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ILAR 2001

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ILAR 2001: The 20th Congress of the International League of Associations for Rheumatology

This supplement to *The Journal of Rheumatology* documents the abstracts of the 20th ILAR Congress — ILAR 2001 — held in the Shaw Convention Centre in Edmonton, Alberta, Canada, from August 26th to 30th, 2001.

This is an exciting time in rheumatology, perhaps most especially from the therapeutic standpoint, and we believe that the Scientific Committee has focused on this excitement in a variety of areas and formats. The program incorporates keynote addresses, symposia, and workshops, and at the end of each day a debate that we hope will stimulate controversy and interaction. We are fortunate in being able to gather clinician scientists from all four of ILAR's regions, i.e., EULAR, PANLAR, APLAR and AFLAR, who will form a team of effective communicators.

ILAR itself has had as its principal message over the preceding 4 years the importance of undergraduate medical education in rheumatology. This Congress focuses on education for the rheumatologist, providing both updates in areas that may have grown unfamiliar, as well as state of the art presentations appropriate even for the expert in the field.

One of the virtues of a truly international meeting of this type is that it allows a degree of interaction between rheumatologists from across the world to meet at both a social and professional level, to develop new ideas and a better understanding of how each proceeds in our own areas. While the professional aspects of the Congress are certainly critical in this regard, we hope that the social areas will also provide enjoyment, entertainment, and a meeting place for new and old friends. We welcome you to ILAR 2001.

ANTHONY S. RUSSELL, MD, FRCPC.
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PAUL DAVIS, MD, FRCPC.
Scientific Chair

20th ILAR CONGRESS
AUTHOR INDEX TO ABSTRACTS

M1

REGENERATION OF ARTICULAR CARTILAGE AFTER MECHANICAL IMPROVEMENT IN KNEE OA

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Department of Orthopaedic Surgery, Yokohama City University, School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan.

Objective: The aim of the current study was to document regeneration of the articular cartilage in the medial compartmental osteoarthritic knee after high tibial valgus osteotomy.

Rationale: The repair of degenerated articular cartilage after non-replacement surgery for osteoarthritis of the knee has not been reported in detail. Improvement of the intra-articular findings need to be investigated in relation to clinical and radiographic outcome.

Methods: The repair of articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis was observed in 146 knees of 115 patients. The mean age of the patients at osteotomy was 64.8±7.0 years (range, forty-seven to eighty). Observations were made through an arthrotomy at the time of removal of the blade plate, an average of two years after the initial osteotomy.

Results: Repair of the degenerated cartilage was classified into three stages. There were no regenerative findings (Stage 0) in twelve knees, partial repair with fibrocartilaginous tissue in the previous degenerated area (Stage I) in eighty-seven knees, and total coverage by new regenerated fibrocartilage or hyaline-like cartilage (Stage II) in forty-seven knees. Mature regeneration (Stage II) was observed more frequently in the knees with advanced degeneration with exposure of the subchondral bone than in those with cartilage remaining in the weight-bearing portion, in the knees with increased width of the medial joint space after high tibial osteotomy than in those with unchanged width ($p<0.05$), and in the knees with more than 5 degrees of anatomical valgus angulation after osteotomy than in those with less than 4 degrees ($p=0.05$). O'Driscoll's histological and histochemical grading score was higher in the Stage II group ($p<0.02$).

Conclusion: Degenerated articular cartilage is well-repaired in the weight-bearing portion of the medial compartmental osteoarthritic knee after adequate correction of varus deformity by high tibial osteotomy.

M2

PATHOGENIC ASPECTS IN GONARTHROSIS

V. CEPOI; G. COVALCIUC; N. MIERCIUC; A NEGRESCU; D. CEPOI; L. CHERTOACA
University of Medicine Farmacy "N. Testemiţanu", Chişinău, R. Moldova

Objective: To study the extrajoint lesions compared to and in complex with joint lesions in patients with gonarthrosis(GA) and their role in the pathogeny.
Rationale: Development mechanisms are studied insufficiently, that determines the inadequacy of the treatment in most cases.
Methods: Anthropomentrics radiological, nuclear investigation (muscular microcirculations, synovial membrane, bone histological (biopsy of the synovial membrane, cartilage, biomechanics (force, tonus, time of contraction). Syncronized recording of lateral angle EMG and phases of EMG.
Results: There were recorded anthropometrical and biomechanical changes in regional muscles in patients with GA. At early stages (0-1) blood circulation of regional muscles decreases with 20-25%, in stage II with 30-45%, EMG amplitude and speed of sensitive and motor transmissions in lamb nerves is decreased. Histological: muscular changes in stage I – 25-30%, stage II – 100%.
Conclusion: The extrajoint formations in GA are affected in early stages: the syniovial membrane and cartilage get affected much later, depending on certain favouring factors.

M3

DEMONSTRATION OF MITOTIC FIGURES IN NORMAL ARTICULAR CARTILAGE AND WITH OSTEOARTHRITIS IN AN EXPERIMENTAL MODEL.

D. Bañuelos-Ramírez, E. Gómez-Conde, M.C. López-Robles. E. Orozco-Orozco. IMSS. CIBIOR. CICATA. Puebla, Pue., and México city. México. CP 72040.

Background: The very specialized tissue loss the capacity of reproduction; in the case of the articular cartilage (AC) it has not been demonstrated that it happens mitosis of their fundamental cells, the chondrocytes (Cdr) in convincing form. The existent studies asum that mitosis exist for the incorporation of tritriated timidine; howewer in stricte sense this alone it indicates that the cells enter to S phase, it doesn't demonstrate that they are divided.
Objective: to demonstrate the mitosis of the Cdr in normal AC and with OA with mitotic figures and the preferential places in that happens.
Methods: We obtained AC of rats Wistar of different ages conformed in 3 groups: normal, with OA postchirurgic and postinfiltrations of steroids, making tints HE, propidio iodure, acridine orange and with previous incubations with RNAse and Ab anticentromere. In all groups negative control were made. We use light microscopy, fluorescence and immunofluorescence to identifity phases of the mitosis and their structures. The protocol was approval of the investigation department.
Results: figures mitotics were identified in clear form including the ultraestructure in AC. They persist in AC with steroids (although they disminish) and they get lost in lesions poschirurgics.
Conclusion: the mitosis exists in CA in diverse conditions and ists induction good be future therapeutic utility.

M4

INTRARTICULAR HYLAN G-F 20 (SYNVISC)® IN THE TREATMENT OF PATIENTS WITH OSTEOARTHRITIS OF THE KNEE.

J. Shariati, M. Hatef, M. Jokar. Department of Rheumatology, Mashhad University of Medical Sciences, Khorassan, Iran.

Objective: To evaluate the effectiveness and safety of Hylan G-F 20 (Synvisc)® versus acetaminophen and a nonsteroidal antiinflammatory drug (diclofenac) for gonarthrosis.

Method: The test was carried out on three-hundred and sixty patients. A series of 3 weekly intraarticular Hylan G-F 20 (Synvisc)® was compared to acetominophen or diclofenac for a period of 6 months, double blind, simple sampling clinical trial. The primary measurement was the Western Ontario and McMaster Universities Osteoarthritis index (stiffness, pain, functional capacity) and also pain experienced on a 50 foot walk test.

Result: In primary assessment a significant improvement with respect to pain was observed in patients receiving Hylan G-F 20 compared to acetaminophen and diclofenac ($P < 0.005$). 61% of patients who are treated with Hylan G-F 20 had >= 28 mm reduction in the VAS from week 6 compared to 35% of patients treated with acetaminophen and 43% diclofenal treated patients. In secondary outcome, Hylan treated patients were significantly better at month 6 regarding to the WOMAC pain and physical function relative to diclofenac ($P = 0.05$). Gastrointestinal adverse effect were seen more in diclofenac treated patients. Injection site pain reported only in 2 patients (1%).

Conclusion: This study confirms that 3 weekly IA injections of Hylan in gonathrosis generally provide sustained reduction of pain and function improvement, and are well tolerated compared to acetaminophen and diclofenac.

Key words: Osteoarthritis, Treatment, Intraarticular, Hylan.

M5

RESULTS OF ROTATIONAL ACETABULAR OSTEOTOMY WITH EXCISION OF THE CAPITAL DROP OF THE FEMORAL HEAD FOR ADVANCED COXARTHROSIS

K. Okano, H. Enomoto, S. Harada, S. Ito and H. Shindo
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Objective: Rotational acetabular osteotomy (RAO) is one of the reconstructive pelvic osteotomies for dysplastic hips . We evaluated the results of rotational acetabular osteotomy (RAO) with excision of the capital drop of the femoral head for advanced coxarthrosis.
Patients and Methods: RAO was performed on 45 hips to treat advanced coxarthrosis caused by acetabular dysplasia in 44 patients between 1985 and 1994. In 35 patients (36 hips) with a median age of 44.0, RAO only was performed (non excision group) and followed up for 5 to 13 years postoperatively (mean 7.3 years) . Another 9 patients (9hips) with a median age of 38.8 were treated by RAO with excision of the capital drop of the femoral head (excision group) to obtain good congruency and sufficient covering by the transfered acetaburum. These patients were followed up for 8 to 13 years postoperatively (mean 10.8 years). The functional and radiological results were compared between these two groups. The functional results were evaluated by Merle d'Aubigne and Postel score, and the radiological results were evaluated by osteoarthritic stage at the time of follow up.
Results: The mean preoperative and postoperative Merle d'Aubigne and Postel score was 9.8 and 10.2 respectively in the excision group, and 11.5 and 14.0 respectively in the non excision group. The postoperative Merle d'Aubigne and Postel score were better than before surgery only in the non resection group (p=0.03). In the excision group, 6 hips had progressive osteoarthritic change, 3 hips had no change. No hip had a decrease in osteoarthritic stage. In the non excision group, 12 hips had progressive osteoarthritic change, 5 hips had no change and 19 hips had a decrease in osteoarthritic stage.
Conclusion: In RAO procedure for advanced coxarthrosis, excision of the capital drop of the femoral head is not a useful additional procedure.

M6

EFFICACY AND TOLERABILITY OF NIMESULIDE VERSUS CELECOXIB IN OA

N.A. SILVA, L.R. MARCZYK, DEPARTMENT OF RHEUMATOLOGY, MEDICAL SCHOOL OF THE FEDERAL UNIVERSITY OF GOIÁS, GOIÂNIA, BRAZIL

Objective: To compare the efficacy and tolerability of nimesulide versus celecoxib in the treatment of OA (OA).
Rationale: The first comparative study between nimesulide and a coxib in OA
Methods: 57 patients were allocated in 1 of 2 treatment groups, in a 30-day treatment with nimesulide (tablets) or celecoxib (capsules), 100 mg bid of either one. The severity of pain (at rest, movement and night), morning stiffness, the degree of functional impairment (HAQ), functional classification (ACR-1991) and severity index for knee OA were evaluated. For those with OA in knee or hip, the time to walk 15 meters was measured. All adverse events were reported during study period.
Results: There was a significant and similar decrease in the averages of the pain scale at movement and rest for both groups at all visits. The night pain averages were similar at the end of the study (p=0,152). The means of the duration of the morning stiffness decreased significantly in the nimesulide group throughout the whole study, and began only from the third visit on for the celecoxib group, becoming similar at the end (p=0,993). The mean time to walk 15 meters decreased significantly for the nimesulide group only at visit 4 (p<0,001), and all the means from the second visit on were lower than those for the celecoxib group. There was a significant and constant decrease in the means of functional impairment (HAQ scale) for the nimesulide group, while in the celecoxib group this decrease appeared on visit 4, where the means became similar (p=0,517). The severity index of The Lesquesne & Samson's (1991) for OA of the knee for the nimesulide group decreased significantly from the third visit on, which did not happen with the celecoxib group. Both groups developed similarly in the functional classification (ACR-1991) throughout the whole study. Efficacy and tolerability were similar in both groups when evaluated by patients and only efficacy, when done by the physicians.
Conclusion: Nimesulide demonstrated similar efficacy and tolerability to celecoxib in the treatment of OA.

M7

RETROSPECTIVE 10YEARS LARGE SCALE EVALUATION OF GASTROINTESTINAL TOXICITY ASSOCIATED WITH NSAIDs IN 9084 PATIENTS WITH RA AND OA AND PROPHYLACTIC EFFICACY OF TEPRENONE AGAINST NSAIDS ULCERS.

A. Yanagawa[1], T. Endo[2]. [1]Institute of Medical Science, [2]Endoscopy Center, St.Marianna University, Kawasaki, Kanagawa, 216-8512 Japan.

Objective: Conventional NSAIDs therapy includes the risk of developing significant injury to upper gastrointestinal (GI) tract ulcer complication in NSAIDs users ranged from 2% to 4%. In a Japanese survey of 1,068 patients with GI mucosal damages in 1989, high figures were obtained for gastric lesion, i.e., about 15% for gastric ulcers, while the figure was under 2% for duodenal ulcers, unlike in other countries. To determine whether the frequency of NSAIDs GI toxicity in recent 10 years has a lower incidence of GI toxicity compared with before and also we evaluated the prophylactics efficacy of teprenone (T), gastric defensive drug, against NSAIDs ulcer.
Material and Methods: We investigated in a large-scale survey of prevalence of upper GI ulcers in total patients with RA (5,915 cases) and OA (3,377cases) who were required NSAIDs therapy and also evaluated NSAIDs ulcer prevention by co-administration of teprenone. Evaluated period was ranged from 1991 to 1999.
Results and conclusions: The GI ulcer complications were seen more than 2% from 1991 to 1993. However, incidence of lesions was gradually deceasing from 1994 to 1999, occurrence rate of GI ulcers was less than 0.5% in 1999. A comparison of incidence of GI ulcers between T co-administered group (T group) and none treatment group (none T group) revealed that the incidence was significantly lower for the T group than none T group.
These results indicated that the incidence NSAIDs induced GI ulcers in Japan were obviously decreasing and teprenone has a strong prophylactic effect against NSAIDs induced lesions.

M8

GREATER EFFICACY OF DICLOFENAC/MISOPROSTOL (ARTHROTEC) COMPARED TO ACETAMINOPHEN IN A RANDOMIZED, DOUBLE BLIND, CROSSOVER CLINICAL TRIAL IS MOST EVIDENT IN PATIENTS WITH MORE SEVERE OSTEOARTHRITIS (OA) OF THE HIP OR KNEE.

T. Sokka, T. Pincus. Vanderbilt University, Nashville, TN 37232

Objective: To compare responses of patients with OA of the hip or knee in a clinical trial, according to baseline OA severity.

Rationale: Acetaminophen is recommended as the initial drug therapy for OA, while reports indicate that most patients prefer NSAIDs.

Methods: 227 patients with hip or knee OA received either 6 weeks of diclofenac/misoprostol (Arthrotec,ARTH) or acetaminophen (ACETA), and then 6 weeks of the other drug. Changes in scores on the Western Ontario McMaster (WOMAC) OA scale and pain visual analog scale (VAS) were analyzed according to baseline tertiles for these measures.

Results: WOMAC pain scores were improved by 7.8 of 100 units (p<0.001), and pain VAS scores were improved by 14.6 of 100 units (p<0.001), while taking ARTH versus ACETA. Changes in WOMAC and VAS scores while taking ARTH versus ACETA were significantly higher for patients in the highest baseline tertile compared to those in the middle and lowest baseline tertiles for WOMAC or VAS (p<0.001).

Conclusion: ARTH is much more likely than ACETA to be efficacious in patients with more severe OA of the hip or knee. Patients with mild OA have similar responses to ARTH and ACETA, possibly because they have less capacity for improvement.

M9

ADVERSE EVENTS WITH ACETAMINOPHEN ARE COMMON OVER 6 WEEKS IN A RANDOMIZED CONTROLLED DOUBLE-BLIND CROSSOVER CLINICAL TRIAL

T. Pincus, T. Sokka, Vanderbilt University, Nashville, TN 37232.

Objective: To analyze the incidence of adverse events in patients who took acetaminophen (ACETA) and then diclofenac/misoprostol (Arthrotec-ARTH) in a randomized double-blind crossover clinical trial

Rationale: Acetaminophen is recommended as the initial drug therapy for OA, while reports indicate that most patients prefer NSAIDs.

Methods: Patients took either 6 weeks of ACETA and then 6 weeks ARTH or the same drugs in reverse order in a crossover clinical trial. Adverse events were reported on standard Food and Drug Administration (FDA) case report forms, and tabulated for each drug.

Results: ARTH had significantly greater efficacy than ACETA (p=<0.001). 46% of 210 patients reported any adverse event while taking ACETA compared to 54% of 203 patients while taking ARTH (p=0.46). GI adverse events were reported by 24% with ACETA versus 34% with ARTH (p=0.006), including diarrhea – ACETA-14%, ARTH-20% (p=0.07); dyspepsia – ACETA-8%, ARTH-10% (p=0.53); nausea/vomiting – ACETA-4%, ARTH-8% (p=0.09); abdominal pain – ACETA-2%, ARTH -7% (p=0.001).

Conclusion: Adverse events were more common with ARTH compared to ACETA. However, 46% of patients reported an adverse event in 6 weeks of taking ACETA, including a GI adverse event in 24%. The impression of low GI toxicities of ACETA compared to nonsteroidal anti-inflammatory drugs (NSAIDs) may reflect in part a possible reporting bias concerning ACETA, as adverse events were common in patients who took ACETA in a 6 week clinical trial.

M10

OPEN STUDY OF A STATE OF PEROXIDE OXYDATION OF LIPIDS AND ANTIOXIDANT SYSTEM AT PATIENTS WITH OSTEOARTRITIES.

Orugov M.A. ,Abasov. E.S, Ashirov M.G. Republic Arthrological Center, Baku, Azerbaijan.

Objective: In this work our aim is to study a state of peroxide oxydation of lipids on the basis of evaluation of malono dealdehyde (MDA) and peroxide H_2O_2,and natural antioxidant system on the basis of indices of α—tokopherol (Vitamin-E) in blood of patients with osteoartrities (OA) .

Rationale: It was defined that at patients in comparison with healthy Persons (control group) occurs disturbance of membrana lipids oxydation and natural antioxidant system.

Possibly, it definitly results in redoubling and regeneration of Articulate cartilage in OA .

Methods: Patients included 36 males and 10 Females in the age of 45-65 with osteoartrities many of whom equally with others had defeat of knee joints. On Kollgren gradation I – III range. 20 healthy persons (10 males and 10 females) were included for control purposes who-se parameters in blood earlier indicated were also studied. Received datas were statistically treated.

Results: Holded invetigation showed that content of MDA in blood at patients with OA inc rea-sed to 7,231n\mole\ml (+4,886 nmole\ml, p< 0,01), and also increased a content of H_2O_2 at patients 0,284mk mole\l (control – 0,190mk mole\ l). Also was observed reduction Of α—tocopherol content in blood. Patients with OA (1,258 mlg% control 1,724 mlg% p < 0,05) these results were of the same type at both sexes. More striking changes were observed at patients with OA in presence of reactive sinovit in knee-joints. Received results evidence that OA is the reason of antioxidant Indices reduction, which promotes to (intermediate products oxydation of membrana lipids). Possibly this disbalance plays definite role in redoubling of pathological processes and degeneration of articulate cartilage in OA.

Conclusion: On this basis we recommend using of antioxidant preparations in complex therapy of patients with OA.

M11

SELECTIVE COX-2 INHIBITION AND ACID-INDUCED GASTRIC LESIONS: EFFECT OF MELOXICAM, NIMESULIDE AND PIROXICAM

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Objective: To determine the effect of selective COX-2 inhibition on HCl-induced gastric lesions in the rat.

Rationale: COX-2 selective agents are associated with fewer GI side effects, however, the effect of selective COX-2 inhibition on gastric ulcer formation induced by other causes has not been well examined.

Methods: Gastric lesions were induced in male rats (n=10/group) using 0.45 N HCl 60 min after administration of meloxicam, nimesulide or piroxicam (1.5 or 3.0 mg/kg sc). One hour later the animals were killed, the stomachs removed, rinsed and photographed. Severity of lesions was quantified as total area of lesions compared to total fundus area using computer-assisted planimetry of digital images.

Results: Fundus area of all groups was comparable. Absolute ulcer area (mm^2) and percent lesion:fundus area compared to control is shown in Table 1 for the lower (1.5 mg/kg) and higher (3 mg/kg) doses of the compounds tested (*p<0.05).

	Meloxicam		Nimesulide		Piroxicam	
Dose:	low	high	low	high	low	high
Ulcer Area	117±24	105±16	99±18	137±21	141±21	166±15*
% of Control	10.2	-3.1	-10.4	27.0	33.9	55.5*

Meloxicam and nimesulide did not affect gastric lesions as compared to positive controls, though a trend to larger lesion area was seen with nimesulide. Piroxicam significantly augmented HCl-induced ulcer severity in a dose-dependent manner.

Conclusion: The selective inhibition of COX-2 has less effect on the severity of acid-induced gastric ulcers in rats than non-selective inhibition.

M12

SUCCESS-1 IN OSTEOARTHRITIS (OA) TRIAL: CELECOXIB VS NSAIDS AND RISK OF SERIOUS UPPER GI (UGI) COMPLICATIONS

G. Singh[1], J. Goldstein, W. Bensen, N. Agrawal, G. Eisen, J. Fort, A. Bello, S. Boots. [1]Dept of Medicine, Stanford University, Palo Alto

Objectives: SUCCESS-1, the largest double-blind, randomized study in rheumatology, compared the efficacy and tolerability of 2 therapeutic doses of celecoxib to conventional doses of NSAIDs to closely parallel clinical practice in worldwide settings in OA of the knee, hip, and hand

Methods: GI safety and tolerability were assessed globally: celecoxib 200 mg/d (n=4421) and 400 mg/d (n=4429) were compared to naproxen 1000 mg/d (n=914) and diclofenac 100 mg/d (n=3510). An independent Gastrointestinal Events Committee (GEC) categorized potential clinically significant UGI events in a blinded fashion as ulcer complications or symptomatic ulcerations.

Results: The mean age was 62 years; baseline aspirin use and UGI bleeding history were comparable. UGI symptoms were consistently and significantly lower with celecoxib.

	Celecoxib (n=8800)	NSAIDs (n=4394)	OR, 95% CI
UGI Tolerability, n (%)			
Dyspepsia	422 (4.8)*	259 (5.9)	1.2 (1.1-1.5)
Abdominal pain	423 (4.8)*	274 (6.2)	1.3 (1.1-1.5)
Nausea	207 (2.4)*	151 (3.4)	1.5 (1.2-1.8)
Serious GI events, n (inc/100 pt yrs)			
Possible events†	83 (4.8)	61 (7.1)	1.5 (1.1-2.1)
Ulcer complications‡	2 (0.1)*	7 (0.8)	7.0 (1.5-33.8)
Symptomatic ulcer complics‡	18 (1.0)*	18 (2.1)	2.0 (1.0-3.8)

†investigator-determined; ‡confirmed ; *p<0.05

Conclusion: Compared to conventional NSAIDs, celecoxib reduced the risk of ulcer complications by almost 87.5%, while providing equivalent efficacy and better tolerability. Sponsored by Pharmacia Corporation and Pfizer, Inc.

M13

SUCCESS-1 IN OSTEOARTHRITIS (OA): CELECOXIB HAS SIMILAR EFFICACY TO THE CONVENTIONAL NSAIDS

G Singh,[1]; J Goldstein,; J Fort, A Bello, S Boots, [1]Dept of Medicine, Stanford University, Palo Alto

Objectives: SUCCESS-1 is a long-term study that compared the efficacy, tolerability, and safety of celecoxib and the most commonly prescribed NSAIDs in 39 countries in the treatment of signs and symptoms of OA of knee, hip, and hand.

Methods: In a double-blind, randomized study, 13,194 patients from 1142 centers in Europe and S. Africa, Asia, Latin America, and US/Canada were treated with celecoxib (200 or 400 mg/d) and common NSAIDs (naproxen-1000 mg/d in US/ Canada; diclofenac-100 mg/d in other countries). Efficacy was assessed by country/ region based on mean change in arthritis pain (VAS) and night pain at week 12.

Results: Most patients were female (76%); the mean age was 62 years. Baseline aspirin use and history of upper GI bleeding were comparable. In European countries, no significant differences between celecoxib 200 mg/d compared to celecoxib 400 mg/d or to diclofenac 100 mg/d were observed; comparable efficacy between celecoxib and NSAIDs was demonstrated in other countries/ regions.

Patient's Assessment Mean changes	Arthritis Pain (VAS) mm[1]		Night Pain[1]	
	Celecoxib 200mg/d	Diclofenac 100mg/d	Celecoxib 200mg/d	Diclofenac 100mg/d
Central Europe	-22.1	-20.4	-0.73	-0.69
Germany	-28.3	-25.7	-0.89	-0.67
Italy	-17.6	-20.6	-0.50	-0.54
Nordic regions	-13.4	-14.2	-0.36	-0.38
Spain/Portugal	-18.4	-21.0	-0.68	-0.66
UK/Ireland	-10.9	-11.9	-0.33	-0.38

[1]0–100=none to most severe pain; [2]5 pt scale:1=very good, 5=very poor; p≥0.18

Conclusion: In various settings that closely follow local clinical practice around the world, celecoxib demonstrated similar efficacy to common regimens of diclofenac in OA treatment. Sponsored by Pharmacia Corporation and Pfizer Inc.

M14

PHARMACODYNAMIC DISSECTION OF DOSE-RESPONSE TO MELOXICAM IN OSTEOARTHRITIS USING THE WOMAC INDEX.

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Objective: Evaluate the performance of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and its subscales as sensitive measures of treatment differences in a placebo-controlled, active-controlled (diclofenac) multi-dose study of the non-steroidal anti-inflammatory drug (NSAID) meloxicam, in osteoarthritis (OA) patients of the hip or knee.

Methods: A total of 774 patients were randomized and treated in a 12-week double-blind, double-dummy, parallel group trial comparing daily oral meloxicam of 3.75 mg, 7.5 mg and 15 mg doses to placebo and diclofenac 50 mg twice a day. Patients were required to flare upon discontinuation of their previous NSAID, with flare defined in terms of patient pain, patient global assessment and physician global assessment of disease activity. The WOMAC index was evaluated with respect to the ability to identify dose response, relationship to other covariates including age, and the ability to identify failure in patients discontinuing for lack of efficacy (LOE).

Results: WOMAC total and all three subscales (pain, function and stiffness) showed a clear dose response relationship across the ranges from placebo to high dose (15mg) meloxicam. In addition, improvement in WOMAC scores was significantly associated with age, with older patients showing less improvement. WOMAC scoring allowed differentiation of patients discontinuing due to LOE (mean score 1.0 below baseline) and other patients (mean score 20.2 below baseline). The below table shows results.

WOMAC Total change from baseline (mean)	Placebo	Meloxicam 3.75 mg	Meloxicam 7.5 mg	Meloxicam 15 mg	Diclofenac 100 mg
All patients (N=774)	10.2	14.2	15.3	18.9	21.2
Discontinuing due to LOE (N=171)	-0.2	0.3	0.6	3.0	5.1
Not discontinuing due to LOE (N=603)	16.7	19.5	18.4	22.5	22.7

Conclusions: The WOMAC scale demonstrated good sensitivity, showing efficacy at the 7.5 mg and 15 mg doses of meloxicam and activity, but insufficient efficacy, at the 3.75 mg dose. WOMAC sensitivity to differences in response on the basis of age, and to the lack of improvement in patients who discontinued therapy due to lack of efficacy are important for the design and analysis of future trials.

M15

COMPARATIVE STUDY OF 2 REGIMENS OF INTRAARTICULAR INFUSION OF HYALURONAN (HYALART, FIDIA, SPA) IN KNEE OSTEOARTHRITIS

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Introduction: The use of hyaluronan is currently well established in the treatment of knee osteoarthritis (OA), but there is still no agreement about the most appropriate regimen. This open and randomized study compares the effectiveness of 2 different regimens.

Patients and methods: 200 patients suffering from knee OA were randomly assigned into 2 groups (A: 5 infusions/6 months, B: 3 infusions/3 months). There was no significant difference between the 2 groups regarding demographic data, disease severity and radiological category. Evaluation of the clinical response was performed at 6 and 12 months interval, based on the Lequence's index (LI), the pain VAS and the evaluation of clinical response by the patient and the doctor.

Results: 73 patients from group A and 86 from group B completed the study. At 6 months, there was a clinical improvement per 2.87 (24%) units and 3.72 (31%) units at the LI ($p<0.001$) and at 12 months the change was 2.96 (24.8 %) units and 5.7 (47.3%) units respectively. Pain in the VAS decreased in 6 months by 48.9% in group A and 51.5% in group B ($p<0.001$) and in 12 months by 49.7% and 51.5% ($p<0.001$) respectively. Clinical results were superior in group B for both parameters. 67% of patients in group A and 79% in group B assessed the response as satisfactory ($p<0.001$) while the doctor evaluated the result as satisfactory in 57.5% and 65% of cases ($p<0.001$) respectively. There were no side effects other than 3 cases of transient local pain.

Conclusions: Intra-articular administration of hyaluronan (Hyalart) is a safe and effective treatment of knee OA. The regimen of 3 infusions every 3 months proved to be more effective, resulting in a better clinical outcome and higher patient compliance.

M16

CLINICAL EXPERIENCE WITH INTRA-ARTICULAR HYALURONATE IN OSTEOARTHRITIS OF THE KNEE

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Objective: To evaluate the continued efficacy and safety of intra-articular hyaluronate in an open study of 2+ years in 112 knees in 92 patients with osteoarthritis of the knee.

Methods: This report includes a 6 month extension with 20 additional knees, of a previously completed trial of 92 knees. Five intra-articular injections of 20 mg sodium hyaluronate were administered at weekly intervals. Outcomes were determined by physical examination, assessment of pain including visual analog scale of 1 to 10, monitoring of any adverse reactions, and yearly standing AP radiographs of the knees.

Results: 74% of patients achieved greater than 50% improvement for one year or longer. 23 patients (25%) have been followed for over 2 years. Outcome measures of response included reduction of pain and tenderness, improved functional capacity and walking ability. Adverse effects were infrequent, and included minimal after pain", minor bruising at site of injection, and a few instances of headache. No patient dropped out because of any side-effect. 15 of 18 patients previously considered for TKR no longer needed the procedure. Only 10 patients (11% of knees) failed to show any beneficial response. "Booster" (supplemental) injections were given to 18 patients (20 knees) approximately 6 weeks after completion of the injections, with improvement in 14 knees (70%).

Conclusion: Intra-articular hyaluronate is an effective and safe treatment in OA of the knee Quality of life effects, such as walking, steps, and getting in and out of a car frequently showed improvement.

M17

CAN JOINTS OTHER THAN KNEES BE SUCCESSFULLY TREATED WITH INTRA-ARTICULAR HYALURONATE?
Pilot studies on osteo-arthritis of the first MC-C joint.

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Rationale: Hyaluronate injections have been shown to be effective in providing pain relief in some patients with osteo-arthritis (OA) of the knees and have become a popular local therapy in many centers. To date no studies have been reported to evaluate the use of such injections into other joints. We have initiated a pilot study at 1st MC-C joints.

Objective: To begin evaluate feasibility and potential value of intra-articular injection of hyaluronate into osteo-arthritic first carpo-metacarpal joints.

Methods: Seven patients with x-ray proven painful osteo-arthritis at a 1st MC-C joint have volunteered for open treatment with hyaluronic acid (Hyalgan) 1cc weekly for 5 weeks. Joints were injected via a dorso-radial approach with a 23-gauge needle. All subjects had pain scores on a visual analog scale (VAS), documentation of tenderness or crepitus, pinch strength measured in pounds and in 2 cases functional test with a nine-hole peg test. All observations were repeated before each injection and monthly after completion of the treatment.

Results: All 1st MC-C joints easily tolerated injection of 1cc hyaluronic acid. Local bruising in one patient was the only complication. Pain scores of 5 patients were improved at measurements after the fifth injection. Mean pain score for all 7 before treatment was 5.5 and after treatment 3.6. Improvement has been maintained for up to 6 months. Pinch strength improved in 5 patients. Time to complete the nine-hole peg test improved in 1 of 2 patients tested to date.

Conclusion: First MC-C joints easily tolerate injection of 1cc hyaluronic acid without any worsening or significant complication. Five patients have had improvement as measured by pain on VAS and strength by pinch test. Hyaluronic acid injection deserves further study for use in joints other than the knee.

M18

INSIGHT INTO THE STRUCTURAL BASIS OF SELECTIVE CYCLOOXYGENASE-2 INHIBITION

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Cyclooxygenase-1 and -2 (COX-1/COX-2) catalyze the rate-limiting step in prostaglandin (PG) synthesis and are the targets of non-steroidal anti-inflammatory drugs (NSAIDs). The evidence is strong that the selective COX-2 inhibitors have reduced GI side effects in patients treated for rheumatic conditions.

Objective: The molecular basis of binding affinities and COX-2/COX-1 selectivity are explored using an approach that combines experimental results from X-ray analyses and docking experiments from computational chemistry.

Methods: The reported X-ray structures of COX-1 and COX-2 were used for computational optimization of the interaction between the different NSAIDs and COX isoforms using the established computer program Sybyl/Molcad.

Results: The inhibition of COX can occur by compounds with high degree of structural diversity and various types of mechanisms. The results show that COX-2 selective inhibitors are belonging to several structural distinct classes: arylalkanoic acids, enolcarboxamids, acidic sulfonamids and diarylheterocycles. Two fundamental differences between the active site of COX-2 and COX-1 are responsible for the COX-2 selectivity: COX-selective diarylheterocycles (DuP 697, celecoxib, rofecoxib) are exploiting the side pocket and enolcarboxamid (meloxicam) and acidic sulfonamids (L745.733, NS 398, nimesulide) the extra space at the top of the channel.

Conclusion: This work illustrates the value of novel docking procedure for determing the binding of NSAIDs to the COX-enzyme. The structural insights into the binding mechanism indicate that COX-2 selectivity can be obtained by at least three chemically distinct classes of NSAIDs of which meloxicam, nimesulide, celecoxib or rofecoxib are representatives.

M19

Clinical results of rotational acetabular osteotomy for dysplastic hips.

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Objective: In Japan , more than 90 percent of osteoarthritic hips (OA) have a history of congenital hip dislocation and / or congenital acetabular dysplasia. Rotational Acetabular Osteotomy(RAO) or circumacetabular en bloc osteotomy has mainly been performed for these patients in our hospital. In the present study, a clinical assessment was done on 78 hips which had been followed more than three years.

Material and Methods : Seventy-eight hips including five hips from five male patients and seventy-three hips from sixty-three female patients were assessed according to the JOA (Japanese Orthopaedic Association) hip score and radiological indices. The mean age at operation was 29 years (12 to 61). 44 hips were prearthrotic, 27 were early stage coxarthrotic and seven were advanced. In five hips with poor congruity , intertrochanteric valgus osteotomy was also applied. The mean follow-up period was 6.4 years (3.0 to 15.1 years).

Results : Clinical results in most cases were favorable. Preoperative JOA scores averaged 76 and postoperative scores 87 points. Mean preoperative and postoperative center-edge angles were -2 degrees and 30 degrees respectively.

Conclusion: Prearthrosis and early stage cases of OA have proved to be good indications for RAO. But in some of the advanced cases, joint space-narrowing progressed postoperatively, and clinical results were rated as poor.

M20

JOINT LAVAGE ARE BENEFICIAL PAIN TREATMENT IN KNEE OSTEOARTHRITIS

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Objetive: To evaluate the efficacy ant tolerate of joint lavage in the treatment of patients with symptomatic knee osteoarthritis(OA)

Methods: Two hundred forty two patients with painful tibiofemoral OA were enrolled in a prospective trial of 6 months'duration.Outcome mesures evaluated at baseline,week 1,week 4, week 12 and week 24 included severity of pain 100 -mm visual analog scale(VAS), patients'and physicians' global assessment,and the WOMAC OA index.

Results: All the measures evaluated was significantly improved between basal and at 24 week ($p<0.00005$). Patients global assessment was better in 54,88%; fair in 24,27% and poor in 9,87%.Pain walking on a flat surface assessed according to the WOMAC index improve a 13% and the stiffness a 50%.Adverse events was found in 2% (1 acute gout,1phhlebitis and 3 hypotension).

Conclusion: Joint lavage significant relieved pain and functionalimpaiement in knee OA patients.The effect of joint laveage persisted up to week 24.

M21

VISCOSUPPLEMENTATION WITH SODIUM HYALURONATE FOR THE TREATMENT OF OSTEOARTHRITIS

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Objective: To determine efficacy of intraarticular sodium hyaluronate in the treatment of patients with osteoarthritis (OA) of the knee.
Rationale: Hyaluronan is administered to synovial joints for the treatment of OA. This mode of therapy is called viscosupplementation because clinical improvement is thought to be based on supplementing the viscous and elastic properties of pathologic synovial fluid.
Methods: Twenty-one patients with OA was treated with 5 weekly intraarticular sodium hyaluronate (Orthovisc) injections into the knee at a dose of 2 ml (15 mg/ml). Knee joint mobility, WOMAC stiffness and WOMAC pain scores were evaluated at baseline, weeks 5, 9, 16, and 21.
Results: A total of 175 injections were performed in 21 patients involving 35 knees. The time course of the study measures are shown in Table.

	Baseline	5. week	9. week	16. week	21. week
Knee flexion angle	98 ± 11	105 ± 8[a]	108 ± 11[a]	104 ± 11[b]	108 ± 8[a]
Morning stiffness	2.7 ± 0.9	1.4 ± 0.8[a]	1.5 ± 1.1[a]	1.9 ± 1.0[b]	1.8 ± 0.8[c]
Gelling	2.9 ± 0.9	1.4 ± 0.5[a]	1.5 ± 1.2[a]	2.1 ± 1.0[c]	1.1 ± 0.8[a]
Total pain score	14.8 ± 3.3	7.6 ± 2.5[a]	9.0 ± 4.3[a]	12.2 ± 4.5[d]	8.0 ± 5.2[c]

[a] p<0.001, [b] p=0.001, [c] p<0.01, [d] p<0.05

Conclusion: This trial suggests that intraarticular injections of sodium hyaluronate are generally well-tolerated and may represent a valuable alternative approach to the treatment of patients with OA.

M22

EFFECT OF SODIUM HYALURONATE (500-730 KDa, HYALGAN®) ON JOINT SPACE WIDTH IN OSTEOARTHRITIS OF THE KNEE.

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Background: Clinical studies have shown that a series of 3-5 weekly intra-articular injections of hyaluronan of molecular weight 500-730 kDa (Hyalgan®) reduces pain and improves function in patients with osteoarthritis of the knee and that this effect can be long lasting. There is also some evidence from pilot clinical studies to suggest that this product may slow osteoarthritis.
Objective: To examine the effect of Hyalgan® on the radiological joint space in patients with osteoarthritis of the knee. The primary end point is the change in radiological joint space between baseline and one year in the medial tibio-femoral compartment, measured by digital image analysis, analyzed by mixed linear models with intention to treat of available paired radiographs. There is a secondary analysis of osteoarthritis severity using the 6 point LINK scale.
Method: A multicentre, randomised, placebo-controlled, double blind (masked observer) study was conducted in 17 centres in the UK. Weight bearing antero-posterior radiographs were taken using a standardised technique. Patients were randomly assigned to receive 3 courses of 3 intra-articular injections of hyaluronan or 2ml of saline during the one year study. Uncontrolled use of analgesics and NSAIDs was permitted.
Results: 408 patients were enrolled and there was complete data for 273 patients. Mean patient age was 64.2yrs, 68% were female. The two groups were comparable at entry. The group of patients with greater joint space at entry, treated with hyaluronan, showed reduced progression of joint space narrowing. In the hyaluronan group the mean loss was only -0.13 (sd=1.1), while in the placebo group the mean loss was -0.55 (sd=1.0) [p = 0.02]. There was an agreement between the LINK and the digital image analysis.
Conclusions: Repeat cycles of Hyalgan® give a statistically significant delay in radiological joint space narrowing within one year in patients with osteoarthritis of the knee.

M23

EVALUATION OF CHONDROPROTECTIVES IN O.A. KNEE

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OBJECTIVE: To evaluate chondroprotective efficacy of,glucosamine- sulfate (GS) and glucosamine hydrochloride (GSH)+ chondroitin sulfate (CS), in composition to Nsaid - placebo.

RATIONALE:-Rofecoxib(R) an analgesic Nsaid and weak chondroprotective . GS is a slow Nsaid and symptom modifying drug but with combination of GSH and CS, these actions are bit early and prolonged.

METHODS:- This was a randomized, multicentre double blind and double dummy study. 2000 patients with O.A. knee were received into 4 groups. 1st group with placebo, 2nd group with (R) 3rd group with (GS) and 4th group GSH+CS. The clinical efficacy was evaluated by assesing Lequesene index, spontaneous pain using the (Huskisons visual analog scale), pain on load (using 4 point ordinal scale) and paracetamol consumption.

RESULTS:- Though encouraging initially with (R), but long term efficacy of chondroprotective are well appreciated clinically.

CONCLUSION : slow acting symptom modifying drugs gsh+ cs and gs seem to have slow but gradually increasing clinical efficacy in O.A. there benefits for a long period after the end of treatment. Of the two consumption of GSH+CS showed a shade better efficacy than GS group in our study, though very early to conclude

M24

ROFECOXIB RELIEVES SYMPTOMS AND CONTROLS PROGRESSION OF OA KNEE

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Objective: Rofecoxib (R) is affective in relieving symptoms of O.A.

Rationale : cox-II inhibitors are metaloproteases inhibitors thus act as chondroprotective drugs.

Methods : 54 patients with O.A. Knee (A.C.R. criteria) were randomly assigned, double blindly to a continuous treatment for six months with oral 25 mg per day and placebo. Weight bearing, antero posterior radiograph of each knee were taken at initial and then every 3 months, standardizing patient position and radiographic procedure. Total mean joints width of the medial compartment of the tibio femoral joint was asserted by digital image analysis by a validated computerized algorythm , with the narrowest middle joint space at enrolment being taken for primary evaluation , (single joint) symptoms was scored at each 2 monthly visits by the total womac index data were drawn at 2 monthly intervals.

Results : The two groups of patient were comparable for demographic and disease characteristics. Rofecoxib treated patients had a increase of JSW 0.04/6 months. The symptoms worsened under placebo while they were relieved under (R). The results were - (mean<01>SE) on the I.T.T. patients are here under summarized.

Conclusion : Rofecoxib is an symptom modifying drug, however it can be used as structure modifying drugs .

M25

DIFFERENTIATION OF HYALURONATE PRODUCTS BY QUALITATIVE DIFFERENCES OF IMMUNOGENICITY IN RABBITS – RELATIONSHIP TO CLINICAL FLARES? W. Bucher, T. Otto. Lampire Biological Labs, Inc, Pipersville, PA, 18947 USA.

Rationale: Two hyaluronates (HA), Synvisc®, hylan G-F 20 (SYN), and Hyalgan®, sodium hyaluronate (HYL), have been marketed in the U.S. since 1997 for the treatment of pain of osteoarthritis. SYN is chemically crosslinked while HYL is purified intact. Both products specify a less than 1% protein and lack of immunogenicity (FDA-PMA submissions) although SYN in primates induced antibodies to hylan and/or chicken proteins (CP) in 1/3 of the animals tested. Related clinical reports with SYN (Puttick, et al. 1995) of product-specific severe acute inflammatory reactions (SAIR) also documented high titer anti-hylan and/or CP antibodies in a patient's sera.
Objective: Evaluate the comparative immunogenicity of hyaluronate products as an explanation for clinical reports of product SAIRs.
Methods: 12 rabbits (4 per group) received 7 injections (0, 1, 4, 8, 12, 18 and 24 wks) of 400ug HA equivalents of either crude rooster comb preparation (CRCP), SYN, or HYL. Endpoint antibody titers for HA and CP were determined.
Results: None of the HA preparations elicited a significant specific response to HA (endpoint titer greater than 1:20). The limited titers to HA appeared to be limited to primary responses. In contrast, 100% of the CRCP and 75% of the SYN rabbits elicited significant titers to CP (endpoint titer greater than 1:100) while none of the HYL rabbits had a significant titer. These data suggest that during crosslinking a qualitative change in the immunogenicity of residual proteins may be induced to SYN, which is in contrast to the naturally derived HA product, HYL. Differences in immunogenicity may explain product specific SAIRs and have clinical implications in their repeat use.

M26

COPRESCRIPTION OF ASPIRIN (ASA) TO NSAID THERAPY IN OSTEOARTHRITIS (OA) IS A RISK FACTOR FOR DEVELOPING GASTROINTESTINAL (GI) ADVERSE EVENTS. Frank Degner. Boehringer Ingelheim GmbH, 55216 Ingelheim am Rhein, Germany.
Objective: To evaluate the effect of ASA coprescription to non-steroid anti-inflammatory drug (NSAID) therapy on reported gastrointestinal adverse events (AEs) in OA patients treated with the selective COX-2 inhibitor meloxicam compared with diclofenac and piroxicam.
Rationale: Coprescription of ASA to NSAIDs is known as a risk factor for NSAID related GI toxicity, while meloxicam has demonstrated a favourable GI tolerability profile compared with the non-COX-2 selective NSAIDs diclofenac and piroxicam.
Methods: Two four weeks double-blind randomised large-scale clinical outcome trials were performed in a total of 17979 OA patients (MELISSA and SELECT, BJR 1998; 37:937-951). Data from both studies were analysed regarding the effect of ASA coprescription to NSAID therapy with either meloxicam 7.5 mg (n=4635 and n=4320), diclofenac 100 mg (n=4688) or piroxicam 20 mg (n=4336) on reported GI adverse events.
Results: Overall meloxicam 7.5 mg had significantly fewer GI adverse events than diclofenac 100 mg ($p<0.001$) and piroxicam 20 mg ($p<0.001$). The favourable GI tolerability of meloxicam was maintained with coprescription of ASA, although the risk to experience a GI adverse event was increased for all treatment arms in patients receiving ASA coprescription. The below table shows results.

	MELISSA		SELECT	
Treatment group	Meloxicam 7.5 mg	Diclofenac 100 mg	Meloxicam 7.5 mg	Piroxicam 20 mg
Patients treated	4635	4688	4320	4336
on ASA	259	224	203	226
not on ASA	4376	4464	4117	4110
GI AEs reported	13.3%	18.7%	10.3%	15.4%
on ASA	15.3%	23.3%	13.3%	19.9%
not on ASA	13.2%	18.6%	10.2%	15.2%

Conclusion: Meloxicam is associated with fewer GI adverse events compared with diclofenac and piroxicam, even when taking into account concomitant ASA use. However, ASA coprescribed for cardiovascular prophylaxis is a risk factor for experiencing GI adverse events during NSAID therapy.

M27

A RANDOMIZED CONTROLLED TRIAL EVALUATING EFFECTIVENESS AND COST-EFFECTIVENESS OF HYLAN G-F 20 IN PATIENTS WITH KNEE OA
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Objective: To determine the effectiveness, cost effectiveness and cost utility of hylan G-F 20 for the treatment of knee osteoarthritis (OA), a prospective, randomized, one-year, open-label, economic trial was conducted in Canada.
Rationale: Health economic evaluations are increasingly important to the adoption of new technologies in rheumatology.
Methods: 255 patients were randomized to: Appropriate care with hylan G-F 20 (AC+H) or Appropriate care without hylan G-F 20. Societal costs related to the treatment of OA in the knee and other joints were collected. Effectiveness was measured using the WOMAC, SF-36 and Health Utilities Index Mark 3.
Results: AC+H was clinically and statistically superior for all primary and secondary effectiveness measures. The mean annual incremental cost per patient was $710 for AC+H. The largest contributor ($676) to this cost difference was the price of hylan G-F 20. The second largest contributor ($-279) was the savings in other costs of treating knee OA. AC+H had a statistically significant gain of 0.071 quality-adjusted life years (QALY), and a societal cost of $10,000 Canadian per QALY gained.
Conclusion: Clinical effectiveness exceeded the clinically important difference established a priori. Cost utility ratio is below the suggested Canadian threshold for adoption. Results provide strong evidence for adoption of treatment with hylan G-F 20 in patients with knee OA.

M28

OPEN STUDY OF OMEGA-3 SUPPLEMENTATION IN THE TREATMENT OF OSTEOARTHRITIS
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Objectives: to evaluate the benefit of Omega-3 polyunsaturated fatty acids supplementation in patients with osteoarthritis (OA).

Rationale: Omega-3 has been researched in Rheumatoid Arthritis patients. The research shows that Omega-3 succeeds in declining pain and inflammation's process on the joint. So far, the effect of Omega-3 in patients with OA has not been researched.

Methods: This study used a random trial open method. The 22 OA patients included in Altman's criteria were divided into two groups. One of the groups was given 0.6 g/day Omega-3 soft capsule (0,36 g EPA, 0,24 g DHA) for 12 weeks. OA patients' health status was investigated by giving AIMS 2 forms and Lequesne index scores.

Result: A significant difference was observed in Lequesne index scores between two groups. Furthermore, this study had no significant difference for AIMS 2 scores between Omega-3 group and control group.

Conclusions: The supplementation of Omega-3 based on Lequesne index score was useful for patients with OA.. Prolongation of this study with more samples and dosage of Omega-3 is necessary to find further effect of Omega-3 in the therapy of OA.

M29

Prospective Endoscopic Study Patients with Rheumatic Disesaes Long-Term Treated by NSAIDs in aspects of Helicobacter pylori Infection.

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Objective : To evaluate recurrence of lesions in upper GI tract in rheumatic patients Hp+ vs Hp- chronic treated by NSAIDs.
Rationale:NSAIDs are GI toxic; approx.20% chronic NSAIDs users develop gastroduodenal ulcerations or erosions. Hp is another gastroduodenal(GD) aggresive factor but its role in NSAIDs users remains controversial .
Materials and Methods: 85 patients -69 females and 17 males- treated by NSAIDs at least 3 months due to rheumatic disorders : RA-69, OA-7 or AS-9 were enrolled to the study. All the patients were referred to the Endoscopy Room because of symptoms or signs suggesting GI ulcerations.Studied group (n=21) was Hp + eradicated effectively. Control groups were Hp +(n=37) not eradicated and Hp- (n=27). The groups were no significant different in demographic aspects and NSAIDs consumption period. The GI symtoms was graded in scale 0-3. Endoscopic GD lesions were assessed according Lanza score (1981).Biopsy specimens (2 antrum and body) and for urease test were taken during endoscopy. Oesophagus was evaluated according to the 4 grade scale of Savary - Millera.Mean period of observations-12 months. Patients underwent gastroduodenoscopy at baseline ,post 3 months, 6 months and 12 months and of the medical indications. Patients were treated by proton pump inhibitors (PPI) and half of Hp+ was given 7 day therapy Amoxicillin +Clarithromycin +PPI
Results:Mean GI Symptom Index (GISI) was changed in comparison to baseline value respectively ;Hp (-) 0,63-0,39;Hp(+) 2,02-1,7;Hp(+)/Hp(-) 1,8-0,26 ($p<0,01$). GI symptoms was decreased after Hp eradication significantly. Incidence of duodenal ulcer DU (16,7-3,6%), but no gastric ulcer -GU(31,8-15%) decreased after eradication Hp.Incidence of GU in Hp+ was not changed significantly(24,3-16,2%). The least incidence of GU was observed in group Hp (-).
Conlusion:GISI decreased after eradication significantly. Hp eradication decreased significant incidence of DU but no GU in chronic NSAIDs users.

M30

EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTION OF HYLAN GF-20 (SYNVISC) FOR THE KNEE

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Objective: To determine the safety and efficacy of intra-articular injection of Hylan GF-20 (Synvisc) in the treatment of osteoarthritis (OA) of the knee.

Rationale: Hylan GF-20 (Synvisc) is a biologically similar to hyaluronan. Hyaluronan is a component of synovial fluid which is responsible for its viscoelasticity. Viscosupplementation with Hylan GF-20 has been widely used in the treatment of OA.

Methods: There were 35 patients (14 male, 21 female, mean age 65,5 years) with bilateral symptomatic knee osteoarthritis with effusion. Hylan GF-20 injected intra-articular in the knee ones weekly over three weeks. Patients were examined weekly during the treatment period and after 12 weeks. Assessment included recording of : visual analog scores (VAS) for pain in rest and pain of movement, range of movement and side effects. Control group was another knee of the same patient.

Results: Pain on movement reduced in 70% patient, and 82% patient reduced pain at rest. Results showed the best efficacy in reduction pain symptoms and in improving joint mobility after the period of 12 weeks after the last injections Hylan GF-20 in comparison with another knee. No systemic and local adverse reactions were observed.

Conclusion: These results suggest that viscosupplementation with Hylan GF-20 (Synvisc) is safe and effective in treatment of knee OA.

M31

LONG-TERM STUDY IN THE CHONDROPROTECTIVE TREATMENT OF OSTEOARTHRITIS

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The incidence of arthritis increases with age and lifespan, being the most common cause of invalidity after a certain age. In the category of disabilitating chronic diseases arthritis only comes second after cardiovascular diseases.
The study involved 282 patients hospitalized for coxarthritis (61.53%), gonarthritis (19.23%), and gonarthritis and coxarthriti (19.23%). The study group was further divided into three subgroups. The first subgroup (194 patients) was treated with *Alflutop*, a bioactive concentrate containing marine organisms rich in mucopolysaccharides. The patients received ten intraarticular injections, every other day, followed by intramuscular injections for three weeks. The treatment was repeated three times a year. The second group (50 patients) was treated with intramuscular injections with *Zeel P*, containing extracts of cartilage, placenta, umbilical chord, symphytum and coenzyme a. the third group (36 patients) was treated with a combination of both products in alternative series, and *Dona* every second month.
Clinically, the treatment resulted in the disappearance of pain, improvged functionality, improved radiological index of articula space, stable biological and immunological levels.
The best results were obtained in the early stages of the disease and in those cases without severe cartilage and articular damage. the primary role of this medication in degenerative rheumatism being prophylactic and curative.

M32

TYPE OF WORKING ACTIVITY AS OCCUPATIONAL HAZARD FOR OSTEOARTHRITIS OF CERVICAL SPINE

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AIM: To assess the correlation of radigraphic manifestations of cervical spine osteoarthritis in patients (pts) with clinical manifestations of chronic cervical syndrome, with age, sex, type of working acitivity(sitting position, standing or moving), and employement duration.
PATIENTS AND METHODS: Group of 170 pts, 142 females and 22 males, age 25-62 years (median 45), employement duration 90-39 years (median 23). RESULTS: Most of the pts (106) were working in sitting position with flexed neck, (employement duration 20-29 years), and 63 pts were standing or moving during the work. On cervical spine radiographs reduced extension was detected in 149 pts, discarthrosis in 73 pts, osteoarthritis of cervical spine joints in 36 pts. Diffuse sceletal hyperostosis was found in 19 pts. Pts who were working in sitting position with flexed neck had higher, but not significantly higher, frequency of radigraphic manifestations of cervical spine osteoarthritis. There was positive but insignificant correlationof frequency of radigraphic manifestations of cervical spine osteoarthritis with age, sex, and employement duration.
CONCLUSION: There was no significant diference in frequency of radigraphic manifestations of cervical spine osteoarthritis in patients with chronic cervical syndrome, acording to age, sex, type of working acitivity(sitting position, standing or moving), and employement duration.

M33

CHANGES OF GASTRIC AND DUODENAL MUCOSA AT RHEUMATIC DISEASES (RD)

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Aim. To assess clinical diagnostic, and endoscopic aspects of gastric and duodenal mucosal damages nonsteroid antiinflammatoire medicaments (NAM).

Materials and methods. Clinical examination and gastroduodenoscopy with tardet biopsy were performed in 32 RD patients treated by NAM/

Results. Erosive and ulcerative disturbances were found in all cases. 14 (43.7 %) had similar changes in stomach and 18 patients (56.3 %) - in initial part of duodenum. Only 6 men (18.8 %) showed an ulcerative anamnesis. Endoscopic researches defined an acute inflammation submucous hemorrhages, acute erosive and ulcerative defects. It was found that emergency gastroduodenal endoscopy allows to diagnose the bleeding point and to use endoscopic hemostasis, and his reability. The mucosae damage is more intensive in the distal part of stomash.

Summary. Clinical and endoscoic disturbances in RD pts recieved NAM are connected with morphological changes. Endoscopic investigation can be considered - the special attention should be paid on rational treatment in patients with gastric bleeding.

M34

Chondroprotector effects of Hyaluronan in experimental osteoarthritis. Morphologic and scanning microscope evaluation.

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Objective: to study the effects of Hyaluronan in experimental osteoarthritis in rabbits by partial meniscectomy.

Material and methods: Hyaluronan was administered directly to the articulation in a group of rabbits in an early phase and at a late phase of the illness, each group with its respective controls. The macroscopic and microscopic morphologic aspects were evaluated. The relative concentration of calcium in the cartilage, the trademark and the subchondral bone, were determined by microscopy scanning.

Results: The groups of rabbits which received Hyaluronan presented in macroscopic evaluation, smaller percentage of extension of the damage of the cartilage, between 2 to 5 times less, in relation to those that didn't receive treatment as it is pointed out in table II. The level of calcium in proportional terms by local mass fraction, diminished in subchondral plate regions in the groups, which received Hyaluronan, with tendency to approach to the group control.

Conclusion: We conclude that Hyaluronan is effective showing less aggressive extension and depth of the lesion in the cartilage and the size of the osteophites when compared to die control group. It was also determined that the subchondral region's density decreased in the groups that received treatment without regard to the phase in which the treatment was administered.

Key words: Hyaluronan. Experimental Osteoarthritis. Scanning Microscopy

M35

RENAL FUNCTION AND URATE (UA) DURING AND AFTER MINI-ASPIRIN IN ELDERLY PATIENTS.

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Objective. Use of mini-aspirin is prevalent. It has been shown to cause UA retention and creatinine (Cr) retention in elderly patients, especially if hypoalbuminemic (1). While UA retention was transient, Cr excretion remained depressed 1 week after withdrawal of aspirin. Aim: to study these effects a longer period after aspirin withdrawal in a larger group of elderly patients.

Methods. Long-term care in-patients (N=83, F:M=67:16, mean age 80.7±9). Exclusions: Cr>1.6, gout, active ulcer, bleeding or use of anticoagulants, aspirin or NSAIDs. Aspirin Rx: 100mg/day/ 2 weeks. Lab x 5 weeks (2 on and 3 off aspirin).

Results. After 2 weeks mini-aspirin CCT and UA excretion decreased in 61and 55 out of 83 patients, respectively. 3 weeks after withdrawal mean UA returned to baseline, while CCT improved only partially. Mean values (% change from baseline) are presented on **table 1** (* p<0.05):

Week (Rx.)	0 (pre asp)	2 (2 weeks on asp)	5 (3 weeks off asp)
BUN mg/dL	17.5±7.5	21.9±9.7 * (+25%)	19.3±8.4 * (+10%)
Creatinine mg/dL	0.72±0.26	0.77±0.27* (+7%)	0.72±0.27 (0%)
24 hrs. Cr mg	692±341	537±315 * (-22%)	592±330 * (-14%)
CCT ml/min	71.2±35	52.4±32.7* (-26%)	61.6±34 * (-13%)
Serum UA mg/dL	4.35±1.4	4.66±1.7 * (+7%)	4.37±1.5 (+0.5%)
24 hrs UA mg	422±186	364±179 * (-14%)	412±213 (-2%)
UA clear. ml/min	7.5±4.3	6.0±3.4 * (-20%)	7.3±4.7 (-3%)

Predisposing factors: Lower serum albumin levels were found in patients whose CCT reacted adversely. Low basal renal function, age, hypertension and diuretics did not enhance this response to mini-aspirin.

Conclusion. Mini-aspirin affects renal function and UA in the elderly. Low renal function was not a risk factor. Changes of renal function (and less so UA) persisted 3 weeks after withdrawal, suggesting separate mechanisms as well as clinical alert.

(1) Caspi D, Lubart E, Graff E, Habot B et al. Arthritis & Rheum, 43:103-8, 2000.

M36

LIMITED VALUE OF SPOT URINE URIC ACID TO CREATININE RATIO IN THE ESTIMATION OF URIC ACID OVERPRODUCTION IN PRIMARY GOUT

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Objective: To assess whether or not uric acid to creatinine ratio (Uua/Ucr) in spot urine is useful for the estimation of uric acid overproduction in primary gout patients.

Subjects and Methods: One-hundred thirty male primary gout patients and 33-non-gout male control subjects were enrolled in the current study. Early morning urine and/or a portion of 24-hour-collected urine (24-hour urine) were used as spot urine samples. Uric acid overproducers were defined as those with a 24-hour urinary uric acid excretion greater than 1000 mg/day, while uric acid underexcreters were defined as those with a uric acid clearance below 6 mL/min.

Results: There was a significant relationship between 24-hour urinary uric acid excretion and early morning urine Uua/Ucr in gout patients. However, no significant difference in Uua/Ucr was observed between gout patients and control subjects, or in Uua/Ucr between gout uric acid overproducers and underexcreters in early morning urine. In contrast, a significant difference in this value was observed between the two groups in the 24-hour urine specimens. Although the diagnostic accuracy of gout uric acid overproduction was 87.2% when using early morning urine and 89.6% when using 24-hour urine, the sensitivity of gout uric acid overproduction was only 25.0% when using early morning urine and 25.0% when using 24-hour urine, when the cut-off value of Uua/Ucr was settled at 0.63 and 0.64, respectively.

Conclusion: Uua/Ucr using spot urine, especially early morning urine, is not an accurate indicator of uric acid overproduction in gout patients.

M37

EFFECT OF A COMBINATION THERAPY WITH LOSARTAN AND ANTI-HYPERURICEMIC AGENTS ON URIC ACID METABOLISM IN GOUT PATIENTS WITH HYPERTENSION

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Objective: To evaluate the effect of a combination therapy with losartan and anti-hyperuricemic agents on uric acid metabolism in gout patients with hypertension.

Subjects and Methods: Losartan (50 mg/day) was administered together with allopurinol (200 mg/day) or benzbromarone (50 mg/day) to 19 gout patients with hypertension. They had received allopurinol (200 mg/day) or benzbromarone (50mg/day) for 1 month prior to the administration of losartan. Before and after the combination therapy of losartan and anti-hyperuricemic agents, 24-hour urine was collected and blood was drawn. Serum uric acid level, 24-hour urinary uric acid excretion, uric acid clearance, and creatinine clearance were determined.

Results: 1. Losartan decreased blood pressure from 163±9/102±11 to 132±5/84±7 mmHg (P<0.01). 2. Serum uric acid level was decreased from 5.3±1.0 to 4.7±0.9mg/dl after the administration of losartan (P<0.01). 3. Losartan increased the clearance and 24-hour urinary excretion of uric acid from 5.5±2.1ml/min and 482±133 mg to 7.7±2.8 ml/min (P<0.01) and 590±179 mg (P<0.01), respectively.

Conclusion: Losartan is effective for the treatment of hyperuricemia even in a combination therapy with anti-hyperuricemic agents.

M38

EFFECT OF FENOFIBRATE ON THE PLASMA CONCENTRATION AND URINARY EXCRETION OF PURINE BASES AND OXYPURINOL

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Objective. To investigate whether fenofibrate increases the clearance of purine bases (hypoxanthine, xanthine, and uric acid) and oxypurinol.

Methods. We administered it (150 mg) 3 times a day for 3 days, and then allopurinol (300 mg) 4 hours after the last administration of fenofibrate, to 5 healthy subjects. Ten hours later, clearance study was done.

Results. Following the 3-day administration of fenofibrate, the fractional clearance of xanthine, uric acid, and oxypurinol increased by 41% (P<0.05), 100% (P<0.01), and 51% (P<0.01), as compared to the respective base line values, while the respective plasma concentrations decreased by 46% (P<0.05), 46% (P<0.05), and 19% (P<0.05).

Conclusion. These results suggest that fenofibrate, fenofibric acid, or fenofibrate derivatives can increase the fractional clearance of xanthine, uric acid and oxypurinol by acting on their common renal pathways. Furthermore, it is suggested that the hypouricemic effect of a combination therapy using allopurinol and fenofibrate may be less than additive.

M39

CHANGE IN OXIDIZED LOW-DENSITY LIPOPROTEIN AND PLASMA TOTAL ANTIOXIDANT STATUS BY ALLOPURINOL IN GOUT

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Objectives: We investigated oxidation product of low-density lipoprotein, oxidized LDL antibody (oLAb) and plasma total antioxidant status (P-TAS) in gout patients who have hyperuricemia. Moreover, Those factors were compared between before and after treatment of antihyperuricemic agent.

Subjects and Methods: Age-matched male patients with primary gout (n=50) and healthy adult male (n=30) were included in the study. P-TAS was measured by a colorimetric method using a kit (Total antioxidant status, Randox Laboratories Ltd., UK). Serum oLAb was measured by an enzyme immunoassay using a kit (oLAb ELISA, Biomedica, Austria).

Results; Serum uric acid (SUA) and P-TAS was significantly higher in gout than control (8.2 +/- 1.8 vs 5.1+/- 0.9 mg/dL, p<0.0001 and 0.66 +/- 0.26 vs 0.42 +/- 0.10 micromol/L, p<0.0001, respectively). Serum oLAb too (575 +/- 442 vs 363 +/- 188 mU/mL, p<0.05). P-TAS was significantly correlated with SUA (r=0.76, p<0.0001), while serum oLAb was not. Multivariate analysis demonstrated that SUA was a strong contributor of P-TAS. P-TAS was significantly decreased while using antihyperuricemic agent.

Conclusion: Uric acid contributes, in part, to an increased P-TAS. However, it is suggested that SUA does not play a role in inhibition of LDL oxidation in gout.

M40

SEVERE HYPERPARATHYROIDISM. A REPORT OF 68 CASES.

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Hyperparathyroidism is the most frequent endocrinopathy after diabetes mellitus and, hyperthyroidism. It is now more easily diagnosed at an early stage of the disease and severe forms are rarely reported. However, they remain not rare in some countries as ours.

Objective : to study the frequency and type of osteo-articular involvement in severe forms of hyperparathyroidism.

Material and methods : Type of the study : retrospective. Studied period : 1990-1999. Criteria for inclusion : Serum calcium and phosphorus, PTH assays and or histological proof. Clinical and radiographical data were collected for each patient.

Results : 68 cases were collected (51F/17M) . Mean age : 43 ans ± 11 ans [17 ; 68 ans]. Osteo-articular manifestations were : bone pains in 52 cases (76,47%), lacunas and fractures in 15 cases (22,05%), bone swelling in 8 cases (11,76%) , bone deformities in 6 cases (8,82%) and arthralgias in 8 cases. Chondrocalcinosis was noted in 2 cases. The diagnosis was fortuitous in 2 cases. Hypercalcemia was noted in 63 patients. PTH was elevated in 32 cases . The preoperative localization of parathyroid nodule was based essentially on ultrasonography exam in 40 patients and has demonstrated parathyroid nodule in 29 cases (60,41%). Surgery was performed in 66 patients. Histological study objectived adenoma in 58 cases and diffuse hyperplasia in 8 cases. The post operative morbidity was dominated by permanent hypoparathyroidism in 35 cases (51,47%).

Conclusion: severe forms of hyperparathyroidism are not unusual. The involvement of joints and bone leads to severe complications as fractures. They obviously have to be prevented by an early diagnosis.

M41

HYPERPARATHYROIDISM AND FAHR DISEASE. Report of a case.

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Fahr's disease associates various degrees of neuropsychological impairment and calcium deposits in the basal ganglia.

Case report: B.D, 18 years, was developing Fahr's syndrome revealed by neuropsychiatric disorders. Brain CT scan which identifies calcium deposits in the basal ganglia and laboratory results demonstrated idiopathic hypoparathyroidism.

Discussion: Clinical expression of Fahr's syndrome greatly varies. Diagnosis requires CT brain. The main cause is hypoparathyroïdism, whether primary or post operative.

Conclusion: This case report illustrates the good prognosis of Fahr's syndrome since correcting the impaired calcium phosphorus metabolism.

M42

HYPERURICEMIA IN POST RENAL TRANSPLANT INDIAN PATIENTS

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Background: Hyperuricemia is a common yet often overlooked metabolic complication in renal transplant recipients. Despite renal transplantation being the commonest solid organ transplantation performed in India, no data on hyperuricemia/gout in these patients is available from the country.

Objectives : (1) To study the frequency of hyperuricemia in post transplant patients (2) To assess the role of various variables like age, sex, BMI, diuretics, cyclosporine etc. in these patients.

Patients and Methods : All renal transplant patients attending the transplant clinic at a large teaching hospital in India were included. Hyperuricemia was defined as serum uric acid ≥ 7 mg% in males and ≥ 6 mg% in females. Patients with serum creatinine >3mg/dl were excluded from the study. Mean follow up was 2.5 years.

Results : Our cohort comprised 265 patients of whom 33 were excluded due to impaired renal function. 174 of the 232 patients studied (male 211, female 21) exhibited hyperuricemia (serum uric acid levels 9.38 ± 2.39 mg%). The vast majority of hyperuricemic patients were on cyclosporine A. Age, sex, BMI, diuretic use were not contributory factors. Clinical gout was seen only in 1 patient.

Conclusions : Hyperuricemia is seen 75% of post renal transplant Indian patients. Cyclosporine A is one of likely contributing factors. Clinical gout, at least over a mean follow up of 2.5 years, is uncommon.

M43

FENOFIBRATE LOWERS SERUM URATE IN PATIENTS TREATED WITH ALLOPURINOL

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Background: Fenofibrate is well established in the treatment of hyperlipidaemia and is a unique fibric acid derivative due to its urate lowering properties. This effect has not, however, been investigated in patients with hyperuricaemia established on allopurinol therapy.

Objective: To assess the short-term urate lowering effect of fenofibrate in patients with interval gout associated with hyperuricaemia on current treatment with allopurinol.

Methods: 11 patients (10M:1F), age range 38-74, were assessed in an open crossover study. All had received allopurinol ≥ 300mg/day for ≥ 3 months and had been gout-free for ≥ 1 month. Serial biochemistry, including serum and urine urate and creatinine, were undertaken at [1] baseline, [2] after 3 weeks micronised fenofibrate 200mg/day and [3] 3 weeks after cessation of fenofibrate. Allopurinol was continued throughout the study period.

Results: Fenofibrate was associated with a 24% reduction in serum urate at 3 weeks (mean 0.36±0.11 vs 0.29±0.07mmol/l; p=0.002). The urate-lowering effect was rapidly reversed on its withdrawal. There was a mean rise in uric acid clearance of 56% (6.7±3.1 vs10.5±5.6ml/min NR 6-11; p=0.005). Both cholesterol and triglyceride levels fell (neither statistically significant). Alkaline phosphatase activity was reduced in each patient, confirming compliance with fibrate therapy. Importantly, none of the group developed acute arthritis whilst taking fenofibrate, and the three who continue to take the drug remain free of gout.

Conclusion: Fenofibrate rapidly reduces serum urate by a significant degree in patients with hyperuricaemia already established on allopurinol prophylaxis. Fenofibrate is a potential novel treatment for hyperuricaemia and the prevention of gout, particularly when these are coexistent with hyperlipidaemia or are resistant to conventional therapy.

M44

SERONEGATIVE OLIGOARTHRITIS AS PRESENTING MANIFESTATION OF PRIMARY HYPERPARATHYROIDISM

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Objective: The case of a patient with primary hyperparathyroidism in whom the presenting manifestation was seronegative oligoarthritis is presented.
Rationale: The association of calcium pyrophosphate crystal disease with hyperparathyroidism has been described. Acute arthritis as postoperative complication of parathyroidectomy in patients with hyperparathyroidism has also been described.

CASE REPORT: A female patient, aged 63 years, presented with chronic remitting oligoarthritis of a year's duration affecting the left carpal joint and the left knee.Radiografic examination of the involved joints was negative for erosions. Laboratory examinations revealed mild anemia, increased erythrocyte sedimentation rate, normal C-reactive protein, negative rheumatoid factor and negative antinuclear antibodies. Serum calcium levels were elevated, being in the range of 10,7-12,5 mg/dl and serum phosphate levels were decreased. Chest and abdomen computed tomography imaging and whole body scintigraphy with with Tc 99m did not reveal sarcoidosis or malignancy. Serum parathyroid hormone was in the high normal range (PTH=45 pg/ml,normal range 10-65 pg/ml), plasma c-AMP was increased, being 4,0 nmoll/dl(normal range 1,6-2,9 nmoll/dl), nephrogenous c-AMP was increased, while 25(OH)vitaminD3, 1,25(OH)vitaminD3 and parathyroid hormone related protein were in the normal range. Thyroid-parathyroid scintigraphy with 99mTc MIBI and 99mTcO4 revealed the presence of an area in the lower pole of the thyroid compatible with hyperfunctioning parathyroid tissue.
Conclusion: The case of a patient with primary hyperparathyroidism where the presenting manifestation was seronegative oligoarthritis is described. Increased calcium levels, low phosphate, increased nephrogenous and plasma c-AMP were observed and parathyroid scintigraphy revealed the presence of hyperfunctioning parathyroid tissue.

M45

THE LOCOMOTOR SYSTEM IN DIALYSIS PATIENTS

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Objective: Patients receiving maintenance haemoldialysis suffer from various problems of the joints, soft tissues and tendons. To establish the incidence and nature of osteoarticular disease in patients receiving long term treatment with hemodialysis we surveyed all our patients who had received dialysis.

Methods: The subjects were 122 patients who were dialyzed for one year to 22 years. We also analyzed clinical factors such as age, duration, underlying disorder of chronic renal insufficiency, hemotologic parameters. All patients were seen at an extra clinic attendance when they were asked to evaluate pain and stiffness in each joint. A diagnosis of dialysis associated arthropathy was made by three investigators, using as criteria single or combined presence of carpal tunnel syndrome, erosions and bone cysts of the joints and destructive spondylarthropathy. Plasmaure, creatinin, hemoglobin, ferritin, calcium, phosphorous, urate, parathyroid hormone concentrations, alkaline phosphatase, magnesium, aliminium, ß2 microglobulin, osteocalcin, vit. D, hepatitis markers were measured before dialysis in patients. Radiographs of the hands and painful joints were obtained in patients. We used DEXA to detect changes in bone mineral density (BMD). Hamilton despression scale was used for depression.

Results: We found carpal tunnel syndrome in 29 (23.8%), spondylarthropathy in 14 (11.5%), skeletal deformities in 29 (23.8%) tenosynovitis in 6 (4.8), perioarthritis in 10 (8.2) patients and bone cysts in 26(20.7%) patients. When we compared groups according to duration of hemodialysis treatment, carpal tunnel syndrome, bone cysts and periarthritis were found more frequently in the patients receiving hemodialysis treatment for longer time ($p<0.01$). BMD was reduced in dialysis patients of both sexes in comparison with the healthy subjects. There was significant correlation between BMD and the mean serum ß2 microglobulin, magnesium, creatinin, ferritin, alkaline phosphatase levels. Strong relationship was found among hemodialysis duration and osteoporosis. Depression was observed in 66.3% of patients.

Conclusion: Changes of the locomotor apparatus in prolonged hemodialysis treatment determine the quality of life with all its consequences for the patients.

M46

EFFICACY OF CELECOXIB VS NAPROXEN IN THE TREATMENT OF ANKLE SPRAIN

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Objectives: A COX-2 specific inhibitor, celecoxib, may be as effective as conventional NSAIDs in the treatment of ankle sprain.

Methods: A randomized, double-blind study evaluated celecoxib 400 mg/d (n=198) or naproxen 1000 mg/d (n=198) over 8 days. Patients had a baseline grade 1 or 2 ankle sprain and moderate-to-severe pain on weight bearing (≥45 mm, 100mm VAS).

Results: Most patients were male; mean age was 30 years. The first study dose was taken within 48 hours after the injury occurred. Covariate-adjusted analyses of the primary endpoints (Patient's Global Assessment of Ankle Injury responder rate, and Patient's Assessment of Ankle Pain VAS on weight-bearing) demonstrated that celecoxib was as effective as naproxen in improving the signs and symptoms of ankle sprain.

	Responder Rates [n (%)] on Patient's Global Assessment of Ankle Injury*		Patient's Ankle Pain (VAS), mm** Mean (SE)	
	Celecoxib	Naproxen	Celecoxib	Naproxen
Baseline	..	..	68(14.5)	68(13.1)
Day 4	139(71%)[‡]	142(72%)	32(2.0)[†]	29(1.9)
Day 8	175(89%)[‡]	178(90%)	15(1.7)[†]	15(1.7)

*Improved by ≥1 grade on 5-pt scale from 1 (very good)-5 (very poor); **covariate-adjusted; [‡]celecoxib not inferior to naproxen based on 95%CI; [‡] p ≥.51; [†]VAS=Mean(SD)

Conclusion: Celecoxib is as effective as the maximum recommended dose of naproxen for pain in treating ankle sprains. Celecoxib, with its platelet-function-sparing properties, may offer an advantage over naproxen in managing ankle sprain injuries.

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M47

ACUPUNCTURE – OLD OR NEW METHOD FOR TREATMENT OF BACK PAIN?

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Recently acupuncture is being applied in almost all diseases of mankind. It was brought from China and has since been gaining an ever stronger scientific basis in the modern world, especially in the analgetic sense. The author who is mostly concerned with low back pain and the changes in that part of the spinal column has been using it successfully for the past 15 years.

In the period of time from 1995 to 2000 250 patients with low back pain were treated only with acupuncture. All other methods of medicaments and physical therapy were excluded, with the exception of resting. 160 patients had syndromes of vertebral character, 90 had vertebrogenous syndromes with radicular symptomatic. Only those patients who had their first attack of pain in the low back region were taken as samples, so as to avoid eventual simulators and malingerers. Eight acupuncture sittings were carried out every day. Most patients were treated as outpatients, some were hospitalized on account of their poor state of health.

Results: In the group with acute low back pain without radicular symptomatic, in which the author commenced with the treatment 2 days after the appearance of pain, an almost complete sanation of the disease was reached after 8 days of acupuncture. In the group in which acupuncture was begun 3 or more days after the appearance of pain, only a partial clinical and subjective improvement was noted towards the end of acupuncture therapy. The second group of patients, who had a discoradicular conflict and were treated within 2-3 days after the appearance of the disease, had equally good analgetic results, acute pain was diminished to almost one half, but the discoradicular conflict symptoms mostly remained. In patients in which acupuncture was begun a few or several days after the initial disease only a minimal clinical improvement was noted.

In conclusion the author suggests the application of acupuncture in acute low back pain and advises to commence treatment with acupuncture immediately, within 2-3 days after the initial low back pain of any character. Good results can not be obtained by a later approach. Counterindications other than the general ones are not known.

M48

BACK PAIN TREATED BY LOW FREQUENCY PULSATING MAGNETIC FIELDS

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Low back pain may be the result of diseases of different etiology, but most frequently the cause lies in degenerative changes of the spine: first and most often affected is the lumbosacral dynamic segment which is the nucleus of vertebrogenerated pain and functional disturbances of the sacral part of the spine.

This paper is part of a research study on the influence of low-frequency pulsating magnetic fields of low intensity on biosystems. 72 patients with low back pain of a degenerative nature were included in the study: hernia disci, ankylosing spondylitis, degenerative changes in spinal small joints. The patients were divided at random into two groups. In the first group there were 48 patients (average age 38 years, range from 28 – 68 years, 62% women) treated by pulsating magnetic field (50 Hz, 60 G = 6 mT), kinesi- and hydrotherapy. The magnetic field was applied daily for 30 minutes, for 15 days in all. In the second group there were 24 patients with similar pathology and of the same age, treated only by kinesi- and hydrotherapy. Subjective (low back pain, sensitiveness to palpation, pain on rising from the bending forward position) and objective parameters (Lasegue's sign, the distance between the fingertips of outstretched hands in the bending forward position and the ground) were evaluated before and after therapy and treated statistically. The results showed a statistically significant difference ($p = 0.05$) in the subjective decrease of low back pain, the reduction of sensitiveness to palpation and the reduction of pain in rising from the bending forward position, as well as in the objective signs (bil. Lasegue, improved mobility of the lumbosacral segment) – the results were significantly better in the group with magnetotherapy.

The authors conclude that low frequency pulsating magnetic fields of low intensity are a useful new additional method of treatment of low back pain.

M49

JOINT HYPERMOBILITY IN PATIENTS WITH SPONDYLOLISTHESIS

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Objective: To study the relation between joint laxity and spondylolisthesis.

Patients & Methods: Fifty-five patient with spondylolisthesis were compared with that in an age, sex, and body mass index (BMI), matched control group without spondylolisthesis. Joint mobility was scored on a scale of 0-9.

Results: Backache was the chief complaint in all patients radicular pain was reported in 40, step deformity in 35, and increase in lumbar lordosis in 15 patient. Spondylolisthesis was of grade I or II, it is mainly at L5/S1 or L4/5 level, 32 patient showed isthmic defect and 23 showed degenerative spondylolisthesis. Disc space narrowing was reported in 27 patient, which was mainly between L5/S1 and L4/5. The number of patients with hypermobile joints and the total mobility scores were higher in the spondylolisthesis group ($P<0.01$) which also had more spinal hypermobility ($P<0.1$) when compared with the control group.

Conclusion: Joint laxity may be contributing factor for the pathogenesis of spondylolisthesis.

M50

CHRONIC LOW BACK PAIN INFLUENCE TO THE HEALTH

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The **objective** of the study was to analyze the relationship between chronic low back pain (CBP) and physical, psychological symptoms and physical capacity.

Methods. A sample of 1,030 subjects being aged 25-74 was randomly selected in the vicinity of two main urban outpatient clinics. All the subjects were interviewed according to a standard questionnaire. Two groups of respondents were identified: the first- met the ACR 1990 definition for CWP, the second- satisfied the standard definition of CBP but not the ACR definition for CWP. A follow-up screening of the subjects who reported CBP was carried out after 6 months. The subjects who still reported CBP were classified as "persistent" CBP sufferers and who did not- "nonpersistent" CBP cases.

Results. The response rate was 83.01%. The prevalence of CBP was 12.28%. After 6 months 72.38% of subjects with CBP participated in the follow-up screening. "Persistent" CBP was present in 47.37% of respondents. They more often reported musculoskeletal, somatic, psychological symptoms, fatigue, poor health status ($p<0,05$, $\chi^2= 38,6$; C 0,3), poor quality of life ($p<0,05$, $\chi^2= 29,6$; C 0,3), restricted everyday life physical activity ($p<0,05$, $\chi^2= 39,8$; C 0,4) than the subjects with "nonpersistent" CBP. The average score of vegetative-functional complaints was 24.13±2.69 for subjects with "persistent" CBP and 5.67±3.01 with "nonpersistent" ($p<0.05$). The average score of depression symptoms was 15.45±7.89 and 8.83±4.62 respectively ($p<0.05$). The average score of physical capacity of subjects with "persistent" CBP was significantly lower (59.14±11.48%) compared with "nonpersistent" CBP cases (72.43±12.65%) ($p<0.05$).

Conclusion. Results of this study demonstrate the importance of "persistent" chronic musculoskeletal pain to the health.

M51

TRAMADOL THERAPY IN TREATMENT OF LUMBAGO

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Objective:To test the efficacy and tolerance of tramadol in patients suffering from low back pain.

Methods: We monitored two groups of patients in two centres in Croatia. The groups were made up of patients with the first attack of lumbago during the monitored year. The current attack lasted about 7 days on average. The study excluded patients over 65, patients with impaired liver and/or kidney function, and those taking MAO inhibitors. Following tramadol therapy (as the only used analgesic) with the regime of 3 x 50 mg over 4 days, and then 2 x 100 mg over 6 days, pain relief was tested (VAS scale from 0 to 10), along with objective improvement of the lumbal spine function, adverse events and overall eff icacy (scale 1=poor to 5=excellent).

Results: A total of 90 patients from two centers provided data.All were under 65 (average age 42). Most patients were men (61%), employed (62%) and all were suffering from a first attack of lumbago in that year.After 10 days tramadol provided pain relief (range 3,5- 4). The improvement of lumbal spine function was in correspondence with pain relief. The most frequent adverse events were: nausea(19%), somnolence(15%), headache(8%).Overall efficacy of medication was rated"excellent" by 39% of patients.

Conclusion: Tramadol has proved its efficacy in treatment of lumbago, acting as an analgesic with an acceptable percentage of adverse events.

M52

MODIFIED INITIAL TREATMENT OF LOW BACK PAIN

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Aim of the study: Musculoskeletal pain is a major health problem for people in height of active life, causing increasing costs of absence from work, highly expensive diagnostic and treatment procedures, as well as compensation claims. A standard, inexpensive and simple diagnostic and treatment protocol was proposed for primary treatment, before the involvement of more aggressive measures.

Methods: 165 patients were reported to authors for episodes of low back pain. Patients were divided in two groups. First group of 72 patients, (43%) were treated by simple NSAID medication (piroxicam, LUBOR, Belupo, 3 x 100 mg/day), and by modification of daily activities. Second group of 93 patients (57%) was worked up in standard diagnostic procedure (x-ray and EMG work up). If patient did not improve after two-week treatment, further diagnostic procedures were extended as needed.

Results: 56 (78%) patients form the first group significantly improved after treatment involving continuos and controlled NSAID medication and change in daily activities. This considered exclusion of heavy exercises, but not a bed rest. 16 (22%) needed further diagnostic investigation, but in only 7 (10% of initial group) morphological substrate of their problems could be distinguished. In second group of patients a significant x-ray finding was found in 34 (36%), and 20 (21%) patients had positive EMG findings. In only 19 patients (20%) these findings could be connected with patients specific troubles.

Conclusion: Patients with low back pain could be effectively treated by simple measures consisting of controlled NSAID medication and specific modification of daily activities. Bed rest and extensive diagnostic procedures should be spared for patients with the evidence of neural involvement and for those with prolonged pain.

M53

ASSESSMENT OF A BIOFEEDBACK PROGRAM TO TREAT CHRONIC LOW BACK PAIN

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Background: Low back pain is a common problem that can affect up to 80% of adults during their lives.The symptoms of these chronic pain patients include affective, cognitive and behavioural components. Many interventions have been found to be beneficial in the rehabilitation of chronic low back pain patients, one of them is biofeedback.

Objectives: Assess the efficacy of a biofeedback program for chronic low back pain patients and its impact in their pain, disabilities, and depression and anxiety symptoms, and promove higher abdominal muscles contraction levels without increasing paraspinal muscles contraction levels

Methods: Sixty patients with chronic low back pain were randomly assigned into a control and a treatment group and were oriented to take analgesics when necessary. The treatment group participated in a biofeedback program (8 weeks) that included: global relaxation trainning and abdominal strength exercises with and without biofeedback and cognitive restructuring techniques. The outcome measures used were Visual Analogue Scale (VAS), Roland-Morris questionnaire, Schöber Index, Beck Depression Inventory (BDI) and State-trait Anxiety Inventory (STAI) in the begining and at the end of the observation period. Contraction (EMG) levels of abdominals and paraspinal muscles were also registered

Results: At the end of the observation period treatment group patients improved significantly on VAS (p=0,012) and STAI (p=0,003). Roland-Morris questionnaire improved in both groups without differences between them (treatment p=0,0001 and control p=0,006). The control group improved significantly on BDI (p=0,013). There were no differences in the contraction levels of abdominals and paraspinals muscles, and neither in the Schöber Index

Conclusion: Our biofeedback program reduced pain and anxiety symptoms of chronic low back pain patients. The disabilities improved in both groups. The program didn't change depression symptoms and the paraspinal contraction levels while contracting abdominal muscles

M54

CAN THE INTERNET AFFECT OUTCOMES? A RANDOMIZED ONE-YEAR BACK PAIN TRIAL.

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The Back Pain Internet Education Study was developed to determine the effectiveness of a moderated Internet discussion group in improving health status and health care utilization. Subjects were randomized to take part in an email list where all members received the posts of all other members, or a control group that received a popular magazine subscription. All subjects continued with their regular medical care.

Subjects were recruited during 1998 and early 1999. The recruitment process included, 1) reaching the back pain study web page, 2) filling out a screening questionnaire to determine eligibility for the study, 3) reading and submitting an informed consent and 4) completing a baseline questionnaire. All of these activities occurred on line.

The subjects come from 49 states, are 62% male, mean age 45.3 years (SD=11.6) and mean education 16.6 (SD=2.8) years. In the past 6 months they had averaged 3.9 physician visits and 4.2 chiropractic visits. During the first year there were approximately 2500 posts to the list with 68% of the subjects posting at least once.

At one year 190 (69%) treatment subjects compared to 232 (89%) control subjects demonstrated less disability (Roland disability scale), health distress, and interference in their daily activities; increased self-efficacy to manage their symptoms, and increased orientation toward self-care (all p<.01). There is also a trend toward fewer back related visits to physicians (p=.07). All analyses are ANCOVAs controlling for age, sex, ethnicity, marital status, education, and baseline status of the dependent variable.

These results suggest that a simple moderated email discussion group can have important effects on health status and may reduce health care utilization. These effects are in addition to those received from traditional medical care. Thus, such Internet groups may be a low cost means of enhancing outcomes for large numbers of patients.

Yahoo! donated banner advertising for this study

M55

EFFECT OF TRAIMCINOLONE DIACETATE INJECTIONS IN EARLY DUPUYTREN'S CONTRACTURE AND STENOSING TENOSYNOVITIS OF THE HAND.

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Objective: To determine the effectiveness of steroid injections in slowing the progression of fibrosis and contractures in early Dupuytren's disease and related conditions causing stenosing tenosynovitis of the hand.

Rationale: Fibrosing conditions are initiated by inflammation followed by deposition of collagen and ground substance. Glucocorticoids inhibit both mechanisms leading to fibrosis.

Methods: Twenty-three patients studied included 12 men and 11 women (age range from 35 - 72 years). Eighteen patients had Dupuytren's contracture, 15 bilaterally. None of them had contractures in the PIP joints. Two had bilateral De Quervain's tenosynovitis and 3 had isolated fibrous nodules in a single flexor tendon. All patients received 1-2 triamcinolone diacetate injections of 2.5 to 5mg in the fibrous nodules, cords and tendon sheaths. Additionally, 5 patients received nonsteriodal anti-inflammatory agents for 1-2 weeks.

Results: Patients with Dupuytren's contracture demonstrated softening of the symptomatic cords, improvement of grip strength and partial resolution of nodules. The other patients had a complete resolution. Patients were followed for 1-7 years and maintained their functional improvement. No patient progressed or required surgery. There were no complications such as hematoma, infection, decrease in grip strength, or flexor deformity of the fingers.

Conclusion: These observations suggest that treatment of early Dupuytren's disease and other fibrosing tenosynovitis of the hands with injections of triamcinolone diacetate is safe and effective and appears to prevent progression of these conditions.

M56

MULTIVARIATE ANALYSIS OF SYMPTOMS AND SIGNS OF SOFT TISSUE DISORDERS (STD) OF THE ARM: A MULTICENTRE STUDY

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Lack of agreed criteria has hampered research on STD.

METHODS; Multivariate analysis of 1045 consecutive cases at 5 clinics has identified core variables for diagnosis of the commonest STD. Logistic regression modeling of these with clinican's diagnoses as the independent variable was undertaken.

RESULTS: STD cases were included when there were 50 or more. The remainder were other new cases of arm pain.

Significant variables positively discriminating for each were;

NONSPECIFIC ARM PAIN, 458 cases; Pain in hand or wrist, neck pain, discomfort &/or pain, weakness arms or hands, dropping things or clumsiness.

CARPAL TUNNEL S, 56 cases; Paraesthesiae or numbness in median nerve area, pain at night, weakness in relevant muscles.

EPICONDYLITIS, 87 cases; Pain or tenderness, or pain at epicondyle on loading relevant muscle.

TENOSYNOVITIS, 63 cases; Pain on moving tendon or swelling of sheath or triggering or locking or nodule of any wrist tendon.

SHOULDER TENDONITIS, 157 cases Abduction shoulder <140 degrees, painful arc, pain in shoulder, sleep disturbance.

FIBROMYALGIA, 124 cases; widespread pain, tender points,

ARTHRITIS (INFLAMM), 29 cases;Morning stiffness, finger pain

Areas under ROC curves showed acceptable discrimination.

CONCLUSIONS; Multivariate analysis in a large number of cases from 5 centres defined clinically plausible groups of variables suitable for use in surveillance criteria.

M57

ANTI-Jo-1 AUTOANTIBODY POSITIVE MYOSITIS: CLINICAL FEATURES AND SURVIVAL IN FRENCH CANADIAN PATIENTS.

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Objective : To describe a subset of French Canadians (FCs) with idiopathic inflammatory myopathies (IIM) expressing anti-Jo-1 autoantibodies (Abs).

Methods: From a cohort of 100 adult FCs with IIM, patients positive for anti-Jo-1 by clinical laboratory ELISA were retrospectively analyzed.

Results: Seven women and 5 men (12% of the cohort) were anti-Jo-1 positive. Anti-Jo-1 positivity was confirmed by immunoprecipitation from HeLa cell extract in 10 of 11 sera tested. IIM diagnoses were polymyositis (PM, n=7) and dermatomyositis (DM, n=5). The median age at diagnosis was 40 years (range 27-60 years). The mean followup was 7.5 years (range 8-185 months). The dominant initial manifestations were: myalgias, arthritis, carpal tunnel syndrome and polyarthralgias (17% each). At diagnosis, «antisynthetase syndrome» features were: arthritis (75%), fever (41%), dyspnea due to pulmonary fibrosis (PF, 33%), and Raynaud's phenomenon (RP, 25%). Mechanic's hands were absent. Other manifestations were: proximal muscle weakness (91%), myalgias (58%), DM rash (41%), puffy hands (41%), carpal tunnel syndrome (41%), dysphagia (25%), and generalized edema (25%). Laboratory features were: high CK levels (100%) (mean 7870 U/L, range 439-18795), hypoalbuminemia (66%), rheumatoid factor (33%), anti-Ro (17%), anti-topo I (17%), anticentromere (8%), anti-Sm (8%) and anti-DNA (8%). On followup, arthritis (92%) with erosions (25%), PF (66%), RP (41%), mechanic's hands (17%), scleroderma (SSc, 17%) or DM-type (8%) calcinosis, and sclerodactyly (8%), were noted. The initial treatment was corticosteroids in 11 (92%) patients. Although complete responses were noted, clinical and/or CK flares were evident at tapering in all patients, requiring addition and maintenance of a second line agent. Remission was achieved with MTX in 5 patients (mean dose 17.5 mg/week; range 12.5-30). Cumulative 5-year survival was 100%.

Conclusion: Anti-Jo-1 Abs in FCs with IIM are markers for a peculiar overlap syndrome characterized by PM or DM, PF and, at times, RA and SSc features. Myositis control requires a second line agent. The 5-year survival is good.

M58

ETIOLOGIES OF TALALGIAS IN A NORTH AFRICAN POPULATION. A PROSPECTIVE STUDY OF 100 CASES.

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Objective: to evaluate the frequency and etiologies of talalgias in a non Euro-american population.

Material and methods: Prospective study over a of 6 months period. Were studied all the patients examined for talalgias .

Results: 100 patients were included (58 women and 42 men) . Their mean age was 37,5 ± 11,1 years [16-75]. During the studied period, the frequency of talalgias was 1,3% of all the motives for consultation. The talalgia was mechanical in 94% of cases. Its site was low in 90 patients, posterior in 10 , low and posterior in 16. Talalgia was bilateral in 20% of cases : 6 of them were inflammatory and made possible the early diagnosis of ankylosing spondylitis. The talalgia was frequent in works requiring a prolonged standing position (30%) and when overcharged weight (40%). The kind of the shoe (slippers, commonly used) appears important. The statics of the rear foot shows a varus (14%) of the cases and a valgus in (20%). These curvatures are associated to a more complex distortion of the foot (flat foot 20%, hollow foot 40%). The X-ray of the rear foot shows a new bone formation on calcaneum in 55% of cases, and Haglund diseases in 4 cases.

Conclusion : although it is usually of mechanical origin, the diagnosis of talalgias may lead to diverse etiologies, among them ankylosing spondylitis in our country.

M59

REFLEX SYMPATHIC DYSTROPHY SYNDROME OF THE HIP. A report of 10 cases.

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Reflex sympathic dystrophy syndrome (RSDS) of the hip (RSDSH) usually represents 10-15% of the lower limbs RSDS. Its etiopathogeny is particular.

Objective: to study RSDSH in a rheumatology department .

Material and methods: Type of the study: retrospective. Studied period: 1988-2000.

Criteria Inclusion: Doury criteria of the RSDS. Localization: hip .

Results: from 84 RSDS , 10 (8,4%), are localized on the hip (left hip N=7 , right hip N=6) which represents 20,9% of the lower limbs localizations. Mean age of the patients (6M/4W), is 47,6 years ±15,02 (30-80). Other localizations are the knee (N=4) , shoulders and thorax. Recurrent forms are noted in 3 cases. Etiological factors are as follows: traumatism or micro-traumatism (N=4), pregnancy (N=1), abscess of the psoas (N=1), neurogical complaints (N=1), idiopathic forms (N=3). Pains and lameness were found in all the patients. X-rays were normal (N=4), showed demineralisation (N=9). Scintigraphy performed in 4 patients showed hyperfixation (N=3), hypofixation (N=1). Treatment used calcitonine then rehabilitation in all patients . No guanethidine block was needed . All the patients improved after 9,7 weeks±4,37 (5-17).

Discussion: RSDSH is infrequent. Recurrent, see-saw forms and those associated to another localization (50%) are frequent. Most of the cases occurred after traumatisms. Pregnancy was responsible in one case. Idiopathic forms represented one-third of the cases .

M60

REFLEX SYMPATHIC DYSTROPHY SYNDROME (ALGODYSTROPHY) : a report of 84 cases.

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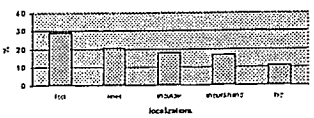
Introduction : RSDS are still a complex and polymorphic disease. Therefore their diagnosis may be difficult.

Material and methods : Retrospective study (1988-2000); criteria for inclusion: Doury's criteria .

Results : 84 patients were included (50F-34M) .Mean age: 50,7 years ±14 [17-80] . Mean interval for diagnosis : 13,7 weeks ± 11,8 [1-48]. Typical form wass reported in 31 patients.



Primitive forms		Secondary forms	
N	%	N	%
10	12	74	88
Etiologies		%	
traumas		52,4	
neurologic		16,7	
diabetes		13	
rheumatisms		9,5	
malignancy		4,7	
drugs		3,5	
pregnancy		2,4	

X-rays : heterogenous osteoporosis (52,4%) . Scintigraphy (n=18): increased uptake (88,9%) . Treatment used : calcitonin (71,4%) , griseofulvin (41%) . NSAIDs (41,6%) , analgesics (21,4%) . often combinated . Physical therapy (53,6%) . Recovery was reported in 63,7% of the cases (average delay = 9,12 weeks±6,5 [2-28]) . Recurrent forms were noted in 13% of the cases.

Discussion : in our serie, RSDS occur most often in the lower limbs. They are most often secondary to traumas. Multifocal and recurrent forms are present in the third of the cases .

M61

EFFICACY OF CELECOXIB IN THE TREATMENT OF ACUTE SHOULDER PAIN.

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Objective: To evaluate and compare the efficacy of 14-day treatment with celecoxib 200 mg BID and naproxen 500 mg BID in patients with acute shoulder pain.
Methods: In a double-blind controlled, multicenter study, patients with pain onset within the previous 14 days and pain intensity of ≥40 mm on a 100-mm VAS were randomly assigned to one of two parallel groups. The primary assessment was pain at rest.
Results: Baseline characteristics were similar (47 ± 12 years of age; mean duration of acute episode, 5.6 ± 5.1 days). The mean decrease in pain at rest was not statistically significantly different between the two groups after 14 days of treatment. Celecoxib was at least as effective as naproxen. Fewer patients experienced epigastric pain with celecoxib (7 patients vs 14 with naproxen).

	Changes from Baseline		Difference Between Groups
	Celecoxib (n=99)	Naproxen (n=103)	
Pain at rest (VAS 0-100 mm)	-47.9 (± 2.5)	-42.3.0 (± 2.5)	-5.6; p=0.1167 95% CI (-12.5, +2.0)

Conclusion: Celecoxib is at least as effective as naproxen in acute shoulder pain. Unlike previously published randomized controlled trials with celecoxib, observed upper GI events rates based upon limited sample size of this study do not permit inference of improved GI safety.
Sponsored by Pharmacia Corporation and Pfizer, Inc

M62

JOINT HIPERMOBILITY SYNDROME: A PROSPECTIVE STUDY OF ARTICULAR AND NON-RHEUMATIC MANIFESTATION IN A VENEZUELAN POPULATION.

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Objective: Although Joint Hypermobility Syndrome (JHS) is a common condition, there are clearly a number of articular and non-articular manifestations. Because of this, one study of subjects with JHS was performed in our country.
Patients and Method: A prospective,descriptive and analytical of 41 patients attending our Unit from February up to September 1999, and who fullfilled the Beighton Scale (BS) for JHS was made.The mean age was 32 years,35 were females and 6 males.All over the group were evaluated through Beighton Scale (BS),being 4 points the lowest and 9 points the highest.All subjects were examined for echocardiogram and a gynecological exam was performed in all sexually active women.
Results: 11 patients (26.8%) had 9 points in the BS and 1 patient (2.4%), being the mean of the group of 6 points.The dorsiflexion of fifth finger was found in all subjects.When comparing pasive aposition of the thumb of the flexor aspect of the forearm,with the highest point,there was a good correlation (p=0.003). Patients under 30 years had higher points in the BS (p=0.005). Arthralgia was present in 29 subjects (70.78 %), mainly in women(p=0.001).Flat feet was found in 23 patients (56.09%) and Marfanoid habitus in 23 patients. Mitral valve prolapse (MVP) was found in 24 patients (58.53%), the great majority under 30 years and with higher points in the BS. Uterine prolapse was diagnosed in 12 women of the 24 examined (50.0%), most of them over 30 years, no significance correlation was showed between uterine prolapse and points in the BS.
Conclusion: In our study arthralgias particularly of the knees was found, and among extrarticular MVP was the commonest one. We also found a higher incidence of uterine prolapse than expected for women in this age.

M63

INCREASED GASTROINTESTINAL BLEEDING IN HOSPITALIZED ADULT DERMATO-MYOSITIS PATIENTS.

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Objective: Previously reported gastrointestinal (GI) involvement in adult dermatomyositis (DM) has been limited to pharyngeal and esophageal dysfunction. Following a number of serious GI bleeds in hospitalized DM patients, we sought to determine the incidence of clinically important GI bleeds in hospitalized DM patients using patients with polymyositis (PM) as a control.

Methods: A retrospective study of all patients with DM or PM admitted to a single tertiary care centre from April 1979 to October 1999 was performed. Charts were identified by ICD-9 codes. Probable and definite cases of DM and PM by the 1974 criteria of Peter and Bohan were included. GI bleeding was defined as melena, hematemesis, or hematochezia; or hypotension and positive fecal occult blood; or endoscopic lesions with stigmata of bleeding; all associated with a drop in hemoglobin. Variables included in univariate and multivariate analysis were: diagnosis, presence of GI bleeding, steroid dose, use of NSAIDs and GI prophylaxis, ACR functional class, and malignancy.

Results: There were 154 patients with diagnosis at discharge of DM or PM. Seventy-eight cases were excluded as follows: not DM or PM (35); overlap syndrome (23); juvenile onset (3); diagnosis prior to 1974 (3); insufficient information (14). One chart was unavailable. DM was confirmed in 35 cases and PM in 40 cases. Univariate analysis revealed no difference between the DM and PM patients with regard to age, NSAID or GI prophylaxis use, ACR functional class, presence of malignancy, or steroid dose. There was a significantly higher rate of GI bleeds in the DM group at 28.6% versus 7.5% in the PM group ($\chi 2$ p=0.016) with most being upper GI ulcerations. Univariate analysis of DM patients alone revealed no difference between those with and without GI bleeding with respect to age. NSAID or GI prophylaxis use, steroid dose, functional class, or malignancy. Multivariate analysis of all patients revealed the presence of DM vs PM as the only predictor of GI bleeds (OR 5.3, 95% CI 1.2-24.1).

Conclusions: We found a significant increase in the frequency of serious GI bleeding in adult DM patients over that in PM patients. This has not been previously described and could not be explained by traditional risk factors for GI bleeding. Muscle biopsies in DM typically reveal perivascular pathology, and ischemic GI ulceration is well described in juvenile onset DM. Extension of a vasculopathic process into the GI tract may explain the frequency of bleeding in adult DM patients. Regardless of etiology, the absolute rate of bleeding bears noting as an important clinical complication and may merit use of routine GI prophylaxis.

M64

LOW EXTREMITIES PAIN IN JOINT HYPERMOBILITY AND IT'S ASSOCIATION WITH FLAT-FOOT.

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Objective: To study prevalence of chronic ankle and knee pain in benign joint hypermobility syndrome (BJHS) patients with and without pes planus.

Rationale: Pain, especially of ankle and knee joints, is the principal source of distress among patients with BJHS. The causative factors are often remained elusive. It is a common thing also to see secondary moderate orthopedic abnormalities, such as pes planus, in pts with BJHM.

Methods: 156 patients (110 w, 46 m), age 16-30 (mean 22,3 year), with BJHS were studied by plantagraphy for pes planus presence. Only 2 and 3 degrees of pes planus were registered. The Beigthon score was 5 and more in all pts.

Results: Moderate or severe pes planus was found in 36 cases of all BJHS pts. Chronic ankle and knee pains were present in 21 of them (58,3%). 120 BJHS pts didn't demonstrate signs of significant pes planus. Ankle and knee arthralgias were present in only 23 cases in the group (19,2%). The difference was highly significant (p=0,000, χ^2).

Conclusion: Moderate orthopedic abnormalities (pes planus) may be a causative factor of low extremities arthralgia in pts with BJHS. Pes planus should be recognized and treated in symptomatic BJHS pts.

M65

DEVELOPMENT OF AN EXPERIMENTAL PROTOCOL TO ASSESS INTEREXAMINER RELIABILITY OF PUTATIVE SPINAL DYSFUNCTION

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Objective: To assess interexaminer reliability of a protocol evolved from clinical practice to diagnose cervical spinal dysfunction (SD).

Rationale: Spinal adjustment/manipulation is a useful intervention for spinal pain. An operational definition of SD, to which manipulation is directed, has eluded investigators.

Methods: A protocol consisting of global range of motion (ROM), tenderness (T) and restricted intersegmental motion (RIM) was assessed in 3 studies. Pilot Study 1 (n=17) involved 'gestalt' SD-present decision by a chiropractor, and a rheumatologist who applied the protocol. In Pilot Study 2 (n=48) two chiropractors each applied the protocol. In Study 3 (n=50) two chiropractors applied the protocol on their own patients prior to treatment.

Results: Pilot Study 1: Concordance between SD present and 2 out of 3 criteria was fair (Kappa=.393) in the upper cervical spine. Concordance was poor for side-specific and other findings. Pilot Study 2: ROM Kappas ranged from <0 to .7. Tenderness Kappas in the upper cervical spine (headache subjects) ranged from .4 to 1. Concordance was poor for assessment of RIM.

Study 3: Concordance between examiners was poor.

Conclusion: ROM & T, and using 2 out of 3 findings may have potential as indicators of SD. The use of RIM should be reconsidered. At this time an operational definition of SD remains elusive and existence of a specific manipulable lesion is speculative.

M66

BONE DENSITY IN BENIGN JOINT HYPERMOBILITY SYNDROME(BJHS) PATIENTS

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Objective: The aim of this study was to evaluate osteopenia or osteoporosis in subjects diagnosed as BJHS.

Rational: Changes in properties of connective tissues in BJHS may also involve bone tissue and result in decreased bone mineral density.

Methods: In this study performed in Istanbul University Cerrahpaşa Medical Faculty PMR Department 39 patients and 20 controls were enrolled. BJHS was diagnosed in patients with Beighton Scores of equal to or exceeding 4/9 points. Physical examination, laboratory analysis and bone mineral density assesment by DEXA were performed.

Results: Patients with BJHS had statistically significant osteopenia at trochanteric and intertrochanteric regions compared to control group ($p<0.05$).

Conclusion: It was concluded that bone mineral density should be assessed in BJHS patients with an additional osteoporosis risk factor.

M67

KININASE II, KALLIKREINS AND KININOGENS IN PLASMA OF PATIENTS WITH PRIMARY FIBROMYALGIA

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Objective: To evaluate kininogen levels and the activity of kallikreins and kininase II in plasma of patients with primary fibromyalgia.

Rationale: Since kinins produce pain and since fibromyalgia is associated with diffuse musculoskeletal pain, multiple tender points, fatigue and sleep disturbance, in this study we evaluated the kinin system components in primary fibromyalgia.

Methods: A total of 18 patients (17 women) with primary fibromyalgia and 18 controls matched to patients for sex and age were studied. Low-molecular weight (LKg) and high-molecular weight kininogen (HKg) levels were determined by ELISA. The activities of tissue kallikrein (Tkal) and plasma kallikrein (Pkal) were determined by their amidolytic action on selective chromogenic substrates. Kininase II (Kin II) activity was measured using the specific substrate Hippuryl-His-Leu.

Results: Compared to controls, the levels of LKg and HKg, and the activities of Tkal, Pkal and Kin II were significantly increased in plasma of patients presenting with primary fibromyalgia (Median values are shown in the Table)

INDIVIDUALS	TKg µg/mL	HKg µg/mL	LKg µg/mL	Pkal U/mL	Tkal µmol/mL	Kin II nMol
Controls	1.15	0.47	0.71	1.77	1.57	5.20
Fibromyalgia	2.15	1.05	1.09	2.57	2.55	9.45
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Conclusion: The results reported here indicate an increased production of kinins in fibromyalgia. Although serotonin has been implicated as one of the major mediators in fibromyalgia, this study also emphasizes the possible participation of kinins, since most of the kinin system components are activated. **Financial support: FAPESP**

M68

NEW TREATMENT METHODS IN FIBROMYALGIA

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Objective: To study the efficiency of new treatment methods in patients with fibromyalgia (FM) – plasmoionic therapy.

Rationale: FM is rather frequent in the population, despite the fact that their evolution mechanisms and treatment are insufficiently studied.

Methods: Clinical assessment included EMG of 48 patients with FM: 31 females, 12 males, average age 37 years; disease duration 2-10 years. The control group included 10 patients receiving drug treatment. The treatment was realized by application of plasmoionotherapy, based on oxygen ions flux over the damaged areas on the biologically active zones. For that we used a device with spectral activity named "Rotor" (designed by V. Rudenco). The time of ion action was about 10-15 min in mcA. The active electrode ionizes the air oxygen and puts it through the damaged tissues acting over the nervous receptors and causing production of nervous mediators (noradrenalin, acetelcolin, DOPA) and exhausting autoblocation of nervous receptors.

Results: In 34 patients the treatment was favourable causing disappearance of the pain syndrome, fibromuscular spasms (contractions), 9 patients – with normal functioning; 3 – were having profound degenerative modifications, which didn't allow any improvement in their status, there were not observed any side effects in both groups.

M69

HYALURONIC SERUM LEVELS IN FIBROMYALGIA (FM), NON-SPECIFIC ARM DISORDER (NSAD) AND CONTROLS (C).

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Yaron et al (1) reported clearly higher serum hyaluronic acid (HA) levels in FM than in pain free controls (CT) or rheumatoid arthritis (RA) cases. Barkhuisen et al (2) failed to confirm this with a small sample of FM cases. Yaron et al (3) showed a much less definite difference in a second study. HA had been not been tested in NSAD.
METHODS; HA mcg/l. (4) was measured in mid afternoon in 19 women with FM, 22 with NSAD & 22 CT of comparable age.
RESULTS; The mean HA levels were within normal at 25 for FM, 23 NSAD & 22 for CT with no difference between groups before and after adjusting for an increase of HA with age ($R=0.54$ $p<0.01$). Mean tender point count (TP) was for FM, 13, NSAD, 2 & CT, 1. TP score and attribution to occupation were not related to HA.
As higher morning HA levels had been noted in RA (4) five subjects with currently active FM (Mean of 15.5 ARC TP) had HA mean levels of 56 at 8 AM, 41 at 9 AM and 35 at 3 PM. All HA levels were within published and internal (CT) normal limits.
CONCLUSION; Serum hyaluronic acid levels were not raised in fibromyalgia or regional arm pain cases.

1. Yaron I, Buskila D, et al. Elevated levels of hyaluronic acid in the sera of women with fibromyalgia. J Rheumatol 1997; 24: 2221-2223.
2. Barkhuizen A Bennett R.M. Elevated levels of hyaluronic acid in the sera of women with fibromyalgia. J Rheumatol 1999; 26: 2063-64.
3. Yaron M. Reply, J Rheumatol 1999; 26 :2064.
4. HA test, Kabi Pharmacia Diagnostics AB S-752 Upsala, Sweden.

M71

PSYCHOPATHOLOGIC STUDY IN PATIENTS WITH FIBROMYALGIA

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Objetive: Fibromyalgia is considered a psychosomatic disease.This study was conducted to assess psycophatology changes in patients with fibromyalgia.
Methods: We have evaluated secuential out patients with ACR criteria of fibromyalgia,through interviews by a clinical psychologist,a psychiatrist and tests for general psychopathology (Golberg), depression (Beck) and anxiety (Stai).
Results: 29 patients were evaluated (4 men). Psycopathologic results: 8 patients were totally normal.Psicopathology (Golberg'test): 12 patients were normal. 5 had mild and 12 severe alterations. Depression (Beck'test): 13 patients were normal. 4 suffered from mild depression, 4 moderate, 4 severe and 4 more severe depression.Anxiety (Stai'test): Ten patients didnt have anxiety. Eighteen were trait anxiety and sixteen state anxiety.Interview: 19 patients had sleep problems. 24 were fatigued and 15 had relapse thinking.
Conclusion: The absence of psychopatology in 28% of patients with fibromyalgia, and the mild changes in others, allows us to differentiate between psychogenic rheumatism and fibromyalgia, and obliges us to establish a psychogenic evaluation in these patients.

M70

OPEN LABEL PILOT STUDY OF HYDROXYCHLOROQUINE IN PATIENTS WITH FIBROMYALGIA

P. A. MacDonald, Rheumatology Associates and M. H. Ellman, The University of Chicago, Chicago, Il 60612 Objective: To determine if hydroxychloroquine (hcq) will benefit fibromyalgia patients by raising the pain threshold and decreasing levels of substance P. Rationale: Hcq may increase the pain threshold in pts with primary fibromyalgia that may translate into reduction of painful symptoms resulting in improved sleep, less fatigue and depression. Methods: Pts included 8 females and 2 males meeting ACR criteria for Fibromyalgia. All had normal laboratory tests (CBC, Chemistries, WESR, RF, TSH and ANA). There were no significant intercurrent illnesses. All pts received 200 mg BID of hcq for 16 weeks. Stable doses of previously prescribed anti-depressant and analgesic medications were continued. Pts were evaluated weekly for the first month and then monthly. Evaluations including Dolorimeter monitoring of trigger points, patient and physician global scores, modified HAQ, Beck's Depression and Anxiety Scale and Fibromyalgia Impact Questionnaire. Evaluations for potential ophthalmic toxicity included Amsler grid testing and fundoscopic exams routinely. Eight of ten were women with the mean age of 47.7 years, range 33-66 yrs. One pt was dropped from the study at week 4 for non-compliance. RESULTS: The VAS scores and pt and MD global assessment reflected improvement or non-improvement the Beck and the FIQ scores closely mirrored improvement. Monitoring trigger point tenderness was not helpful in determining improvement or lack of improvement. Four pts experienced no improvement and in one of these pts, the symptoms worsened coinciding with a marked increase in depression. The mean VAS values in the five pts that improved, declined from 7.6 to 2.5. Only 2 of the pts opted to continue hcq therapy after the study, None of the 3 pts stopping therapy experienced worsening of their fibromyalgia. There were no observed side effects. CONCLUSION: Five out of 10 patients showed significant improvement as measured by VAS scores for pain and FIQ although only two patients opted to continue hcq and the other 3 did not worsen when hcq was stopped. We think hcq is a treatment option for select patients with fibromyalgia, however a placebo-controlled study is warranted.

M72

PSYCHOLOGICAL DYSFUNCTIONAL DIMENSIONS IN PATIENTS WITH FIBROMYALGIA: DEVELOPMENT OF AN ITALIAN QUESTIONNAIRE

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Objective: To observe whether psychological dysfunctional dimensions of pain could be detected in fibromyalgic patients through the development of a new questionnaire.

Methods: An original questionnaire composed of 51 items was given to 250 patients (185 females and 65 males, mean age 55±12.8 years) suffering from chronic fibromyalgia according to the criteria of the Multicenter Criteria Committee of the American College of Rheumatology. A Varimax computerized program of factorial analysis with ortogonal and oblique rotation of the axes was used to analyse the data.

Results: Five strong independent factors were identified: 1) catastrophizing and 2) external control beliefs (cognitive); 3) alexythymia (emotional); 4) restless behavior (behavioral); 5) need for support (relational) . Two weaker factors were: lack of reactivity and lack of autonomy .

Conclusion: Our questionnaire is a preliminary development of an Italian language psychological characterization of FM patients which may be relevant and useful for clinical/psychological treatment of these patients.

M73

THE IMPACT OF NEWBORN LITTER INDUCED ARTHRITIS EVENT IN MATERNAL BEHAVIOR, PAIN THRESHOLD AND SLEEP PATTERN.

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Objective: To evaluate in animal study the role of neonate litter induced arthritis as a stressful event to the mothers.

Rationale: Stressful events can contribute to increase in nociceptive transmission in painful disorders such as fibromyalgia.

Methods: Arthritis was induced in the litter of 9 Wistar rats with complete Freund's adjuvant (2:1) injection in one paw. Controls were 9 rats which litter received saline injection. The behavior of the of the arthritic pups' mothers (APM) and control mothers (CM) was observed during 3 hours after day 1 and at day 21. At day 21 elevated plus maze test was performed for anxiety evaluation and at day 22, hot plate (50°C) for pain threshold. At day 29 electrodes were implanted in the cortical fields, and neck muscle. Polysomnography was performed (Nihon Kohden QP 223, 6 channels for each mother).

Results: After day 1 APM spent more time looking for the pups than CM (106.7 ± 26.5 vs. 40.0 ± 15.0 min., $p < 0.01$), 88.9% of them showed hyperkinesia vs. none of the CM ($p<0.01$) and 55.6%, increase in sniffing vs. none of the CM ($p<0.01$). At day 21 no difference was observed between the behavior of the APM and CM. Compared to CM, the APM presented decrease in % of time spent in the open arms of the plus maze (44.7 ± 13.3 vs. 13.4 ± 12.1, $p < 0.05$), shorter permanence on the hot plate (61.2 ± 16.9 vs. 39.0 ± 16.4 min., $p < 0.01$) and reduction in % sleep efficiency (63.5 ± 21.7 vs. 48.9 ± 19.4, $p<0.01$).

Conclusion: Induced arthritis in the neonate litter was stressful to the mothers resulting in anxiety, decrease in pain threshold and sleep disturbances, persistent even after normalization of the pup's condition.

M74

„QUALITY OF LIFE AND WORK DISABILITY IN FIBROMYALGIA PATIENTS IN COPARISON WITH RHEUMATOID ARTHRITIS PATIENTS".

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Objective: The purpose of the study was to evaluate the influence of fibromyalgia syndrome (FMS) complaints on patients' quality of life and work status.
Methods: Present health status questionnaire was sent to 177 fibromyalgia patients. The ACR 1990 FMS criteria were used. Clinical and basic laboratory examinations were performed in 86 FMS female patients (aged 39 – 70) who agreed to cooperate in this study. The group of 77 FMS patients was compared with the control group of 73 rheumatoid arthritis (RA) patients (aged 21 – 75). Nine FMS patients were excluded from the analysis (4 patients with pSS and 5 patients with no further features of FMS). The activity of RA group was moderate and duration of the disease ranged between 0,5 and 29 years. They were asked about their present pain status, other complaints, mental and work status. Moreover, in all cases the FIQ answers were obtained.
Results: The pain was described as "great, sometimes unbearable" in 30 FMS patients (38,9%) and in 17 RA patients (23,3%) ($p<0,04$); it was described as "awful" or "terrible" by 43 FMS patients (55,8%) and 28 RA patients (38,4%) ($p<0,05$). Intensity of pain in VAS was similar in both study groups. Exacerbation of complaints was described as weather depended in 40 FMS patients (51,9%) and 32 RA patients (44%) (NS). Sleep disturbances were reported in 66 FMS cases (85,7%) and in 68 RA patients (93,1%) (NS). Morning fatigue was significantly more frequent in FMS patients– 53 (68,8%) than in RA patients– 25 (34,2%). Morning stiffness was significantly more frequent in RA patients- 31 (42,5%) than in FMS patients- 20 (26%). Depressed mood, tension, nervousness, anxiety were reported with similar frequency in both groups. Physical ability (according to FIQ) was significantly more reduced in FMS than in RA patients. Work disability was assessed similarly in both patients' groups. Forty seven (61%) FMS patients and 50 (68,5%) RA patients were pensioned.
Conclusions: Some FMS patients complain of the pain of greater intensity than RA patients. In spite of different pathogenesis and course of the diseases the intensity of morning stiffness, fatigue were comparable in both groups. Regardless of nondestructive character of the disease, FS patients present physical and mental disability similar to serious destructive arthritis. Careful management as well as social and professional rehabilitation are necessary to help FMS patients to return to normal life activity.

M75

CLINICAL OBSERVATION OF PATIENTS WITH LONG-LASTING FIBROMYALGIA SYNDROME".

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Objective: The study was undertaken for the purpose of assessing the natural course of fibromyalgia syndrome (FMS) and verifying the diagnosis of the disease.
Methods: Present health status questionnaire was sent to 177 FMS patients. The ACR 1990 criteria of fibromyalgia were used. Duration of FMS ranged between 3 and 40 years. One hundred and fifteen answers were received. Thirty three patients (28,7%) had no pain. In the remaining cases the same or higher intensity of pain was noted. Clinical and basic laboratory examinations were performed in 86 FMS female patients (aged 39 – 70) who agreed to cooperate in this study. They were asked about their present pain status and other complaints, mental and work status, as well as their understanding of the disease. In all cases the FIQ questionnaire examinations were performed. In some cases additional tests were done.
Results: During examination only 5 patients (5,8%) had no pain in musculoskeletal system and felt very well; they did not fulfill tender points (TPs) criteria. In 81 patients (94,2%) different intensity of pain was noted. Less than 11 of 18 TPs were found in 11 patients (12,8%), however in these patients other manifestations of FMS were present (anxiety, depressed mood, sleep disturbances, fatigue). In the remaining 70 patients (81,4%) all ACR criteria of FMS were still present. Four patients (4,7%) fulfilled criteria for diagnosis of primary Sjögren's Syndrome (pSS)- ocular and oral dryness appeared later in the course of the disease than widespread pain. There were no features of other connective tissue diseases in the remaining 82 patients. Other musculoskeletal disorders were observed in some cases: the most frequently carpal tunnel syndrome (21 patients- 24,4%), enthesopathy of different sites (15 patients- 17,4%), coxarthrosis (6 patients- 7%), gonarthrosis (4 patients- 4,7%).
The majority of FMS patients (61- 70,9%) did not understand the matter of the disease and were anxious about their future. Thirty two patients (37,2%) regarded FMS as a type of rheumatism, leading to physical disability. Forty four (51,2%) patients believed, that hospital management is necessary. Nine patients (10,5%) were afraid about the possibility of cancer. Since the time of the diagnosis the majority of FMS patients were treated by different specialists (the average number of specialists 4,16). All patients were treated with NSAIDs, this treatment was effective only in 31 cases (36%). Forty three patients (50%) were treated with antidepressants, with satisfactory clinical effect in 12 cases (14%).
Conclusions: Despite the treatment, FMS symptoms were still present by several years in the great majority of patients. Nevertheless the complete recovery is sometimes possible. Similarity of FMS symptoms and early stage of primary pSS can be the cause of misdiagnosing. No serious somatic diseases developed in these patients. The results confirm that ACR criteria for FMS diagnosis are useful in everyday practice.

M76

SUPRACLAVICULAR SWELLING IN FIBROMYALGIA POSSIBLE SIGN OF CORD IRRITATION.

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Objective: To determine if there is any significance to the finding of non-adenopathic supraclavicular swelling in patients with fibromyalgia in relation to status of cervical cord compression.

Rationale: Supraclavicular swelling is sometimes found in patients with chronic fatigue syndrome and attributed to adenopathy. However, this has never been studied. This is sometimes observed in patients with fibromyalgia, a condition similar to chronic fatigue syndrome. An index patient was worked up and no adenopathy was found. Because she demonstrated positive Hoffman's sign and hyperreflexia, a cervical MRI was done and showed compressive deformity of the cord. As subsequent patients were noted to have same findings, this survey was done to determine if there is a correlation.

Method: Consecutive fibromyalgic patients with supraclavicular swelling were identified prospectively. Those who have had cervical MRIs are included in the study.

Results: Over a 21 day period, 37 fibromyalgic patients were identified with supraclavicular swelling. There was no adenopathy present. Cervical MRIs were available in fifteen. One had Cushing's features from chronic Prednisone use and is excluded. Eleven showed cervical disc disease resulting in abutment against or compression of the cervical cord. In cases where the finding is unilateral, the abutment is ipsilateral. Patients also demonstrated positive Hoffman's sign. Three patients did not show any cervical cord compression. One has single level DDD with spondylolithesis, one with single level mild DDD, and one with repetitive strain syndrome. Compared to those without this sign, patients with this finding are more severely affected with marked fatigue, pain, and weakness.

Conclusions: Non-adenopathic supraclavicular swelling may be a sign of ipsilateral cord abutment in fibromyalgia. This may support the hypothesis that irritation of anterior cord may result in muscular hyperirritability that characterizes fibromyalgia.

M77

RISK FACTORS FOR OSTEOPOROSIS IN HEALTHY PREMENOPAUSAL WOMEN

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Out of 667 citizens of Belgrade, randomly selected from the population register, we chose 101 healthy women aged 20-40 yrs, to establish risk factor for osteoporosis using standardized questionary.

The study was carried out in Institute of Rheumatology in Belgrade and bone mineral density (BMD) of lumbar spine was measured using a Lunar DPX-L device.

Osteopenia was found in 12 (11,88%) and osteoporosis in 2(1,98%) women. We were assessing 24 risk factors for osteoporosis and 11 of them were detected in our group: sedentary type of work (50%), sedentary type of life (64,3%), smoking (78,6%), alcohol abuse (7,1%), coffee abuse (100%), low calcium intake (50%), low sun exposure (14,3%), late menarche (50%), nulliparae (35,7%), long breast feeding (35,1%), low or normal BMI (92,9%). Statistical analyses (Chi square test, T- test) confirmed, that only, extensive smoking and low BMI have significant negative effect on BMD in our group of healthy women aged 20-40 yrs.

For further confirmation of this conclusion we need larger investigation group. The most of these risk factors we could modify and we have to do it, for prevention of osteoporotic fracture.

M78

DENSITOMETRIC BONE GAIN IN RHEUMATIC POSMENOPAUSICAL PATIENT TO A YEAR OF TREATMENT WITH SODIC ALENDRONATE.

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Background: In patient with rheumatic diseases (RD) that receive corticosteroids and posmenopausical status the risk factors for osteoporosis they are increased.
Objective: to value the effect of the treatment with a antiresortive drug administered at least one year.
Methodology: 64 female outpatients with RD, posmenopausical and that previous received in prophylxis form calcium and calcitriol to their first DMO. Value of T (in DMO) was –2.5 or lower betwen two DMO of the same region and with the same apparatus and were included to intake Alendronate (10mgs) during one year. The concomitant treatment for de RD same non stoped, including steroids (dose average 12.5mg/d) and some recommendations.
Results: the increase average of DMO was of 4.1%; the observed maximum gain was of 11.9%; a patient was with non change and another decreased 12.7% for voluntary suspensión of the treatment. In the following square summary the values of the patients.

Previous 1 year				Postreatment values		
DMOg/cm	DMOg/cm	%	T	DMOg/cm	%	T
Hip	0.696	70	- 2.5	0.799	80	-1.7
L2-L4	0.722	64	- 3.6	0.877	73	-2.7

Conclusión. The prevention for OP is insuficiet in RD treated with corticosteroid and amerited antiresortive drugs.

M79

RICKETS AND OSTEOMALACIA IN NORTHEAST OF IRAN

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Objective: To determine the clinical, laboratory and radiologic features of rickets and osteomalacia in northeast of Iran.

Methods: In a prospective study during 11 years period from 1989 to 1999 we followed up all cases of osteomalacia and rickets in the rheumatology clinic and department of Imam Reza Hospital. Diagnosis was based on the clinical, laboratory and radiographic findings. All patients were treated with vit D and calcium.

Results: We had 797 patients (795 female, 2 male). Their age was between 8-74 years. Most cases were in a second decade. Clinical findings were: bone pain 96.4%, (most common in knee, back and pelvic), muscle weakness 81%, abnormal gait 43%, and bone deformity 19.6% (often genuvalgus and genuvarus). Laboratory findings were: osteopenia 63%, epiphyseal growth plate alterations 74.4%, ground glass appernce 26.8% and looser's zones 26.5%. The response to treatment with Vit. D and calcium was significant. Only four patients were Vit.D resistant.

Conclusion: Rickets and osteomalacia are common disorders in our region. Females especially in growing age are often involved. The most common cause is Vit. D deficiency probably due to inadequate sun exposure. It is suggested education to women for taking suitable sun rays and adding vit D to dairy products will be preventive and effective in this health problem.

Key words: Osteomalacia, Rickets, Diagnostic techniques and procedures, Female, Male, IRAN.

M80

POLYOSTOTIC FIBROUS DYSPLASIA

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Fibrous dysplasia is a rare disease characterized by the presence of mesenchymatous tissue in the bone. It exposes to various risks. We report one case.

Case report : A 37 year-old man presents since he was 10 years old, bone pains and multiple fractures without any endocrine disorder. At his admission in our department in 1998, he had limb deformities and thoracic hyperchromic stains. There was hypocalciuria and the PAL were at 1274 UI/ml. Endocrine biological explorations were normal. Radiographs showed polyostotic lacunas especially at the right hemibody and at the skull and a right trochanterian fracture. TDM of the face and skull didn't show any nerve compression. The histological analysis confirmed the fibrous dysplasia. Vitamino-calcic treatment and preventive measures were established.

Discussion : PFD is a congenital disease with variable radiological aspects. It exposes to deformities risk, fractures, osteomalacia (like in our case), neurological compression and potentially sarcomatous transformation. A recent treatment with bisphosphonates seems to be effective for pains and probably for fracture prevention but was not available in our practice.

M81

THE CORRELATION OF AP AND LATERAL BONE MINERAL DENSITY MEASUREMENTS WITH LUMBAR DEGENERATİVE CONDITIONS

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Aim:Degenerative changes in the lumbar spine (endplate sclerosis, osteophytes,facet joint sklerosis) have considerable influence on spinal bone mass measurements.Therefore we aimed to assess difference between AP and lateral supine measurements and the correlation with degenerative changes.
Methods:Postmenopausal osteoporotic 54 subject and premenopausal 21 controls aged 30 – 40 years were included. Degree of degeneration was evaluated by lumbosakral radiographies. BMD was assessed by DEXA at lumbar spine, AP and lateral supine and femur.Difference between BMD of AP and lateral supine spine measurements in both groups was statistically evaluated and correlated with degenerative changes.
Results:In the patient group AP total BMD was found to be 0.86±0.15, lateral supine total was 0.63 ± 0.15 ($p<0.001$),in the control group AP total BMD was 0.98±0.1,lateral supine total BMD was 0.80± 0.08 ($p< 0.001$).In both groups degenerative changes showed negative correlation with lateral BMD($r =0.675$).
Conclusion:In the presence of lumbar degenerative changes BMD assessment by lateral supine DEXA measurements seen to be an important method for the evaluation of ostoporosis.

M82

BONE MINERAL DENSITY (BMD) AFTER TRANSPLANTATION: EFFECT OF PHYSICAL ACTIVITY

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Objective: To evaluate the role of physical activity on BMD in patients with renal, hepatic, and cardiac transplantation (Tx).
Rationale: Tx should offer a good quality of life to patients having benefited from organ donation. The use of immunosuppression, while decreasing the risk of organ rejection has been complicated by bone fragility, and fractures. Physical activity should help to maintain bone integrity.
Methods: Patients included 20 male Tx patients, 10 physically active and 10 sedentary. The level of physical activity was assessed by a self-administered questionnaire. BMD of the lumbar spine (L), of the upper extremity of the femur (F) and of the whole body were measured by DXA (QDR-2000+, Hologic Inc). Body composition was also measured by DXA.
Results: The L- and F-BMDs were non significantly higher in the active Tx group. There was a significantly higher proportion of active Tx patients with a Z-score of L-BMD higher than or equal to 0, as compared with sedentary patients ($p < 0.05$). A positive correlation was observed between total hip BMC and the sport index score ($r = 0.48$; $p < 0.05$). There was a trend toward higher values of fat mass and fat percentage in both the whole body and in the trunk in sedentary Tx patients. Sporting activity was accompanied more by fat loss than by muscle mass gain.

L-BMD expressed in	Z-score < 0	Z-score ≥ 0	Total
Active	3	7	10
Sedentary	8	2	10
Total	11	9	20

$p < 0.05$

Conclusion: Physical activity may exert a positive influence on bMD and particularly on L-BMD in transplanted patients. A trend was observed for the Tx patients with high activity to have lower values of fat content and fat percentage at the trunk level, which could constitute a diminished risk factor for cardiovascular diseases, a well-known cause of mortality in the long-term after Tx.

M83

EVALUATION OF PHYSICAL CAPACITY AND DISABILITY IN OSTEOPOROTIC WOMEN

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Introdution. The vertebral osteoporotic fractures result in increased kyphosis angle. This alteration could led to disturbance in physical capacity.
Objective. Our objective was to evaluate the physical capacity and disability in a group of osteoporotic patients.
Material and Methods. Fifteen women with osteoporosis and vertebral fracture (G1), 20 women with osteoporosis without vertebral fracture (G2) and 20 normal women (G3) were selected. The variables of physical capacity were measured in the belt conveyor. The patients stayed 4 minutes in standing quietly, 4 minutes walking at 3 Km/h and 10 minutes walking at 4 Km/h. It was also applied the questionary SF-36.
Results. Our results showed that women with osteoporosis and vertebral fracture had increased kyphosis angle (median=60°) and the group 2 was 43.5 and group 3 was 37°. G1 showed oxygen consumption (VO2 (Kg)), METS and energy expenditure (Kcal/h) in standing quietly bigger than G2 (G1 vs. G2, p=0.016; p=0,017 and p=0,012, respectively). There wasn't significant difference in the energy expenditure during the walk between three groups. The energy expenditure during walking at 3 Km/h and at 4Km/h, showed correlation with thoracic kyphosis in G1 (p= 0,01 and p= 0,017, respectively). It wasn't find difference in SF36 between three groups.
Conclusion: Energy expenditure showed correlation with the angle of thoracic kyphosis. Patients with or without osteoporosis had the same energy expenditure during the walking. The SF36 score was similar between three groups.

M84

EVALUATION OF PULMONARY FUNCTION IN PATIENTS WITH OSTEOPOROSIS

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Introdution. By and large vertebral osteoporotic fractures result, in increased kyphosis angle. This alteration could led to disturbance in the pulmonary function. Spinal deformity is associated with alterations in pulmonary function.
Objective. Our objective was to evaluate the pulmonary function in a group of osteoporotic patients.
Material and Methods. Fifteen women with osteoporosis and vertebral fracture (group 1), 20 women with osteoporosis without vertebral fracture (group 2) and 20 normal women (group 3) were selected. All performed spirometry in the Vitatrace-130 SL spirometer.
Results. Our results show that women with osteoporosis and vertebral fracture had increased kyphosis angle (median=60°), decreased forced vital capacity (1 vs. 2, p=0.020; 1 vs. 3, p=0.039) and forced expiratory volume in the first second (FEV1)(1 vs. 2, p=0.008; 1 vs. 3, p=0.014) when compared with women with no vertebral fracture and no osteoporosis . There was a negative correlation between thoracic kyphosis and the predictesd value of expiratory forced volume in one second (p=0.003). Since 55° of thoracic kyphosis the pulmonary function showed compromised (p= 0,021).
Conclusion: We conclude that women with vertebral fracture have an increase of their kyphosis angle and a decrease of pulmonary function.

M85

OSTEOPOROSIS DIAGNOSIS AND TREATMENT IN SENIORS IN A REHABILITATION FACILITY AFTER HIP FRACTURE

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Objective: To evaluate the diagnosis and treatment of osteoporosis in seniors in rehabilitation facility after hip fracture, and to compare this to their acute care diagnosis and treatment.

Rationale: Mortality within a year of hip fracture is 6-44%. Appropriate pharmacotherapy reduces the risk of further fragility fractures. Rehabilitation is focused on discharge planning and function, and so should facilitate osteoporosis treatment.

Methods: A retrospective chart review on consecutive hip fracture patients (over 65yrs) admitted to a tertiary care hospital. Osteoporosis diagnosis and treatment was recorded. Patients were followed in the rehabilitation facility. The results from the two groups were compared.

Results: Data was collected on 311 patients in acute care. (Average age 86 years).226 patients were followed up in the rehabilitation facility. Osteoporosis was diagnosed on admission to rehabilitation in 9.7% compared to 11.9% in acute care (p=NS); and on discharge from rehabilitation in 11.2% and 15.4% (p=NS) in acute care. Osteoporosis treatment (any) in acute care hospitals was 13% on admission and 9.7% on discharge and in rehabilitation facilities 12.8% and 10.2% respectively (p=NS). Most often treatment was calcium alone, specific osteoporosis treatment was used in <4% in both groups.

Conclusion: Rehabilitation facilities are no better than acute care hospitals at diagnosing and pharmacologically treating osteoporosis in seniors after hip fracture. The rate of treatment in both groups is unacceptably low, in spite of exposure to numerous medical specialists.

M86

BIOCHEMICAL MARKERS OF BONE TURNOVER AFTER A FIFTEEN AND TWO MONTHS ETHANOL WITHDRAWAL

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Objective: Analyze the effect of alcohol intake in bone biochemical markers (BM); their evolution after a 15 days and 2 months period of ethanol withdrawal; compare the initial values with those of a healthy population; compare bone mineral density between this two groups. Rationale: Alcohol abuse is considered an important cause of osteoporosis. Many data suggest a direct inhibitory effect of ethanol on osteoblastic function. Methods: We measured BM of bone formation (osteocalcin-OC and bone specific alkaline phosphatase-BAP) and resorption (C-terminal telopeptide-NTX and urine deoxypyridinoline-DEP) after an overnight rest, in noncirrhotic alcoholic patients (pts) (Group 1) and in healthy non-alcohol addicted controls (Group 2). In group 1 alcohol intake was greater than 100 gr/day, for a mean period of 18,2 years . In group 1 we compared the values at days 0, 15 and 60 after alcohol withdrawal. Results: We study 54 pts in group 1 (74% males) and 26 in group 2 (58% males). The two populations were similar in terms of sex, mean age, body mass index, coffee and milk ingestion and regular exercise. There were more smokers in group 1 (42,5% vs 19,2%, p=0,002). At day 15 and 60 DEP showed a significant increase (p<0,005). NTX values were in normal or high at days 0, 15 and 60. The mean value of OC showed a tendency to increase. Group 1 had more pts with reduced lumbar spine BMD values (26% vs 53%, p=0,04).

	Day 0	Day 15	Day 60
OC	5.43	5.75	6,96
BAP	27.5	27.9	27.2
NTX	55	50	64.5
DEP	3.6	5.3	6.6

Conclusion: This study suggests that there is a disruption between bone formation and resorption among alcoholics. There was a trend towards normalisation of osteoblastic function in group 1 after ethanol withdrawal, although no statistical difference was found. The bone resorption biological markers (NTX and DEP) tended to be normal or high during this 2 months period. There are more patients with osteopenia/osteoporosis among alcoholics.

M87

RISEDRONATE IS ASSOCIATED WITH A LOWER INCIDENCE OF GASTRIC ULCERS THAN ALENDRONATE: RESULTS FROM TWO COMPARATIVE STUDIES

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Bisphosphonates (BPs) are effective treatments for osteoporosis, but some have been associated with GI injury. We compared the incidence of gastric ulcers after treatment with risedronate (RIS), a pyridinyl BP, and alendronate (ALN), a primary amino BP, in 2 similar endoscopic studies. METHODS: In both studies, healthy postmenopausal women were randomized to receive RIS 5 mg or ALN 10 mg daily for 14 days. Subjects received ALN as original round tablets in Study 1 and as wax-polished oval tablets in Study 2. In Study 2, subjects were stratified by *Helicobacter pylori* (HP) status before randomization. Evaluator-blind assessment of the esophageal, gastric, and duodenal mucosa was performed at baseline and on Days 8 and 15 of each study. RESULTS: In both studies, the overall incidence of gastric ulcers ≥3 mm was significantly lower in the RIS group than in the ALN (table).

	RIS 5 mg		ALN 10 mg		
	N	n (%)	N	n (%)	*P*-value
Study 1	221	9 (4.1)	227	30 (13.2)	<0.001
Study 2	300	18 (6.0)	297	36 (12.1)	0.013

Mean gastric erosion scores were significantly lower in the RIS group than in the ALN group at Day 8 and 15 ($P \leq 0.001$) in both studies. Mean esophageal and duodenal endoscopy scores were similar in the 2 groups at Days 8 and 15. Esophageal ulcers were noted in none of the evaluable subjects in the RIS group and in 3 in the ALN group in Study 1, and in 1 evaluable subject in the RIS group and 2 in the ALN group in Study 2. Duodenal ulcers were noted in 2 evaluable subjects in the RIS group and 1 in the ALN group in Study 1 and in none of the evaluable subjects in Study 2. In Study 2, HP infection did not increase the incidence of BP-related GI injury. CONCLUSIONS: In 2 large, comparative studies in which RIS and ALN were given at doses for the treatment of osteoporosis, the incidence of gastric ulcers was significantly lower among RIS-treated subjects than among ALN-treated subjects. Results were consistent in the 2 studies despite the difference in the shape and polish of the ALN tablets used. These findings support the hypothesis that BPs differ in their potential to produce upper GI mucosal damage.

M88

THE EFFECT OF RISEDRONATE ON HIP FRACTURE RISK IN ELDERLY WOMEN WITH OSTEOPOROSIS.

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Objective: To evaluate the effects of risedronate in the risk of hip fracture in elderly women with osteoporosis or with risk factors for hip fracture other than low bone mineral density. Methods: The risedronate Hip Intervention Program (HIP) was the first clinical trial to investigate a bisphosphonate with hip fracture efficacy as a primary endpoint Patients (n=9331, mean age=78) were enrolled into one of two groups. Group 1 (N=5445) patients were 70-79 years of age and enrolled on the basis of low FN BMD (T-score < -3) and at least one additional clinical risk factor for hip fracture. Women ≥ 80 years of age were enrolled in Group 2 (N=3886) on the basis of at least 1 clinical risk factor for hip fracture or low FN BMD (T-score <-4), 84% and 16% of patients respectively. Women in each of the two groups were randomized to receive risedronate (RIS) or placebo daily for 3 years, 1 g/d calcium, and were supplemented with up to 500 IU vitamin D daily if levels were low. Fractures that occurred during the treatment period and those that occurred in patients who discontinued treatment prior to end of the study but returned for the scheduled 3-year visit are included in this analyses.

Results: Risedronate significantly reduced the risk of hip fracture in Group 1 patients at 3 years as shown in the table below. In Group 1 women with both low FN BMD and ≥ 1 prevalent vertebral fracture, the risk of hip fracture was reduced by 60% vs. control (p=0.003). In Group 2 controls, the incidence of hip fracture in those subjects without BMD assessment was similar to those with FN T-score > -2.5, (3.2 and 5.6, respectively) compared to those with FN T-score <-2.5 (9.7%). This observation suggests that Group 2 patients were generally not osteoporotic. Significant BMD increases were observed in patients from Group 1 and Group 2 as early as Month 6 and continued throughout the study. Consistent with previous risedronate studies, the overall safety profile of patients treated with risedronate was similar to placebo-treated patients.

Hip Fracture Risk Reduction at 3 Years RIS vs. Control			
Population	Risk Reduction vs. control	95% CI	p-value
Group 1	40%	10-50	0.009
Group 1 with ≥ 1 prevalent vertebral fracture	60%	20-80	0.003

Conclusion: Risedronate treatment significantly reduced the risk of hip fracture in women with confirmed osteoporosis. Study findings suggest that clinical risk factors alone are not predictive of a response to anti-resorptive therapy. Therefore, it is important for physicians to properly identify patients who will benefit from anti-resorptive treatment to reduce the risk of hip fracture.

M89

TWO YEAR RESULTS OF ONCE-WEEKLY ADMINISTRATION OF ALENDRONATE 70 MG FOR THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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The therapeutic equivalence of alendronate (ALN) 70 mg once weekly (OW) (provided by Merck and Co., Inc., Whitehouse Station, NJ, USA), ALN 35 mg twice weekly (TW), and ALN 10 mg once daily (OD) in the treatment of postmenopausal osteoporosis for one year has been reported previously (Schnitzer et al, *Aging* 12:1-12, 2000). We will present preliminary two-year BMD results from a one-year extension. We compared the efficacy of treatment with OW ALN 70 mg (n=519), TW ALN 35 mg (n=369), and OD ALN 10 mg (n=370) over 2 years in a double-blind, multicenter study of postmenopausal women (age 40 to 90) with osteoporosis (BMD of either the lumbar spine or femoral neck $\geq$ 2.5 SDs below peak mean, or prior vertebral or hip fracture). The primary efficacy endpoint was change in lumbar spine BMD. Secondary endpoints included changes in BMD at the hip and total body. Results: Mean BMD increases at the lumbar spine, total hip, femoral neck, hip trochanter, and total body sites for each treatment regimen after two years were similar, with no clinically meaningful differences.
Conclusions: These findings confirm that once-weekly ALN 70 mg is therapeutically equivalent to once-daily ALN 10 mg in patients with postmenopausal osteoporosis. In addition, the two-year results demonstrate that once-weekly ALN 70 mg is generally as safe and well tolerated as ALN 10 mg once daily.

M90

DESIGN, RATIONALE AND BASELINE CHARACTERISTICS OF THE FRACTURE INTERVENTION TRIAL LONG TERM EXTENSION (FLEX)

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The Fracture Intervention Trial (FIT) and other studies have established that alendronate (ALN) can continue to decrease fracture risk and reduce bone loss for at least 4 years. However, the optimal duration and dose of long-term use of ALN is not known. To address these issues, we are performing a follow-up randomized trial to FIT. After the conclusion of FIT, 2856 women from 10 of the 11 FIT clinical centers who had been assigned to ALN were offered the possibility of participating in a new study in which they would be re-randomized for an additional 5 years to either: ALN 10 mg (30%), ALN 5 mg (30%) or placebo (40%). The primary endpoint of the study is change in total hip BMD over 5 years. Secondary endpoints include spine, total body, and hip sub-region BMD, biochemical markers, height loss, and safety. Assessment of the incidence of vertebral and non-spine fractures is an exploratory objective. An interim analysis will be performed and published after 3 years.
Women were eligible for the FIT Long Term Extension (FLEX) if they had been assigned to ALN in FIT and had used ALN for at least 3 years prior to FLEX. A total of 1099 women (about 34% of those originally randomized to ALN) were recruited into FLEX. Among the 1713 women who were screened but did not participate, the most common reasons for non-participation included a desire to remain on open-label ALN (21%), less than 3 years of prior ALN use (19%), and use of excluded bone-active medications (13%). At FLEX baseline, the average age was 73.6 years; 42% were >75 yrs and 15% were >80 years. Mean prior ALN use was approximately 5 years. The mean femoral neck BMD T-score at FLEX baseline was -2.2, an increase of 4.2% from FIT baseline and unchanged from FIT closeout. The FLEX study will address some of the important clinical questions about the optimal duration and dose of long-term alendronate use.

M91

THE EFFECT OF ALENDRONATE ON AGE-SPECIFIC INCIDENCE OF KEY OSTEOPOROTIC FRACTURES

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Objective: To describe the behavior of the relative risk (RR), absolute risk reduction (ARR), and number needed to treat (NNT) by attained age for the hip, spine or forearm for alendronate treatment in women with osteoporosis. Design: 3658 women with osteoporosis from the Fracture Intervention Trial were followed for 3 to 4.5 years and treated with alendronate (ALN) at 5 mg/day for 2 years followed by 10 mg/day for the remainder of the trial. The age groups used in the analysis were: 55 – 65, 65 – 70, 70 – 75 and 75 – 85. All fractures were confirmed by x-rays. Results: Risk reduction of hip, spine and forearm fractures were 53% (RR = 0.47, p <0.01), 45% (RR = 0.55, P < 0.01) and 30% (RR = 0.70, p = 0.038) respectively. The reductions did not depend on age. The ARR increased with age for each of the fracture sites. For the hip, the ARR increased from 0.13 women per 100 patient-years at risk (PYR) for the 55 to 65 group to 0.53 women per 100 PYR for the 75 to 85 group. The corresponding increases in ARR for the spine were 0.14 and 0.86. The NNTs for 5 years for the hip were 157 for the 55 - 65 year old and 45 for the 75 to 85 year old women. The corresponding numbers for the spine were 140 and 23. For the composite endpoint, the NNTs (for 5 years) were 38, 25, 17 and 13 for the age groups 55 – 65, 65 – 70, 70 – 75 and 75 – 85 respectively. Conclusion: Alendronate is very effective in reducing the risk of osteoporotic fractures, regardless of age.

M92

ALENDRONATE REDUCES THE RISK OF CLINICAL VERTEBRAL FRACTURE IN OSTEOPENIC WOMEN: DATA FROM FIT

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Objective: To determine the effectiveness of alendronate in reducing the risk of clinical vertebral fractures (CVFX) in women with osteopenia who do not meet the BMD criterion for osteoporosis.
Design: We studied 3737 women, age 55 to 80, from the Fracture Intervention Trial who had BMD T-score > -2.5 at the femoral neck: 940 with an existing morphometric vertebral fracture (MVFX) and 2797 without. 1859 were treated with PBO and 1878 were treated with ALN 5mg per day for the first two years and 10mg for the remaining period for up to 2.5 years. All CVFX were confirmed by a physician. **Results:** The absolute risk of CFVX was about 4 to 5 fold greater in women with existing MVFX than in those without. Alendronate significantly (p = 0.005) reduced the overall risk of CFVX by 60% (RR = 0.40 (0.19, 0.76)). The reductions were consistent among those with and without MVFX: 0.34 (0.12, 0.84) and 0.46(0.16, 1.17) respectively. The effect was observed very early. There were no CFVX in the first year among the alendronate patients.
Conclusion: Alendronate was equally effective in reducing the relative risk of painful clinical vertebral fractures in women with and without existing MVFX. The effect of alendronate was seen early.

M93

SAFETY OF ONCE-WEEKLY ALENDRONATE 70 MG IN PERIODONTAL DISEASE

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Periodontal disease, the leading cause of tooth loss in adults, is a chronic inflammatory process which leads to a local imbalance between bone formation and bone resorption. Alendronate sodium (ALN) is a potent and selective inhibitor of osteoclastic bone resorption used for the treatment and prevention of osteoporosis in postmenopausal women. In postmenopausal osteoporotic women, ALN 70 mg once weekly has demonstrated efficacy comparable to those of ALN 10 mg daily and very good safety and tolerability. However, there has been no direct comparison between ALN 70 mg once weekly and placebo. To further investigate the safety profile of once weekly ALN, as well as efficacy in periodontal disease, we are conducting a randomized, placebo-controlled, multicenter, 2-year study. Three-hundred and thirty-five patients aged 30 to 79 with periodontal disease were randomized to either placebo (PBO) or ALN 70 mg once weekly. The overall and upper gastrointestinal (GI) safety and tolerability profile of ALN after one year of treatment was very favorable compared to placebo, as shown below.

Adverse events (% patients)	ALN (N=167)	PBO (N=168)	Upper GI adverse events (% patients)	ALN (N=167)	PBO (N=168)
Any	81.4	84.5	Any upper GI	10.8	11.9
Drug-related†	9.0	11.9	Drug-related†	4.2	6.5
Discontinued	2.4	3.0	Abdominal pain	4.8	4.8
Serious○	5.4	4.8	Dyspepsia	2.4	4.8

†Drug-related indicates that the investigator considered the event possibly related to study drug while still blinded to treatment allocation.

○Serious adverse events include those requiring hospitalization or causing death.

In summary, 1-year data show that ALN 70 mg once weekly was very well tolerated in men and women with moderate to severe periodontal disease.

M94

A Randomized, Double-Blind, Placebo-Controlled Endoscopy Study Comparing the Effects of Oral Alendronate Once-Weekly and Placebo on the Upper Gastrointestinal Mucosae.

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Background: Alendronate 10 mg daily has been shown in long term clinical trials to be an efficacious treatment of postmenopausal osteoporosis, with a safety and tolerability profile similar to placebo. A weekly dosing regimen of alendronate is preferred by both patients and physicians as it has the potential to provide greater convenience and enhance adherence. In a one-year clinical trial, alendronate 70 mg once weekly was equally efficacious and at least as well tolerated as the 10-mg daily dose in the treatment of postmenopausal osteoporosis.[Schnitzer et al, *Aging* 12:1-12, 2000] We hypothesized that mean endoscopic gastric erosion scores would be similar in subjects receiving alendronate 70 mg once weekly and those receiving placebo.

Methods: We conducted a double-blind, placebo- and active- controlled endoscopy study. 277 subjects (90 men and 187 women) were randomized to one of three treatment groups: alendronate once weekly for 10 weeks (N = 126), placebo once weekly for 10 weeks (N = 126), or placebo weekly for 10 weeks followed by aspirin 650 mg 4 times daily for the last week as the positive control (N = 25). Esophagogastroduodenoscopy was performed 5 to 7 days after the last dose of alendronate or matching placebo.

Results: The mean gastric erosion scores (Lanza scale) were similar between subjects given alendronate 70 mg once weekly and those given placebo [0.32 vs. 0.35, respectively, 95% CI for difference = (-0.22, 0.16) p = 0.75], whereas scores in both groups were significantly lower than those given aspirin (3.09; p<0.001). Endoscopic gastroduodenal ulcers occurred in 0 alendronate (0%), 2 placebo (1.7%) and 5 ASA (23.8%) subjects. The mean erosion scores in the esophagus and duodenum between alendronate and placebo were also similar. The incidence of upper GI symptoms was similar between the alendronate and placebo subjects and did not suggest a relationship with endoscopic lesions.

Conclusion: The effects of alendronate 70 mg once weekly on the gastric, duodenal, and esophageal mucosae are similar to that of placebo.

M95

INCREASES IN BONE MINERAL DENSITY EXPLAIN THE REDUCTION IN INCIDENCE OF NONVERTEBRAL FRACTURES SEEN WITH ANTIRESORPTIVE THERAPY IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS.

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A published meta-analysis of randomized, placebo-controlled trials of antiresorptive agents in postmenopausal women found a significant relationship between increases in bone mineral density (BMD) and reductions in risk of radiographic vertebral fractures, as well as a small risk reduction not explained by change in BMD (J Clin Endocrinol Metab 2000;85:231-6). In the current analysis, we examined the extent to which increases in BMD during antiresorptive therapy are associated with reductions in risk of nonvertebral fractures (nVFx). We performed a meta-analysis of all randomized, placebo-controlled trials of antiresorptive agents conducted in postmenopausal women with osteoporosis with available relevant data. A total of 15 such trials with usable data were identified including a total of 1911 women with incident nVFxs over 54,952 women-years of followup. Poisson regression was used to estimate the association between increase in BMD (change in the treatment group - change in placebo group) and relative risk (RR) of nVFXs across all trials; separate models were constructed for change in spine BMD and change in hip BMD. Both models found a significant relationship between increases in BMD and reductions in nVFx risk. For each 1 percent increase in bone mineral density at the lumbar spine, there was a 4.3 percent decrease in risk of nVFx (P = 0.029); for each 1 percent increase in bone mineral density at the hip, there was a 8.8 percent decrease in risk of nVFx (P = 0.016). In neither model was there a significant decrease in risk of nVFxs in the absence of increase in bone mineral density. Thus, an agent that increases spine BMD by 8% reduces nVFx risk by about 40%, and an agent that increases hip BMD by 5% also reduces nVFx risk by about 40%. These data demonstrate that larger increases in BMD at both the spine and hip are associated with greater reductions in risk of nVFxs. Antiresorptive agents which do not produce large increases in BMD do not appear to and would not be expected to decrease the risk of nVFXs.

M96

A SIMPLE CLINICAL TOOL TO IDENTIFY ASIAN WOMEN WITH OSTEOPOROSIS.

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The objective of this study was to develop and assess a statistical model for predicting osteoporosis (femoral neck BMD T < -2.5) in postmenopausal Asian women, using risk factors obtained by questionnaire. A simple scoring index was developed based on multiple variable regression modeling. The full index with 11 variables achieved 95% sensitivity and 47% specificity. The area under the curve (AUC) was 0.85. Removing all variables except patient age and weight did not materially reduce predictive ability (sens = 91%, spec = 45%; AUC = 0.79), but substantially improved simplicity. To calculate this index, age was multiplied by -2 and body weight was multiplied by 2, the last digit was dropped from each, and the resulting values were added together. For example, age 66 becomes 13, 61 kg becomes 12, and the index is (-13) + 12 = -1. Three risk categories were identified. Almost two-thirds (61%) of high risk patients (representing only 8% of all women in the study, index < -4) had osteoporosis -- physicians might be advised to consider intervention and measure BMD. Among women with low risk (representing 40% of all women, index > -1), only 3% had osteoporosis, and BMD measurements are probably not necessary. Approximately 15% of the moderate risk women (index = -4 to -1) had osteoporosis; the decision to measure BMD for this category may vary by community, depending on available resources. In summary, this index had acceptable predictive ability and was easy to use. This free and simple tool could help clinicians actively assess osteoporosis and determine the need for intervention or BMD measurements before fractures occur.

M97

PREVALENT VERTEBRAL FRACTURE AND OTHER PREDICTORS OF PHYSICAL IMPAIRMENT

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Background: Vertebral fractures are a hallmark of postmenopausal osteoporosis and an important end point in trials of osteoporosis treatment, but the clinical significance of prevalent fractures remains uncertain.
Objective: To examine the associations of prevalent vertebral fractures and other characteristics with physical functioning among 589 Japanese women ages 40 to 90 years.
Methods: Lateral spine radiographs were obtained and radiographic vertebral fractures were assessed by quantitative morphometry, defined as vertebral heights more than 3 SD below the normal mean. A self-administered questionnaire was used to survey participants about difficulty in performing selected basic and instrumental activities of daily living (ADL).
Results: The prevalence of vertebral fractures increased significantly with age. Half of women ages 80 and over had vertebral fractures. Impaired function was defined as difficulty performing 3 or more ADLs. Each vertebral fracture increased the odds of impaired function by 1.4 times (95% CI: 1.1,1.8) in an age-adjusted logistic regression model. The number of vertebral fractures remained a significant predictor independent of age, number of painful joints, and BMI in multiple variable logistic regression models; the odds ratio of impairment for number of vertebral fractures was 1.5 (CI: 1.2, 2.0). Additional adjustment for back pain did not alter these findings.
Conclusions: Prevalent vertebral fractures contributed significantly to impaired function. The association was independent of age, back pain and the number of painful joints. The results also suggest that vertebral fractures may impair physical function even when back pain is not present.

M98

ALENDRONATE IS MUCH MORE EFFECTIVE THAN CALCITONIN AND ALFACALCIDOL FOR PREVENTING NONVERTEBRAL FRACTURES.

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It is unlikely that trials of sufficient size will be conducted to compare the antifracture efficacy of various agents. We previously developed a method for estimating and comparing the antifracture efficacy of various antiresorptive agents, expressed as the relative risk reduction (RRR) and number needed to treat (NNT) to prevent one case of fracture. These predictions are based on the observed effects on BMD from head-to-head (HTH) trials, together with the relationship between changes in BMD and fracture risk reductions derived from meta-analyses of antifracture trials. This approach provides a more accurate estimate of each agent's efficacy than relying on the results from a single trial, especially when fracture trials of adequate size are not available (e.g., alphacalcidol). Using BMD results from HTH trials avoids the potential for bias related to differences in baseline characteristics or other factors between trials. We previously reported the results comparing alendronate to calcitonin and alfacalcidol with regard to the predicted effects on vertebral fractures; now we report similar analyses for nonvertebral fractures. The predicted nonvertebral fracture RRR was 28% for alendronate 5 mg/day, based on BMD changes in a HTH trial; this is similar to the published value in large clinical trials, thus validating the method. Assuming a nonvertebral fracture incidence of 19% over 3 years in untreated women with prior vertebral fractures (based on a large epidemiological study), the number needed to treat (NNT) to prevent a new vertebral fracture was 19 for alendronate, and 84 for alphacalcidol; similar results were observed for calcitonin. We conclude that alendronate is 3 to 4 times more effective for reducing nonvertebral fracture risk than alphacalcidol or calcitonin.

M99

THE EFFICACY OF NASAL CALCITONIN ON THE TREATMENT OF OSTEOPOROSIS IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS

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Objective: Osteoporosis is a prominent feature of ankylosing spondylitis (AS) as suggested by an uncoupling of bone formation and resorption. The aim of this study was to determine the lumbar bone mineral density (BMD) and evaluate the efficacy of nasal calcitonin 200 mg daily (Miacalcic®) in a group of male AS patients with osteoporosis.
Methods: Thirty-two consecutive AS patients with a mean age of 35.1±11.4 years and with a mean duration of 14.8 years were included to the study. Demographical, clinical and laboratory characteristics of the patients were recorded. Lateral spine radiographs were taken and lumbar lateral BMD were determined for the assessment of vertebral fractures and osteoporosis, before and after the study. Patients who were defined as osteoporotic according the WHO criteria were received nasal calcitonin 200 mg daily for one year. The primary outcome measure was the percentage of change in the lumbar spine BMD.
Results: Osteoporosis was determined in 11 (34.3%) of patients and 10 patients (31.2%) had osteopenia. Although not statistically significant, at the end of 12 months with calcitonin therapy, the lumbar spine BMD of osteoporotic patients was increased (0.81±0.47 vs 0.85±0.34) ($p>0.05$) and a trend toward a decrease in the incidence of new vertebral fracture was also observed. Calcitonin was well tolerated and no adverse event was reported.
Conclusion: We conclude that nasal calcitonin 200 mg daily may be effective in the treatment of male AS patients with established osteoporosis. Further studies are needed to confirm these preliminary findings.

M100

MANDIBULAR RATE OF BONE LOSS IS A RISK FACTOR TO VERTEBRAL AND FEMORAL OSTEOPENIA AND OSTEOPOROSIS.

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Background: Considering the architectural characteristics of the alveolar bone tisse at the mandible, with trabecular and cortical bone constitution, should be expected to occur the same changes in DMO that aging and menopause induce on vertebral and femoral bone.

Objetives: A group of 39 caucasoid women from 48 to 83 years old was studied , to determine the correlation between mandibular, vertebral and femoral bone mass.

Methods: All the them were submitted to densitometric DMO evaluation by means of DEXA (DPX LLunar equipment) at the lumbar spine and femur, as well as at the mandible in three differents sites.

RESULTS: The correlation coefficient between the means, calculated for each site, from the obtainde results (Pearson' s equation), shows a significant and positive correlation between DMO in the three sites of mandibles referred to spine and femur. This correlation showed to be closer between mandible and spine.

Conclusion: The reproduction of these results in other larger casuistics can confirm if mandibular bone mass (or bone loss) should be used as a predictor factor of vertebral and femoral bone loss in osteoporotic patients.

M101

OPEN STUDY OF SIMVASTATIN IN THE TREATMENT OF THE GLUCOCORTICOID INDUCED OSTEOPOROSIS

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Objective: To evaluate the anti-osteoporosis properties of the simvastatin (lipex), lipid lowering drug, in rheumatoid arthritis pts., with the glucocorticoid induced osteoporosis.
Rationale: The primary action of Statins is to inhibit HMG-CoA reductase, the enzyme in the cholesterol biosynthesis. Recently, it has been noticed that Statins have a positive impact on the bone remodeling and osteoporosis.
Methods: Patients included 33 total in each of two group. The first group (Group 1) received Simvastatin (Lipex) 1o mg at bed time plus Calcium 5oo mg daily for three months. The second control group (Group 2) received only Calcium 5oo mg dose. Clinical assesment, BMD test i.e. T score was evaluated at the baseline and three months after. The laboratory tests and risk factor stratification for osteoporosis was screened at the same time of BMD testing.
Results: A significant improvement was observed in Group 1 pts three months after the therapy. The BMD score was improved by 24% in this group No improvement was seen in Group 2 patients. The lipid profile was improved in Group 1, but no in Group 2 patients.
Conclusion: The results obtained in this study suggest another therapeutic profile of Statins in our case simvastatin (lipex). It is Osteoporosis which could be safely treated .

M102

EFFECTS OF INTRAVENOUS PAMIDRONATE IN THE TREATMENT OF METABOLIC BONE DISEASES

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Objective: To evaluate therapeutic and side effects of pamidronate (DP) i.v. infusions in the treatment of various metabolic bone diseases.
Rationale: Disoddium pamidronate, 3rd generation bisphosphonate is analog of pyrophosphate today used primarily in diseases with increased bone resorption and bone loss.
Methods: Patients included 32 females and two boys: 18 women with postmenopausal osteoporosis (PMO), 8 with Paget's disease of bone (PD), 3 with reflex sympathetic dystrophy syndrome (RSDS), 3 with heterotopic calcifications (HC) of legs, while boys had osteogenesis imperfecta (OI). Pts with PMO and boys with OI received pamidronate as a 30-mg i.v.infusions every 3 months during 12 months. In pts with PD and RSDS pamidronate was administered as a single i.v. infusion of 60 mg and 30 mg, respectively. HC were treated with 30 mg of pamidronate as a monthly i.v. infusion, during 6 months. Clinical assessments included the osteodensitometry with LUNAR-DPX IQ at baseline and after 12 months. Efficacy of treatment in PD and RSDS was estimated by pain scalling score and by serum alkaline phosphatase (AP) every month.
Results: In pts with PMO we did not notice significant increase of bone mass density (from 0.770±0.100 g/cm^2 to 0.777±0.09 g/cm^2). Boys with OI improved bone mass density for 8%. Patients with PD and RSDS lost pain and serum AP level in PD was normalised with permanent course during 6 months. HC were gradually decreased during 6 months. As the only adverse effect of pamidronate we noted transient pyrexia in 20 (69%) patients.
Conclusions:I.v. pamidronate is effective and well tolerated in pts with PD, RSDS, OI and HC. At doses that we administered, bone mass density loss in women with PMO was detiorated.

M103

TREATMENT OF CORTICOSTEROID INDUCED OSTEOPOROSIS IN RHEUMATOID ARTHRITIS PATIENTS - A 3-YEAR RESULTS -

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Objective: To compare the bone mass effects of vitamin D, intermittent cyclic ethidronate and vitamin D plus intermittent cyclic ethidronate therapy in patients with corticosteroid induced osteoporosis for rheumatoid arhtritis.

Ratiomale:Bisphosphonate and vitamin D suppress progressive bone loss.

Methods: Fifty two female RA patients who had established corticosteroid induced osteoporosis and were receiving predonisone therapy (>=5mg/day) were enrolled in a prospective 36-month study. We divided them into 3 groups. Seventeen patients were received daily oral vitamin D (A group), 21 patients were received cyclic ethidronate therapy consisting of ethidronate 400mg/day for 14 days followed for 76 days (B group), and 14 patients were received daily oral vitamin D plus cyclic ethidronate (C group). Bone mineral density (BMD) of the spine and proximal femur were measured by dual-energy x-ray absorptiometry at baseline, 12 months 24 months and 36 months. Serum calcium, phosphorus, alkaline p hosphatase and biochemical markers were measured for 1 years. We also measured activity of rheumatoid arthritis, Lansbury's index(L.I), serum CRP, and modified health assessment questionaire(mHAQ).

Results; Treatment with vitamin D plus cyclic ethidronate for 36 months resulted in significant increases of 5.0% in BMD of the spine (P<0.05 versus base line). A and B group did not increase the BMD of the spine significantly. BMD of the proximal femur did not change significantly during the study in three treatment group. Serum calcium only increased significantly in A group. And also L.I and CRP did not change significantly.

Conclusion: 1)Vitamin D plus cyclic ethidronate therapy prevented significantly progressive loss of BMD of the spine in female patients with corticosteroid induced osteoporosis for rheumatoid arthritis. 2)There was no apparent anti-inflammatory effects on rheumatoid arthritis patients.

M104

NATRIUM ALENDRONATE THERAPY IN TYPE I AND TYPE II OSTEOPOROSIS

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Objective: To assess the effectiveness of therapy with Natrium Alendronate in type I and type II osteoporosis, over a period of 5 years.
Material and methods:Out of a total of 586 patients we selected 190 females, aged between 45 and 75 years. The predominant age groups were those between 50-59 and 60-69 years. 165 patients came from an urban background and 25 came from a rural background. 170 had type I osteoporosis and 20 (aged over 70) had type II osteoporosis. The clinical exam was accompanied by lab findings focusing on the serum resorbtion bone markers (urine hydroxiproline, alkaline phosphatase), the serum synthesis bone markers (acid phosphatase), urine calcium, urine N telopeptide, osteocalcine and bone densitometry. The tests were carried out at the beginning of the treatment, after 6 months and after 1 year.
Results: After 6 months and 1 year of treatment with Natrium Alendronate an increase in the T score, of maxiumum 0.2 standard deviation was noticed. This increase was accompanied by a decrease in the articular and dorsal pain and insignificant alterations of the biological data.
Conclusions: The medication was well tolerated by the patients, without any adverse reactions. The therapy with Natrium Alendronate resulted in an increase in bone mass and improved clinical symptomatology. The best results were obtained in those patients who avoided risk factors and associated kinetotherapy with the medical treatment.

M105

SYSTEMIC MASTOCYTOSIS AND OSTEOPOROSIS

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Objective: Osteoporosis is increasingly recognised in men.The recognition of pathological causes of osteoporosis is crucial, as in men 30%to 60% of those presenting with vertebral fractures have another illness contributing to osteoporosis. In this study systemic mastocytosis as a cause of osteoporosis in a male patient is described.

CASE REPORT: A patient, male, aged 47 years, presented with urticaria pigmentosa. Skin biopsy and bone marrow biopsy were performed. He was diagnosed to have systemic mastocytosis.The patient was suffering from spinal pain. Bone mineral density was performed which revealed the presence of osteoporosis, T-score being -2.93 SD. Biphosphonates were administered and spinal pain improved. Mastocytosis is a rave disease of mast cell proliferation with involvement of the reticuloendothelial system including skin and bone. Systemic mastocytosis is characterised by a combination of symptoms than relate to the mast cells release of vasoactive substances.A well recognised roentgenographic feature observed in patients with mastocytosis is diffuse osteolysis and osteosclerosis, affecting primarily the axial skeleton and the ends of the long bones.Rarely, bony involvement consists of generalized osteoporosis. The pathogenesis of osteoporosis in mastocytosis may be related to the release of biologically active substances by the mast cells, which act on osteoblasts and osteoblasts.

Conclusion: Osteoporosis appears to be a complication of mastocytosis. Thus mastocytosis appears to be one of the causes of osteoporosis and should be considered in the differential diagnosis of osteoporosis in men.

M106

OSTEOPOROSIS IN A FEMALE RHEUMATOID POPULATION

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Objective: To evaluate the prevalence of osteoporosis (OP) in a female Portuguese rheumatoid population, using both dual X-ray absorptiometry (DXA) and quantitative ultrasound (QUS), and correlate them with disease parameters and bone markers.
Methods: In 55 patients (age: 54.9 ±9.2 years; disease duration: 14.7 ±9.0 years; post-menopausal: 78,2%), randomly chosen from our outpatient clinic, the following parameters were assessed: body mass index (BMI), years since menopause (YSM), dose and duration of steroid therapy, rheumatoid factor (IgM-RF), ESR, CRP, bone markers, history of osteoporotic fractures (OF), disability and pain scores (HAQ). Bone mineral density (BMD) was measured by DXA (LUNAR Expert 1320) at lumbar spine (LS), femoral neck (FN) and hip. Left calcaneal QUS parameters (BUA and SOS) were determined by Osteometer DTU-one.
Results: 38 patients (74,5%) had low bone mass (OP: 37.25%; osteopenia: 37.25%) and 14.5% had a previous OF. LS, FN and hip BMD were negatively correlated with age and YSM. Only the FN and hip BMD had a positive correlation with BMI and a negative one with ESR ($r= -0.35$, $p<0.05$). While SOS showed a negative correlation with age, YSM and the mean daily steroid dose ($r=-0.47$, $p<0.005$), BUA correlated only with YSM. Osteocalcin inversely correlated with both the mean daily ($r=-0.44$, $p<0.01$) and cumulative ($r=-0.34$, $p<0.05$) steroid doses. D-pyr positively correlated with ESR ($r=0.49$, $p<0.01$), years of steroid therapy ($r=0.41$, $p<0.05$) and disease duration ($r=0.40$, $p<0.05$). ß-crosslaps correlated positively only with ESR ($r=0.49$, $p<0.005$) and NTx with HAQ score.
Conclusions: The low bone mass found in most of our patients was correlated with the classical bone mass determinants (YSM and age). Our data also suggest that disease severity parameters and the steroid therapy increase the bone turnover, contributing to osteoporosis in RA.

M107

A MULTIVARIATE ANALYSIS OF RISK FACTORS FOR WOMEN'S OSTEOPOROSIS

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OBJECTIVE:
To determine, in a multivariate analysis, risk factors for women's osteoporosis in HNERM.

METHODS:
Cases were selected from women who were studied for osteoporosis in Rheumatology Service of Hospital Rebagliati between 1998 to 2000.
Medical records review and an interview were done in 1843 women in order to obtain information regarding age, height, weight, tobacco, alcohol, coffee or calcium consumption, immobilization, physical activity, family history of fracture, postmenopause, rheumatoid arthritis, thyroid disorders, diabetes mellitus, early menopause, total hysterectomy, corticosteroid use, anticonvulsivants use, race and history of fracture. The diagnosis of osteoporosis was made by dual energy X-ray absortiometry.

RESULTS:
Multiple logistic regression analysis confirmed that age more than 50 years old ($p<0,001$), postmenopause ($p<0,001$), weight less than 50 kg ($p<0,001$), consumption of more then 2 cups of coffee per day ($p<0,001$), history of fracture ($p<0,001$) and diabetes mellitus ($p=0,014$) increased the risk for osteoporosis.

CONCLUSION:
Age, postmenopause, weight, coffee consumption, history of fracture and diabetes mellitus were risk factors for women's osteoporosis in HNERM patients.

M108

THE RELATION BETWEEN HIGH CHOLESTEROL LEVEL AND BONE MINERAL DENSITY (BMD) IN POSTMENOPAUSAL OSTEOPOROTIC WOMEN.

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Background. Some studies suggest that osteoporosis may have a relation with cardiovascular risk factors.
Objective. To assess the femoral and lumbar BMD (by DXA) in postmenopausal osteoporotic women (PMO) with normal (<240 mg/dl) and high cholesterol (≥240 mg/dl) levels.
Methods. Postmenopausal osteoporotic women according to WHO criteria, without antilipid treatment and sedentary life history were recruited randomly. Subjects classified as high cholesterol level and normal cholesterol leveled patients. Cholesterol level ≥240 mg/dl accepted hypercholesterolemia. The relation between groups was assessed by Mann-Whitney U test. $P<0.05$ was significant.
Results. Thirty-four PMO women (11 with high cholesterol) were taken into the study. There were not significant relation between the ages and BMI of both groups (similar groups). The relations between BMD of women with normal and high cholesterol levels were not significant at all measured regions.

	Cholesterol (mg/dl)		
	<240 X (SD) n=23	≥240 X (SD) n=11	p value
Age	59.57 (6.51)	62.82 (6.27)	0.153
BMI (kg/m^2)	28.30 (3.46)	28.36 (6.10)	0.663
First menstruation age	13.48 (1.73)	14.64 (1.96)	0.123
Duration of menopause	17.91 (9.59)	14.73 (6.87)	0.403
Cholesterol	193.78 (24.54)	266.27 (25.16)	<0.0001
Triglyceride (mg/dl)	123.30 (57.08)	166.18 (55.43)	0.084
Tscore-L3	-3.03 (1.00)	-2.36 (1.56)	0.611
Tscore-L1-L4	-2.58 (0.95)	-1.78 (1.50)	0.123
Tscore-Femur Neck	-2.00 (1.02)	-2.01 (0.81)	0.800
Tscore-Trochanteric	-1.92 (1.37)	-1.87 (0.69)	0.971
Tscore-Ward's Triangle	-3.24 (1.11)	-3.45 (0.61)	0.363

Conclusion: There are not significant relation between BMD level and hypercholesterolemia in PMO women.

M109

THE SHORT TERM EFFECT OF NASAL SALMON CALCITONIN ON BONE MINERAL DENSITY AND BONE TURNOVERS IN POSTMENOPAUSAL OSTEOPOROSIS.

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Objective: To assess the short-term effect of nasal salmon calcitonin on bone mineral density (BMD) and bone turnovers in postmenopausal osteoporosis.

Method: Subjects with osteoporosis according to WHO criteria (T ≤ -2.5) were recruited randomly into our study. Patients with secondary osteoporosis and under estrogen replacement therapy were excluded. Subjects were divided into two groups. First and second groups were taken 100IU and 200IU nasal salmon calcitonin respectively and 500 mg elementary calcium. The blood osteocalcin and urine deoxypyridinoline levels and BMD assessed at baseline, 3 and 6 months.

Results: Twenty subjects for each group were recruited randomly (mean ages: 57.90±6,66 and 59.95±7.85). The serum osteocalcin and urine deoxypyridinoline levels were decreases significantly at 3rd and 6th months of the treatment in both groups. In calcitonin 200 IU group there was insignificant augmentation of BMD at L1-L4 and femur neck region as well calcitonin 100 IU group's at Ward's triangle in 3 months. BMD was decrease in all other regions in 3 months. In 6 months there was insignificant augmentation of BMD in all areas in 200 IU group. In calcitonin 100 IU group there was a BMD augmentation in only L1-L4 and Ward's triangle region. There was not any significant difference of scores between groups.

Conclusion: Because of the minimal augmentation of the BMD at 6th months in all areas we may pointed out that the fracture risk was decreased in patients with nasal salmon calcitonin 200IU/day treatment in short term. The diminution of the bone resorption and formation markers also showed that the fracture risk was decreased. Further investigations with long follow up period are necessary to assess the accurate effect of nasal salmon calcitonin in long term.

M110

PREVALENCE OF OSTEOPOROSIS IN A COHORT OF URBAN POPULATION IN GUATEMALA CITY

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Objective: To evaluate the prevalence of osteoporosis in a population that consulted for clinical suspicion of osteoporosis in Guatemala City.

Rationale: With the development of more precise methods for evaluation of risk of fracture due to osteoporosis, by bone densitometry, we evaluated 945 patients that consulted for bone densitometry from January 1999 to December 2000.

Methods: Of those 945 patients studied 441 were found to have osteoporosis (T-score < –2.5) 46.6%, of those, 402 (91%) were females rate of age 7-95, median 60 year old. According to source of referral, patients were separated in three groups.

a) Guatemalan Institute of Public Health 235 (53%)
b) Guatemalan Association Against rheumatic diseases 32 (7.2%)
c) Private patients 174 (39.4%)

All patients underwent forearm bone densitometry with Densitometer DTX 200.

Results: Osteoporosis was found in almost half of patients tested, most of them females, about 60 year old.

Conclusion: Osteoporosis is not rare in urban Guatemalan females, particularly in patients in the working class and high middle class 53% and 39.4% respectivelly.

M111

BONE MASS MEASUREMENTS IN ADULTS WITH RHEUMATIC DISEASES IN CUBA.

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INTRODUCTION:The Bone Mass Density Meassurements can be used to establish a diagnosis of osteoporosis, estimate future fracture risk, and monitor medical conditions that contribute to the progression offering therapeutic intervention. The rheumatic diseases patients can developed secondary osteoporosis for differents medical disorders and mecanisms.

OBJECTIVE: The aim of this study was establish the DMO in patients with Osteoarthritis, Rheumatoid Arthritis, Systemic Lupus Erythematosus and evaluated the involve risk factors.

METHODS: We performed Dual X-Ray Absorpciometry (DXA) of Femoral neck and Lumbar L2-L4 spine in 154 patients with rheumatic diseases.The studied groups are : Group I-AR (48 patients), II-OA (60 patients), III-Systemic L. Erythematosus.(30 patients), IV-Miscellanea (16 patients). All subjects fulfilled a complementary Socio-Demographic and clinical questionnaire .

RESULTS. The prevalent groups were females 132(85.7%), Europoides 96 (62.3%), with 48 years old +(10.8%). The more frequent risk factors were sedentarism 126(81.6%), smoking 56(36.4%), alcohol 12(7.8%), low calcio intake 42(27.3%), steroids consume 76(49.3%). Underwent fracture 16(10.4%) 11 in femoral neck 5 in spine.The general DMO was in Osteopenic range in 96 (62.3%) patients, and Osteoporotic range in 26 (16.8%).The A.R. group was the most low BMD.

CONCLUSIONS: Our study confirm the relationship between Rheumatic diseases and low Bone Mineral Density measurement and associate risk factors and fracture.

M112

ULTRASONOGRAPHY OF THE KNEE IN RHEUMATOID ARTHRITIS

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Objective: To compare ultrasonography(US) with clinical examination(CE) in the detection of soft tissue inflammation of the knee in rheumatoid arthritis(RA).

Methods: 19 patients with RA underwent independent clinical and ultrasonographic examination of both knees for suprapatellar bursitis(SPB), knee effusion(KE) and Baker's cyst(BC). US was performed using an ATL HDI 3000 machine with L7-4 MHz and CL10-5 MHz probes. Patients with previous knee surgery were excluded from the study.

Results: A total of 38 knees were examined at a total of 112 sites (1 patient was unable to lie prone for US of popliteal fossae). US detected soft tissue inflammation(SPB, KE or BC) at 47/112(42%) sites while CE detected soft tissue abnormality at 29/112(26%) sites. US detected 14(37%) cases of suprapatellar bursitis in 38 knees, 5(13%) of which were detected on CE. US detected 24(63%) knee joint effusions in 38 knees, 13(34%) of which were detected on CE. US detected 9(25%) Baker's cysts in 36 knees, 2(6%) of which were detected on CE.

		SPB	KE	BC
Clinical Examination*	Sensitivity	0.36	0.54	0.22
	Specificity	0.88	0.64	0.96

*compared to US as gold standard

Conclusion: Taking US of the knee as the "gold standard", CE was specific but not sensitive in the detection of suprapatellar bursitis, knee effusion and Baker's cyst of the knee in RA.

M113

ULTRASONOGRAPHY OF LOWER LIMB ENTHESES IN SERONEGATIVE SPONDYLOARTHROPATHY.

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Objective: To compare ultrasonography(US) with clinical examination(CE) in the detection of entheseal inflammation of the lower limbs in seronegative spondyloarthropathy(SpA).

Methods: 35 patients with SpA (AS=27, PsA=7, ReA=1) underwent independent clinical and ultrasonographic examination of both lower limbs at 5 entheseal sites:- superior pole(SP) and inferior pole(IP) of patella, tibial tuberosity(TT), achilles tendon(AT) and plantar aponeurosis(PA). US was performed using an ATL HDI 3000 machine with L7-4 MHz and CL10-5 MHz probes in order to detect bursitis, structure thickness and bony erosion and proliferation.

Results: A total of 350 entheseal sites were examined (2 being obscured by psoriasis). US detected entheseal abnormality in 195/348(56%) sites (SP=37, IP=40, TT=44, AT=36, PA=38) while CE detected entheseal abnormality at 75/348(22%) sites (SP=19, IP=17, TT=11, AT=15, PA=13). In 18 entheseal sites with bursitis on US, only 6 were detected on CE.

		SP	IP	TT	AT	PA
Clinical Examination	Sensitivity	0.30	0.23	0.18	0.22	0.21
	Specificity	0.76	0.72	0.88	0.79	0.84

*compared to US as gold standard

Conclusion: The majority of entheseal abnormality in SpA is not detected at clinical examination. US is superior to CE in the detection of entheseal abnormality of the lower limbs in SpA. A quantitative US score of lower limb enthesitis is proposed.

M114

A COMPARISON OF IMMUNOFLUORESCENCE (FANA) AND ENZYME IMMUNOASSAY (EIA) ANTINUCLEAR ANTIBODY (ANA) TESTING.

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EIA for ANA screening are used to decrease cost and test variability. However, most clinicians were trained to use FANA and there are limited studies that guide the interpretation of EIA tests in clinical practice. We performed HEp-2 FANA and EIA tests from 8 companies (Biorad, Diamedix, Diasorin, Helix, Inova, Pharmacia, Sanofi and Wampole) on 525 consecutively referred sera. Testing was performed according to manufacturer's instructions. Odds ratios, Goodman-Kruskal Gamma measure of association and disconcordant pairs percent of total were calculated for FANA and EIA results.

	ODDS RATIOS							
FANA(n)	Kit 1	Kit 2	Kit 3	Kit 4	Kit 5	Kit 6	Kit 7	Kit 8
NEG(75)	0.19	0.17	0.34	0.14	0.21	0.07	0.07	0.60
1:40(142)	0.45	0.38	0.60	0.23	0.39	0.14	0.10	1.03
1:80 (19)	0.19	0.27	0.46	0.36	0.27	0.06	0.06	1.38*
1:160(94)	0.92	0.92	2.62*	0.71	0.84	0.24	0.52	3.48*
1:320(42)	2.82*	2.0*	3.20*	2.50*	1.47*	0.62	1.63*	9.50*
1:640(41)	4.86*	2.42*	4.86*	2.15*	2.15*	0.58	1.73*	4.86*
1:1280(56)	8.33*	6.0*	4.09*	4.60*	2.50*	0.93	3.67*	27.0*
>1:1280(56)	27.0*	7.0*	13.0*	55.0*	8.33*	2.73*	5.22*	27.0*

*95% confidence intervals of Odds ratios significantly different than 1. There was strong association (Gamma>0.72) when comparing each of the EIA tests. Most comparisons showed <5% disconcordance.

Conclusion: A positive result by EIA test was most likely to be detected at higher FANA titers, corresponding to FANA of ≥1:320 for most companies. There was high association (Gamma) between all the EIA tests.

M115

IMMUNOFLUORESCENCE AND ENZYME IMMUNOASSAY (EIA) ANTINUCLEAR ANTIBODY (ANA) TESTING IN RHEUMATOLOGY REFERRALS.

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EIAs were developed to improve efficiency and reproducibility of ANA testing. Studies have assessed the sensitivity of EIA testing in SLE; however, there is little data to assist in interpretation of results with other connective tissue diseases (CTD) or non-specific rheumatic complaints. We performed HEp-2 ANA (FANA) and EIA testing from 8 companies (Biorad, Diamedix, Diasorin, Helix, Inova, Pharmacia, Sanofi and Wampole) on 525 consecutively referred sera. Clinical diagnoses were made according to ACR or other standard criteria. Odds ratios were calculated for EIA positivity in each disease group.

	% POSITIVE AND EQUIVOCAL OF TOTAL								
Disease (n=)	FANA ≥1:160	Kit 1	Kit 2	Kit 3	Kit 4	Kit 5	Kit 6	Kit 7	Kit 8
SLE(69)	87.0*	88.4*	89.9*	89.9*	87.0*	82.6*	66.7*	84.1*	88.4*
UCTD(61)	72.1*	64.0*	57.4*	62.3*	55.7*	60.7*	31.1	47.5	78.7*
CTD (44)	83.7*	86.0	79.1*	79.1*	86.0*	67.4**	67.4*	69.8*	90.7*
RA(30)	56.6*	40.0	43.3	60.0*	36.7	46.7	23.3	30.0	66.7*
Arthral (118)	41.5	40.7	33.1	41.5	25.4	30.5	15.3	18.6	56.8*
No CTD (69)	42.0	34.8	30.4	50.1	33.3	31.9	7.2	24.6	63.8*

* Odds ratios significantly different from 1, CTD=MCTD, Sjogrens, scleroderma, myositis.

Conclusion: Most EIA kits and FANA detect the majority of SLE and other CTD patients. The proportion of patients with a positive FANA (≥1:160) or EIA was similar in all rheumatic disease groups. EIA tests, in general, have similar sensitivity and specificity for the detection of autoantibodies when compared to FANA testing.

M116

RADIOLOGIC SCORING OF RHEUMATOID ARTHRITIS: COMPARISON OF DIGITAL AND ANALOG IMAGES

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Objective: To compare the reproducibility of semiquantitative scoring of erosion, joint space narrowing (JSN), and their combination (Total) in the hands of patients with rheumatoid arthritis, using laser-digitized images on high-resolution monitors from a picture archiving computer system (PACS) versus the original radiographs.

Methods: Hand radiographs of 60 patients were obtained at 2 visits (baseline, 6 to 24 months follow-up), digitized at 100 and 50 μm pixel sizes, blinded to sequence, and independently scored by 3 experienced readers using the Genant or Sharp methods.

Results: Inter-technique intra-reader correlation coefficients (r) for each of the two visits were 0.95-0.99 erosion, 0.90-0.96 JSN, and 0.93-0.98 Total; and 0.93-0.98 erosion, 0.82-0.97 JSN, and 0.92-0.98 Total for progression between the two visits. Intra-technique intra-reader r was 0.92-0.99 erosion, 0.86-0.94 JSN, and 0.90-0.98 Total for the two visits; and 0.92-0.97 erosion, 0.86-0.95 JSN, and 0.94-0.97 Total for progression. Intra-technique inter-reader r was 0.73-0.93 erosion, 0.66-0.76 JSN, and 0.75-0.84 Total for the two visits; and 0.90-0.91 erosion, 0.72-0.84 JSN, and 0.85-0.92 Total for progression. Inter-technique intra-reader r for new lesions in intact joints at baseline was 0.85-0.98. Over all, the Genant and the Sharp methods showed similar reproducibility and close correspondence.

Conclusion: Scoring directly off digitized images on high-resolution monitors provides highly reproducible results, comparable to those of the original radiographs.

M117

ULTRASOUND IN THE DIAGNOSIS OF DISCUS HERNIATION

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Background: One major advantage of ultrasound (US) is that it can be performed bedside by the clinician. In an attempt to implement US in the diagnosis of disc herniation some authors have previously described sensitivities and specificities approximating those of the conventional methods. Within the last decade, however, there have only been sparse reports on this subject, and the role of US is still unclear.

Objectives: To evaluate in a blinded fashion US in the diagnosis of disc herniations at the three lower lumbar levels performed by an experienced specialist.

Methods: 18 males and 19 females (mean age 39.7 years, range 24-65 years) with no previous back surgery were included due to suspected disc herniation. The US investigation was performed transabdominally with the patient in the supine position. An Acuson Sequoia with a 4 MHz vector transducer was used. MRI or CT was obtained at the lower three lumbar levels. The two modalities (US vs. CT/MRI) were performed and evaluated blinded to each other. The endpoints were existence of herniation or protrusion in contrast to normal findings and the corresponding level of the abnormal finding.

Results: A total of 97 disc levels were visualised by US. Fourteen levels were not visualised. There were 45 disc abnormalities (herniations or protrusions) found by CT/MRI, and of those 12 (26.7%) were also found by US. Fiftytwo discs were found to be normal by CT or MRI, but of those 11 (21.2%) were suspected to be abnormal by US. A total agreement between US and CT/MRI was found in 53/97 (54.6%) of the cases . The sensitivity of US was 12/45 (26.7%) and the specificity 41/52 (78.8%). The false positive rate was 47.8% and the false negative rate 44.6%. The over all *kappa* value was 0.18. The findings stratified at levels gives a *kappa* value for level L5/S1 of −0.18 and a *kappa* value for the levels L3/4 and L4/5 of 0.13 and 0.25 respectively. At levels L3/4 and L4/5 a total agreement of 40/63 was found.

Conclusion: At level L5/S1 US does not seem to be of any diagnostic value. At the levels L3/4 and L4/5 US was in agreement with CT/MRI in about 2/3 of the patients and could be of potential use at these levels. Further investigations are needed to establish the role of US.

M118

ULTRASONOGRAPHIC EVIDENCE OF INTRA-ARTICULAR INJECTIONS IN THE HIP

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Objective: Our goal was to evaluate the use of US as guidance when performing injections in osteoarthritic hips using air as contrast medium.

Rationale: In order to validate intra-articular medical treatment of osteoarthritis in the hip joints it is imperative to have documentation of the correct placement of the injection. Radiographic methods imply a radiation load, while ultrasound (US) is harmless.

Methods: A total of 30 injections were given to 11 Patients with hip-osteoarthritis (ACR criteria)(Age mean 60 y Range 44-86 y).

The femoral head and neck was scanned with a 8-13 MHz linear transducer.

The probe was placed below the inguinal ligament in parallel with the axis of the femoral neck. Placement of a gauge 21 needle into the hip joint (anterior/inferior capsule below the femoral head) was monitored with a B mode (grey scale) scanning allowing a continuous visual guidance.

Preceding the treatment, a small(0,5-2 ml) amount of atmospheric air was injected.

Results: The position of the needle was evident on the screen in all cases. The injections of air into the joint was demonstrated in 29 cases presenting a small hyperechoic brim inside the joint capsule. However, in one case in spite of a seemingly correct placement of the needle the hyperechoic air brim was clearly positioned outside the joint. Placement of the needle was subsequently corrected. Still picture of the setting as documentation revealed air presence without difficulty, however the needle tended to be less recognisable when not in motion

Conclusion: The sole use of grey scale US as guidance device gives a good view of the intra-articular placement of a needle. However use of air as US contrast before an injection or aspiration, enhances the precision and allows photographic documentation of the set-up.

M119

SYNOVIAL INFLAMMATION IN THE WRIST IN PATIENTS WTIH ARTHRITIS – A COMPARISON BETWEEN DOPPLER ULTRASONOGRAPHY AND MRI.

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Backgound: Synovial membrane volumes obtained by Magnetic Resonance Imaging (MRI) have been suggested as a marker of joint disease activity. Graded power Doppler images has been able to detect treatment response in joint synovium. If ultrasonographic parameters correspond with findings in MRI an alternative method in assessing inflammatory activity would be available.

Objective: To compare Doppler ultrasonography (DUS) with MRI and clinical findings in determining synovial activity in the wrist of patients with rheumatic disease.

Methods : 11 patients (5 women and 6 men, median age 53 years, range (32-69)) with arthritis were included. All patients were examined by DUS with a 15 MHz linear transducer and by 1.5 T MRI before and after contrast injection. The area and thickness of the synovial membrane were outlined after contrast injection on MRI. US flow pattern of the synovium in the wrist was evaluated by quantitative spectral DUS (n=10), recording resistance index (RI). The relative RI (rRI) = mean RI/extra synovial RI, was calculated to adjust for changes in peripheral resistance unrelated to the joint. The synovial vascularisation was determined by colour Doppler (n=10). Using a colour recognition function, all marked pixels were changed to a reference colour and the total amount of pixels finally depicted using a colour histogram.

Each patient was evaluated by ESR, CRP and joint assessment.

Results: The colour Doppler pixel (CDP) measurements correlated significantly with both max area and thickness of the synovial membrane on post contrast MR images (Rs = 0.88 and 0.84, P< 0.002). Also the rRI values correlated significantly with both max area and thickness of the synovial membrane on post contrast MR images (Rs = 0,89 and 0,93, P<0,001). Kappa statistics were made on MRI and DUS : Kappa was 0,8 between the max area and thickness of the synovial membrane on post contrast MR images and the CDP measurements. Kappa was 1,0 between the max area and thickness of the synovial membrane on post contrast MR images and the rRI values. No correlation was found between ESR,CRP and joint assessment and the imaging modalities.

Conclusion : The estimation of synovial inflammatory activity on DUS was comparable with post contrast MRI . DUS appears to be an alternative method to determine inflammatory activity in patients with arthritis.

M120

KNEE OSTEOARTHITIS PROGRESSION EVALUATED BY MAGNETIC RESONANCE IMAGING AND A NOVEL QUANTIFICATION IMAGING SYSTEM.

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Knee osteoarthritis (OA) is a prevalent disease characterized mainly by cartilage degradation. Existing methods used to evaluate OA progression are imperfect. The aim of this study was to evaluate the role of a novel software tool using data obtained with successive MRI of the knee in assessing cartilage degradation in patients with OA.

Forty patients with symptomatic knee OA were recruited for the study and had MRI acquisition of the knee at baseline, 6 months and 1 year of follow-up. These images were systematically analyzed and quantified using the software. The attrition of cartilage volume is computed by contrasting the MRI at 6 months and at 1 year to the baseline value. The disease progression was also contrasted at each time point to classic knee OA evaluation variables, co-medication consumption, physical examination of the knee and standardized semi-flexed knee radiographs done at baseline and at 1 year. Grade IV radiographs was an exclusion criteria.

Patients' mean age was 63.1 years (range 39-78), 74% were female, with an average BMI of 31. Preliminary data on knee OA progression (cartilage volume losses in % from baseline) computed on 35 patients at 6 months and 1 year of follow-up are already striking and statistically significant (mean and S.E.M.):

	Total Cartilage	Medial Compartment	Medial Femoral Condyle
6 mos.	-1.81 % (0.43)	-2.11 % (0.65)	-3.34 % (0.96)
1 year	-2.38 % (0.51)	-3.91 % (1.41)	-5.03 % (1.33)

p value = < 0.001 for all the measurements, t-test at 6 months, ANOVA at 1 year.

Data will be presented on the 40 patients followed for 1 year and compared to the clinical and radiological data. This new imaging system could dramatically change the way clinical research is established to evaluate the progression of knee OA.

M121

UNIQUE ULTRASONOGRAPHIC FINDINGS IN PATIENTS WITH THE HEREDITARY INCLUSION BODY MYOPATHY

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Objective: To demonstrate the facility of the use of gray scale and power Doppler sonography as a non-invasive diagnostic procedure in the evaluation of a the Hereditary Inclusion Body Myopathy (HIBM).
Rationale: HIBM is an autosomal recessive disorder characterized histologically by the presence of ß amyloid fibrils in myofibers and clinically by muscle weakness and atrophy with quadriceps sparing. This disorder is seen in different ethnic groups including members of Iranian Jewish families where it has been mapped to chromosome 9q1-p1. The onset is usually in the 2nd to 3rd decade of life, with slow progression leading to severe involvement of multiple muscle groups, ultimately resulting in immobilization.
Methods: We studied 4 Iranian Jewish patients diagnosed with HIBM. Ultrasonographic examinations of the quadriceps femoris and hamstring muscle groups were carried out in these patients. Echogenecity, as determined by gray scale assessment, was used to detect disordered muscle and atrophy, and power Doppler sonography was used to assess vascularity.
Results: The initial symptom in all was "footdrop" due to anterior tibial muscle weakness. Two patients with disease duration of seven years developed pelvic girdle and shoulder girdle weakness. Two patients with twenty-eight years of disease were restricted to wheelchairs with severe myopathy of upper and lower extremities. All had significant family histories consistent with HIBM. An unusual and unique pattern of central atrophy of muscle with peripheral sparing was observed in all four patients. Vascularity was markedly reduced in the affected areas with relatively increased blood flow in the peripherally-spared areas. We referred to this as a "fried-egg" or "bull's eye" appearance.
Conclusion: Our study demonstrates the use of both gray scale and power Doppler sonography as a helpful non-invasive procedure in the evaluation of HIBM. Their ability to define a unique centrifugal, "fried-egg" myopathic abnormality may be diagnostic for this disorder.

M122

SOUND MEASUREMENT FOR THE QUALIFICATION AND QUANTIFICATION OF CREPITUS IN KNEE OSTEOARTHRITIS (OA), COMPARED WITH OTHER CONVENTIONAL METHODS

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Objective: Develop an equipment capable of analyzing the crepitus of knee caused by cartilage modifications which occur in the osteoarthritis (OA), qualifying the responses to allow a differentiation by groups. Preliminary results of 30 cases will de presented, compared with control group.
Method: The crepitus, possibly, caused by a modification on the knee structure cartilage produce a sound wave, with the joint movement, that varies in time, frequency and intensity. Using a sensor for frequencies captivation with latitude from 5 to 40 hertz it is possible to identify the frequency produced in each knee and, by a data treatment system, to quantify the result comparatively with conventional methods (clinical semiology and radiology). The proposed system uses a mathematical analysis to distinguish the patients according to the variation of the frequency and the sound intensity produced by the joint.
Preliminary Results: A frequency from 0 to 5 Hz was noticed in normal patients which would mean, comparatively, classification 0 in Kellgren & Lawrence grading criteria for radiographic severity of knee OA. In patients with OA, frequencies from 10 to 20 Hz were noticed and in these cases the generated wave amplitude showed apexes that were quantified and identified.
Conclusion: Preliminary studies indicated a good results' combination comparing the conventional methods for diagnosis with the one proposed in this object of study, which improves precision on the qualification and quantification of crepitus in knee osteoarthritis (OA).

M123

SONOGRAPHIC STUDY OF THE HIP IN RHEUMATIC DISEASES

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Background: Pain in the hip region may arise from different anatomic structures and it is often difficult to identify the site of changes clinically. Sonography (SN) studies the hip region carefully and evaluates most alterations of many articular and periarticular structures. The aim of the study was to identify with SN the site and the entity of alterations in patients with hip pain.
Methods: 84 patients with hip pain were examined (73 females and 11 males; mean age 54.9 years; range 20-80). In 45 cases bilateral involvement was present; in 39 it was monolateral. Totally 129 joints were studied. 17 patients had a clinically suspected diagnosis of OA, 13 of RA, 7 of periarticular disorders of soft tissues of the hip; in 47 no clinical diagnosis had been made yet. The hips of 54 healthy control subjects were examined (39 females and 15 males; mean age 51.4 years; range 22-69). With a combination of already reported techniques SN was performed using a 3.5 MHz linear transducer. The chi square test was used for statistical analysis.
Results: Changes were revealed in 92 joints (71.3%). In particular hip joint effusion was found in 38 cases (29.5%); in 22 it was slight, in 8 moderate, in 8 abundant. Irregularities of the bone surface were showed in 46 joints (35.6%). The presence of trochanteric bursitis was revealed in 38 cases (71.3%). In healthy control subjects irregularities of the bone surface were found in 6 joints (5.5%). Differences were statistically significant (p=0.0000).
Conclusions: SN is a valuable imaging diagnostic method for the detection of changes in patients with painful hip and it can be successfully applied also for the therapy monitoring.

M124

VALIDATION OF A NEW SYSTEM OF BMD MEASUREMENT USING SINGLE-PHOTON RADIOABSORPTIOMETRY OF THE PHALANX

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Background: A new method for the measurement of bone density of the phalanx using digitised conventional X-ray films of the hand has been developed in our centre.
Objectives: To test the reliability and validity of our method, especially regarding the digitalisation process and the software developed for segmentation and optical density analyses.
Methods: The non-dominant hand is radiographed together with an alumínium wedge used for calibration and correction of the variability associated with the XR technique and digitalisation process. A single exposure at 46 kV is performed and the resulting film is read with an AgfaScan T1200 device with predefined settings.
Results: To assess the reproducibility of our technique, XR hand films of 17 patients were scanned 5 times in different days. CV was found to be 0,913 (95% CI 0,650-1,825) for the middle phalanx; 0,632 (95% CI 0,470-1,265) for the proximal phalanx; and 1,194 (95% CI 0,918-2,387) for the central area of the third metacarpal. A test-retest experiment with 2 films in 50 patients gave an almost perfect internal correlation (Pearson's R of 0,985; 0,995 and 0,986) for these same sites. Construct validation was performed in a sample of 171 women with a clinical diagnosis of osteoporosis using conventional lumbar spine and hip DXA (Lunar) and phalanx DXA (AccuDXA). Correlations between BMD in several sites ranged from 0,851 (Middle to proximal phalanx RXA) to 0,510 (AccuDXA to lumbar DXA).
Conclusion: The reproducibility and internal correlation of measurements made with our newly developed technique is very high for the three areas of the hand studied. Correlation of BMD of the hand with BMD in the lumbar spine and hip is moderate and similar to that found among these places themselves.

M125

ULTRASONOGRAPHIC MEASUREMENT OF CARTILAGE AND CLINICAL FINDINGS IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

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AIM. To evaluate the presence of correlations between knee cartilage thickness and clinical findings (pain assessment, functional capacity and range of motion) in patients with osteoarthritis (OA) of the knee.

METHOD. We measured the thickness of the cartilage of the knee joint in 20 patients with OA of the knee. The thickness of cartilage was measured with ultrasound unit (Acuson, Sequoia) using electronic linear probe 5-8 MHz, in weight bearing area of the medial and lateral compartment of the knee joint. Measurements were performed at the middle point of the distance between the apex of the condyle and intercondylar notch. Assessment of the pain was estimated by visual analogue scale (VAS) according to Haskinson, and functional capacity by index of severity for OA of the knee (Lequesne`s questionary). Also we measured the range of motion of knee joint. Results of the study were statistically calculated using standard programs.

RESULTS. We found that the mean value of the cartilage thickness in both knees was lower (right – 1.94± 0.61 mm; left – 1.93±0.37 mm) then described in the current literature. When we calculated medial and lateral compartment of both knees, we found that lower values were in medial compartment (left: lateral – 2.1±0.45 mm, medial – 1.77±0.45 mm ; right: lateral – 2.1±0.61 mm , medial – 1.94±0.46 mm). We did not find any correlation between the cartilage thickness and VAS of the pain. Also, there was no correlation between cartilage thickness and index of severity of OA of the knee as well as with the range of motion.

CONCLUSION. Thickness of the knee cartilage in patients with OA is not in direct correlation with clinical symptoms. Influence of some other factors (secondary synovitis etc.) may be more useful in clinical explanation of patients compliances then anatomical damage of joint cartilage.

M126

ULTRASONOGRAPHIC CHANGES OF THE CARTILAGE IN THE OSTEOARTHRITIS OF THE KNEES.

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Objective: The aim of this study was to establish and compare validity of the diagnostic ultrasound (US) and clasical plain radiography in the early phase of the osteoarthritis of the knees.

Methods: The study was conducted in the group of 60 outpatients with clinical diagnosis of the osteoarthritis of the knees and 20 healthy subjects. Following parameters are measured: cartilage thickness of the femoral condyles at the 3 characteristic sites and changes of the articular cartilage. US findings were compared with radiographic features of the disease (radiographic grades by the Kellgren-Lawrence classification).

Results: Cartilage thickness was 1.8 mm in the early phase of the osteoarthritis (radiographic grade 0 or 1), and in the late OA of the knees (radiographic grades 2, 3 or 4) thickness was 1.6 mm. Cartilage thickness was significantly lower at the all measurement sites in both OA knees, compared to the normal cartilage thickness in healthy subjects (2.1 mm). Changes of the synovial space-cartilage interface were found in 65% OA patients in the early phase of the disease. Only 31% of the same patients have had changes of the bone-cartilage interface.

Conclusion: In the absence of the clear radiographic features of OA of the knees (radiographic grades 0 or 1) US was showed like much more sensitive diagnostic method, comparing to the radiographic imaging of the knees.

M127

VEGETATIVE SYNDROME AT RHEUMATIC DISEASES (RD)

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Aim. To investigate vegetative nervous system (VNS), vegetative reactivity and vegetative activity maintenance in patients RD and correlation of mediatory exchange with VNS disturbances.

Materials and methods. Vegetative status, catecholamine metabolism, mediatory exchange, vegetative regulation of cardiac rhythm were performed in 150 RD patients.

Results. Lowering of vegetative tonus both sympatic and parasympatic VNC, was assessed. 67 % of pts demonstrated relative parasympathotonia, in 53.6 % -ascending of asymmetry, in 60 % - cranio-caudal differences with large downstroke at the left and in the legs (76.8 % and 66.6 %), that confirms segmentary shifts of vegetative regulation with generalized disturbances of VNS tonus.

A close positive relationship exists between ercotropic activity and vasospastic reactions, level of vasoactive amines and pressory prostaglandinus. The vasospastic and ischemic syndromes were prevailed. Skin ulcero-necrotic change vere cyaracterized by relavive parasympa-thotonia with significant rising of inflammatory mediators (histamine and serotonin) and also depressory prostaglandins with relative decrea-sing of inhibitory system functions.

Conclusion. At RD pressory prostaglandins and also dystonic re-actions and ergotropic activity may be associated with vasospastic synd-romes.

It is suggested that an increase of histamine and the ration hista-mine/histaminase in patients with acute and subacute forms suffering from ulcero-necrotic skin changes may serve a marker of acute phase of immunopathologic process.

M128

INFECTIOUS OSTEITIS PUBIS. A STUDY OF 20 CASES

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Background : Osteitis pubis covers several different entities and may lead to nosologic confusion. Infectious osteitis pubis (IOP) should be used when underlying infection is found.

Objectives : To analyse the main characteristics of IOP in a monocenter series.

Methods : Retrospective study about IOP with analysis of clinical, biological, imaging, bacteriological and pathological features. Inclusion criteria : osteitis pubis with favorable outcome under antibiotics.

Results : Twenty cases were analysed : 13 men, 7 women, aged 16-77 years. IOP followed surgical procedure of the pelvis or urinary tract (8/20), was post-traumatic (2/20), regional infection related (3/20), or of unknown origin (7/20). Two cases of diabetes and one chronic steroid treatment were present. Pain was constant, with a delay in diagnosis of over 1 month. Elevated ESR (15/20), hyperleukocytosis (6/20), positive cultures of blood (3) or urine (4) were found. X-rays modifications were constant. Cultures of suppurative scars were positive in 4 cases, whereas cultures of pubis biopsies were positive in 1 out of 9 cases (S-aureus). Mononuclear subacute osteomyelitis was found histologically in 5/9 biopsies, without suppurative or necrotic changes. Outcome was favorable in all cases under antibiotics in a period of 1 to 12 months. Spine or sacro-iliac extension occured in 3 cases.

Conclusion : IOP should be considered as a septic arthritis to reduce the delay in diagnosis and in instauration of targeted antibiotherapy.

M129

RHEUMATIC MANIFESTATIONS IN HIV INFECTION

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Rheumatic manifestations are reported in 50% to 70% of HIV patients.
Objective: To identify osteoarticular features in a HIV population.
Methods: Prospective study started in January 2000 involving patients who attended the Infectious Diseases outpatient clinic. The HIV infection was classified according to the 1993 CDC classification for this syndrome. Evaluation of the patients in the first visit included an interview and a clinical examination. The level of CD4+ T cell count was determined by flow citometry in each patient. 44 patients were evaluated: 33 males (75%) and 11 females (25%). Age range was 19 to 67 years (mean age: 37,2).
Results: 26 were HIV-positive (59%) and 18 have AIDS (41%). 39 were HIV 1 positive (88,6%) and 5 were HIV 2 positive (11,4%). Rheumatic manifestations occurred in 25 patients (56,8%): Fibromyalgia (36%); Regional rheumatic pain syndromes (28%); Back pain (20%); Painful articular syndrome (12%); Lower limb arthritis (12%); Raynaud's syndrome (4 %); Sicca syndrome (4%). The CD4+ T cell count was below 200/µL in 62% of patients with rheumatic manifestations. The fibromyalgia patients were treated with magnesium and amitriptyline. The pain in the regional rheumatic syndromes respond to anti-inflammatory medication and/or intra-articular steroids.
Conclusions: Rheumatic manifestations are very common in HIV infection. Usually they are benign and respond to anti-inflammatory medication. The CD4+ T cell could be important in the pathogenesis of the rheumatic involvement.

M130

SEPTIC ARTHRITIS. A REPORT OF 45 CASES.

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Objective : to study clinical , epidemiological and evolutive data of septic arthritis (SA) in Rheumatology in Africa.
Material and methods:
Type of the study : retrospective (1983-2000). Criteria for inclusion: bacteriological confirmation in or out the joint, healing under antibiotics treatment without any relapse after one year.
Results : 45 patients were included. Mean age: 45,8 ± 19,5 years [15-81]. Sex Ratio W/M: 1,8. Mono-arthritis were noted in 33 cases (73%), oligo-arthritis in 9 cases (20%) and polyarthritis in 3 cases (7%). SA most often involves the knee (57%). Predisposing factors were dominated by steroid infiltration (25%), diabetes mellitus (20%). The germ has been recovered in the joint in 60% of cases (27/45). Staphylococcus aureus is the most common (37%) . 8 gonococcal arthritis were found . SA was decapitated by a previous antibiotics treatment in 11 patients. The diagnostic delay (mean delay of 14 days) explained the high frequency of the severe radiological lesions in 77,5% of the cases. Except for gonococcal arthritis, the treatment associated parenteral use of two-antibiotics for 4,5 weeks. Joint washing was necessary for 6 patients. As sequelae, joint effusion in 4 cases, flessum and secondary osteoarthritis in 3 cases were noted.
Conclusion: SA are frequent in underdeveloped countries. Their remaining high incidence underlines the obvious necessity of education for patients and for GP who may have, to take care of rheumatic patients and who often (mis)use corticoid infiltrations.

M131

SPINAL EPIDURAL ABSCESS

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Spinal epidural abscess is a rare localization of the central nervous system infection . It is a diagnostic and therapeutical emergency. Potential deterioration with clinical neurological deficit may be fully
reversible with an early aggressive treatment. We report one case.

Observation : L. K, a nineteen years old woman , right- handed , is inadmitted for paraplegia associated with inflammatory spinal pains, tenderness and fever .MRI revealed a spinal epidural and muscular abscess. Surgery was performed for diagnosis (presence of staphylococcus aureus) and medullary decompression .The evolution was favourable with antibiotics .

Discussion : Spinal epidural abscess is a rare infectious disease. Because of the absence of specific clinical signs, diagnosis may be late. MRI allows the best imaging study.

M132

MULTIPLE INFECTIOUS ARTHRITIS.

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Objective : to study clinical, biological, radiological features and evolution of multiple infectious arthritis.

Material and methods : Type of study : retrospective. Studied period: 1983-2000.
Criteria for inclusion: arthritis involving more than 2 joints with bacteriological confirmation.

Results : 7 men and 4 women were included. The average age was 41 ± 19 years (16-65). Joint involvement realized biarthritis in 5 cases, oligoarthritis in 3 cases, ploy arthritis in 3 cases. The knee was the most commonly affected joint. The average period for diagnosis was 14 days. Risk factors were diabetes mellitus (n=3), corticoid infiltration (n=2), rheumatoid arthritis (n=1), pregnancy (n=1). Bacteriological confirmation was obtained in 7 cases. Isolated microrganisms were gonococcus (n=5), staphylococcus aureus (n=1), and streptococcus B (n=1). All the patients received antibiotics. The average period for the treatment was 3.5 weeks (2- 8 weeks). Joint lavage was performed in 3 patients. 5 patients had functional sequelae : joint effusion (n=2), flessum (n=2), osteoarthritis (n=1).

Conclusion : multiple infectious arthritis occurs in about 24% of septic arthritis. This high incidence is related in our serie to the diagnosis delay, the incidence of gonococcal infection (50%), high incidence of corticoid infiltration in a non rheumatological practice , and diabetes mellitus. An early diagnosis and treatment are of obvious importance.

M133

Les manifestations articulaires du VIH

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76 patients séropositifs, infectés par le virus de l'immunodéficience humaine (VIH) représentant 90% des atteintes articulaires, ont été hospitalisés du 1er janvier 1993 au 31 décembre 2000 dans le service de Rhumatologie du CHU de Brazzaville pour une oligo ou une polyarthrite. Le VIH représente en effet la 1ère cause des arthrites inflammatoires et le 2ème motif d'hospitalisation dans le service avec une séroprévalence de 7-8% de la population au Congo -Brazzaville.

Résultats : 76 patients : 39 hommes et 37 femmes, extrêmes :19 à 70 ans, moyenne d'âge = 37 ans, tous hétérosexuels. Les manifestations articulaires sont : la polyarthrite = 59 cas (70%), l'oligoarthrite = 17 cas (20%) et l'arthrite septique = 8 cas (10%). Les arthrites siègent sur le genou : 90%, la cheville : 65%, le poignet : 45%, le gros orteil : 34%, le coude : 30%, les IPP, MCP et autres MTP : 29%. Tous les malades (100%) sont au stade IV - CDC: IVC2=52%, IVA= 34%, IVC1= 8%, IVB2= 5%, IVB1= 1%. Il existe un important syndrome inflammatoire avec une VS supérieure à 100 mm à la 1ère heure dans 90% des cas.

Conclusion : Les manifestations articulaires du VIH sont représentées essentiellement par une polyarthrite (78%) ou une oligoarthrite (22%), parfois inaugurale, à distribution grossièrement symétrique, touchant les grosses et petites articulations des 4 membres, non destructrice. L'atteinte du gros orteil est très évocatrice chez un sujet jeune, amaigri et fébrile. L'évolution est lentement régressive en 4-8 semaines sous AINS. Les corticoïdes ne sont pas plus efficaces.

M134

THE ROLE OF VIRAL INFECTION IN DEVELOPMENT OF ARTHRITIS IN LYME BORRELIOSIS AND OTHER RHEUMATIC DISEASES.

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Objective: To evaluate wheather a viral infection is associated with arthritis in Lyme borreliosis (LA) or another rheumatic disorders A total of 140 synovial fluid samples (SF) from adult patients with LA and various rheumatic disorders were tested.

Rationale: Electron microscopy (ELM) is a powerful tool for the investigation of infectious processes. It is widely applied in the diagnosis of viral illnesses, but can be used to detected infections with other agents such as bacteria, mycoplasmas, and fungi.

Methods: Direct electron microscopy was used. The 300 - mesh copper ELM grids pre-coated with Formvar and carbon were floated on the viral suspension for 20 min. Stained grids were examined with a JOEL 100 CX transmission electron microscope.

Results: Viral particles of the families Herpesviridae,Picornaviridae, Parvoviridae and Paramyxoviridae were detected in 59 SF. In 28 SF from a total of 97 patients with LA Herpesviridae and in 2 Parvoviridae were detected. Only in 9 cases an acute infection of herpesvirus was proven.. Another presence of herpesvirus in 21 SF was probably due to pathogenic effect of Borrelia burgdorferi The Herpesviridae were found in 13 SF and Picornaviridae in 12 SF of the patients with other rheumatic disorders.The Parvoviridae and Paramyxoviridae were found only in 2 SF. The results were confirmed by Solid-Phase Immune Electron Microscopy(SPIEM)

This work was supported by grant NI/6128-3 IGA of Czech Ministry of Health.

M135

RHEUMATIC MANIFESTATION IN PATIENT WITH RECENT CMV INFECTION

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Objective: Purpose of this report, is the description of a patient, with CMV infection and oligoarthritis.

Rationale: It is well known that viral infections could appear with Rheumatologic manifestations as arthritis, polymyositis, vasculitis e.t.c. Parvovirus, B19, Rubella virus, RNA viruses, alpha viruses, Coxsackie's, enteroviruses, picorna viruses, HBV, HCV, HIV, Ross river virus, EBV, rubeola but more often arthralgies and myalgia occur.

CASE REPORT: We present a young adult 20years old, who came to our department with fever and asymmetric oligoarthritis of right elbow, left wrist and right knee joint. It's personal history was free. Patient suffered from sorethroat and in physical examination, tracheal and inguinal lymph nodes were enlarged.At the same time an acne like rush spread through back, face, thigh, knees, elbow and to a lesser degree through the trunk. In some places lesions were confluent and hemorrhagic. His general condition was good during his hospitalization. Laboratory data was negative, except from high title of IgM, Abs of CMV virus in patient's serum. From dermatologic lesion biopsy, typical data of leukocytoclastic Vasculitis was found. Patient was treated with roxythromycine with great improvement of arthritis and dermal lesions. In two months time, title of IgM Abs decreased whether IgG title of CMV was increased.

Conclusion: We presented a case report of a young, non-immunosupressed patient with CMV infection, oligoarthritis and leukocytoclastic vasculitis, as well as it's impressing therapeutic result. Although CMV is a common virus until now very little cases have been reported. Consequently, in cases with fever associated with oligo or polyarthritis we should exclude the possibility of viral infection.

M136

INVOLVMENT OF LOCOMOTOR SYSTEM IN LYME BORRELIOSIS

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Objective: To evaluate symptoms of locomotor system and response to the treatment in Lyme borreliosis.
Methods: Complaints and clinical symptoms of 49 patients with Lyme borreloisis were analyzed.
Results: Symptoms from locomotor system were observed in 36 (73,5%) patients – arthralgia in 19 (38,8%) and arthritis in 17 (34,7%).Knees joints were the most common site of arthritis (13/17), in 3 cases small joints of hands were involved. 8 (16,3%) patients had recurrent or permanent effusion in knee joints. High titers of IgG antibodies against Borrelia burgdorferi by ELISA in serum or/and synovial fluid were detected in all cases of arthritis. In 5 cases the diagnosis was confirmed by PCR.All patients recived antibiotic therapy (Doxycycline or Amoxycilline or Ceftriaxon) for 30 days.
Due to recurrence or persistence of arthritis in 13 cases antibiotic therapy was repeated after 1 – 3 months interval.
In 4 patients with recurrent knee effusion hypertrophy of synovium 6 knee joints synovectomies were performed with good result.1 person presented borrelial lymphocytoma on ear lobe.
Conclusions: In Lyme borreliosis recurrent arthritis despite antibiotic treatment is quite common and requires repeated antibiotic courses or synovectomy.

M137

PATTERN OF BONE and JOINT TUBERCULOSIS IN CIPTO MANGUNKUSUMO HOSPITAL JAKARTA - INDONESIA

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Objective: To assess the pattern of bone and joint tuberculosis in Ciptoo Mangunkusumo Hospital-Jakarta.
Method: A retrospective study on 118 medical record was reviewed between Jan 1994-Dec 1999 for bone and joint tuberculosis.
Result: Among 118 patient of bone and joint tuberculosis 68 was male(58%) and 50 female (42%).The mode of patient lies within < 400 years 90 (81%), 58 (49%) patients accompanying with pulmonary tuberculosis and 60 (51%) patients without any evidence of lung involvement . Five (8,6%) patients with miliary tuberculosis and 15 (15,7%) patients with others extrapulmonary tuberculosis manifestationn i.e.meningitis,pleural effusion, lymphadenitis, colitis, peritonitis and paravertebral abcess.Only 20 (17%)patients with positive mantouxt test (recal antigen). None of patient with history of steroid user and 33 patients with diabetes and 1 patient with hepatic cirrhosis. The mostt common site affected in these patient on thoracal vertebrae 82 patientss (71,19%) and lumbar vertebrae 54 (45,76%) . Twenthy two (18,64%) patients was affected at lumbar 1 level and 21 (17,79%) patients att thoracal 12 level. About 30 (51,52%) patients with pulmonary involvement underwent the examination acid fast bacilli and 3 patientss demonstrate positive result.
Conclusion: Bone and joint tuberculosis was most affected in male, at productive age. Lumbar 1 and thoracal 12 level of the vertebrae was the most affected site. The incidence of patient with pulmonary tuberculosis compare to tuberculosis without pulmonary involment was appropriate equal.

M138

ASYMPTOMATIC GASTROCNEMIUS MUSCLE BIOPSY: AN EXTREMELY SENSITIVE AND SPECIFIC TEST IN THE PATHOLOGIC CONFIRMATION OF SARCOIDOSIS PRESENTING WITH HILAR ADENOPATHY.

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Objective: To evaluate asymptomatic gastrocnemius muscle biopsy as a tool in the histologic confirmation of the diagnosis of sarcoidosis.

Methods: Twenty two patients, admitted over a two year period to our department, with bilateral hilar adenopathy and a variety of symptoms compatible with sarcoidosis, were studied prospectively. Besides a complete history, physical and routine laboratory, serum angiotensin converting enzyme (SACE) determination, pulmonary function, slit lamp eye examination, PPD skin test, gallium 67 scan and gastrocnemius muscle biopsy under local anesthesia, after informed consent, were performed.

Results: The biopsy revealed non caseating granuloma in all the patients, confirming the diagnosis of sarcoidosis. No other patient in our department received this diagnosis over the two year period of the study. The procedure was well tolerated by all patients and almost zero morbidity was noted. Erythema nodosum was present in 68.2% of the patients, PPD was negative in all of them, SACE was elevated in 59.1% and pulmonary function was normal in the majority.

Conclusion: The impressive sensitivity of the employed biopsy, its safety and ease of performance, along with the extreme rarity of muscle involvement by other granulomatous diseases, included in the differential diagnosis, may render it the procedure of choice for the histologic confirmation of sarcoidosis, presenting with hilar adenopathy.

M139

RHUPUS SYNDROME: A REPORT OF 2 CASES

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Rhupus syndrome was describe in 1988 by Panush. It is characterized by an overlap between Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE). Usually appears in woman and have a good prognosis. The authors reported 2 cases of this overlap syndrome. Case 1: 45 years old woman with chronic symmetric polyarthritis, malar rash, photosensitivity, oral ulcers and immunological disorders: raised antinuclear antibody (ANA) and antinative DNA antibody binding. The title of ANA was 1:320 with a homogenous pattern. The X-ray showed osteopenia, erosive arthritis involving several metacarpophalangeal (MCP) and proximal interphalangeal joints (PIP) of both hands. The symptoms improved with sulphasalazine (2g/day), prednisone (7,5mg/day) and hydroxychloroquine (400mg/day).
Case 2: 45 years old woman with a history of monoarthritis of the right wrist since she was 23 years old. Six months ago she's started with symmetric polyarthritis involving hands (several MCP and PIP joints) and feet (metatarsophalangeal joints). At the same time the physical examination showed malar rash and photosensitivity. The laboratory: positive rheumatoid factors test, positive ANA (homogenous;1:320) and raised antinative DNA antibody binding. The X-ray showed osteopenia, erosive arthropathy involving the MCP joints, the PIP joints and the fifth metatarsophalangeal joint. She's asymptomatic with prednisone (7,5mg/day) and hydroxychloroquine (400mg/day). Conclusion: This overlap syndrome is very rare. The diagnosis is based in the ARA Classification Criteria for both diseases. The treatment and prognosis differ from patients having RA or SLE alone.

M140

EXTENSIVE MULTIPLE ENCHONDROMATOSIS

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Extensive multiple enchondromatosis (ME) is a rare bone disease characterized by the development of multiple chondromas in the bones. We report a case with main radiological aspects. Evolutive risks and therapeutic difficulties are discussed.

Case report: A 40 year-old woman was admitted in our department in 1998. She was complaining of diffuse bone pains for 10 years. Clinical exam showed limb deformities. Radiographs showed multiple large lacunas blowing long and tubular cortical bones in hands and feet extensive through the past 10 years. The histological exam confirmed enchondromatosis. The treatment was only symptomatic.

Discussion: A predominance of radiological aspects in tubular bones in hands, feet and long bones metaphysis with micro-calcifications suggests ME , as in our case. This disease exposes to malignancy transformation risk which asks for regular examination. Regular extensive involvement of the bones remains rare. The treatment is only symptomatic.

M141

COXITIS IN CROHN'S DISEASE (Report of 3 cases)

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Destructive lesions of the hip are rare in Crohn's disease. Clinical , radiological and evolutive data of coxitis in Crohn's disease are reported about 3 cases.

Case report. 1 : S.L., 15 years old girl, treated with Salazopyrine for Crohn's disease since the age of 10 years. A chronic polyarthritis appeared 3 years after the beginning of digestive symptoms. Clinical exam showed multiple synovitis and a limitation of the hip movements . X-rays showed bilateral destructive coxitis. The evolution was favourable under glucocorticoid therapy and rehabilitation.

Case report 2 : K.K. , 43 years old woman, is affected since the age of 17 years by a Crohn's disease associated with erosive polyarthritis. X-rays showed a triple rail pattern at the spine, synostosis of the hips and destructive lesions of several articulations. The evolution was unfavourable in spite of symptomatic therapy.

Case report 3 : Z.K., 58 years old woman, is affected since the age of 41 years by a Crohn's disease associated with a spondylarthropathy. Clinical exam showed a painful limitation of the hips movements. X-rays showed bilateral destructive coxitis. The patient was treated by salazopyrine and diclofenac; the evolution was favourable.

Discussion : Coxitis in Crohn's disease may be destructive (obs.1 and 3) or synostosant (obs. 2), isolated or associated to a spondylarthropathy. Symptomatic treatment may control the disease. However, synoviothesis is often needed as well as hip prothesiswhen disability becomes severe (case report 2)

M142

CHEIROARTHROPATHY IN DIABETES TYPE 1.
Report of a case.

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Cheiroarthropathy may complicate badly controlled type 1 diabetes. It may be frequent in childhood and adolescence. We report one case.

Observation: A.A., a 16 years old boy, treated with insulin for type 1 diabetes mellitus since he was 4 years old. 4 years later, he presented with arthralgias associated and low back pain, hands and feet stiffness. The physical exam showed height and weight backwardness, bilateral elbow and knee flessum and a retraction of the fingers and the toes. The skin was thickened. Biological and radiological investigations were normal. The skin biopsy showed thickening and fibrous infiltration of the skin. The evolution was favourable with diclofenac and naftidrofuryl.

Conclusion: There is no specific treatment for cheiroarthropathy, but this syndrome should be carefully investigated because of possible microvascular complications.

M143

RELAPSING POLYCHONDRITIS – A CASE SERIES FROM SINGAPORE

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Introduction: Relapsing polychondritis (RPC) is a rare systemic inflammatory disorder, characterised by recurrent inflammation of cartilaginous tissues that may potentially be debilitating and life threatening. RPC has been described mainly in Caucasian populations. Reports from other ethnic groups are lacking.

Objective: To study the clinical characteristics, management and outcome of RPC patients seen in an Oriental population.

Method: The case notes of RPC patients treated in the department from 1989 to 2001 were reviewed. Among 10 patients treated as RPC only 8 fulfilled the diagnostic criteria suggested by Damiani and Levine and these were studied.

Results: Although most previous studies reported an equal sex distribution, the female-to-male ratio in our series was 3:1. There were 6 ethnic Chinese and 2 Malay patients. The age of onset of symptoms range from 3 to 43 years, with a median of 30 years. A diagnosis was made from 2 weeks to 3 years after onset, with a median of 6 months. There were 7 patients with auricular chondritis, 4 nasal chondritis, 5 ocular inflammation, 5 vestibular symptoms or reduced hearing, 7 articular involvement, 5 laryngotracheal involvement, and 4 associated with fever. None of the patients had valvular, cutaneous, renal or central nervous system involvement. Six had raised ESR at presentation. One patient developed DLE 2 years later. All 8 patients received prednisolone but only 2 did not require additional immunosuppressants. Two patients had resistant disease failing to respond adequately to azathioprine, methotrexate, cyclophosphamide (oral or IV), cyclosporin, mycofenolate mefotil, chlorambucil, and intravenous immunoglobulin in various combinations together with prednisolone. None of the patients died. Four of the 5 patients with laryngotracheal involvement had tracheostomy and 1 of them had airway stenting as well.

Conclusion: Our series suggests that the clinical manifestations of RPC are similar in the Oriental and the Caucasian populations.

M144

CLINICAL STUDY OF CHORESTEROL SHOWER EMBOLI

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Objective: Cholesterol shower emboli has been well-known a high mortality and morbidity and often misdiagnosed for the collagen diseases because of systemic disorders and clinical features. We examinated the clinical features in cholesterol shower emboli cases to evaluate the early diagnosis and effects of steroid therapy.

Materials and Methods: We described five males cases developed acute renal failure (ARF) as a result of cholesterol embolism. In three cases, cholesterol embolism occurred after the angiographic procedures and two cases were onset spontaneously. These cases had eosinophilia, positive reaction of autoantibody, livedo, hypertension, and ARF. There was no case with positive reaction of MPO-ANCA. The diagnosis was based by skin biopsy and clinical features. Two cases were treated with methylprednisolone pulse therapy and plasma exchange and these renal function were improved. In two cases treated with prednisolone therapy only, these renal function were not recovered and became maintenance hemodialysis (HD) therapy. In one case with HD therapy only, he died by interstitial pneumonitis, 20 days after.

Results: This disease was misdiagnosed for vasculitis because of eosinophilia, fever, positive reaction of autoantibody and livedo, in spontaneous cases especially. The skin biopsy was useful for the definite diagnosis. The prognosis of cholesterol embolism with ARF has a poor outcome. In case without fully therapy, his prognosis was poor. In cases with intensive care, they survived and well outcomes.

Conclusion: These clinical data suggests that the skin biopsy is useful tool for diagnosis and intensive care schedule may reduce the mortality of patients with multivisceral cholesterol shower emboli.

M145

OSTEOPOIKILOSIS: REPORT OF A CLINICAL CASE AND REVIEW OF THE LITERATURE

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Osteopoikilosis is an uncommon benign sclerosing bone dysplasia. Herein we report a 45-year-old man with characteristic roentgenographic findings of osteopoikilosis and clinical findings of cervical myelopathy. The importance of the differential diagnosis in symptomatic cases of osteopoikilosis is emphasized with the review of the literature.

M146

THE EFFICACY OF ELECTROMAGNETIC FIELD TREATMENT IN DIABETIC DISTAL SYMMETRIC POLYNEUROPATHY.

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Objective: To evaluate the efficacy of electromagnetic field treatment(EFT) in patients with diabetic distal symmetric jkx polyneuropathy.
Rationale: EFT affects the cell metabolism stimulating Na+/K+ pump at cell membrane level; increases oxygen content of tissue and blood flow. It gains analgesia and stimulates tissue repair agent.
Methods: 46 Type II diabetic patients with distal symmetric polyneuropathy were entered this research. Patients were randomized between control (placebo) or EFT group. Treatment was given for 8 weeks. All patients were assessed before the treatment, after the treatment and three months later then the treatment by thermal sensoryal analyzer, Michigan Neuropathy Screening Instrument (MNSI), grading pain reproduced from Kumar and Marshall, Nottingham Health Profile (NHP) parameters.
Results: In the EFT group, cold sensation threshold ($p<0,05$), cold pain threshold ($p<0,01$), MNSI questionnare ($p<0,001$) and form ($p<0,01$), pain scoring values ($p<0,01$), pain ($p<0,001$), physical activity and sleep ($p<0,05$) subgroup of NHP showed significant improvement after the treatment. It's effective was significant statistically after 3 months.When compared with the control group, EFT didn't showed significant improvement.
Conclusion: In diabetic distal symmetric polyneuropathy treatment, placebo and EFT didn't showed superiority to each other

M147

OSTEONECROSIS OF FEMORAL HEAD IN PATIENT WITH FAMILIAL HIP DYSPLASIA AND HASHIMOTO THYROIDITIS

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Objective: The case of a patient with familial hip dysplasia, Hashimoto thyroiditis and dyslipidemia in whom the presenting aseptic necrosis of femoral head.

Rationale: Aseptic necrosis or osteonecrosis is a cellular death of bone minerals. Osteonecrosis is not concerned of a disease of itself, but the outcome in pathologic manifestations, group of which aim at the arterial web of the bone.Diseases related to aseptic necrosis are: SLE, Rheumatoid Arthritis, hemoglobinopathies, trauma extended or not, Weber-Christian disease, alcoholism, corticosteroid abuse, atheromatosis, diabetes mellitus, disturbances in lipid turnover, familial dysplasias, lipoid infusion of liver, hyperuricemia e.t.c.

CASE REPORT: A female patient, agent 60 year's, mother of 4 children with Hashimoto thyroiditis, been in menopause last 10 years, who is treated with thyroid hormone replacement therapy, for 5 years after thyroidectomy. Her personal previus history includes dyslipidemia type IV according to Frederickson and familial dysplasia of right hip (coxa plana I).Her problem occurred 8 months before with pain of the right hip and no restriction in movement at the beginning, sharp pain reminded of sciatica with knee referance, deteriorating with time, independent from movement and position. Poor improvement was noticed after administration of analgesics or NSAIDs, there was additional pain in movement and after some months, movement disability, shortened leg and rotational movements disappeared. Patient underwent MRI and total arthroplasty followed by excellent result.

Conclusion: Aim of our presentation is the coexistence of many causative agents in the diagnosis, as well as the help of MRI in diagnosis of aseptic necrosis.

M148

PREVALENCE OF RHEUMATIC MANIFESTATIONS IN DIABETIC PATIENTS IN A CLINIC SPECIALIZED IN RHEUMATIC DISEASES (GUATEMALAN ASSOCIATION ANTI RHEUMATIC DISEASES: AGAR)

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Objective: To evaluate the frecuency of musculoskeletal manifestations in diabetic patients seen at our clinic from January to December 2000.

Rationale: It has been described an increased number of rheumatic manifestations in diabetic patients in comparison with normal population.

Methods: During the year 2000, 500 patients non diabetic consulted for musculoskeletal complaints, among these we found 22 diabetics (4,4%), all 22 type II (100%) 16 (73%) controlled with po hypoglicemic drugs, 2 (9%) with subcutaneous insulin. 15 (68%) were females, median age 48 range (15-38), 13 (59%) had osteoarthritis, 3 (13,6%) with flexor tenosynovitis of hands, 1 (4,5%) frozen shoulder, myofasceitis 1 (4,5%), talalgia 2 (9%), polymyalgia rheumatica 1 (4,5%) with psoriatic arthritis.
Among this group, 8 had diabetic peripheral neuropathy (36,3%)

Conclusion: Rheumatic manifestations are frecuent in diabetic patients ussually associated with peripheral neuropathy which makes diagnosis of the late difficult.

T1

WITHDRAWN

T2

INCREASED CCR4 EXPRESSION IN ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS.

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Objective: To determine the clinical relevance of the expression of CCR4 in active systemic lupus erythematosus (SLE).

Rationale: CC chemokine receptor (CCR) 4 is selectively expressed on Th2-type T cells, and has been shown to be responsible for Th2-dominant immune responses.

Methods: CCR4 expression was examined on peripheral blood CD4+ T lymphocytes of patients with SLE and healthy controls by FACS analysis using anti-human CCR4 monoclonal antibody.

Results: Higher expression of CCR4 was found on peripheral blood CD4+ T lymphocytes of active SLE patients than healthy controls and inactive SLE patients. The CCR4 expression significantly correlated with the SLE disease activity index (SLEDAI) scores. The expression was dramatically decreased after the corticosteroid therapy using high dose prednisolone in parallel with serum level of double-stranded DNA antibody and SLEDAI scores. Moreover, we found that serum levels of IL-10, a Th2 cytokine, were increased in active SLE patients, and significantly correlated with the CCR4 expression.

Conclusion: This study suggests that Th2 immune response is predominant in the active state of SLE, and CCR4 may have relevance in regard to the disease course in SLE patients.

T3

ROLE OF LEUCOCYTES IN HEMORHEOLOGY AT A SYSTEMIC LUPUS ERYTHEMATOSUS

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The purpose: Studied resistance of leucocytes to a tension in mediums with low osmotic and there regulator opportunity for an ill systemic lupus erythematosus (SLE).

Methods: Explored a blood from a ulnar vein for 36 women from with SLE, medial age - 37 years. For learning kinetics of a bloating and osmoregulatory responses on 10 mkl of a concentrated suspension of leucocytes positioned in test tubes of volume 2 mls, added îî100 mkl of one of solutions NaCl (0,9 %, 0,45 %, 0,2 %) and calculated volume of white blood cells.

Results: In hypoosmotic medium (0,45 %) at an exacerbation for ill SLE is marked the expressed bloating of granulocytes (398,6±161,7; p ‹ 0,05) and agranulocytes (163,9 ±10,4; p < 0,05) as contrasted to by check, that obliquely points augmentation of a passive permeability of a membrane caused by inflammatory processes which are flowing past in a connecting tissue. At an incubation till 1 hour volume of these cells is reduced worse (239,3 ±17,5; p < 0,05 and 124,6±8,6; p < 0,05), than in the check.

Deductions: The disorganization of a connecting tissue (SLE) is attended by changes of osmoregulatory responses of leucocytes, the infringement of their ability to strain and, therefore, watches rheological infringements influential on " leukocyte plugging ".

T4

ANTICARDIOLIPIN ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: To evaluate the presence and the relation between high levels of IgA isotype of anticardiolipin antibodies (ACA) and systemic lupus erythematosus (SLE) and their association with increased thrombotic risk.
Rationale: Antiphospholipid antibodies, including anticardiolipin antibodies and lupus antikoagulant (LAC) are associated with a prolongation of partial thromboplastin time and with tendency of thrombosis, strokes, recurrent miscarriages and thrombocytopenia. They were among the first serologic abnormalities found in SLE and antiphosholipid syndrome, especially moderate to high levels of IgG and IgM ACA.
Methods: IgA ACA were assayed by an enzyme linked immuno-sorbent assay (ELISA), using the modified method by Smolasky in 49 patients with SLE and 40 healthy volunteers as controls.
Results: Elevated IgA ACA were found in 14 out of 49 (28,57%) patients with SLE, compared to 1 out of 40 (2,5%) positive sera (in small titer) in the control group. The difference between IgA ACA titers of SLE patients and normal human sera was statistically significant (p=0,000). Among the 14 patients with elevated levels of IgA ACA 2 had different vascular complications. One female patient developed mesenteric venous thrombosis with acute abdomen and one had deep leg venous thrombosis.
Conclusion: The presence and the association of elevated levels of IgA ACA and thrombotic complications in SLE patients may suggest that IGA ACA could be involved in pathogenic mechanisms of developing vascular complications in those patients, although is considered that IgG and IgM isotypes are more specific for increased thrombotic risk in SLE.

T5

SUPPRESSION OF EXPERIMENTAL SLE IN MICE BY AN ANTI-TNFα MONOCLONAL ANTIBODY or BY PENTOXIFYLLINE.

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We have previously shown that the clinical manifestations of experimental systemic lupus erythematosus (SLE) correlate with an early increased production of the proinflammatory cytokines TNFα and IL-1. In the present study, we examined the efficacy of two therapeutic modalities which lower TNFα production, on the clinical manifestations of mice afflicted with experimental SLE.

Experimental SLE was induced in naive C3H.SW mice by priming and boosting with the human monoclonal anti-DNA antibody that bears the common idiotype, 16/6 Id. The latter was previously shown to induce in mice an SLE like disease that resembles lupus in patients in its serological and clinical manifestations. Two weeks after booster injections, treatment with either an anti-TNFα monoclonal antibody (mAb), or pentoxiphylline (PTX) was started. Anti TNFα was given twice a week (50 µg/mouse) and PTX daily (100 µg/mouse) both for a period of 6 weeks. Production of TNFα (by splenocytes) and IL-1 (by peritoneal macrophages) was determined 3 and 7 months after disease induction. The experimental mice were also followed for disease manifestations.

Both anti-TNFα mAb and PTX treatments reduced the production of the two proinflammatory cytokines, TNFα and IL-1 in mice with experimental SLE. Anti-DNA antibodies were significantly lower in the mice treated with both anti-TNFα therapeutic protocols. In addition, the latter had significant beneficial effects on the clinical manifestations tested including leukopenia, proteinuria and immune complex depositions in the kidneys of the treated mice.

Conclusions: Abrogation of TNF α and IL-1 production in the early stages of experimental SLE by anti-TNFα mAb or by PTX improves the clinical status of mice afflicted with this autoimmune disease.

T6

DOWNREGULATION OF EXPERIMENTAL SLE AND APS BY TNFα DNA VACCINATION

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Naked DNA encoding TNFα was introduced to BALB/c mice with experimental SLE induced by 16/6 Id and to mice with experimental APS induced by β2GPI. Administration of naked DNA encoding TNFα resulted in the generation of immunological memory to its gene product. Upon induction of either SLE or APS, this memory inhibited the development of high titers of anti-ssDNA anti-histones and antiphospholipid and anti-β2GPI antibodies (32%-41% reduction as compared to the untreated group vaccinated with control naked DNA) in experimental lupus. Downregulation of TNFα in the mice with the autoimmune conditions affected the balance between Th1/Th2 cytokines by suppression of IL-4 and IL-10 expression.. Administration of TNFα DNA construct led to amelioration of the clinical manifestations of experimental lupus and experimental APS. The murine anti-TNFα antibodies which developed in the DNA vaccinated mice and could adoptively transfer the beneficial effect of the vaccine to other mice with the disease.

T7

CD31 (PECAM-1) DEFICIENCY ACCELERATES LYMPHADENOPATHY AND AUTOANTIBODY PRODUCTION IN MURINE LUPUS

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Objective: CD31 or platelet-endothelial cell adhesion molecule-1 (PECAM-1) is expressed by endothelial cells, platelets, neutrophils, and lymphocytes. CD31 has been postulated to play a role in transendothelial migration of leukocytes and negative regulation of T cell signaling. We investigated the role of CD31 in murine lupus.

Methods: CD31-deficient mice were backcrossed into MRL/lpr mice for 6 generations. Lymph node cellularity, spleen size, and cell populations were analyzed. Autoantibodies were measured by ELISA. Pathology of kidneys and lungs were examined.

Results: CD31-deficient mice showed accelerated lymphadenopathy and splenomegaly at 18 wk of age. Cell populations did not differ between CD31-deficient and wild-type mice. Anti-dsDNA antibody levels of IgG2a class were increased in CD31-deficient mice. Renal and pulmonary disease was similar in both types of mice.

Conclusion: CD31, besides playing a role as an adhesion molecule, regulates lymphocyte activation and anti-dsDNA antibody production in MRL/lpr mice.

T8

ANTI-TOPOISOMERASE I ANTIBODY IN PATIENTS WITH SLE WITHOUT SCLERODERMA

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Case Report:
The sera of two patients with classical SLE and secondary sicca syndrome were repeatedly tested positive to topo I antibody by anti-Scl-70 specific ELISA following a positive screening by ANA ELISA (ANA-EIA). Both patients had no clinical evidence of scleroderma (SSC). One patient remains well nearly three years from the first positive serological test, while the other expired after developing renal and cardiopulmonary complications including Libran sacks endocarditis and pulmonary hypertension.

There are only four cases of SLE previously reported in the English literature with positive anti-topoI without features of scleroderma. Also, there are very few reports describing cases of SLE-SSC overlap who tested positive before the onset of SSC suggesting that anti-topoI in SLE may predict the future development of SSC.

Conclusion
The cases presented here and those previously documented are therefore unique in the sense of being a serological challenge to the high specificity of anti-topo I to SSC. In addition, they may also represent a new subset of SLE which is characterized by the absence of features of SSC despite the presence of anti-topo I antibody. Further studies are necessary to examine these postulates.

T9

RELATION BETWEEN PATHOLOGIC CHANGE OF LUPUS NEPHRITIS AND ITS CLINICAL MANIFESTATION

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Objective: To investigate the relation between pathologic features of lupus nephritis (LN) and its clinical findings.
Rationale: Most lupus patients have some clinic and pathologic evidence of renal involvement
Methods: The renal biopsy was made in 47 systemic lupus erythematosus (SLE) patients and 6 types were classified. Then the correlation between pathological features and clinical findings was analyzed.
Results: II, III and IV type LN was often clinically active, but V type LN was inactive. In IV type LN, there was high incidence of hematuria and renal insufficiency. On the other hand, severe proteinuria was found in V type LN. There was no relation between acute activity index of renal pathology and SLE clinical activity index. The same result was found in renal pathological acute activity index and anti-dsDNA antibody levels.
Conclusion: There is a relation between LN pathological change and SLE clinical manifestation, but their degrees are different.

T10

LATE ONSET LUPUS

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Aim: To analyze the clinical and immunological features of SLE with late onset.
Methods: We studied 30 pts (all were postmenopausal women), mean age- 60,8 yrs, mean duration disease- 75 months. 77% pts had 6 and more criteria ACR (1982) for SLE. SLEDAI were equal 25,3 balls.
Results: This study demonstrated that SLE pts with late onset exhibits peculiar clinical features: high frequency of joint involvement (100%- arthritis/ arthralgias), severity features such as nephritis or CNS dysfunction are less common. Malar rash, photosensitivity and pleuro-pulmonary syndrome observed in 50%, 47% and 40% corresponding. 1/3 pts had Raynaud's syndrome. ANF was positive in 77% pts, anti-DNA-in 54%, RF- in 40%. 50% pts had antiphospholipid antibodies, but definite syndrome Huges was diagnosed only in 17% pts. The longer was the postmenopausal period the more rare the renal disturbance and high activity of the disease was observed.
Conclusion: Late onset SLE in Russia tends to run a more benign course and rare major organ involvement.

T11

HEALTH STATUS PERCEPTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS. A STUDY OF 159 ITALIAN PATIENTS WITH AND WITHOUT NEUROLOGICAL INVOLVEMENT

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Objective: to assess health status perception in a large group of systemic lupus erythematosus (SLE) out-patients using MOS-SF-36 in comparison with patients affected by primary Sjogren's syndrome (pSS) or rheumatoid arthritis (RA) and to evaluate the relationships between disease activity and cumulative organ damage with particular reference to neurological involvement.
Patients and methods: 159 patients with SLE (mean age 49.53 years, mean duration of the disease 9.98 years), 70 with pSS, 80 with RA and 80 healthy controls were analyzed. Patients and controls were matched for age and sex. Health status was assessed by self-administered MOS-SF-36 questionnaire (Italian version). In the SLE group, disease activity has been evaluated by SLEDAI and cumulative organ damage has been investigated by SLICC-ACR. Neurological involvement has been rigorously assessed (by clinical and imaging tools) according to the recently published ACR-classification criteria (1999). The mean scores for each subscale of the SF-36 for patients with SLE were compared to those of the other group. Among the SLE group a comparison was also performed for the mean SF-36 scores between the patients with (NP-SLE) and those without neurological involvement. **Results**: Patients with SLE had a poorer global health perception compared to controls, pSS and RA patients. In particular SLE patients had lower scores than those with pSS in many subscales of SF-36 (with the exception of "vitality" and "mental health"). In comparison with RA, SLE patients proved to be more compromised only in the dimension concerning "role limitations : emotional problems" and "social function". Among SLE patients no correlations were found between SLEDAI and the mean scores derived from the subscales of SF-36. Conversely SLICC-ACR and patient's age did prove to be inversely related to many subscale scores of SF-36. Finally, NP-SLE patients had lower scores than those without neurological involvement in three subscales: "physical function", "role limitations: emotional problems", "pain". **Conclusions** : SLE (especially if NP involvement occurs) severely affects the patients' health status perception even more than pSS and RA, thus heavily conditioning their quality of life. Since SF-36 represents a simple, little time-consuming, valid and reliable instrument to evaluate QoL and because of its poor correlation with disease activity index, in a more patient centered perspective it should be routinely used in the follow-up of the disease.

T12

ANTICOAGULANT PROTEIN C SYSTEM IN SLE PATIENTS

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Objective: to evaluate the utility and sensitivity of ProC Global test in 17 SLE patients, in some cases with thromboembolic complications.
Rationale: Thromboembolic complications are often noticed in many SLE patients, mainly caused by lupus anticoagulant (LAC) or anticardiolipin antibodies (ACA). We used ProC Global test (ProC® Lobal, Behring Diagnostics GmbH) as very simple and inexpensive screening test of protein C system assessment for further detailed evaluations (AT, proteinC and S, factorV Leiden), which done separately are more expensive and take more time.
Methods: We included to the study group 17 SLE patients, 15 women and 2 men in age 21 to 63 years. Thromboembolic complications were previously observed in 7 patients: 2 had recurrent thrombophlebitis, 1 retinal thrombosis, 4 had recurrent fetal loss. Antinuclear antibodies were present in all patients, 100% had anti-dsDNA, 17,6% anti-RNA, 35,2% anti-SS-A, 5,9% anti-SM. ACA were present in 6 patients (35,2%), LAC in 3 (17,6%).
Results: In all analysed patients screening clotting times (prothrombin time - 15,1 ± 0,99sec., thrombin time 11,4 ± 0,65sec., aPTT 34,4 ± 1,2 sec.) and fibrynogen level (337 ± 56 mg/dl) were in the normal ranges. Diminished anticoagulant activity of whole protein C system was detected in 12 cases (70,6%) – mean value in normalized ratio (NR) 0,59 ± 0,19, normal NR 0,86 – 1,10. There was also statistically important decrease level of factor V (mean 18,53% ± 7; normal 70-140%) and VIII (mean 59,5% ± 26,2; normal 70-150%). The lowest factor VIII activity (15%) was detected in a patient with immunological thyreoiditis. No statistically significant correlation was found between the coagulation data and antibody or thromboembolic presence.
Conclusions: Most SLE patients have diminished activity of natural protein C system, which may be responsible for thrombotic episodes observed in these patients. ProC Global seems to be very useful and inexpensive test for detection of disturbances in the whole anticoagulant protein C system.

T13

WITHDRAWN

T14

TREATMENT OF LUPUS NEPHRITIS BY ANGIOTENSIN CONVERTING ENZYME INHIBITORS (ACEI) AND LOSARTAN.

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Objective: To clarify the efficacy of ACEI and Losartan on lupus nephritis.

Patients and methods: First we analyzed the usage of hypotonica in 302 patients (24 males and 278 females) with systemic lupus erythematosus (SLE). Then, patients with proteinuria who started hypotonica after the prednisolone (PSL) usage were evaluated on the changes of their blood pressure (BP), proteinuria and creatinine clearance (Ccr). We tried ACEI (Quinapril 10 mg/day or Temocapril 2 mg/day) and Losartan (50 mg/day) in 7 patients who had intractable proteinuria despite low serological lupus activities.

Results: Seventy three patients (24.1%) were taking hypotonica during their admission. There were no differences in the changes of BP and Ccr between patients with Ca antagonists (CA, group A, n=13) and patients with ACEI (group B, n=7), but more reduction in proteinuria was observed in group B ($p<0.0001$). In patients who took CA first and took ACEI later (n=5), there were no reductions in proteinuria before ACEI usage, however, ACEI reduced proteinuria significantly without the reduction of Ccr. Seven patients with ACEI and Losartan showed marked responses and the reductions of PSL, immunosuppressant, statins, and furosemids were available. In 2 patients, ACEI were discontinued due to cough, but Losartan alone was effective.

Conclusion: Inhibition of renin-angiotensin system is important in lupus nephritis. ACEI and Losartan might be a new therapeutic agent for lupus nephritis especially the patients without serological activities.

T15

RETINAL CHANGES AND ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS.

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Background: The incidence of retinopathy in systemic lupus erythematosus (SLE) and its relation to other clinical and laboratory manifestations of SLE are under debate. Great importance is placed on retinopathy in activity criteria according to the scoring system of SLEDAI.

Objective: The goal of the monocenter cross sectional study from the East Bohemian region is to clarify the problem according to the incidence of retinal changes of SLE, and evaluation of the disease activity in SLE according to the descriptors of the SLEDAI in patients with and without retinopathy.

Methods: The group under study consists of 60 SLE patients according to ACR classification (1982, updated 1997). One expert ophtalmologist examined the ocular fundi for the presence of retinal changes fulfilling the definition of the SLEDAI descriptor for visual disturbance, but without any information about other SLEDAI descriptors. Data obtained in SLE patients with and without retinopathy were statistically processed using Wilcoxon's test and Fisher's exact test.

Results: Retinopathy according to the SLEDAI definition was present in 9 (15%), and absent in 51 (85%) SLE patients. The values of the SLEDAI score in patients with retinopathy were significantly higher than in patients without retinopathy ($p < 0.001$). In SLE with retinopathy two other SLEDAI descriptors frequency was significantly more than in patients without retinopathy: arthritis ($p < 0.035$) and increased DNA binding ($p < 0.038$).

Conclusion: The incidence of retinopathy according to the SLEDAI definition in 15% (9/60) of SLE under study, and significantly higher values of the SLEDAI score in SLE subgroup with retinopathy were found. Data obtained also demonstrated that retinal changes of SLE may be significantly more frequent in SLE with arthritis and with increased DNA binding.

T16

THE CLINICAL FEATURES AND THE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS DEPENDING OF SEASON

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Objective: Evaluation of clinical features and activity of the systemic lupus erythematosus (SLE) depending of season in Republic of Moldova.

Rationale: The immune system, adrenocortical function with glucocorticoid secretion and anti DNA antibody level may be influenced by the seasons.

Methods: In the study were included SLE pts who were followed up during a 5 years period. The diagnosis were estableed according the 1982 ARA revised criteria for SLE. The activity by ECLAM score was calculed for each patient and entered into a computerized database. Each encounter was stratified according to the months.

Rezults: We studied 120 pts, 106 f. and 14 male, median age 41.6-1.2 yr. (range 16-63 years). All constitutional symptoms were assessed. The mean fatigue scores were high >1 without seasonal variation. From cutaneous manifestations only photosensitivity was higher in april (1.1+0.2) and lower october – november (0.12-0,1). Malar rash was higher in april and lower in august. Musculoscheletal, neurological and renal manifestations not was found seasonal. Mean ECLAM scores ranged between 4.3+0.9 in november and 8.3+1.2 in march. We did not find any seasonal pattern in the number of patients with ECLAM scores higher than 9. Level of ESR rate, white blood cell and platelet count, the partial tromboplasty time and anti-DNA antibodies showed some variation during the year but we were unable to show any seasonal pattern.

Conclusions: In our study it not was correlation between photosensitivity, systemic manifestations and during of SLE. The seasonal pattern in SLE were unable photosensitivity and activity of SLE but the severity of the disease may be found in individual SLE patients.

T17

LATE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (LOSLE) IN MEXICAN POPULATION: A CASE-CONTROL STUDY OF CLINICAL, FUNCTIONAL AND IMMUNOLOGICAL FEATURES.

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Introduction: LOSLE vary widely among published studies in different populations. This study was undertaken to characterize this subgroup of SLE patients.

Methods: Case records of all SLE patients who attended our Lupus Clinic between 1995- 2000 were reviewed. Patients with a disease onset beyond the age of 50 were recruited as cases, and < 50 years as controls. Clinical charts were reviewed by a single trained observer. Patients filled out several self-administered validated versions of the MEX-SLEDAI, severity of the disease (KATZ index), SLICC/ACR index, Spanish AIMS, HAQ-DI, BECK and global evaluations. Clinical data and new serological evaluation was obtained. Analysis: Descriptive statistics and non-parametric evaluations among groups. Significance was set at 0.05 level.

Results: Twenty five cases and 24 controls are reported. Three were male. Few differences were detected among groups. LOSLE patients had lower education (6.1 vs 9.8, p=0.03); lower movility (4 vs 2.8, p = 0.06); lower social function (2.5 vs 1.5, p=0.02); higher SLICC ACR (4.8 vs 3.4, p=0.03) and higher C3 levels (102 vs 87, p = 0.04) and lower DNA levels (139 vs 186, p=0.05). No differences were detected in functional, disease activity, comorbidity and treatment requirements.

Conclusions: LOSLE does not seem to represent a less severe subset in Mexican patients.

T18

FALSE POSITIVE VDRL TEST (BFP-STS) IN PATIENTS WITH SLE: ASSOCIATION WITH CLINICAL MANIFESTATIONS AND SEROLOGICAL PARAMETERS

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Aim: To investigate the relationships between clinical features and serological parameters in SLE patients with false positive VDRL test (BFP-STS) and those without.

Method: The records of 68 patients with SLE were reviewed. These were divided on the basis of the presence of BFP-STS (N=15) or its absence (n=53). The clinical features and serological parameters were subsequently evaluated in each group.

Results: BFP-STS was found in 15 patients (22%). Clinically they had a significantly higher frequency of malar rash (P<0.001) haematological features (p<0.005) (thrombocytopaenia (p<0.0005), leukopaenia (p 0.05), haemolytic anaemia (p<0.01) and SLE-related antiphospholipid (APL) syndrome (p 0.005). However, neuropsychiatric lupus (p<0.0001) was more frequent in the group without BFP-STS. Moreover subacute cutaneous LE, Raynaud's phenomenon, livedo reticularis and cardiopulmonary complications were present only in the latter group. Although the frequency of positive anti-DNA (ds) was significantly higher in the BFP-STS group (p<0.002), the mean values of the two groups were not different (p=0.71). Anticardiolipin (p<0.02), anti-RNP (p<0.005) and anti-La antibodies (p<0.005) and positive Coomb's (p<0.005) had a significantly higher frequency in the BFP-STS group.

Conclusion: Our patients with BFP-STS appeared to have sparing of certain major organ systems yet there was greater tendency to developing APL syndrome and haematological features. These findings indicate that besides its clinical relevance, BFP-STS appeared to have paradoxical prognostic implications for lupus patients.

T19

NEUROMETABOLIC STUDIES IN NEUROPSYCHIATRIC SLE

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Objectives : To study neurometabolism in neuropsychiatric lupus (NP-SLE) utilizing SPECT and proton MRS.

Patients and Methods : 99m Tc HMPAO SPECT, MRI and proton MRS were carried out in 10 patients of NP-SLE, 10 patient of SLE without neuropsychiatric involvement and 10 healthy controls.

Results : SPECT revealed multiple perfusion defects in 80% of patients with NP-SLE and 10% of lupus patients without neuropsychiatric involvement. None of the controls exhibited any perfusion defects. Multiple perfusion defects were seen in parietal and temporal lobes even with normal MRI. MRS revealed metabolic abnormalities in 100% of cases with NP-SLE. NAA/Cr, NAA/choline and Choline/Cr ratios were reduced in NP-SLE as compared to non NP-SLE and healthy controls (NAA=N-acetyl aspartate, Cr=creatine). No lactate peak was observed. As many as 80% of non NP-SLE patients also revealed reduced neurometabolite ratios. Clinical correlation of defects was low.

Conclusions : SPECT and MRS demonstrated abnormalities even in absence of structural lesions on MRI. MR spectroscopy had high sensitivity (100%) but poor specificity (20%). Reduction of neuronal markers suggests diffuse brain injury with myelin breakdown or cellular inflammation in NP-SLE. Absence of lactate suggests that anaerobic metabolism is not common. Larger studies are needed to assess the exact clinical significance of SPECT and MRS changes in neuropsychiatric lupus.

T20

MYOCARDIAL SCINTIGRAPHY IN NINETY SLE PATIENTS.

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Introduction: Ischemic coronary disease (ICD) is one important cause of morbidity and mortality for SLE patients.

Objective: The aim of this study was to evaluate the ICD prevalence in SLE patients using myocardial scintigraphy.

Patients and Methods: Myocardial scintigraphy with ^{99m}Tc sestamibi at resting and after pharmacological stress with dipyridamole was performed in 90 female SLE patients (> 5 years of disease and 38±10 yo) The prevalence of risk factors (RF) for ICD such as hypertension, diabetes mellitus, dyslipidemia, postmenopausal status, smoking, obesity, and ICD family profile was evaluated.

Results: Abnormal mibi (abmibi) was found in 30 (33%) patients. Considering the perfusion defects, 18% were fixed defect, 24% were reversible and fixed and 57% were reversible defects. We found a significant association between abmibi and RF for ICD (p=0.003). The risk of abmibi was 4 times greater in SLE patients with obesity or hypertension, when compared to patients without these RF. Obesity and hypertension also showed a significant association with angina. The regression logistic model showed that obesity, angina, diminished HDL-c, large vessels vasculites and SLE-DAI score in SLE patients were associated with abmibi.

Conclusion: SLE patients have high prevalence of abnormal myocardial scintigraphy, mainly in patients with obesity or hypertension, confirming the need to control these RF

T21

DECREASED NEUTROPHILS DENSITY IN SLE PATIENTS IS INDEPENDENT OF DISEASE ACTIVITY.

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Objective: The aim of this study was to evaluate the neutrophils density in a gradient of Ficoll-Hypaque in SLE patients, as to study the possible correlation of this alteration and disease activity, disease duration and steroid dosage.

Patients and Methods: Fifty-one SLE patients and 29 controls were studied. The separation of leucocytes was done by centrifugation in a Ficoll-Hypaque (FH) and sodium diatrizoate with density adjusted to 1077 mg/ml, according the Boyum technique revised by Aiuti et al. After centrifugation, leucocytes from the white cloud layer were smeared on to a slide, stained and 500 cells were counted.

Results: The mean percentage of neutrophils in SLE patients was greater than the mean of control group ($p<0,01$). The relation L+M/N was smaller in patients than in controls ($p<0,01$). No correlation was found between L+M/N and disease activity measured by SLEDAI scores, disease duration or steroid dose.

Conclusion: We concluded that SLE patients had significant increase in the percentage of neutrophils in the Ficoll-Hypaque gradient, when compared to normal control. This means that neutrohils of SLE patients have lower density compared to the controls and suggests that these neutrophils were activated or pre-activated. We did not find correlation between diminished neutrophils density and disease activity, disease duration and steroid dosage. More studies will be necessary to understand the mechanisms involved in the decrease of neutrophils density even in SLE patients with controlled disease.

T22

ASSOCIATION OF ANTI-U1RNP ANTIBODIES AND RAYNAUD PHENOMENON WITH "SCLERODERMA-LIKE" NAILFOLD CAPILLAROSCOPIC ABNORMALITIES IN LUPUS PATIENTS.

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Objective: To evaluate the potential association between nailfold capillary and videomorphometric abnormalities and the presence of Raynaud's phenomenon (RP), anti-U1RNP and anticardiolipin (ACL) antibodies in lupus patients.

Methods: One hundred lupus patients were studied. Nailfold capillaroscopy was considered abnormal according five criteria. Three measurements were performed by videomorphometry intercapillary distance (D), capillary width (W) and length (L). Immunodiffusion and ELISA were utilized to search the autoantibodies (U1RNP and ACL).

Results: Capillaroscopic abnormalities were associated with RP, anti-U1RNP antibodies and simultaneous presence of RP and anti-U1RNP antibodies. SD pattern was associated with RP, and simultaneous presence of RP plus anti-U1RNP antibodies. There was negative correlation between ACL antibodies and SD pattern. Higher values for W, D and L were observed in patients with RP.

Conclusions: This study demonstrated significant association between RP, anti-U1RNP antibodies and capillaroscopic alteration in a set of lupus patients. Our results suggest that SLE patients with RP, anti-U1RNP antibodies and capillaroscopy "scleroderma-like" findings may be a sub-group of SLE with association with sub-clinical systemic sclerosis, who may be have a different clinical features and prognosis.

T23

LUPUS NEPHRITIS: OUTCOME OF IV CYCLOPHOSPHAMIDE TREATMENT

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Objectives: To evaluate the outcome and side effects of IV. cyclophosphamide in portuguese SLE patients.

Patients and methods: Twenty-six patients with biopsy proven lupus nephritis, assessed between 1992 and 2001 were included. Patients received a dose of 0.5g/m2 cyclophosphamide associated with oral and IV prednisolone. Clinical and laboratory data were evaluated. Patient's records were reviewed. Outcome was assessed by end stage renal failure and infections.

Results: the mean disease duration was 3.29 years (+/- 5.1). Lupus nephritis OMS class were 23 type IV, 2 type III, 1 type V. Patients received a mean of 10.1 pulses (+/- 5.0). There were significant improvements in the mean of all major laboratory parameters. There is a patient in end stage renal failure, one with renal insufficiency and two patients abandoned treatment: one due to treatment failure and one due to side effects. Most frequent side effects were infections (respiratory and UTI and cutaneous Herpes zooster).

Conclusions: Treatment in this group was successful, with a good tolerance and without significantly serious side-effects.

T24

PREVALENCE OF THYROID DISEASE IN PATIENTS WITH SLE AND PRIMARY SJÖGREN SYNDROME

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Objective: To study thyroid function and morphology, the presence of anti-thyroid antibodies (ATA) in SLE and PSS patients and to correlate thyroid dysfunction with clinical symptoms.

Rationale: Thyroid dysfunction has been described among patients with SLE and primary Sjögren syndrome (PSS).

Methods: We studied the serum levels of thyroid hormones (fT3, fT4), TSH and anti-thyroglobulin and anti-mycrossomal antibodies in 69 consecutive patients (49 SLE and 20 PSS).

Results:

	SLE	PSS
Females (%)	96	95
Age	39+/-12	44,6+/-12
Years of disease	9+/-7,6	7+/-6
Abnormal Thyroid morfology (%)	38	40
Thyroid Autoantibodies (%)	12	25
Thyroid dysfunction (%)	18	20
Asymptomatic Thyroid disease (%	56	75

Conclusion: In this group of patients we found a high prevalence of thyroid morphology abnormalities and thyroid dysfunction. In either group, less than half of the patients with thyroid dysfunction have related symptoms.

T25

DISEASE ACTIVITY IN THE FIRST THREE YEARS IS RELATED TO CORONARY ARTERY DISEASE (CAD) IN SLE PATIENTS

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AIM: To determine whether the adjusted mean SLEDAI (AMS) in the first three years of disease predicts future CAD in SLE patients.

METHOD: An inception cohort of patients seen at the Toronto lupus clinic within one year of diagnosis and who were seen at least once a year in the first 3 years was identified and followed for a minimum of 10 years. This group included 134 patients, 18 of whom had a CAD event (angina or myocardial infarction). To evaluate the average lupus disease activity of patients in their first 3 years of disease, we measured the area under the curve of the SLEDAI over that period and divided this by the time elapsed. This measure is called the Adjusted Mean SLEDAI (AMS). The variability of the SLEDAI over time (variability measure = VM) was estimated by the average change in SLEDAI from visit to visit. Finally, the mean cholesterol level, mean dose of corticosteroids and use of antimalarials, immunosuppressants, ASA and NSAID's was examined for all patients.

RESULTS:

	No CAD (n=116)	CAD (n=18)	p
AMS	6.32 ± 3.73	8.61 ± 2.83	0.0139
VM	1.20 ± 0.76	1.61 ± 0.59	0.0333
Mean Chol. (mmol/l)	5.47 ± 0.76	6.15 ± 1.26	0.0849
Mean steroid dose	6.50 ± 6.30	12.59 ± 12.07	0.0569

There was no statistical difference between the two groups with regards to the use of antimalarials, immunosuppressants, ASA or NSAID's. Finally, in a stepwise logistic regression analysis, the mean dose of steroids was the only significant independent predictor of CAD (OR=1.092, p=0.0063). After removing that variable from the model, the only other independent predictor of CAD was the AMS (OR=1.156, p=0.0260).

CONCLUSION: SLE patients with CAD had a higher disease activity (AMS), variability of their disease activity (VM) and a higher mean dose of steroids in their first 3 years of disease. A higher mean dose of steroid followed by a higher AMS were the two main independent predictors of future CAD.

T26

DOES ANY CHANGE IN CLINICAL AND LABORATORY FEATURES OF LUPUS PATIENTS AFTER THE BIG EARTHQUAKE IN TAIWAN?

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Objective: For the comprehension of the impact by the big earthquake that occurred in Sep. 21, 1999 in Central Taiwan area on our lupus patients, nearly 60 SLE patients living in that area were advised to participate this study.

Methods: A questionnaire will record demographic data and clinical manifestations before and 6 months after earthquake. Laboratory tests including CBC, C3, C4, Anti-DNA, serum creatinine, 24 hours urine protein, urine RBC and ESR etc., were measured.

Results: After earthquake, it showed a few patients had obvious disease flare-up by the evidence of fever, arthralgia, malar rash and photosensitivity, increased protein loss or edema and others. For the clinical parameter in all SLE patients, there is no significant change on fever, arthralgia, edema, fatigue, apatile loss, headache, dyspnea, malar rash, psychosis, hair loss, muscle weakness, chest pain, amenorrhea, and infection. In contrast, the laboratory tests by Wilcoxon signed rank statistical analysis only showed a significant decrease of C4 (p=0.020) and increase of serum creatinine (p=0.022). Leukopenia, thrombocytopenia and increased 24 urine protein loss was found but it did not reach a statistical difference before and after earthquake.

Conclusion: There is no striking change in the clinical aspects for lupus patients although a small number of patients had relapse or emotional disturbance within 6 months after earthquake. However, some laboratory tests were abnormal after earthquake indicate the lupus status may be worsen but in general, is not apparent clinically. It probably needs more time or more cases to follow-up before a definite conclusion can be drawn.

T27

TREATMENT OF LUPUS NEPHRITIS. AN ANALYSIS WITH 180 PATIENTS.

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Objective: To evaluate one year of treatment with immunosuppressive regimen of lupus nephritis according to the World Health Organization's (WHO) Classification System.

Methods: Between 1995 and 1999 we studied 180 patients who had systemic lupus erythematosus according to the criteria at the American Rheumatism Association and lupus nephritis characterized by renal-biopsy evidence. The patients were treated with azathioprine (AZA), cyclophosphamide (CYC) or methylprednisolone pulse (MP) according to the WHO classification. Complete remission was defined as urinary protein excretion less than 0.3g/24hs, normal urinary sediment and serum creatinine and creatinine clearance 15% or less above the base-line values. Treatment failure was defined as urinary protein excretion that remained at 0.3 to 2.9g/24hs and serum creatinine and creatinine clearance more than 15 percent above the base-line values.

Results: Renal involvements observed in the 180 patients with their respective treatment were showed in the Table I

Nephritis	Treatment	Total – n (n/180 - %)	Complete remission n (%)	Treatment Failure n (%)
Class II	AZA	26 (14%)	21 (80%)	5 (20%)
Class III	CYC + MP	24 (13%)	20 (83%)	4 (17%)
Class IV	CYC + MP	94 (52%)	70 (74%)	24 (26%)
Class V	AZA or MP	17 (9%)	11 (64%)	6 (36%)
Class II + V	AZA	9 (5%)	7 (77%)	2 (23%)
Class III + V	CYC + MP	10 (6%)	9 (90%)	1 (10%)

Conclusion: Immunosuppressive therapy in the treatment of nephritis lupus as combination of azathioprine and pulse methylprednisolone or pulse cyclophosphamide has led to a dramatic decrease in morbidity. Improvement in the renal pathological picture can be seen in any histological class treated with appropriate regimens.

T28

QUALITATIVE ASSESSMENT OF URINARY PROTEIN EXCRETION IN A BRAZILIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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OBJECTIVE: To investigate the urinary protein excretion profile in SLE adult patients attended in a University Hospital (Southeast Brazil) without clinical and laboratory evidences of renal disease. METHODS: The profiles of urinary protein excretion were analyzed in 44 SLE patients, without fever, arterial hypertension, pregnancy, diabetes mellitus, non-steroid anti-inflammatory use during the last three months. To determine the urinary excretion of total protein, albumin (MA, glomerular marker), alpha 1 microglobulin (A1M, tubular marker) and urinary sediment analysis, random urine samples and 24-hour collection were obtained. Total protein and creatinine concentrations were assessed on a Cobas-Mira Plus analyzer (pyrogallol red and modified Jaffé rate methods, respectively). MA and A1M were determined by nephelometric method (Array® 360 System-Beckman). Random urine samples were also submitted to a routinely urine analysis for dysmorphic erythrocytes. RESULTS: Hematuria was seen in 5 (11.3%) cases being 3 of them of glomerular origin. The protein excretion varied between 0 t o 0.26g/24hs. Albumin excretion varied from 0.01 to 0.45 µg/min. Microalbuminuria (value range 20 to 200 µg/min) was observed in 5 (11,3%) and tubular dysfunction in 3 (6.8%) of the patients. CONCLUSION: Our data suggests that renal impairment is relatively frequent in SLE even in the absence of clinical signals. The early detection of these alterations permit a careful follow up of these patients, delaying the consequent surge of renal damage.

T29

COGNITIVE DISTURBS IN SYSTEMIC LUPUS ERYTHEMATOSUS EVALUATED BY MAGNETIC RESONANCE IMAGING (MRI)

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OBJECTIVE.To evaluate brain magnetic resonance imaging in SLE patients with cognitive impairment
PATIENTS AND METHOD 40 SLE patients were screened for cognitive impairment (ACR, 1999) using standardized research methods. Systemic disease activity was measured by SLEDAI. Patients with severe anxiety or mood disorders, CNS infections, uremia, diabetes and previous isquemic or hemorragic brain disease were excluded. MRI scans were obtained in a 2T scanner with T1 - and T2-WI, FLAIR, T1 Inversion Recovery and Proton Density axial scans and T1- and T2-WI sagital scans, before and after gadolinium. Statistics were performed by chi-square test and by Fisher's exact test.
RESULTS .Age ranged from 12-62 years (median age 34.2 years) with follow-up from 6-144 months (median time 60 months). Mean SLEDAI score was 12. 50% had mild, 30% moderate and 20% severe cognitive dysfunction. MRI showed small cortical and subcortical lesions hypointensive in T1 and hyperintensive in T2 without gadolinium enhancement in 10% of the scans.
CONCLUSION.We observed 10% of gliose in MRI scans, suggestive of small vessels vasculitis without relation to cognitive dysfunction, disease activity or age. The fact that our findings are less than previous report could be related to strict exclusion criterias.

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T30

Survival and predictor variables for mortality in Systemic Lupus Erythematosus

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Objective.To analyze survival and mortality risks of various clinical variables in a cohort of systemic lupus erythematosus (SLE) patients, followed prospectively in a single center.
Methods. The survival of a cohort of 509 SLE patients followed over a 20-year period according to a standard protocol was studied using the Kaplan Meier lifetable analysis methods. Univariate associations between clinical and laboratory data and drugs used were calculated. The Cox proportional hazard regression model was used to estimate risk ratio of death and to examine the simultaneous effects of multiple prognostic factors.
Results.Over the duration of follow-up of 20 years, 58 (11.4%) died. The survival rate was 97% at 1 year, 90% at 5 years, 81% at 10 years and 75% at 20 years. Age <16 years at diagnosis, hypertension, weight loss, nephritis, ocular involvement, frequent infections, anti DNA antibodies and the absence of artralgia/arthritis were significantly associated with reduced survival in univariate analysis. Using multivariate analysis, hypertension (OR 2.2, 95% CI 1.1-4.5), age <16 years at diagnosis (OR 2.6, 95% CI 1.4-5.0), ocular involvement (OR 4.9, 95% CI 1.9-12.8), no use of antimalarial drugs (OR 2.8, 95% CI 0.15-0.53)and frequent infections (OR 2.3, 95% CI 1.3-4.1) were independent risk factors associated with increased mortality.
Conclusions.Hypertension , age <16 years at diagnosis , ocular involvement, no use of antimalarial drugs and frequent infections were independent risk factors associated with increased mortality.

T31

THE ANALYSIS OF THE ARTERIOSCLEROSIS BY THE DOPPLER ECHO IN THE COLLAGEN DISEASE PATIENT

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Objective:It has been indicated that the complication concerning the arteriosclerosis of cerebrovascular disease and AMI is abounding for SLE. As the background , vasculitis,serum lipid abnormality,The existence of autoantibodies such as the anti-phospholipid antibody and effects of the steroid are raised. Rational:Further the seriousness is increasing as a factor of various complications such as cerebrovascular disorder and cardiopahty.The clinical application is expected that dynamic property change of blood vessel is measured by the noninvasion as an arteriosclerotic diagnosis. Methods: 55patients included women of 42 persons (SLE,RA,MCTD,PN)were studied.The measurement position also made anyway to be the right side over arm. Results:In the collagen disease patient, the degree of arteriosclerosis is dependent on not only age but also affection years steroid administration history, and it was guessed that the collagen disease patient had entered degree of the arteriosclerosis further than the normal subject from this fact. Conclusion:It seems that at present and then, prevention and treatment of the complication of SLE will become more more the importance ever since.Especially,ischemic heart disease and cerebrovascular disorder, clinical research for examination and treatment, Japanese on the management of risk factor of the arteriosclerosis as the basis more and more seem to be going to be necessity in future.Prospective study for clarifying whether the ultrasonic testing is uninvasive and whether it seems to spread even in SLE example of this country, and whether to control SLE patient using such method with the risk factor in future is effective how It seems to be the important.

T32

Immunoadsorption with amino-acid linked PVA-gels in patients with SLE and vasculitides: Influence on specific immune parameters

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Severe autoimmune diseases are often difficult to manage despite the availability of various immunosuppressive agents. Extracorporeal immunoadsorption (IMAD) is a technique that can be used as a selective or a semiselective procedure, which can reduce pathogenic plasma components in autoimmune disease such as circulating immune complexes and autoantibodies. In IMAD with amino acid (AS, phenylalanine (PHE) or tryptophan (TR)) linked polyvinylalcohol (PVA)-gel immunoglobulines, autoantibodies and immune complexes are reduced by the mechanism of hydrophobic interactions. In our cohort (26 patients with SLE, 6 patients with Wegener's granulomatosis (W.G.)) treated with this technique the immunoglobuline fractions of all isotypes (IgG, IgA and IgM) dropped significantly. Moreover in patients with SLE antinuclear antibodies (ANA) and ds-DNA-antibodies were reduced significantly as well as circulating immune complexes (IgG). In 4 of 6 patients with W.G. the c-ANCA titer decreased after extracorporeal therapy.
There was a tendency of lowering the soluble-IL-2-receptor by the extracorporeal therapy. No influence could be seen on TNF-alpha and interleukin-6 after IMAD, all determined with ELISA technique.

T33

SYSTEMIC LUPUS ERYTHEMATOSUS: A FAMILY STUDY

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Objective: To investigate the significance of genetic and environmental factors in the etiology of systemic lupus erythematosus (SLE).

Methods: Eighty first-degree relatives (FDRs) of 58 SLE probands and 34 non-consanguineous spouses have been studied for SLE-related clinical findings, complete blood count (CBC), erythrocyte sedimentation rate (ESR), general urine examination (GUE), and anti-nuclear antibodies (ANA). The FDRs were classified to either household contacts (HHCs) or non-household contacts (NHHCs) to investigate the effects of both heredity and environment, and the spouses were all non-consanguineous to study the effects of environment in isolation from hereditary factors.
Another 50 randomly selected healthy persons were included as a control group.

Results: SLE-related symptoms and signs were observed in 35% of FDRs, 8.8% of spouses, and 6% of controls (P=0.0001).
A significantly greater frequency of ANA positivity was found among FDRs (16.2%) than among controls (2%) (P=0.02), and a significant association was found between rheumatic complaints and ANA positivity.
Household contact appeared to play insignificant role in the development of rheumatic complaints and ANA positivity.

Conclusion: Our results confirm the role of genetic factors in the etiology of SLE and their marked predominance over environmental factors.

T34

VALVULAR DYSFUNCTION IN SLE PATIENTS WITH ANTICARDIOLIPIN ANTIBODIES

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Objective:
To determine the relative risk of valvular dysfunction in patients with SLE and anticardiolipin antibodies in HNERM.

Patients and Methods:
In 27 patients with systemic lupus erythematosus (SLE) of Rheumatology Service in HNERM, we assessed anticardiolipin antibodies (IgG, IgM or IgA) by ELISA method and valvular dysfunction by 2-D echocardiography.

Results:
Six of twenty seven patients with SLE had valvular dysfunction. Four of them had anticardiolipin antibodies.
The relative risk for developing valvulopathy in patients with SLE and anticardiolipin antibodies was 4.

Conclusion:
It seems like patients with SLE and anticardiolipin antibodies would have more risk of developing valvular dysfunction in HNERM.

T35

MEASUREMENT OF ANTIBODIES TO DNA, NUCLEOSOMES AND HISTONES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective:
To analyze the diagnostic value of an anti-nucleosome ELISA compared to anti-dsDNA and anti-histone measurements in patients with systemic lupus erythematosus (SLE).

Methods:
Sera of 157 SLE patients, 100 healthy blood donors and 172 individuals with other inflammatory diseases were tested for anti-nucleosome antibodies by a commercially available ELISA. The results were then compared to the measurements of anti-dsDNA antibodies by Farr-assay and by ELISA as well as to that of anti-histone antibodies by ELISA.

Results:
For most patients, the anti-dsDNA antibody reactivity correlated well with the anti-nucleosome antibody findings. 64% of the SLE patients with anti-nucleosome antibodies showed positive results also in the anti-histone ELISA. Highest specificity (94%) could be found for the Farr-assay which was almost comparable to the anti-nucleosome ELISA (91%). Highest sensitivity could be evaluated for the anti-dsDNA ELISA (88%).

Conclusions:
For the diagnosis of SLE, the measurement of anti-nucleosome antibodies is highly specific. However, due to a low sensitivity it does not replace anti-dsDNA testing by ELISA.

T36

TUMOR NECROSIS FACTOR-ALPHA AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective and Methods: To obtain information about the involvement of tumor necrosis factor-alpha (TNF-α) in the pathophysiology of SLE this cytokine was measured, by an enzyme linked immunosorbent assay, in sera from 109 patients (pts) with systemic lupus erythematosus (SLE) (44 men and 65 women). The results were compared with 20 healthy subjects.
Results: Pts of both groups (males and females) had a significantly higher serum TNF-α than control subjects ($p<0,001$). TNF-α was found positive (more than 3s.d. above the mean in normal controls) in 17 females (26%), 36 males (81,8%) in pts with SLE compared to 1 person (5%) of normal controls ($p<0,05$). Data differed statistically between patients in male and female groups and controls. We found significant positive correlation between TNF-α and ESR ($p<0,02$), arthritis ($p<0,01$), capillaritis ($p<0,01$), lymphadenopathy ($p<0,001$); the negative correlation was observed with serum albumin ($p<0,02$) in females. There was a positive correlation between TNF-α and SLAM index ($p<0,01$), SLEDAI ($p<0,06$), antiphospholipid syndrome ($p<0,01$), IgG-anticardiolipin antibodies ($p<0,03$) in male group.
Conclusion: There are differences between the level, the clinical value of TNF-α in male and female cohorts of pts with SLE. The measurement of TNF-α maybe a useful tool for monitoring disease activity, in the male cohort especially.

T37

MORBI-MORTALITY IN SLE PATIENTS DURING 3 DECADES IN GUATEMALA CITY.

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Objective: Despite significant advances in the understanding of the pathogenesis of SLE, earlier diagnosis and better treatments, little is known about morbimortality of this disease in some third world latin american countries, including our own, therefore we decided to review our experience.

Rationale: Early diagnosis and treatment should improve the survival rate of our patients.

Methods: We analized the medical records of 86 patients who fulfilled at least 3 ACR criteria for diagnosis of SLE during the past three decades.

Results: From 1970/1979: 10 patients (11.6%), 8 females, with duration of disease to diagnosis of more than 1 year: 6 (60%), all lost to follow-up.

1980-1989: 38 patients (44%), 32 females (84.2%), 26 (68.4%) with disease of more than one year duration, 2 patients died (5.2%) from sepsis, 30 lost to follow-up (79%).

1990-1999: 38 patients were diagnosed (44%), 35 females (92.1%), disease of more than one year 12 (31.5%), 3 patients died one from renal disease + sepsis and 2 from sepsis, 20 (53%) lost to follow-up.

Conclusion: We have a large desertion of patients 60 (69.7%) which is decreasing during the last decade, we believe due to economical reasons. Our patients are diagnosed earlier than before, less than 1 year of disease duration 31.5% vs 60% and 68.4% in previous decades.

T38

THE SPECIFIC ROLE OF ANTI-MICROVASCULAR ENDOTHELIAL CELL (EC) AND ANTI-MACROVASCULAR EC ANTIBODIES IN ATHEROGENESIS OF VASCULITIS AND OTHER AUTOIMMUNE DISEASES

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*Res Unit of Autoimmune Diseases and Depart. Med. B, Sheba Medical Center, Tel-Hashomer; Clinical center, Depart. of Rheumatology, Ljubljana, Slovenia; Institute of Hematology, Sorasky Medical Center, Tel-Aviv, Israel; **INSERM U353, Hopital Saint-Louis Paris, France; Weill Medical College of Cornell University, New York, USA.

Affinity-purified AECA F(ab)2 from four patients with TTP or anti-PF4/heparin, from patients with HIT (heparin induced thrombocytopenia), found to bind and differentially activate only microvascular endothelial cells (EC) and not large vessel EC (HUVEC). The activation was expressed by enhanced thrombomodulin, IL-6 and vWF release, raised levels of adhesion molecules (P-selectin, E-selectin, VCAM-1) and CD36 expressed on the EC, followed by an increase in monocyte adhesion to ECs.
Interestingly, specific activation of large vessels ECs (HUVEC) was demonstrated by polyclonal and monoclonal AECA from patients with antiphospholipid syndrome , Wegener's' granulomatosus, Kawasaki vasculitis and Takayasu arteritis (TA).
In sum, AECA which targets either macrovascular or microvascular can activate specifically microvascular or macrovascular EC via elevation of thrombomodulin, NFkB , adhesion molecules expression associated with monocyte adhesion to EC or induce apoptosis. These biological functions of AECA might therefore play a pathogenic role in the development of the vasculopathy.

T39

EXPERIENCE IN IRAN WITH SPECIAL REFERENCE TO BEHCET'S DISEASE (BD).

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Pattern of Rheumatic Diseases in Iran: They have the same frequency and the same pattern as in Western countries. A study from 1993 demonstrated a prevalence of 32.6% among adults (31.4% in the USA, Cunningham 1984). Inflammatory disorders counted for 11% of all rheumatic diseases. The ratio of RA to AS was 8/1 (7/1 in USA), and SLE to Scleroderma 3.5/1 (3.6/1 in USA). Psoriatic arthritis and Reiter's syndrome were rare in Iran while Behcet's disease had much higher incidence. Osteoarthritis counted for 32%, low back pain 27%, and soft tissue rheumatism for 16% of all rheumatic complaints.
Epidemiology of BD: It is seen more frequently in Iran than in Western countries. From 1975 to 2000, 4413 patients were registered in our database. The annual incidence during the last 11 years varied between 250 and 350 new patients (population: 60 millions). The estimated prevalence is 1.5 BD for 10,000 inhabitants. BD is seen more frequently in northwestern part of Iran. The disease is twice more frequent in Turk ethnic group than in Caucasians. The male to female ratio was 1.17/1. The mean age at the onset was 26 ± 9.6 SD, confidence interval (CI) at 95% = 0.3.
Clinical Manifestations were: Mucous membrane 97% of patients (oral aphthosis 96% and genital aphthosis 65%), skin manifestations 72% (pseudofolliculitis 64%, erythema nodosum 23%), ocular lesions 56% (anterior uveitis 42%, posterior uveitis 45%, retinal vasculitis 31%), joint manifestations 36% (arthralgia 16%, mono-arthritis 8%, polyarthritis 18%, ankylosing spondylitis 1.5%), neurological manifestations 3.3% (central 3.1%, peripheral 0.2%), gastro-intestinal manifestations 8%, epididymitis 6%, phlebitis 7%, large vein thrombosis 1%, arterial thrombosis 3 cases, aneurysm 6 cases, pulmonary manifestations 0.7%, and cardiac manifestations 0.6%.

T40

PRECURSOR OF ENDOTHELIN-1 AS A MARKER OF ENDOTHELIAL DAMAGE IN VASCULITIS

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Objective: To assess plasma levels of BET-1 in patients with primary and secondary necrotizing vasculitides and to correlate the obtained data with acute phase reactants.

Rationale: Endothelin-1 is the strongest vasoconstrictory factor and it is synthesized by the endothelial cells. Its precursor big endothelin-1 (BET-1) is biologically inactive.

Methods: Total 6 patients with polyarteritis nodosa, 3 with giant cell arteritis, 6 with leukocytoclastic vasculitis, 4 with rheumatoid vasculitis, 4 with lupus vasculitis, 4 with vasculitis in undifferentiated connective tissue disease were examined. As a control group 10 blood donors were tested. BET-1 concentrations were assayed by ELISA using a commercial kit.

Results: The plasma concentrations of BET-1 were significantly increased in all patients in comparison with healthy controls (p=0.01). Because of small numbers of patients in individual subgroups no differences and correlations with acute phase reactants could be calculated.

Conclusion: Our data suggest that BET-1 could be regarded as a serological marker of endothelial damage in different kinds of systemic vasculitis.

T41

SACROILIITIS IN BEHCET'S DISEASE, A RADIOLOGIC STUDY

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Introduction: The association of Behcet's disease (BD) and ankylosing spondylitis (AS) is still a controversial subject. As the presence of sacroiliac joint (SIJ) involvement is an essential criterion in the diagnosis of AS, we decided to determine the prevalence of SIJ involvement in BD and compare it with control group.
Materials & Methods: We selected randomly 199 BD patients and 168 non-BD cases (CG), in a 12 month period (between April 1998 to May 1999). All were over 20 year of age. Standard anteroposterior radiographs of the SIJ were obtained and interoreted by two Rheumatologists and a radiologist blinded to the diagnosis. The following 5-points scale was employed: Normal (0), pseudo-widening (1), sclerosis (2), erosion (3), and bony fusion (4). To eliminate any doubt about sacroiliitis only grade 3 and 4 were accepted as SIJ involvement. Both groups were evaluated according to their age (before 30/over 30), and sex separately. The mean result in each group (BD/CG) was compared by the chi square test.
Results: Both groups were sex and age matched: There was 98 females in BD vs. 91 in CG (p=0.35). The mean age in BD was 34.9±8.3 vs. 34.9±10 in CG (p=1). SIJ was involved in 9 patients in BD (4.6%, CI:2.9) vs. 7 patients in CG (4.2%, CI:3). The difference was not statistically significant (p=0.93). Comparing the results seperately in males and females, there was not statistically significant difference (p=0.68 in males, p=0.64 in females). Another sub-division according to the age (under and over 30) again showed no significant difference between the 2 groups. There was 64 patients under 30 in BD with 3 SIJ involvement vs. 61 patients in CG with 2 SIJ involvement (p=0.96). In patients over 30, 6/135 in BD vs. 5/107 in CG had SIJ involvement (p=0.69).
Conclusion: In this study of Iranian patients, we found no significant difference in SIJ involvement between BD and controls, while the incidence of AS was higher in BD than in normal population.

T42

LARGE VESSEL MANIFESTATIONS OF BEHCET'S DISEASE, REPORT OF 377 CASES

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Introduction: Large vessel involvement is one of the hallmarks of Behcet's disease (BD). Like the other manifestations of the disease, its prevalence differs due to ethnic variation and environmental factors. The aim of this study is to find the characteristics of vasculo Behcet in Iran.
Materials & Methods: In a cohort of 4429 patients with BD, those with vascular involvement were selected (VB). Different manifestations of the disease were compared with the remaining group of BD patients by chi square test. A confidence interval at 95% (CI) was calculated for each item.
Results: Vascular involvement was seen in 377 cases (8.5%, CI:0.8). Venous involvement was seen in 367 cases: Deep vein thrombosis in 272 (6.1%, CI:0.7), superficial phlebitis in 99 (2.2%, CI:0.4), and large vein thrombosis in 40 (0.9%, CI:0.3). Arterial involvement was seen in 24 casess (21 aneurysms and 3 thrombosis). Twelve patients showed both arterial and venous involvement. The mean age of the patients with VB was slightly higher (27.2 vs. 25.9, p<0.02), but the disease duration was significantly longer in them (10.1±7.3 vs. 8.9±6.8, p<0.002). VB was more common in men (p<0.000001). As the presenting sign, ocular lesions was less seen in VB (p<0.002). VB was associated with a higher frequency of genital ulcers (p<0.00006), skin lesions (p<0.000001), joint involvement (p<0.000001), epididymitis (p<0.000001), neurologic (p<0.00004) and G.I. involvement (p<0.005). The juvenile form was lower in VB (p<0.007). The frequency of false positive VDRL, pathergy, HLAB5 or HLAB27 showed no significant difference between two groups.
Conclusion: In Iranian patients with BD, large vessel involvement is not common. It may be sex related, and is more common in well-stablished disease (with multiple organ involvement and longer disease duration). No relationship seems to exist between vascular involvement and false positive VDRL, pathergy phenomenon and HLAB5 in BD.

T43

COMPARATIVE STUDY OF CLINICAL AND LABORATORY DATA IN PATIENTS WITH BEHCET'S DISEASE WITH AND WITHOUT OCULAR INVOLVEMENT.

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Objective: Behcet's disease is a chronic disease with multisystem involvement. Ocular involvement is a major cause of morbidity in these patients. This study is designed to report the differences in patients with and without ocular involvement.

Methods: Medical records of 48 patients with Behcet's disease who were visited in Rheumatology clinic from 1989 to 1997 reviewed retrospectively.

Results: 26 patients had ocular involvement which was bilateral in 19 and unilateral in 7. 22 patients had other organ involvement. Mean age and SD was 28 ±11.7 years in the first and 38.8 ±16.5 years in the second group. All the patients in both groups had oral aphthosis. Genital aphthosis, CNS, GI involvement, vascular thrombosis, pulmonary vasculitis, arthritis and cutaneous lesions were more common in the second group (p<0.001). Positive CRP detected in 3.84% of the first and 36.36% of the second group. ESR>35 detected in 11.53% of the first and 50% of the second group (p,0.005).

Conclusion: It seems ocular involvement is more common in younger patients and in patients without ocular disease other organ involvement and higher levels of CRP and ESR are more common.

T44

LEFLUNOMIDE (LEF) IN PATIENTS WITH WEGENER'S GRANULOMATOSIS (WG) IN REMISSION: A PILOT STUDY

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Objectives: To investigate the safety, efficacy and maintenance of remission by LEF in 20 WG patients in a 52 week, open label pilot study.
Methods: WG patients in complete/incomplete remission induced by Fauci's scheme received LEF 20mg daily (after 100mg QD for 3 days) increasing at 12 weeks to 30mg daily. Doses were increased to 40mg daily in the absence of complete remission after 24 weeks. Primary efficacy variables were organ involvement assessed by the disease extent index (DEI), Birmingham vasculitis activity score (BVAS), ANCA titer and relapse occurrence. Results: All patients experienced at least one AE (average 8.3 mentions per patient) the most frequent being mild upper respiratory infection (40%). AEs considered to be causally related to study medication were reported in 9 patients. Other AEs reported included hypertension, diarrhea, nausea and alopecia (≤3 patients each). One patient discontinued from the study due to visual field defects, possibly causally related. Mean total DEI scores were 3.2 at baseline and 3.3 at endpoint (final visit), respectively. The mean total BVAS score was 10.6 at baseline and 9.5 at endpoint. No change from baseline was observed in ANCA titer in 25% of patients. Fifty-five percent of patients at endpoint had an increase of more than two titer steps and one patient experienced a decrease in titer levels. Incomplete remission at 24 weeks in 11 patients resulted in a LEF dosage increase to 40mg daily. Nine of these patients had additional organ involvement in their disease, necessitating increased corticosteroid doses in 4 patients. One patient discontinued LEF due to lack of efficacy and new renal involvement was considered as a major relapse. Conclusion: LEF was well tolerated at the doses studied in WG patients. The majority of patients maintained remission and WG activity remained constant throughout the study period.

T45

SEASONAL VARIATION IN THE ONSET OF PRIMARY SYSTEMIC VASCULITIS (PSV) IN NORFOLK, U.K.

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AIMS The onset of PSV has been reported to be more common in winter compared to summer or autumn. We studied seasonal variation in all PSV cases diagnosed within our well defined population, the Norwich Health Authority, from 1988-1998.
METHODS Cases were identified from a prospective register and the month of the first symptom attributable to PSV and ANCA data obtained by case note review and interview of surviving patients(SL). Classification criteria were Wegener's Granulomatosis (WG)-ACR 1990; microscopic polyangiitis (mPA)-Chapel Hill 1994; Churg-Strauss Syndrome (CSS)-ACR 1990 and Lanham 1984] Monthly and seasonal variations were compared by the poisson distribution and ψ^2 respectively [Winter = Dec-Feb; Spring = Mar-Jun; Summer = July-Sept; Autumn = Oct-Dec]
RESULTS The table gives the number of cases by month.

Month	PSV	WG & MPA	CSS	cANCA	pANCA
January	9	7	2	3	3
February	10	7	3	3	3
March	7	5	2	3	1
April	7	4	3	1	1
May	11	9	2	3	4
June	2	2	0	0	0
July	7	7	0	2	1
August	6	3	3	1	2
September	6	5	1	1	0
October	10	10	0	4	2
November	7	6	1	5	1
December	7	7	0	3	1
TOTAL	89	77	17	29	19

Seasonal differences were not significant at the 5% level but data suggests a weak trend to a higher winter and lower summer onset. [June was significantly lower than expected for PSV and MPA/WG (p=0.02, p=0.05)]. CSS onset appears more common in spring but numbers are small.
CONCLUSIONS Data weakly supports a high winter onset and a summer dip in WG[1] and total ANCA +ve[2] vasculitis but does not confirm an observed high winter peak of cANCA vasculitis [3]. 1. Raynaulds et al, J.Rheum, 1993, 20:9 1524- 1526; 2. Falk et al, 1990, Ann In Med, 113:656-663; 3. Tidman et al, J Int Med, 1998, 244: 133-141

T46

LONG-TERM TOXICITY OF CYCLOPHOSPHAMIDE REGIMENS IN PRIMARY SYSTEMIC VASCULITIS (PSV)

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Cyclophosphamide (CYC) has transformed the prognosis of PSV but causes significant toxicity. Risk may be minimised using pulse therapy, shorter CYC duration and alternative maintenance therapy. We aimed to compare long-term toxicity of CYC for oral and intravenous (IV) therapy.
METHODS Case notes of 122 patients diagnosed with Wegener's Granulomatosis (WG), microscopic polyangiitis (mPA) and Churg-Strauss Syndrome (CSS) between 1988-99 were reviewed for duration and cumulative doses of treatment, CYC related deaths, hospital admission for infection, neutropenia ($<2x10^9/l$), haemorrhagic cystitis, cancer and osteoporosis. Comparison was made between pulsed IV CYC alone and oral CYC.
RESULTS 106 Patients were treated with CYC (12 CSS, 43 WG, 34 mPA, 17 WG/mPA overlap). 30 received only IV pulses (5 CSS, 13 WG, 6 mPA, 6 mPA/WG overlap) and 76 received oral CYC± IV. Steroids were used in all cases. Azathioprine (61) and Methotrexate (13) were used as maintenance treatment. The median presentation age was 65yrs (range 32-90 yrs) and duration of follow-up 27 months (1-130). The median cumulative CYC dose for the IV and oral groups was 6.65g (0.5-23g) and 10.05g (0.80-160.85g) respectively, over mean durations of 145 days (1-583) and 129days (1-2073). The log mean cumulative dose was significantly less for IV CYC compared to the oral group ($P<0.01$). There was no significant difference between treatment duration, cumulative steroid dose or CYC dose/day between groups. 7 deaths were related to oral CYC and 1 to IV CYC. 7 cancers were diagnosed in the oral group alone [bladder (3), oesophageal (3) and seminoma (1)] between 1 month and 10 years following a median CYC dose of 13.7g (4.85-160.85g). Haemorrhagic cystitis occurred once following 20.5g oral CYC over 499 days. 13/76 oral CYC cases received Mesna compared to 18/30 IV cases. Other complications were as follows (IV vs oral): infection requiring hospital admission (4 vs 21); CYC induced neutropenia (6 vs 29); osteoporosis (3 vs 7), The cumulative dose of steroids was not significantly higher for patients with infection or osteoporosis.
CONCLUSION Patients treated with long term oral CYC experienced more toxicity compared to IV pulse therapy. This may result from higher cumulative doses and supports current practice of shorter CYC remission regimens.

T47

CRYOGLOBULINEMIA IN BRAZILIAN PATIENTS: ANALYSIS OF 19 CASES

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Objective: To evaluate clinical and serologic findings in patients with mixed cryoglobulinemia.

Methods: Nineteen patients with mixed cryoglobulinemia (6 males and 13 females) were followed up at the Division of Clinical Immunology, School of Medicine of Ribeirão Preto from 1996 to 2000. Diagnosis was made on the clinical basis and the presence of serum cryoglobulins.

Results: Patients mean age was 35 (range: 8-64) years with a mean disease duration of 23 (range: 4-46) months. Main clinical features included purpura (89%), arthralgias (57%), urticaria (31%), peripheral neuropathy (26%), renal involvement (21%), liver involvement (21%), Raynaud's phenomenon (15%) and digital ulcerations (15%). Serological findings showed hypergammaglobulinemia (52%), leukocytosis with lymphocytosis (42%), decreased serum levels of C3, C4 (36%), antinuclear antibodies (26%), antismooth muscle and anti-phospholipid antibodies (10%) and hepatitis C virus (21%). All skin lesions biopsies revealed leukocytoclastic vasculitis. Cryoglobulinemia was associated with other autoimmune diseases in 42% of the cases (systemic lupus erythematosus 26%, rheumatoid arthritis 5 %, primary Sjogren syndrome 5%, Behçet's disease 5%), with neoplasic disease in 10% and there was only 21% of association with hepatitis C virus. In 27% of the cases there were no other correlated diseases.

Conclusion: Cryoglobulinemia is a systemic disease with deposition of immune complexes in several organs and is associated with other autoimmune diseases, particularly systemic lupus erythematosus, and hepatitis C virus in the majority of the cases.

T48

ELECTROENCEPHALOGRAPHIC FINDINGS IN PATIENT WITH ADAMANTIADES – BECHET SYNDROME.

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Objective: Aim of this report is to describe a case study of a patient with Adamantiades-Bechet (A-B) syndrome with epileptic crises and E.E.G. findings which proved it.

Rationale: Adamadiades- Bechet syndrome is a systemic vasculitis of unknown origin which involves arteries and veins of different sizes occurring with relapsing muco-cutaneous and ophthalmic lesions.CNS involvement is up to 5% in (A-B) and occurs usually with intracranial hypertension multiple sclerosis and pyramidal syndrome. Epileptic crises are not referred in the usual symptoms of CNS involvement.
CASE REPORT: Patient 28 years old came to our department with fever, pain and restriction in movements of the right hip and hemorrhagic diaree.In his personal history ulcerative colitis was mentioned 2 years ago and recurrent painful oral ulcers. During his hospitalization, aseptic ostatitis was diagnosed and acne like lesions occurred with sudden loss of vision, psychokinetic and hyper excitation phenomena, as well as typical Grand mal convulsions.CT and MRI of the brain was of non diagnostic value, whereas EEG was definitely diagnostic for epilepsy. Administration of combined iv corticosteroids (for the beginning and per os later) , azathioprine and cyclosporine was given.Vision improvement was astonishing, psychiatric problems and epileptic convulsions disappeared. EEG findings were normalized in two months time. Three years later patient was free of symptoms with the administration of colchicine only per os.
Conclusion: Epileptic convulsions are very rare expression of CNS involvement of (A-B) syndrome. In recent literature review of 4 patients only presented with epileptic convulsions or epileptiform EEG findings. Aggressive treatment in (A-B) syndrome can be of great help in improvement of symptoms and lesions.

T49

STROKE IN RHEUMATIC DISEASES

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Aim: to reveal strokes rate and their cause in some rheumatic diseases (RD).

Methods: a complex clinical and instrumental examination has been conducted in 200 patients with rheumatic diseases; among these 193 females and 40 mates at the age range from 20-45 years.

Results: in the course of the investigation two groups of patients have been singled out – the first group (19%) consisted of patients who developed paralysis in the debut of the disease ("stroke in the debut"). The second group (21%) included patients who developed strokes during the period of time from 1 to 7 years of katamnestic follow up from the debut of the disease ("delayed strokes"). Paralysis has been diagnosed in 67 patients (39.6%). "Stroke in the debut" has proved to be more common in patients with non-specific aortoarteritis (NAA) (32%), in patients with systemic lupus erythematosus (SLE) (24%) and in patients with nodular polyarteritis (NP) (21%). "Delayed strokes" has been mostly diagnosed in patients with systemic scleroderma (SSD) (30%), with non-specific aortoarteritis (26.3%) and with non-differentiated systemic vasculitis (SVn) (20%).

Conclusion: the main causes of paralysis in patients with "stroke in the debut" were immune vascular lesion and unstable arterial hypertension. In cases with "delayed strokes" heart pathology, stahle arterial hypertension, vessel pathology, hypercoagulation in combination with hypercholesterolemia and vertebral syndrome played the main role.

T50

TREATMENT OF VASCULITIS WITH INTRAVENOUS IMMUNOGLOBULIN

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Objective: To evaluate the effectiveness of treatment with intravenous immunoglobulin (IVIg) in patients (pts) with vasculitis.
Methods: 20 pts with the various forms of vasculitis, including, 4 - with Takayasu arteritis (TA), 3 - with polyarteritis nodosa (PAN), 3 - cutaneous vasculitis. 3 - primary antiphospholipid syndrom, 2 - with Henoch-Schonlein purpura (HSP) and 2 - thrombangiitis obliterans (TAO) ,1 with polimialgia rheumatica and giant cell arteritis (GCA), 1 - Wegener's granulomatosis (WG), 1 - Behchet's disease (BD) were surveyed. There were 13 female and 7 male, the mean age – 42.5±13.2. the duration of illness – 6.45±5.1. IVIg was given in a dose of 0.4g/kg body weight in a 4-day-schedule. Nine pts received also maintenance doses steroids and antiplatelets drugs. An estimation of clinical activity has carried out on BVAS before the treatment and on 5-th and 20-th day from its beginning. C-reactive protein (CRP), von Willebrand factor antigen (vWF:Ag) by ELISA, ESR and serum levels of IgG, IgM, IgA at the same times were determinated.
Results: 17 pts (85%) had reductions in disease activity. 4 (20%) of there entered full, clinical remission (2 - with HSP, 1 – with TA and PAN). but 3 of 17 had a temporary response. 3 pts (2 – with TA and 1 - with BD) did not respond to IVIg. Before the start of treatment mean score of BVAS was 5±3.5 and it was decreased on the 5-th - 2.8±1.9 and 20-th days - 2.2±1.8 ($p<0,01$). There were no significant differences mean values of ESR, CRP, vWF:Ag, IG during follow-up.
Conclusion: So. IVIg must be use for treatment both systemic and cutaneous vasculitis in addition to immunosupressive therapy.

T51

ANTIBODIES TO ANTICARDIOLIPIN AND β2GPI IN SYSTEMIC VASCULITIS AND PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Objective: To investigate significance anticardiolipin (aCL) and β2GPI (anti-β2GPI) in patients (pts) with systemic vasculitis and primary antiphospholipid syndrome (PAPS).
Design and methods: The sera from 18 pts with polyarteritis nodosa (PAN), 18 pts with Takayasu's arteritis (TA), 21 pts with thromboangiitis obliterans (TAO), 21 pts with Henoch-Schonlein purpura (HSP), 20 pts with Wegener's granulomatosis (WG) (ACR,1990) and 8 pts with define PAPS (1998) and 20 donors were surveyed. IgG aCL and anti-β2GPI by ELISA (Orgentec, Germany) were studied.
Results: IgG aCL in 7 (38,9%) pts with PAN, in 4 (20%) pts with WG, in 1 (4.8%) pts with TAO, in 1 (4,8%) pts with HSP and in 3 (16,7%) pts with TA in low titers were found. IgG aCL in 8 (100%) of 8 pts with PAPS in medium or high titers were observed. anti-β2GPI in low titers in 4 (22.4%) pts with HSP and in medium or high titers in 8 (100%) pts with PAPS were observed only.
Conclusions: So, we found IgG aCL and anti-β2GPI are importent tests for PAPS, but antiphospholipid antibodies are seldom determinated in pts with systemic vasculitis and their clinical significance are not obscure.

T52

MOLECULAR MIMICRY BETWEEN MICROBIAL PATHOGENS AND β2GPI: THE INDUCTION OF EXPERIMENTAL APS

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Employing a peptide phage display library, we identified three hexapeptides that react specifically with the anti-β2GPI mAbs. Using the Swiss Protein database revealed high homology between the hexapeptides with different bacteriae and viruses. Naive mice were immunized with a panel of pathogen particles. All the immunized mice developed antiphospholipid Abs. However, the most significant levels of mouse anti-β2GPI were detected in the mice immunized with Haemophilus influenzae or with Neisseria gonorrhoeae and bound β2GPI. Affinity purified specific immunoglobulins were infused i.v into BALB/c mice and the development of APS clinical manifestations was studied. Only the mice which were infused with mouse antibodies derived from mice immunized with Haemophilus influenzae or with Neisseria gonorrhoeae, directed to the peptide TLRVYK, had the potential to induce clinical manifestations which resembles experimental APS. We hypothesize, in the current case, that the mechanism of pathogenic anti-β2GPI generation is induced by epitope mimicry.

T53

ANTI-ICAM THERAPY IMPROVES NEUROLOGIC MANIFESTATION OF EXPERIMENTAL ANTIPHOSPHOLIPID SYNDROM - THE ROLE OF INFLAMMATION IN APS.

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Antiphospholipid syndrome (APS) is associated with various neurological complications, but the exact etiopathology is not well defined. Antiphospholipid antibodies (aPL) can induce a procoagulant and proinflammatory endothelial phenotype with enhanced expression of adhesion molecules. In this study we evaluate the anti-inflammatory effect of anti-ICAM monoclonal antibody on the neurologic dysfunction of mice with experimental APS.

Experimental APS was induced in BALB/c mice (n=45) by β2-GPI immunization (10ug/mouse in CFA). Three weeks after immunization, the mice were treated with 5 weekly i.p. injections of 500 μg of anti-ICAM antibody. Five month after immunization β2-GPI- immunized mice displayed impaired motor coordination on rotating bar ($p<0.01$), cognitive dysfunction in T-maze ($p=0.01$) and showed a tendency for hyperactivity in staircase system. Anti-ICAM treatment of β2-GPI immunized mice resulted in a significant improvement of motor coordination, in hyperactivity, but did not change their cognitive abilities. We assume that ICAM-mediated process account for neurological manifestation in APS and might provide a novel target for managing APS.

T54

β2-GLYCOPROTEIN I (APOLIPOPROTEIN-H) AS AN INFLUENCIAL DETERMINANT IN ATHEROSCLEROSIS

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β2-glycoprotein I (β2GPI) is a phopsholipid binding protein, with *in-vitro* anticoagulant properties. Recent data suggests that β2GPI serves as the major antigen against which antiphospholipid antibodies (aPL) react in solid-phase assays. Accordingly, anti-β2GPI antibodies have been shown to correlate closely with aPL, and with the occurrence of thromboembolic manifestations. We have recently suggested that immune response against β2GPI is involved in enhanced atherosclerosis. These data derives from studies in transgenic LDL-receptor and apoE knockout mice showing that induction of an anti-β2GPI immune response by immunization with the respective glycoprotein is followed by accelerated atherosclerosis. *In-vitro* studies support this paradigm by demonstrating that anti-β2GPI antibodies activate endothelial cell inducing adhesion molecule expression and enhance the uptake of radiolabled oxidized LDL to macrophages. It also appears that induction of murine aPL in LDL receptor deficient mice by immunization with human aPL bearing no β2GPI reactivity, is followed by enhanced fatty streak formation.We have also shown that β2GPI is abundantly present in the subendothelial regions of atherosclerotic lesions of humans. Interestingly, CD4 positive cells colocalize in areas in which β2GPI is expressed suggesting that a local immune response to β2GPI may take place within atherosclerotic lesions, potentially influencing its progression. Moreover, oxidized LDL specifically competes with radiolabeled β2GPI on the incorporation into human umbilical vein endothelial cells and into a myelomoncytic human cell line (U937).

Thus, β2GPI is present in atherosclerotic lesions, may be uptaken by its cellular constituents and consequently could elicit a local immune mediated response (upon its structural modification) that can culminate in enhancement of lesion progression. If these assumption are further consolidated, β2GPI may prove to be a target for anti-atherogenic strategies based on selective immunomodulation.

T55

APOPTOSIS OF B CELL SECRETING ANTI- β2GPI DERIVED FROM PATIENTS WITH APS BY SYNTHETIC PEPTIDES

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We present herein effort to develop a model for B cell peptide therapy for APS. Anti-β2GPI corresponding synthetic peptides were used as monovalent, divalent and tetravalent on Fmoc backbone. The peptides as divalent and mostly in tetravalent form, inhibited significantly the secretion of anti-β2GPI by B cells 4 APS patients. The peptides as tetravalent caused apoptosis of the specific B cells. The apoptosis was determined by DNA fragmentation, and could be prevented by caspase 3+8 or transfection with bcl-2. Regulation of anti-β2GPI secretion by the specific B cells upon exposure to the divalent and tetravalent peptides by cytokines was analyzed. The apoptosis was abrogated by IL-10 and IL-15 while TGFβ enhancec the process. IL-2 and IFN γ had no effect on the studied B cell function.

We propose a new attitude for treating B cells secreting pathogenic anti-β2GPI in APS or generally pathogenic autoantibodies.

T56

HLA CLASS II ALLELES ASSOCIATE WITH ANTI-PHOSPHOLIPID SYNDROME (APS) IN JAPANESE PATIENTS

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Objective: To elucidate clinical characteristics and genetic background of APS, we analyzed HLA class II alleles and clinical features in APS patients.

Methods: The first group of 30 patients (Group1), fulfilled the criteria proposed by Harris et al.{4 primary APS (PAPS), 23 SLE, 2 idiopathic thrombocytopenic purpura (ITP), and one systemic sclerosis}. Eighteen of the 30 patients (4 PAPS, 13 SLE, and 1 ITP: Group2) were diagnosed as definite APS by the preliminary classification criteria proposed by the 8th international symposium on antiphospholipid antibodies. HLA-DRB1, DQA1 and DQB1 alleles were determined by using PCR-RFLP method. The results were compared with those of unrelated 62 healthy controls.

Results: Compared to the control, the frequencies of HLA-DRB1 *0803 (0.0 vs control 14.5%, $p^1<0.03$, $p^2<0.04$) and DQA1*0501 (0.0 vs 16.1%, $p^{1,2}<0.05$) were low in both groups. The frequencies of HLA-DQA1* 0103 and DQB1*0601 were lower in the Group1 (20.0 vs 38.4%, $p<0.05$, 16.7 vs 38.7%, $p<0.03$). However, HLA-DQB1 *0602 was more frequent in the Group1 (26.7 vs 8.1%, $p<0.03$).

Conclusion: These results suggest the association of APS with HLA class II alleles.

T57

CHURG-STRAUSS SYNDROME (CSS) IN A PATIENT WITH ANTIPHOSPHOLIPID SYNDROME (APS)

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To our knowledge, the association of CSS with APS is rare: A 55-year old male with a history of asthma and sinusitis had simultaneously developed perforation of duodenal ulcer, eosinophilia, livedo reticularis, paresthesia of lower limbs and persistent proteinuria. Anticardiolipin antibody (aCL), β 2-glycoprotein I-dependent aCL and anti-MPO ANCA were all positive in his serum. Renal biopsy revealed the disruption of elastic lamina and organized microthrombi in renal arterioles. Under the diagnosis of CSS with APS, we treated him with prednisolone (PSL) 40mg/day, azathioprine 50mg/day and aspirin 81mg/day. His clinical conditions were rapidly improved. However, 2 years later, he developed polyarthritis, digital gangrene, bilateral occipital cerebral infarctions and proteinuria. We could successfully treat him with high-dose intravenous corticosteroid pulse therapy (500mg of methyl-PSL daily for 3 days) and warfarin.

T58

PROGRESSION OF PRIMARY PHOSPHOLIPID ANTIBODY SYNDROME (PPAS) INTO SLE.

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Introduction: Phospholipid antibodies (aPL) are associated with an underlying pathology of bland, non-inflammatory thromboses, unlike the small vessel vasculitis found in SLE. Previous studies have suggested that some PPAS patients may progress to develop clinical SLE.

Aim: To determine if PPAS patients progressed to develop clinical SLE.

Patients and Methods: Forty-five female patients followed for >4 years with PPAS were identified from our aPL database. A retrospective chart review of patients actively being followed was performed and patients lost to follow up were contacted and asked to come for a physical examination, blood tests and to complete a questionnaire.

Results: To date nineteen patients have been enrolled into the study, mean follow up 8.4 years range (4 to 15 years). Fifteen patients gave a history of unexplained late fetal wastage, five had a history of venous thrombosis, six had had a stroke or TIA and one had multifocal infarct dementia. At follow up, a full history and examination of these patients revealed one patient had developed polyarthritis (3 ARA criteria for SLE) and four others complained of intermittent mild arthralgias. There was no other clinical history suggestive of SLE. Laboratory abnormalities at follow up included: positive aPL (14), elevated ESR (6), low C4 (4) and low platelet count (2).

Conclusions: PPAS patients usually remain clinically unchanged and do not progress to SLE even after many years of follow up and the persistence of multiple laboratory abnormalities.

T59

THE ROLE OF AUTOIMMUNE DISORDERS IN THE DEVELOPMENT OF SEVERE PREECLAMPSIA

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Objective: Detection of a lupoid anticoagulant in the pregnant women with preeclampsia examined by us and determination of its clinicoprognostic significance.

Method: Determination of the lupoid anticoagulant.

Results: We have studied in detail 124 pregnant women with severe forms of preeclampsia. In 27 of them a lupoid anticoagulant was detected. All of the women had a hereditary history. Thus, 6 women had signs of perinatal losses, 7 had severe preeclampsia complicating previous pregnancy, in 2 previous pregnancy was complicating previous pregnancy, in 2 previous pregnancy was complicated by detachment of the normally located placenta, 3 had fliofemoral thrombosis. The course of preeclampsia in this group of patients was characterized by an early onset at 25-26 weeks of pregnancy and by pronounced manifest symptoms, in particular by high values of diastolic arterial pressure (DAP-110-140 mm Hg), persistent proteinuria (from 1 to 12 g/L), pronounced edemas of a generalized nature with predominant localization on external genital organs. The course of preeclampsia is chracterized by its fatal aggravation: in 9 women preeclampsia was succeeded by eclampsia with clonicotonic convulsions in 7 of them – during the postanal and postoperative periods. In 2 women the postoperatinve period was complicated by coagulopathic bleeding. In one – by hemorrhagic myelitis. Two out of 7 women required prolonged treatment of posteclamptic coma. In 20 (74%) of the patients in this group death of newborns was noted, which occurred within 3 days.

Conclusions: Thus, the presence of a lupoid anticoagulant in the blood of pregnant women is the cause of the early and severe course of preeclampsia which is characterized by a striking manifestation of the classical triad, fatal aggravation and high level of perinatal mortality.

T60

TREATMENT OF THE PREGNANT WOMEN WITH SEVERE PEECLAMPSIA AND A LUPOID ANTICOAGULANT

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Objective. Optimization of drug therapy in hemostasiologic disorders due to the presence of a lupoid anticoagulant (LA) in pregnant women with severe preeclampsia.

Methods: The method of inhalation of fraxiparin and dexamethasone by the ultrasound inhaler.

Results: Group 1: In 17 pregnant women we used 2 ultrasound inhalations with an interval of 12 hours between them. The duration of treatment was 7 days. 17 patients with severe preeclampsia were treated by routine methods together with ultrasound inhalations. In 8 of the 17 pregnant women who received combination therapy we were able to prolong pregnancy. As a result of the therapy carried out, there wasn't any case of eclampsia, as compared to group II. In 10 instances we were able to obtain live infants, in 2 - infants lived 5 days and died on account of profound prematurity, the rest of them (n=5) were born at 27 weeks – they died as a result of the respiratory distress syndrome Group II: In 4 women we were able to prolong pregnancy by 4-6 days. Thirteen required emergency delivary on account of the aggravating nature of the course of preeclampsia. Perinatal losses amounted to 12 newborns. In 7 women preeclampsia was sueceeded by eclampsia, in 5 of them in the postnatal and postoperative periods, in 2 the postnatal period was complicated by coagulopathic hemorrhage. The most important effects of drug inhalations were significant decreases in the concentration of low and high-molecular weight fragments of fibrinogen degradation products and a pronounced decrease in the frequency of positive tests for the lupoid anticoagulant.

Conclusions: The use of low-dispersity aerosols of low-molecular weight heparins and dexamethasone for the correction of hemostasiologic disorders due to the presence of a lupoid anticoagulant in pregnant women with severe preeclampsia with LA allows to prolong pregnancy, thereby promoting a significant reduction of perinatal mortality.

T61

PERIPHERAL NEUROMOTOR APPARATUS CONDITION IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES SYNDROME

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Objective: studied peripheral neuromotor apparatus in patients with antiphospholipid antibodies syndrome (APLS).

Methods: a complex clinical, neurological as well as immunologic and electroneuromyographic (ENMG) examination of the peripheral nervous system has been conducted in 9 patients with APLS.

Results: During the examination of 9 patients with the definite APLS alongside with traditional clinical manifestations of APLS symptoms of polyneuropathy with different degree of expression have also been revealed. Sensory disorders in the form of distal hypaesthesia have been found in 7 patients. Motor disorders in the form of distal paresis, mild or moderate, have been diagnosed in 5 patients. These combined with painfulness of nerve trunks of crus and antebrachium and symptoms of tension. ENMG examination has confirment the presence of neuropathy which was of demyelinizing character in 2 patients and of mixed type with prevalence of demyelinizing process in 5 patients. There was to be found an increased level of antibodies to cardiolipin IgG (on average up to 45.8 GPL) in all patients. The muscle biopsy results showed autoimmune myopathy with activated lymphocytes penetration under the sarcolemma of the muscular fiber with the lysis of sarcoplasma following it with out any signs of an inflammatory reaction.

Conclusion: Patients with APLS alongside with cerebrovascular lesions and skin syndrome with an active immunopathological process as a bachground had peripheral neuromotor apparatus lesion in the form of polyneuropathy, of mostly demielinizing character, as well as autoimmune myopathy.

T62

ANTIBODIES TO CARDIOLIPIN AND β2GPI IN THE GROUP OF WOMEN'S POPULATION WITH THE HISTORY OF RECURRENT SPONTANEOUS ABORTIONS

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Objective: to determine the significance of IgG anticardiolipin antibodies (aCL) and IgG antibodies to β2GPI (anti-β2GPI) in the group of women's population with the history of recurrent spontaneous abortions.
Design and methods: 58 women with one, two, three and more spontaneous abortions were examined. In control groups 12 healthy female donors and 10 normal pregnant were included. IgG aCL and IgG anti-β2GPI were measured by ELISA.
Results: The mean levels of IgG aCL (8,68 ± 2,38 GPL) and anti-β2GPI (3,53 ±6,21 SGU) among normal pregnant patients were not significantly differ when compared with healthy female donors. In the main group in 17 (29,3%) of 58 patients (pts) antiphospholipid antibodies (aPL) - IgG aCL or IgG anti-β2GPI were found elevated. In this group mean levels of IgG aCL was 67,6 ± 57 GPL and anti-β2GPI - 31,2 ±53,7 SGU. In the aPL-negative part of the main group IgG aCL was 7 ± 5,7 GPL, anti-β2GPI - 5,5 ± 3,2 SGU. It wasn't significantly differ when compared with the control group ($p>0.05$). In the aPL-positive group the mean number of fetal losses was 3,1±2,8, than 1,6 ± 0,9 in the aPL-negative part of the main group ($p< 0,05$).
Conclusions: we found important associations between the presence of aPL and recurrent fetal losses.

T63

MACROVASCULAR DISEASE IN SYSTEMIC SCLEROSIS

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OBJECTIVE: To evaluate the changes at the big blood vessels in the patients with Systemic Sclerosis (SS).

RATIONALE: Changes in the small blood vessels precede to other disorders in SS. Fibrosis is the result of disturbed balance of connective tissue metabolism, changes in small blood vessels and immune system too.

METHODS: Study included 19 patients with SS. We analyzed duration of disease, age, sex and risk factors for atherosclerosis. Control group included 12 patients with hypertension. We investigated big blood vessels of the upper and lower extremities using Doppler ultrasound (*Logidop 5 Cardia*) with probe of 8 MHz. We recorded maximal systolic velocity (Vs), maximal diastolic velocity (Vd) and mean velocity (Vm) on both ulnaris and radialis arteries. We also measured ASPI on both legs.

RESULTS: In SS group we found hypertension in all patients (100%) with mean duration of hypertension 4.74 ± 4.58 years. We found statistical significance differences in Vs, Vd, and Vm between SS and control group. In both groups values of ASPI were more than 0.9.

CONCLUSION: We didn't find segmental macrovascular diseases (occlusion and stenosis) which may have influence on hemodynamics on arteries of lower and upper extremities. Analyzing Vs, Vd, Vm we found enhanced peripheral vascular resistance.

T64

U.S. PHASE III TRIAL OF RELAXIN IN DIFFUSE SCLERODERMA. James R. Seibold, UMDNJ, Robert Wood Johnson, New Brunswick, NJ USA for PJ Clements, JH Korn, M Ellman, NF Rothfield, FM Wigley, LW Moreland, Y Kim, RM Silver, DE Furst, VD Steen, GS Firestein, AF Kavanaugh, MD Maves, D Collier, ME Csuka, R Simms, P Merkel and TA Medsger, with M Erikson, S Rocco, J Hannigan and ME Sanders, Connetics Corp., Palo Alto, CA, USA.

Recombinant human relaxin (rhRlx) has antifibrotic and angiogenic effects of potential application to the treatment of scleroderma (SSc). A prior study of 68 patients with stable, moderate-severe diffuse SSc demonstrated that rhRlx at 25 ug/kg/day led to reduction of total skin score, improvement in HAQ and reduced decline in FVC in comparison to placebo (Ann Intern Med 132: 871-879, 2000).

A multicenter prospective double-blind trial was conducted to attempt confirmation by comparing rhRlx administered at 25 or 10 ug/kg/day versus placebo (2:1:2 ratio) by subcutaneous infusion over 24 weeks.

231 subjects were eligible for Intention to Treat efficacy analysis. SSc was early (mean duration 2.2 ± 0.1 yr) and moderate to severe (mean modified Rodnan skin score (MRSS) at entry 27 units). 195 (81.6%) subjects completed all evaluations.

The primary efficacy measure was MRSS which improved in all groups (-4.9 ± 0.7 placebo vs -4.3 ± 1.7 rhRlx 10 ug vs -5.2 ± 0.6 rhRlx 25 ug, NS by one way ANOVA). No treatment related effects were noted in secondary outcome measures including pulmonary functions, HAQ-Disability Index, hand extension, oral aperture, SF-36, patient and MD global assessment. Transient anemia and menometrorrhagia were frequent drug-related adverse events. Systolic and diastolic blood pressure were reduced and creatinine clearance increased while on rhRlx. Discontinuation of rhRlx was associated with 7 significant renal events including 4 with SSc renal crisis.

This was a well-conducted robustly designed trial that failed to confirm an antifibrotic effect of rhRlx in diffuse SSc. No further SSc studies are contemplated although vascular effects suggest utility in non-SSc peripheral vascular disease, MRSS remains an reasonable measure of outcome in reversal-oriented, shorter term studies of SSc although placebo response appears to be substantial. This data set will permit careful definition of the inter-relationship of MRSS with other candidate SSc outcome measures.

T65

PREVALENCE AND CLINICAL FEATURES OF PULMONARY HYPERTENSION IN PATIENTS WITH ANTI-U1RNP ANTIBODY

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Objective: Pulmonary hypertension (PH) is a major complication of mixed connective tissue disease. However, its prevalence and clinical characteristics were not known. We have attempted to determine the prevalence and early detection of PH in patients witn anti-U1RNP antibody using noninvasive cardiopulmonary evaluation.

Patients and Methods: One-hundred four Japanese patients with antiU1-RNP antibody(MCTD 40 cases, SLE 38, SSc 9, UCTD 8, overlap syndrome 3, others 9). Between January and December 2000, we performed Doppler echocardiogram to detect PH in patients with anti-U1RNP antibody. The pulmonary artery pressure(PAP) was estimated by Doppler echocardiography.

Results: The PAP was estimated by Doppler echocardiography in 104 patients. PH (PAP >30 mm Hg) was found 42(37%) in 104 patients by the Doppler method. Fifteen cases were confirmed by right heart catheterization (mean PAP > 25 mm Hg) and/or clinical evaluations. PH were found among MCTD 20 cases, SLE 8, SSc 6, UCTD 3, overlap syndrome 2, other 3. PH were significantly higher in patients with Raynaud phenomenon (p= 0.02), and in those with pulmonary fibrosis (p= 0.007).

Conclusions: These findings suggest that patients with antiU1-RNP antibody are tended to develope PH.

T66

RAYNAUD'S PHENOMENON:CLINICAL,IMMUNOLOGICAL AND NAILFOLD CAPILLARY MICROSCOPY PATTERNS.

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Objective: To determine correlations between clinical,immunological and nailfold capillary patterns in patients with Raynaud's phenomenon (RP).**Methods:**Clinical RP, skin and organ involvement, ANA, and nailfold capillary patterns were assessed in 150 patients referred for evaluation of RP in period 1999-2000.**Results:** 142/8 female/male;mean age:42±15,6years;RP duration:5,7years.47% of RP were referred without diagnosis;5,5% as primary RP and 49% as secondary RP: Connective tissue diseases (CTD) in 73% of cases.Microangiopathic patterns detected were:38% normal, 25% functional,20% CTD pattern without specific capillary abnormalities of scleroderma (SSc), and 17% with SSc-pattern ("slow pattern" 7,6%; "active pattern" 9,7%).Patients with slow pattern SSc were older than the patients with other patterns:mean average: 53,8 years (p<0,05).RP with uniphasic color changes were observed principally in patients with normal o functional pattern and RP with biphasic color changes in patients with SSc-pattern (p<0,02). Significant association between "slow" pattern SSc and anticentromere antibodies was detected (p<0,004) and between "active"pattern SSc and positive ANA with nucleolar pattern.Anticentromere antibodies were detected in 9% of patients showing functional pattern with capillary pallor and "active"pattern SSc was observed in 42% of positive Scl-70. Sclerodermatous skin was associated with SSc-pattern and capillary pallor pattern (p<0,001) and a higher proportion of soft tissue swelling in hands and organ involvement was detected in patients with "slow"pattern-SSc.**Conclusions:**Functional pattern with capillary pallor showed a significant association with uniphasic RP, sclerodermatous skin changes and negative ANA.Only 42% of patients with positive Scl-70 antibodies exhibited "active" pattern.

T67

CYCLOSPORIN A TREATMENT OF SYSTEMIC SCLEROSIS

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Introduction. The efficacy of cyclosporin A (CyA) in improving the symptoms of patients affected by systemic sclerosis (SSc) is assessed by many authors. We recently reported on the efficacy of low-dose CyA (2.5 mg/kg/day) in SSc (1). The results of our open study demonstrated a significant improvement of skin tightness, microangiopathy, oesophageal and lung parameters, after twelve months of CyA therapy. No relevant side-effects were observed in these patients and none had to stop CyA administration, besides a mild not clinically relevant increase of blood pressure was common.

Methods. Eight female SSc patients (mean age 49±4 years) showing progressive microangiopathy as evaluated by nailfold video-capillaroscopy (NVC) (Videocap - DS Medigroup, Milan, Italy) were retrospectively evaluated after 5 years of CyA treatment.

Results. The initial CyA dose was of 2.5 mg/kg/day in all patients. The improvement of nailfold microvasculature was observed in six patients after two years of CyA treatment. Among these, five patients reduced CyA daily dose to 1.5-2 mg/kg since improvement of all SSc symptoms was observed. One patient reduced CyA daily dose to 1.5 mg/kg because of mild hypertension. A progressive worsening of nailfold microangiopathy was observed after CyA dose reduction in all six patients. One patient had to reduce CyA dose to 1.7 mg/kg/day after six months of treatment because of mild hypertension; as a consequence a progression of SSc microangiopathy was observed. A further patient reduced CyA daily dose to 1.7 mg/kg because of sickness and epigastralgia after five months of treatment. Once again a worsening of SSc microangiopathy was observed.

Conclusion. In our experience, the administration of low-dose of CyA (2.5 mg/kg/day) in SSc patients is usually effective, safe and well tolerated. However, CyA daily dose lower than 2.5 mg/kg seems not effective.

(1) G. Filaci et al - Rheumatology 1999; 38: 992-6.

T68

A DEFECTIVE ACTIVATION OF RENAL FUNCTIONAL RESERVE PREDICTS RENAL INVOLVEMENT IN SYSTEMIC SCLEROSIS.

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Objective: To evaluate if the increase in glomerular filtration rate (GFR) elicited by an aminoacid load (renal functional reserve, RFR) is an early marker of renal involvement in systemic sclerosis (SSc).

Rationale: The early phase of SSc is characterized by an impaired vasodilation that affects also the kidney vasculature. We previously demonstrated a blunted RFR, which depends on preglomerular vasodilation, in SSc patients with normal renal function. Structural vascular wall changes may follow this early functional dysfunction.

Methods: Renal function and blood pressure were followed up for 56 to 60 months in 19 SSc patients (2 males and 17 females, age 50.4±11.8 years), normotensive and with no clinical sign of renal involvement at enrollment. Initial evaluation included the measure of RFR, which was normal in 5 (age 51.6±13.3 years, group 1) but totally absent in 14 cases (age 49.9±11.7 years, group 2).

Results: All patients with normal RFR remained normotensive throughout the follow up period, while 6 out of 14 patients without RFR developed systemic hypertension. At the end of follow-up, average GFR change was 1.2±3.0 and -10.7±10.5 ml/min x 1.73 m^2 in group 1 and group 2 patients, respectively (p<0.01). No renal crisis was observed. Changes in GFR were not related to any eventual hypotensive treatment (ACE-inhibitors and calcium- channel blockers, alone or associated).

Conclusion: The measure of RFR represents a useful tool to detect early SSc patients at risk of progressive renal function reduction and development of systemic hypertension.

T69

SF36 AS A POTENTIAL TOOL FOR THE EVALUATION OF THE QUALITY OF LIFE IN SYSTEMIC SCLEROSIS (SSc)

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Background: SSc modifies the patients (pts) self-image and impair the quality of life. Self-administered questionnaires were used to evaluate health status, functional capacities and disability, considering mainly the physical impact of SSc. SF-36 is the most used tool evaluating pts subjective state about the In psychic and physic limitations due to an underlying illness.

Aim: to evaluate the quality of life in SSc pts by SF-36 administration and to correlate SF-36 with clinical and laboratory parameters.

Patients and methods: in 24 (15 limited and 9 diffuse) pts were evaluated ACE, ACA and anti-Scl70; skin involvement by Rodnan modified skin score; heart and lung involvement by DLco, ^{99m}Tc DTPA, HRCT, EKG, Echocardiography. The SF-36 questionnaire was auto-administered. It considers 8 scales measuring: physical activity (PA), role of physical activity (RP), bodily pain (BP), general health (GH), vitality (VT), social activity (SA), emotional problems (EP), mental health (MH).

Results: Reduced ACE levels, linked to a major impairment of microvasculature, are related to a compromised VT (r=-0.480, p=0.024). High values of skin score, index of a more diffuse and serious disease, are linked to impaired RP (r= 0.453, p= 0.026) and MH (r= 0.476, p= 0.022). Significant correlations were found between the SF 36 scales: PA was related to RP (r= 0.477, p= 0.021), BP (r= 0.565, p= 0.005), and VT (r= 0.673, p= 0.001); VT to RP (r= 0.462, p= 0.031), and PB (r= 0.482, p= 0.023). RP to EP (r= 0.626, p= 0.001). MH and EP also correlated (r= 0.689, p= 0.000).

Conclusions: SF36 may evaluate both the physical and psychological aspects and correlates with clinical and laboratory features of SSc.

T70

SURGICAL TREATMENT FOR GASTROESOPHAGEAL REFLUX DISEASE IN SYSTEMIC SCLEROSIS.

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OBJECTIVE: To describe the experience with the surgical treatment for gastroesophageal reflux disease (GRD) in systemic sclerosis (SSc).
PATIENTS AND METHODS: From 202 patients with the diagnosis of SSc attended at the Scleroderma outpatient clinic in the period 1991-2000, ten patients (5%) who presented GRD, with severe chronic esophagitis and stricture, were submitted to surgical treatment. All the patients were female and eight were Caucasian, with seven presenting limited SSc (mean age 53 years and mean disease duration 17 years) and three diffuse SSc (mean age 44 years and mean disease duration 6 years).
RESULTS: The correction of the gastroesophageal reflux was performed through videolaparoscopy in nine patients. Seven patients underwent modified Nissen technique and three patients Lind technique. There was satisfactory clinical response, with significant improvement in the heartburn and dysphagia in all the patients. After a mean followup of 34 months (12-76 months), one patient presented clinical relapse (after 54 months) and another patient needed a surgical ressection of a paraesophageal hernia (Y-Roux).
CONCLUSION: The surgical treatment of GRD represents an efficient therapeutic option in SSc patients with severe esophagitis and stricture.

T71

STATE OF NEUTROPHILS IN PERIPHERAL BLOOD AND ENZYMATIC ACTIVITY FOR AN ILL SYSTEMIC SCLERODERMA

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The purpose: learning of neutrophils in peripheral blood and enzymatic activity of patients with systemic scleroderma (SSD).

Methods: for the patients with a SSD explored a spontaneous chemiluminescence of neutrophils, level of circulating immune complexes, activity of a catalase, superoxiddismutaza, mieloperoxidaza and content of a lysozyme.

Results: the patients with systemic scleroderma reliable differed from group of healthy faces by higher spontaneous (1,57± 0,9 and 114±0,08 accordingly) and boosted (21±0,08 and 17±2,9 accordingly) chemiluminescence of neutrophils, higher content of circulating immune complexes in a blood plasma (67,9±2,8 and 27,8±7,4 accordingly). For the patients with a SSD as indexs of activity superoxiddismutaza (1,01±0,25 and 1,45±0,05 SED/ml accordingly) and catalase (2,79±0,48 and 3,19±0,09 mcmol/min ml accordingly) reliable were higher.

Deductions: the detected state transitions of neutrophils of a peripheral blood reflect presence of current fissile pathological process and heightened ferment activity for the patients with SSD.

T72

SURVIVAL ANALYSIS IN A COHORT OF 309 FRENCH CANADIANS WITH SYTEMIC SCLEROSIS. Senécal JL, Lonzetti L, Raynauld JP, Roussin A, Rich É, Goulet JR, Raymond Y, Joyal F. Centre hospitalier de l'Université de Montréal, Montréal, H2L 4M1.

Objective : To determine the survival of French Canadian (FC) patients with systemic sclerosis (SSc), and to identify predictive factors for mortality.

Methods : 309 FC patients seen by us from 1984 and 1999 were enrolled consecutively at diagnosis in a prospective SSc cohort study and evaluated according to a disease extent protocol encompassing 215 variables. Patients were categorized into one of four SSc subsets based on extent of sclerodermatous skin involvement : *sine* (n=50), limited (n=152), intermediate (n=78), and diffuse SSc (n=29). Mortality status and causes of death were obtained from Institut de la Statistique du Québec.

Results : Of the 309 patients, 66 (21.3%) deceased during the 15-year period of observation. Death distribution was: *sine*, n = 4 (8% of subset population); limited, n = 32 (21%); intermediate, n = 21 (26.9%); and diffuse SSc, n = 9 (31%) (P<0.03). The major causes of death were related to SSc itself, accounting for 35 (53%) deaths. No deaths were SSc-related in the *sine* subset, whereas 44%, 57.1% and 100% of the deaths were SSc-related in the limited, intermediate and diffuse subsets, respectively (P<0.001). The mean survival after inception was 15.3 years in limited, 14.6 years in intermediate and 11.8 years in diffuse SSc. The 10-year cumulative survival rates for these subsets were 89%, 86% and 62%, respectively (logrank test, P=0.0001). The logrank test between intermediate and diffuse SSc was significant (P = 0.03), as well as between limited and diffuse SSc (P=0.0005). In a univariate Cox regression model, variables significantly associated at baseline with mortality were: age, skin involvement of the trunk, abnormal ECG, DLCO <=70% of predicted value, ESR >= 25 mm/hr, hemoglobin (Hb) level <= 12.5 gm/dl and antitopo I antibodies. By forward stepwise Cox regression, the strongest independent predictor variables, were: skin involvement of the trunk, age, DLCO<=70%, ESR >= 25 mm/hr and Hb <= 12.5 gm/dl.

Conclusion : Simple clinical and laboratory variables obtained at baseline are strong predictors of mortality in FC SSc patients.

T73

ANALYSIS OF CLINICAL MANIFESTATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND WITH CREST VARIANT

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OBJECTIVE: Analysis of clinical manifestations in patients (pts) with systemic sclerosis (SS) and in pts with CREST and analysis of clinical manifestations related to skin involvement in both groups.

RESULTS: Since 1993 we have treated 133 pts (120 f and 13 m) with systemic sclerosis (SS). Mean age of pts was 52 yrs and disease duration 11.6 yrs. Ninety pts (67,7%) had limited cutaneous SS (lSS) and 43 (32,3%) diffuse cutaneous SS (dSS). In the same time we have treated 51 pts (49 f and 2 m) with CREST variant of scleroderma. Mean age of pts was 55.7 yrs and diseases duration 10.9 yrs. Thirty-four pts (66.7%) had limited cutaneous form (lCREST) and 17 (33.3%) diffuse cutaneous form (dCREST). Clinical manifestations in our pts are shown in following figure.

Clinical manifestation	Systemic scl. (n=133)			CREST (n=51)		
	lSS	dSS	p	lCREST	dCREST	p
Interst.lung dis	32.0 %	72.0 %	p<0.01	50,0 %	58.8 %	NS
Oesoph.Dysf.	50.0 %	69.7 %	p<0.01	100 %	100 %	NS
Renal invol.	8.9 %	30.2 %	p<0.01	29.4 %	29.4 %	NS
Hypertensio	44.4 %	41.8 %	NS	52.9 %	70.6 %	NS
ECG changes	30.0 %	53.5 %	p<0.01	50.0 %	64.7 %	NS
Arthritis	20.0 %	39.5 %	NS	20.6 %	17.6 %	NS
Tenosynovitis	6.6 %	4.8 %	NS	17.6 %	23.5 %	NS
Resorp.of DPh	27.7 %	37.2 %	NS	58.8 %	82.3 %	NS
Ulcerations	63.3 %	81.4 %	NS	91.0 %	100 %	NS
Sicca Sy	4.4 %	4.6 %	NS	8.8 %	11.8 %	NS

CONCLUSION: Oesophageal dysfunction, tenosynovitis and resorption of distal phalanx were significant more frequently in pts with CREST then in pts with SS. Interstitial lung disease, oesophageal dysfunction, ECG changes and renal involvement were significant more frequent in pts with dSS then in pts with lSS, but in pts with CREST variant, visceral involvement does not depend on distribution of skin sclerosis.

T74

PULSE THERAPY OF CYCLOPHOSPHAMIDE IN TREATMENT OF SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE

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Objective: To assess the efficacy and safety of cyclophosphamide pulse therapy in patients with severe systemic sclerosis and interstitial lung disease, in an opened prospective pilot study.

Methods: Eleven patients, 9 females and 2 males, age of 34-70 years, mean 47 years, and disease duration of 1-10 years, mean 3,2 years, were included. All the patients hag interstitial lung fibrosis and significantly decreased carbon monoxide diffusing capacity. Previous treatment with D-Penicilamine or Methotrexate was ineffective. During the 2 years study period patients were submitted to monthly intravenous pulses of cyclophosphamide, 500 mg/m^2 of body surface. The outcome measurements were: DLCO KCO, changes in Skin Score and Skin Progressing Index (SPI), and patient opinion about the skin softening and improvement of overall health status (visual analog scale). Statistics - Wilcoxon matched pairs test.

Results: Pulmonary function improved insignificanty in first 6 months of treatment, and in next 18 months slow insignificant worsening was detected. Significant skin softening (p=0,015), and significant improvement in overall health status (p=0.015) were observed by the patients (visual analog scale).Two patients deyed from acute myocardial infarction. In other patients no severe adverse events were recorded in the trial period. Mild and transistent adverse events, nausea, vomiting and malaise, dry cough, and headache and gastric pain, only in the first 48 hours after some of the pulse doses.

Conclusion: Cyclophosphamide intravenous pulse therapy in patients with systemic sclerosis and interstitial lung disease during a 2 years trial period resulted in insignificant deterioration of pulmonary function, but, by patient opinion, softening of the skin and significant improvement in overall health status, without severe adverse events.

T75

LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION-CARDIAC INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Objective: The aim of the study was to evaluate cardiac involvement in systemic sclerosis, analyzing left ventricular systolic and diastolic function.

Rationale: Left ventricular dysfunction, may be serious complication in patients with systemic sclerosis. .

Methods: In the study population of 40 pts with systemic sclerosis (mean age 52,85 ±12,44) and 30 healthy controlled subjects (mean age 50,93±8,12), prospective M mode, 2D and Doppler echocardiographic examination were done. Left ventricular systolic function was evaluated by fractional shortening (FS) and ejection fraction (EF). Left ventricular diastolic function, as expressed by echo Doppler transmitral flow indices of left ventricular filling, was defined as E (early diastolic flow velocity) / A (late diastolic flow velocity) ratio. Diastolic dysfunction was present when E /A < 1.

Results: Compared with the control group, patients with SSc had significantly reduced mean values of EF (61,33 % vs 70,10 % , p<0,001), reduced mean values of FS (33,80% vs. 39,43% , p < 0,001). Diastolic function , was significantly reduced in SSc (0,92 ± 0,22 cm/s) vs. controlled group (1,30 ± 0,31 cm/s), p < 0,001.

Conclusion: The use of this index appears to be a useful predictor of global left ventricular dysfunction in patients with systemic sclerosis.

T76

ELECTROCARDIOGRAPHIC ALTERATIONS IN SYSTEMIC SCLEROSIS AND IN RHEUMATOID ARTHRITIS

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Objective: Aim of this study was to evaluate and to compare the frequency and type of ECG alterations in patients with systemic sclerosis and rheumatoid arthritis.

Rationale: Myocardial involvement is a common finding in patients with SSc. It is also present in RA, but very rarely. Different alterations can be revealed by an ECG examination.

Methods: In the study group of 40 pts with SSc (mean age 52,85 ± 12,44) and 22 pts with RA (mean age 51,45 ± 11,41) clinical and ECG examination were done. All the patients with SSc were devided into two subgroup: with diffuse (dSSc) and localised (lSSc) SSc. The ECG data of each of these subgroup were compared . We investigated the existance of ECG abnormalities :ventricular premature beats , supraventricular premature beats, arrhythmia absoluta, left bundle branch, left anterior fascicular block, complete right bundle branch block, atrioventricular block, infarct or pseudounfarct and ST depression.

Results: ECG alterations were found in 65% of SSc patients, but only in 18,19% of RA patients; the difference was significant (p < 0,001). In the dSSc group ECG alterations were found in 6 pts (15%) - not signifficant compared to the group with lSSc (5 pts, 12,5%) p = 0,220

Conclusion: The result of our study showed a significant prevalence of ECG alterations in SSc, but low prevalence in RA.

T77

SYSTEMIC SCLEROSIS AND RAYNAUD'S PHENOMENON : COMPARISON OF CLINICAL GROUPS

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Objective: To compare clinical groups of systemic sclerosis (SSc) and primary Raynaud's disease (PRD) in biochemical and immunological aspect .

Rationale: PRD is common in 10 % of population , but in SSc as secondary Raynaud's disease is very common – 70 % of all the systemic sclerosis patients and it may be the first symptom of systemic sclerosis .

Methods:. 44 SSc and 10 PSD patients was selected and the statistical analysis by ANOVA (one way ANOVA) test was applied.

Results. Quantitative indices of urea and creatinine levels in blood show that renal function was changed in patient with PRD versus CREST syndrome ($P<0.05$), PRD versus SSc ($P< 0.05$) and PRD versus local sclerosis ($P<0.05$) Making comparison of anti Scl 70 antibodies and inflammatory indices (CRP,ESR) between clinical groups the results was following: SSc versus PRD ($P<0.001$) , local sclerosis versus PRD ($P<0.05$) .

Conclusion: The monitoring of urea, creatinine, inflammatory indices and anti Scl 70 antibodies in patients with CREST syndrome, local sclerosis and primary Raynaud's phenomenon is very important to prevent development of diffuse process– systemic sclerosis with involving of kidney in the pathological process

T78

LOCALIZED SCLERODERMA OVER GRAFTED SKIN

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A healthy 47-year-old woman suffered burning lesions over 65% of body surface. She underwent autologus and allogeneic (pig skin) skin graft. Six years later she presented with taut, thickened skin over some areas of the grafted skin, sparing the face. She developed rapidly progressive dermal sclerosis over 6 months. On physical examination she had severe sclerodactily, moderate to severe confluent areas of scleroderma in grafted areas of chest, arms, hands, thighs and ankles, as well as decreased range of motion in limbs, impaired hand function and synovial effusion in knees. Differential diagnosis of scleroderma and chronic graft-versus-host disease (GVHD) was considered. Laboratory tests showed elevated alkaline phosphatase and eritrosedimentation rate as well as positive antinuclear antibodies and anti Scl-70. Skin biopsy findings on light microscopy were consistent with epidermal atrophy, loss of hair follicles, diffuse fibrosis with moderate fascial fibrosis involving the subcutaneous tissue and perivascular lymphocytic infiltrate. These changes can be compatible with any of the two entities; however, although GVHD in sclerodermiform stage can show fibrosis in papilar dermis, collagen fibers tend to be normal and there is no perivascular fibrosis which was found in this patient. Skin contracture was refractory to colchicine, D-penicillamin and piascledine. Symptoms improved with the use of oral methotrexate (MTX) 7.5 mg weekly, Cyclosporine A (CyA) 200 mg daily (3.5 mg/kg/day) and prednisone 10 mg daily which she has been taking for the last 24 months. No systemic symptoms were ever noted.
CONCLUSION: We present a case of sclerodermatous changes over grafted skin which was compatible with scleroderma and showed rapid clinical improvement when MTX and CyA were started. This might be a rare variant of localized scleroderma.

T79

EFFICACY OF LOW DOSE METHOTREXATE (MTX) IN THE TREATMENT OF ANKYLOSING SPONDYLITIS (AS) WITH ARTHRITIS

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Purpose: In this study have shown that low dose MTX is safe and useful in suppressing some of the inflammatory features of AS.

Methods: Patients in the groupe A (10 patients with AS+arthritis) use of antiinflammathory drugs (Rapten K a 50 mg x 2) + MTX 7,5 mg/week and physical therapy; in the group B + Rapten K a 50 mg x 2 and physical therapy. None had a history of viral hepatitis. The following were carried out got all visits (1.0 mth) for one year trough physical examination: durration of back early morning stiffness, VAS for back paine (10 cm), swollen joints, occiput to woll and finger to floor distance, Schoberts test, complete blood cound, renal/liver functions tests and immunoglobulini levels.

Results: Significante improvement was noted in the group A: blood count (p 0,001) and number swollen joints (p<0,0001) and VAS for pain (p<0,0001).
In the groupe B no significant changes was for pain hip range of movement thoracis and lumber spine, CRP and Ig levels.

Conclusions: Our results have shown that low dose MTX is safe and useful in suppreesing some of the inflammatory features of AS with arthritis.

T80

PLANE BONES INJURY IN ANKYLOSING SPONDYLITIS. NOTIONS OF PATHOGENESIS AND EARLY DIAGNOSIS

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Objective:To study the injuries of plane bones in patients with early staged ankylosing spondylitis (AS), and evaluate the imnportance of these lesions in elucidation of pathogenesis and establishment of criteria for early diagnosis.
Rationale: The injuries of plane bones and semimobiole joints in patients with ankylosing spondylitis (AS) are deatected at very early stages of AS and determine their role in ititiation of pathologic process and pathogenesis itself.
Methods: The study comprises 819 patients with ankylosing spondylitis, including 725 males and 94 females, aged 16-65 years old, with an average of 31.5 years. Clinical assessments included: diagnostic radiography, scintigraphy with Th^{131M}, immunological tests, histological examinations.
Results: Our studies revealed clinical signs of ankylosing spondylitis, supported by the results of clinical assessments: radiography (osteosclerosis and osteoporosis), scintigraphy (radionuclide dypercapture in areas distanced from foint surface), histology (both lacunar and smooth resorption modifications), numerous plasmocytes, intensive fibroblast proliferation, osteoid mass deposits, chemosiderosis, immunological test detected the presence of HLHLA-B27 antigen and its B15, 35, 7 phenotype.
Conclusion: Our results revealed the importance of the study of plane bones injury in patients with ankylosing spondylitis for eludcidation of mechanisms of AS pathogenesis for the establishment of certain criteria for early diagnosis of the disease.

T81

KINEZIOTHERAPY EXERCISES AS A TREATMENT FOR PATIENTS WITH ANKYLOSING SPONDYLITIS

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Ankylosing spondylitis is a chronic inflammatory disease of the joints and ligaments of the spine, beginning in the sacro-iliac joints. It affects 1 promiles of the population. It progresses slowly, the natural outcome is bony ankylosis of the affected joints.
Therapeutically we use NSAI drugs to lessen pain and inflammation, but for sustaining mobility of joints there is therapeutic exercise programme only, which can diminish deformities and restore the posture and mobility of whole body. Patients are motivated to carry out exercises daily. The programme must be defined by properly educated physiotherapist.
The majority of Slovenian patients are organised in the Slovenian Society of A.S. Patients. The regional subunits of the Society organise hydro- and kinesiotherapy.
Authors evaluated 42 patients who regularly practise therapy at Department of Physical Medicine and Rehabilitation in Maribor Teaching Hospital once a week. There were 37 men and 5 women, mean age was 42 years. Authors tested functional ability, axial mobility and respiratory function. In observed period (5 years) the group demonstrates no further functional deterioration and patients are still independent in their everyday's activities of daily living.
The study showed evident benefits of long-term and regulars practicing of competent exercise programme for ankylosing spondylitis patients.

T82

PECULIARITIES OF ANKYLOSING SPONDYLOARTHRITIS PROCESS IN FEMALES

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Aim: To study the peculiarities of ankylosing spondyloarthritis (AS) in women of Tadjik nationality.
Material: 35 females and 35 males with reliable AS were studied (median age 32.3±2.2 yrs and 35.3±1.8 yrs correspondingly). Disease duration was 6.6±1.5 yrs in females and 9.3±1.5 yrs in males.
Results: AS in females is characterized by late diagnosis, slow progressing process in the spine and sacroiliitis symptoms, more frequent lesion in cervical spine (ankylosis and arthritis of arcuate processes of joints- in 20% against 5.6% in males) and in females twice more often sternoclavicular joints were involved. Peripheral arthritis of lower extremities was more characteristic for males (34% against 28% in females). AS peculiarities in females were also characterized by rarity of extraarticular manifestations. Cardiac disturbances were found in 14% of males and 2.8% of females. Eye pathology and renal disturbances were not found. Growth og IgA and IgM levels were noted in peripheral form of the disease. CIC level in males was higher than in females with AS. Among disease preceding factors pregnancy and childbirth are of importance (in 20%) which enables us to regard them as risk factors for AS.
Conclusion: Distinguishing of AS variants associated with sex is promoting early diagnosis and timely beginning of adequate therapy.

T83

THE SIGNIFICANCE OF HEPATITIS B VIRUS INFECTION IN ANKYLOSING SPONDYLITIS HLA B27 POSITIVE

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Objective: To investigate the prevalence and the possible pathogenic significance of hepatitis B virus (HBV) infection in ankylosing spondylitis (AS) associated with the class I antigen HLA B27.
Methods: Patients included 13 males and 10 females with definite AS and no previous immunization against HBV. We performed immunology tests, X-rays and osteoarticulary scintigraphies, HLA, auto antibodies (Ab) against HCV, HBs and HBe antigen (Ag), anti HBs, HBc and HBe Ab, serum HCV-RNA and HBV-DNA if necessary.
Results: 19 patients (82.6%) were HLA B27 (+) and 4 patients (17.4%) HLA B27(-). In B27 (+) group all patients had no signs of present or previous HCV infection. 8 patients (42.1%) had HBs Ag positive in their sera and 7 patients (36.8%) had signs of previous HBV infection. This group was characterized by elevated ESR up to 100mm/h, bilateral grade II-IV sacroiliitis, ANA positive, homogenous. As for the B27 (+) group without signs of HBV infection (4 patients, 21%), clinical manifestations were mild, with bilateral sacroiliitis grad II-III and moderate ESR values, up to 40mm/h. In HLA B27 (-) group only 1 patient had positive tests for HBV and 1 a HCV Ab with no serum HCV-RNA confirmation. The patients were characterized by mild disease activity.
Conclusions: There is a high prevalence of HBV infection in AS HLA B27 (+) group (79% of the patients), 42% having signs of present infection. The disease is characterized by a severe course. There is no high prevalence of HBV infection in AS HLA B27 (-) group. It is possible not only gram-negative bacteria (Klebsiella) but also HBV may trigger the development of AS in genetically susceptible individuals.

T84

SERUM PROLACTIN LEVEL IN SERONEGATIVE SPONDYLOARTHROPATHIES

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Objective: To determine serum prolactin (PRL) levels in patients with seronegative spondyloarthropathies.
Methods: One hundred and two patients with spondyloarthropathies (44 Reiter's syndrome, 44 ankylosing spondylitis and 14 psoriatic arthritis) were evaluated. All satisfied the European Spondyloarthropathy Study Group (ESSG) classification criteria. Controls were 40 healthy volunteers. Morning blood samples were collected from all patients and controls. Serum PRL levels were measured by radioimmunoassay (RIA). Clinical evaluation included detailed questioning about articular and extraarticular symptoms. All subjects underwent complete physical examination. Other laboratory investigations included full blood count, ESR, CRP, RF and HLA-B27.
Results: Mean serum PRL levels were 24 ng/ml, 16,5 ng/ml, 15 ng/ml and 9 ng/ml in Reiter's syndrome, psoriatic arthritis, ankylosing spondylitis and controls respectively. (Normal 0-20 ng/ml). Hyperprolactinemia (>16 ng/ml in males and >25 ng/ml females) was found in 14 (31.8%) patients with Reiter's syndrome and 2 (14.2%) patients with psoriatic arthritis. Serum PRL levels were normal in all ankylosing spondylitis patients and controls.
Conclusion: PRL, which is thought to be a factor playing role in pathogenesis of autoimmune disease, was found elevated levels in Reiter's Syndrome and psoriatic arthritis, but not in ankylosing spondylitis.
Key words: Prolactin, Ankylosing, Spondylitis, Reiter's Disease, Psoriatic, Arthritis, Biological Markers.

T85

SAPHO Syndrome. A report of 2 cases.

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SAPHO syndrome "syndrome acne, palmo-plantar pustulosis (PPP), hyperostosis, osteitis" associates articular and bony signs associated with dermatosis. We report 2 cases.

Case 1: Ms M.M, 55 years, is presenting since 10 years chronic inflammatory pains affecting thorax, sacro-iliac joint and spine. In 1994, ESR at 60mm was relevant. Sacro-iliac and sterno-clavicular (SCC) X rays were normal. Increased radioisotope uptake was showed in right SCC, CT scan was normal. NSAIDs intake improved the patient. 6 years late, she presented painful joints and ESR at 80 mm. The exam showed PPP, SCC and manubrio-sternal synovitis, pain on the left sacro-iliac joint, sternal hypertrophy. There was HLA B27 antigen. Syphilis serology was negative. Once more, NSAIDs treatment improved her.

Case 2: Mr K.A, 22 years old is presenting for 5 years inflammatory polyarthralgias, buttock pains, talalgias, and inflammatory pains in left sterno-clavicular joint, synovitis of the knees and wrists, hyperostosis in right shoulder and in inferior third part of the right shenbone, painful sacro-iliac joint, acne on the thorax. Scintigraphy showed an increased radioisotope uptake in inferior third part on right shenbone, in upper end of the right humerus, in left wrist, left sterno-clavicular and sacro-iliac joints. X Rays demonstrated hyperostosis in them.

Conclusion: both cases show, throughout time, the relationships between SAPHO syndrome and spondylarthropathies. However, this syndrome seems to be rare, in a geographical area where spondylarthropathies are frequent.

T86

PREVALENCE OF ARTICULAR MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE.

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Objective: Data regarding the prevalence of articular manifestations in Inflammatory Bowel Disease (IBD) are disparate in the different published series. The aim of our study was to determine the prevalence of peripheral arthritis and axial involvement in patients with IBD.

Methods: A series of 112 consecutive patients diagnosed of IBD attending a Gastroenterology Unit were evaluated by a rheumatologist. A radiological assessment of X-ray films of the SI joints and lumbar spine was made by a radiologist and a rheumatologist. Radiographs were read independently and blindly, differences in grading were settled by mutual consensus. The HLA-B27 typing was determined by a microlymphocytotoxicity technique.

Results: A total of 100 patients (89%) had complete data for statistical analysis, 59 with Crohn's Disease (CD) and 41 with ulcerative colitis (UC), of which 57 were female. Peripheral arthritis (PA) by medical history was elicited from 21% patients; ankylosing spondylitis (AS) was found in 8%; sacroiliitis > stage 2 (but without fulfilling diagnostic criteria for AS) was found in 5% of patients. A clinical diagnosis of spondiloarthropathy (SpA) using ESSG criteria was present in 35%. History of inflammatory back pain (IBP) was referred by 20%. HLA-B27 was positive in 8% of CD patients and 19% of UC patients. A summary of these data is shown in the table below.

Finding	PA	AS	SI	SpA	IBP	B-27
CD (59)	19 %	5 %	5 %	34 %	20 %	8 %
UC (41)	24 %	12 %	5 %	37 %	19 %	19 %
IBD (100)	21 %	8 %	5 %	35 %	20 %	13 %

Conclusions: In our study we found a high prevalence of articular involvement in patients with IBD. The presence of the HLA-B27 antigen increases the risk for developing inflammatory axial involvement. We observed a higher frequency of HLA-B27 and ankylosing spondylitis in UC in relation with CD.

T87

ENBREL® (ETANERCEPT) IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

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Background: Results have been presented from a 12-week, double-blind placebo-controlled study of 60 patients with psoriatic arthritis (PsA) and psoriasis (Mease Lancet 356:385-90 2000). ENBREL was well tolerated and provided clinically significant benefit to patients with PsA and psoriasis. All patients could receive open-label ENBREL in this 24-week extension study evaluate the longer-term safety and efficacy.

Methods: As in the blinded study, this study evaluated improvements in patients with PsA according to PsA response criteria (PsARC) and ACR criteria. Patients with psoriasis were evaluated using the Psoriasis Area and Severity Index (PASI).

Results: Fifty-eight patients from the 12-week study received open-label ENBREL in the 24-week extension study and were evaluated according to PsARC and ACR criteria. Thirty-seven patients with psoriasis were evaluated using the PASI. The original ENBREL patients sustained their improvement in both PsA and psoriasis in the extension study. The original placebo patients demonstrated similar improvements once they began receiving ENBREL. At 36 weeks, 81% of all patients achieved the PsARC, 74% achieved the ACR 20, and 55% achieved the ACR 50. The patients with psoriasis achieved median improvements of 62% in the PASI and 50% in the target lesion response. Of the 28 patients taking concomitant methotrexate (MTX) at baseline, 43% (12/28) have decreased their MTX dose and 25% (7/28) patients have discontinued MTX. Similarly, of 18 patients on corticosteroids at baseline, 67% (12/18) have decreased their steroid dose and 44% (8/18) have discontinued steroids. At 36 weeks, 28% of patients had zero tender joints, 41% had zero swollen joints, and 40% had a disability score of zero. ENBREL continued to be well tolerated, with no serious adverse events or infections and no increases in adverse events with extended exposure.

Conclusion: ENBREL continues to be safe and effective in reducing the clinical signs and symptoms of PsA and psoriasis for up to 36 weeks.

T88

TNF-α BLOCKADE WITH INFLIXIMAB IN PATIENTS WITH ACTIVE SPONDYLOARTHROPATHY: FOLLOW UP OF ONE YEAR MAINTENANCE REGIMEN.

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Background & Aims : In an open pilot study, the anti-TNF-alpha monoclonal antibody, infliximab, induced a rapid and significant improvement in global, peripheral and axial disease manifestations of patients (pts) with active spondyloarthropathy (SpA), without major side effects.* The aim of this study was to determine whether repeated infusions of infliximab would effectively and safely maintain the observed effect.

Methods : The safety and efficacy of a maintenance regimen (5 mg/kg IV infliximab every 14 weeks) was evaluated using the same measurements reported in the open label study.* Of the initial 21 pts 19 completed the 1 year follow-up for efficacy. Two pts (1 psoriatic arthritis, 1 undifferentiated SpA) changed to another dosing regimen of infliximab after week 12 due to partial lack of efficacy. However, these pts are still in follow-up and are included in the safety analysis.

Results : Efficacy : After every retreatment (at week 20, 34 and 48) a sustained significant decrease of global, peripheral and axial disease manifestations was observed ($p \leq 0,05$ compared to baseline). Before retreatment, recurrence of symptoms was observed in 3 pts (16%) at week 20, 13 pts (68%) at week 34 and 15 pts (79%) at week 48. Safety : No withdrawals due to adverse events occurred. No significant laboratory abnormalities were detected. No major peri-infusional allergic reactions were observed. Three infectious episodes (pyelonephritis, otitis media, and tooth abscess) were observed. During the 1 year follow-up 12 pts (57%) developed on at least 2 occasions antinuclear antibodies; in 4 of these pts (19%) antibodies to dsDNA were detected. However, no lupus-like syndromes occurred.

Conclusion : In this open follow-up study of infliximab in pts with active SpA, the significant improvement of all disease manifestations was maintained over a 1 year follow-up period without major adverse events. Since recurrence of symptoms was observed in a rising number of patients with every retreatment, the maintenance regimen (5 mg/kg every 14 weeks) probably needs adjustment (shorter interval or higher dose).

* Ann Rheum Dis 2000;59:428-33.

T89

QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS: RELATION WITH FUNCTIONAL MEASURES

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OBJECTIVE: Ankylosing spondylitis (AS) is characterized by inflammation of axial skeleton with sacroiliac involvement. The aim of this study was to evaluate quality of life in patients with AS and to assess the relation with clinical and functional measures.
PATIENTS AND METHODS: Twenty-eight patients (18 male, 10 female) with AS and 20 healthy control subjects were included in this study. The mean age was 37.6±10.1 years in AS group and 33.8±8.0 years in control group. Quality of life was evaluated with Nottingham Health Profile (NHP). NHP is a self-administered questionnaire that measure six dimensions: energy, pain, physical mobility, emotional reactions, sleep and social isolation. BASDAI, BASFI, BASMI, BAS-G and HAQ-S were also performed.
RESULTS: The mean scores of physical mobility, pain and sleep dimensions of NHP were significantly higher in AS group compared with the control group ($p<0.001$). Energy, emotional reactions and social isolation scores were not different between groups. HAQ-S, BASFI and BAS-G were found to be correlated with all dimensions of NHP but BASDAI and BASMI were not correlated. NHP scores were not correlated with age, duration of disease and laboratory parameters like ESR and CRP.
CONCLUSION: Our findings suggest that AS patients with increasing functional disability have a reduced quality of life especially in the physical dimensions. The scores of psychosocial dimensions were not statistically different from the control group.

T90

IN ANKYLOSING SPONDYLITIS CHANGES IN SERUM OSTEOCALCIN CORRELATE WITH CHANGES IN ESR

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In view of the predominant pathology osteocalcin may be suspected to be a useful marker of disease activity in ankylosing spondylitis. For this reason changes in serum osteocalcin were correlated with changes in ESR, which probably is still the best marker of inflammation in AS.
In 89 patients with ankylosing spondylitis (75 male, 14 female; age 43 ±11 yrs.; disease duration 14 ±9 yrs.) venous blood was taken at the start and at the end of a three week rehabilitation treatment including physical exercise, physiotherapy, massage therapy, electrotherapy, exercises in water and radon therapy according to individual presciptions by the physician. Patients were advised not to alter medication. ESR was determinded according to Westergreen, the result at the first hour being used for calculations. Serum was frozen at –18°C until further analyis. Osteocalcin was measured in one batch with a commercially available test kit (IRMA, Biocis, Wien; normal range according to manufacturer: 7.5 – 31.5 ng/ml in men, 3.7 – 31.7 in females). Results are given as median (25^{th}, 75^{th} percentile). Mann-Whitney Rank Sum Test and Spearman Rank Order Correlation test were used to test significance.
At the first measurement were ESR = 18 (8; 28) mm and serum osteocalcin = 25 (20.5 ; 32.8) ng/ml. Osteocalcin serum concentration was within the normal range in 66 of the 89 patients, 23 patients showed increased serum concentrations. At the end of the treatment were ESR = 16 (8; 26.5) mm and osteocalcin = 26.1 (18.9 ; 32,7) ng/ml (no significant changes). ESR and osteocalcin at first examination did not correlate significantly (r_s 0.07; p 0.5). Changes in ESR [1 (-4, 6) mm] and changes in osteocalcin [–0.5 (-2.6 ; 5.7) ng/ml] showed a significant correlation (r_s 0.28; $p < 0.01$).
In cross-sectional investigation no significant correlation between serum osteocalcin and ESR exists. Changes in osteocalcin after three weeks were, however, significantly correlated with the changes in ESR. In view of the weak correlation (r_s = 0.28) osteocalcin may, however, not be a very reliable marker of disease activity.

T91

SPINAL DISEASE ASSESSMENT IN PSORIATIC ARTHRITIS (PsA)

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Objectives: PsA patients have features of both peripheral and axial disease. While the peripheral joints are assessed by the actively inflamed joint count, there are no standard tools for assessment of spinal disease in therapeutic studies for PsA. We aimed to determine whether the Bath Ankylosing Spondylitis (AS) tools for Activity (BASDAI) & Function (BASFI) were valid spinal assessment measures in PsA patients.
Methods: 100 consecutive patients attending the Toronto PsA clinic completed the BASDAI & BASFI, and were then assessed according to a standard protocol. Data were analysed using student's t-test, Spearman rank correlations, and Cronbach' alpha for internal consistency.
Results: 55% of patients were male. Mean age was 46.9 (sd 13.0), with mean disease duration of 13.9 years (sd 12.3). 33% had spinal involvement. Internal consistency of the instruments was good with Cronbach's alpha of 0.85 (BASDAI) and 0.94 (BASFI). Mean BASDAI was 3.6 (1.9), BASFI was 2.7 (2.2). The BASDAI and BASFI did not correlate with presence of back involvement. However, there was a significant association with the presence of back ($p<.05$) or neck stiffness ($p<.0005$). The strongest discrimination was between those with and without fibromyalgia or fatigue. Both BASDAI & BASFI correlated moderately with functional class (r=.43 & .56), active joint count (r= .45 & .49) and duration of morning stiffness (r= .61 & .49). The BASFI had a positive correlation with finger to floor distance and deformed joint count ($p=.005$).
Conclusion: The BASDAI & BASFI have good internal consistency, and correlate well with spinal stiffness, fibromyalgia and fatigue in PsA patients. However they do not correlate with back involvement, and are therefore unlikely to be useful measures in PsA clinical trials.

T92

INFLIXIMAB THERAPY IN 15 PATIENTS WITH PSORIATIC ARTHRITIS (PsA).

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Objectives: The anti-TNF agent infliximab, has proven effective and safe in the treatment of rheumatoid arthritis. Our aim was to assess its efficacy and toxicity in chronic resistent PsA.
Patients: PsA patients who had failed at least two prior DMARDs and had at least 6 actively inflamed and 2 swollen joints were studied. Infliximab infusions (5mg/kg) were given at weeks 0, 2, 6 and subsequent doses were given at 6-8 weeks intervals, dependent upon response. All were assessed with a standard protocol at each infusion.
Results: Of the 15 patients (mean age 47.7, disease duration 15.3 years) given infliximab all reported improvement by 2 weeks. In the 10 patients who received at least 4 doses there was no significant reduction in the mean tender joint count (22.7 vs 18.7) or swollen joint count (8.9 vs 5.6). However 7 achieved our definition of response (40% reduction in swollen joint count). Skin assessment (PASI) significantly improved from 4.6 to 0.86 ($p<.001$); 8 patients achieved a 30% reduction in PASI score. 4 patients with follow-up to 18-22 weeks maintained their response.

Adverse events included: severe allergic response halting therapy (1 pt.); Infections (7 patients): lobar pneumonia (2), septic arthritis (1), draining abscess at a site of surgical fusion (1), strep. throat (1), URTI (1), severe diarrhoea (2). Elevated LFTs were noted in 9 patients, severe enough to stop therapy in 1 case. Testicular pain/swelling developed in 2 patients.
Conclusion: Though infliximab may be effective in managing both skin and joint symptoms in some patients, the incidence of adverse events remains unacceptably high in this group of patients. A randomised controlled trial is required.

T93

GROSS VASCULAR CHANGES OF PSORIATIC KNEE JOINT SYNOVITIS.

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Objective. To assess the gross features and extent of synovial vascular abnormalities in psoriatic (PsA) compared to rheumatoid (RA) knee joint synovitis (KJS) and to evaluate their clinical relevance and comparing recent-onset and long-lasting KJS.
Methods. Thirty-nine knees (20 PsA, 19 RA) affected by refractory KJS, 18 with recent-onset KJS (mean KJS duration:1.5 yrs) underwent standard arthroscopy. Videorecording of the examination was reanalysed using a computed image analysis system and dedicated software. Vascular markings (VM) were assessed and separately scored for the areas of distinct architectural structures of synovium inflammation: capsular VM, villous VM (sum of capillary widening- and meandering) and pannus VM. ESR and local KJS inflammation (clinical index) were obtained before arthroscopy. The Spearman test was used to correlate the clinical and arthroscopic indices, and the Mann-Whitney test to compare them with the PsA- and RA-KJS groups.
Results. Distinct VM patterns were observed between PsA and RA-KJS. Moreover, the capillary figures considered unique to psoriatic skin were found in PsA synovial villi.Compared with RA, the total PsA-KJS group had significantly higher VM scores, apart from pannus VM. No significant differences were found between recent-onset and long-lasting RA-KJS subgroups, in either PsA or RA. Conclusions. The higher intensity, distinct gross patterns and different clinical relevance of synovial vascular marking in PsA, compared with RA-KJS. as well the sharing by skin and synovium of typical capillary figures, support the theory of specific vascular abnormalities in psoriasis and related arthritis.

T94

SPONDYLODISCITIS IN ANKYLOSING SPONDYLITIS

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Objective: Spondylodiscitis is an uncommon but well known complication of ankylosing spondylitis (AS). The aim of this study was to evaluate the incidence of spondylodiscitis and to determine the clinical and radiological appearance in a group of patients with AS.

Methods: Thirty-eight patients with a mean age of 36.4 ± 11.4 years were recruited to the study. Demographical, clinical and radiological characteristics of the patients were recorded. Bone scintigraphic evaluation and computerized tomography (CT) of the suspected lesions were determined.

Results: None of the patients had a history of trauma or other chronic disease except AS. Five (13.1%) patients had radiogarphic abnormalities including irregular narrowed disc space borders and bony sclerosis of the adjent vertebral bodies in the thoracic and lumbar regions. All these patients had low back pain and the clinical activity parameters were higher in 3 (7.8 %) of 5 patients. No fracture or pseudoarthrosis were observed. Skeletal scintigraphy and computerized tomography of the vertebrae were performed in these patients. Technetium scan showed increased uptake in the intervertebral disc space and vertebral end plates (L4-5. T12-L1) in 2 (5.2 %) of 5 patients and only 1 (2.6 %) of 5 patients had typical CT findings including widening, irregularity and sclerosis at the lumbar 4-5 intervertebral space.

Conclusion: Spondylodiscitis may have variable clinical or radiological manifestations and advanced imaging techniques are needed to identify this rare complication in patients with AS.

T95

BONE MINERAL DENSITY AND BONE TURNOVER MARKERS IN A GROUP OF MALE ANKYLOSING SPONDYLITIS: RELATIONSHIP TO DISEASE ACTIVITY

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Objective: Conflicting data have been published as to osteoporosis and bone turnover markers in patients with ankylosing spondylitis (AS). The aim of this study was to determine bone mineral density (BMD) of the lateral lumbar spine in a group of male patients with AS and to investigate the relationship between clinical parameters and markers of bone turnover.
Methods: Thirty-two consecutive AS patients with a mean duration of 14.8 years and 32 control subjects were included. Demographical and clinical characteristics were recorded, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to determine the activity of disease. Bone mineral density (BMD) was determined for the lateral lumbar spine in both patients and control groups. Deformities of vertebral bodies were recorded. Serum osteocalcin and urinary N-telopeptide (NTx) were measured as bone turnover markers in patient and control groups.
Results: Nine patients (28.1 %) were categorized as mild, 6 patients (18.7 %) moderate disease and 17 patients (53.1 %) with severe disease. Ten (31.2 %) of the patients had a vertebral fracture compared to 2 (6.2 %) of the controls.Although the mean values of lumbar BMD were lower than in the control group, the difference was not statistically significant. Osteoporosis was observed in 11 (34.3 %) of AS whereas in 2 (6.2 %) of the control group. Osteocalcin levels were significantly higher in AS patients in comparison with control subjects ($p<0.05$). In the subgroup analysis according to the activity of the disease; ESR and NTx levels were significantly higher in the severely active group when compared with that in mild or moderate disease. When we compared the active AS patients with control group; we observed significantly lower BMD and significantly higher NTx levels in the patient group ($p<0.05$). The levels of BASDAI scores and NTx values correlated significantly with each other.
Conclusion: Our study indicates that the incidence of osteoporosis is high in AS patients and especially patients with active disease are at risk for developing osteoporosis.

T96

EVALUATION OF FUNCTIONAL STATUS AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Objective: The aim of this study was to evaluate the functional status and quality of life and to determine the relationship between disability and clinical variables in a group of patients with ankylosing spondylitis (AS).

Methods: Fifty-one patients with a mean age of 37.2+10.8 years were included to the study. Data about demographical characteristics and clinical variables including; pain measured by visual analog scale (VAS), functional indices by Bath ankylosing spondylitis functional index (BASFI), Dutch functional index (DFI) and Dougdas functional index (FI), metrology by Bath ankylosing spondylitis metrological index (BASMI) and disease activity by BASDAI were studied. Radiographs of the patients were scored by Bath ankylosing spondylitis radiological index (BASRI) and quality of life (QOL) was assesssed by Nottingham health profile (NHP). Erythrocyte sedimentation rate (ESR) and C-reactive protein levels of the patients were also recorded.

Results: The scores of BASMI and BASRI were correlated with disease duration and BASDAI scores. Functional loss assesssed by BASFI, DFI and FI was strongly correlated with BASDAI, BASRI and BASMI. Patients with peripheral joint involvement had greater disability. Functional loss was more correlated with the levels of CRP than ESR. NHP scores best correlated with functional indexes followed by BASDAI.

Conclusion: The functional loss should be considered in evaluation of AS patients. The functional indexes can help to assess the patients more objectively and monitorize the treatment in order to increase the QOL in patients suffering from this chronic condition.

T97

Mono-oligoarthritis as a clinical manifestation of *Chlamydia* induced arthritis (CIA).

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Study assumptions: CIA is not always manifested by typical SARA syndrome but may have a course of disease with partial clinical symptoms in the form of mono-oligoarthritis (MoA). Signs of urinary and reproductive tract infection may be subtle and not always come to the attention of the patient and physician. The cause of MoA is not always linked to *Chlamydia trachomatis* (*C.t.*) infection.

Study aim: Clinical assessment of MoA patients with special attention to previous *Chlamydia trachomatis (C.t.), Yersinia enterocolitica (Y.e), Salmonella enteritidis (S.e.)* infections.

Method: Clinical assessment, radiological and serological examinations for presence of antibodies to *C.t.*, *Y.e.*, *S.e.* detected by ELISA method. In chosen patients the presence of *C.t.*DNA was studied by PCR method. In patients with proven *C.t.* infection eradication with azithromicine (1g/week for 12 to 16 weeks) was conducted. After eradication period clinical and serological assessment was repeated.

Material and results The studies were performed on 34 patients (25 females and 9 males)with symptoms of MoA aged x=36,2±24,2. Arthritis afflicted mainly knee joints – 19(56%) patients and tarsal joints–8 (23%) patients. Presence of IgG antibodies to *C.t.* in pathological concentrations were present in 13(38%) patients, in IgM and IgG classes in 11(32%) patients and in IgG and IgA classes in 9 (26,5%) patients. In those patients no antibodies to *Y.e.* and *S.e.* were detected. In 20(58%) of the patients, on the basis of clinical signs and serological examinations, not complete SARA syndrome was diagnosed. After eradication in 45% patients withdrawal of clinical signs of arthritis and serological reactions to *C.t.* antibodies was seen. **Conclusions:** MoA patients should be observed for not complete SARA syndrome after *C.t.* infection.

T98

PULMONARY INVOLVEMENT IN ANKYLOSING SPONDYLITIS.

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OBJECTIVE: To analyse the subclinical pulmonary involvement in a series of patients with ankylosing spondylitis (AS).

PATIENTS AND METHODS: Prospective study analysing 52 patients with the diagnosis of AS according to the modified New York criteria. The patients were asymptomatic about lung complaints and were submitted to a pulmonary investigation that included plain chest radiography, pulmonary function test (PFT) and thoracic high-resolution computed tomography (HRCT). The results were compared with sex, race, dorsal spine involvement, thoracic diameter, smoking status and HLA-B27.

RESULTS: PFT presented a restrictive pattern in 52% of the patients. Thoracic HRCT showed abnormalities in 21 patients (40%), predominantly nonspecific linear parenchymal opacities (19%), lymphadenopathy (12%), emphysema (10%), bronquiectasis (8%) and pleural involvement (8%). Male sex was statistically associated with dorsal involvement. Non-Caucasoid race was associated with bronquiectasis and pleural involvement. Smoking patients presented more linear parenchymal opacities. Negative HLA-B27 was associated with an altered plain chest radiography. Dorsal spine involvement was associated with restrictive pattern at PFT and linear parenchymal opacities.

CONCLUSION: Subclinical pulmonary involvement is frequent in AS. The restrictive pattern at PFT is associated with dorsal spine involvement and a low thoracic diameter, whilst the thoracic HRCT presents a series of nonspecific alterations, predominating the linear parenchymal opacities

T99

DURBAN CLASSIFICATION OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) FOR OLIGOARTHRITIS.

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AIM: To determine the proportion of cases with "unclassifiable" JIA according to the Durban classification for JIA with less than 5 joints involved initially and to compare with a modified hierarchic system.

METHOD: Chart review of 50 children with JIA with fewer than 5 joints involved at presentation, arthritis for > 12 months, and systemic arthritis excluded. Cases were classified according to EULAR criteria, Durban criteria and modified hierarchic Durban (the Durban classification subjected to hierarchy, with the order being: systemic arthritis, rheumatoid factor positive arthritis, psoriatic arthritis (arthritis and psoriasis or a combination of dactylitis and psoriatic nail changes), enthesitis related arthritis (arthritis and HLA-B27+ after exclusions listed above), with the remainder of children being classified as having RF- polyarthritis, or RF - oligoarthritis, according to joint numbers. (ref: Manners PJ: Mod Rheumatol (2000) 10:68-77)

RESULTS: Of 50 children, at least 20 were studied retrospectively. Of these 15 had never been tested for RF, as there had been no clinical indication, but are presumed negative. These cases would otherwise be "unclassifiable". This problem is particular to retrospective classification studies of JIA. Of 50 children, 33 (66%) were "unclassifiable" by the Durban system. By the modified hierarchic Durban system 1 (2%) was "unclassifiable". Reasons for "unclassifiable":(I) Inadequate family history of psoriasis or B27 disease due to either patient/parent being adopted, one/both parents unavailable or unknown, no communication with wider families, diagnoses not medically confirmed nor dermatologically confirmed (psoriasis). In addition accuracy of family history was open to interpretation (II) Psoriasis in family, not in proband and insufficient to classify psoriatic arthritis. (III) B27 negative proband with family history of B27 associated disease.

CONCLUSIONS: (I) The Durban classification of JIA fails to adequately classify a significant proportion of children with arthritis mainly because of family history, particularly where diagnoses need to be confirmed medically or by a dermatologist. (II) The accuracy of family history is open to interpretation, and lacks precision. (III) It may be appropriate to modify the Durban classification using hierarchic system and excluding family history.

T100

LONG-TERM EFFICACY AND SAFETY OF INFLIXIMAB TREATMENT OF ANKYLOSING SPONDYLITIS

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In contrast to rheumatoid arthritis and Crohn's disease there is scant data concerning infliximab-therapy in ankylosing spondylitis (AS).

Two short term studies with a total of 22 patients with AS showed a rapid and significant improvement of disease activity lasting 3 months after 3 infliximab-infusions. However, there is no published data about the long term efficacy and safety of infliximab in patients with AS.

A 35 year old HLA B27 positive male patient diagnosed with AS in 1981 was previously treated with sulfasalazine and NSAIDs and continued to have high disease activity. Therefore, infliximab therapy was initiated in a dose of 5mg/kg body weight in February 2000 in the conventional manner (intravenous infusions in week 0, 2, 6, and then every 6 weeks). A total of 10 infusions were given over a period of one year.

Bath Ankylosing Spondylitis Activity Index (BASDAI), Functional Index (BASFI), Metrology Index (BASMI), pain on visual Analogue Scale (VAS), CRP and ESR were measured every 6 weeks. In addition, protein expression on peripheral blood mononuclear cells was examined. The ileosacral joints were examined by MRI.

Clinical improvement commenced one week after the first infusion and continues until now. Before therapy, BASDAI was 3.9, CRP 4.2 mg/dl (normal < 0.5). After 4 weeks BASDAI had decreased to 1.4 and CRP had decreased to normal. Comparable results were obtained for the other parameters. Before therapy, there was mild activity of sacroileitis detected by MRI, which was not present on MRI at week 14 and week 41. There was no loss of therapeutic effect at the end of the intervals between the 6-weekly infusions or at the end of the 12 month observation period.

The treatment was well tolerated. No adverse events were observed. Thus, infliximab monotherapy could be a safe and effective therapy in patients with AS also with long term application.

T101

MEASUREMENT OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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Aim of the study was to examine and compare objective and subjective disease activity signs in psoriatic arthritis (PsA).

Patients and methods: We examined 100 patients with psoriatic arthritis. Distribution of the painful and swollen joints were recorded on a mannequin. Ritchie index were calculated. Patients were asked to mark the extent of pain on a 100 mm visual analogue scale. Psoriasis area and severity index (PASI) was determined. At the same time the ESR, haemoglobin, and platelet count were recorded.

Results: Mean age of the patients was 47.4 years (25-67). Good correlation was found between the extent of pain, marked on VAS and the number of painful joints (r=0,246), the morning stiffness (r=0,322), and Ritchie index (0,455). Correlation was low between the ESR and the number of painful joints (0,173). No correlation was found between PASI and VAS, We and PASI. There was no correlation between the Westegreen and the number of swollen joints (r=0,0064).

Discussion: The only time, we've found correlation is the number of painful joints and VAS. Since both of them are subjective clinical symptoms they aren't suitable for objective measurements. We do need further investigations to find or create an optimal disease activity score to be able to measure the severity of PsA, or the effectiveness of the therapy.

T102

SIGNIFICANT CLINICAL AND RADIOLOGICAL (MRI-DEFINED) IMPROVEMENT IN REFRACTORY ANKYLOSING SPONDYLITIS WITH INFLIXIMAB: AN OPEN LABEL STUDY.

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Objective: To examine the efficacy and safety of infliximab in the treatment of ankylosing spondylitis (AS) refractory to conventional therapies. TNFα has been demonstrated in sacroiliac joint synovium and preliminary clinical reports describe short-term efficacy in AS with predominantly axial disease. We have studied patients with both axial and peripheral joint disease and also used subtractive dynamic magnetic resonance imaging (sdMRI) to document efficacy.

Methods: We studied 11 patients (M:F=8:3) of mean age 41.3 years (range 26-60) and mean disease duration of 18.7 years (range 13-33) who continued to receive stable background NSAID therapy. Infliximab, 3mg/kg IV, was given at 0, 2, and 6 weeks. Clinical assessments included the BASDAI, BASFI, BASGI, BASMI, and swollen joint count at baseline and 14 weeks whilst laboratory assessments were the CBC, CRP and ESR. The first six consecutive patients were also studied by T1 SE, T2 GE, STIR, and dynamic MRI with gadolinium augmentation acquiring 3 coronal slices at 10 second intervals for 160 seconds. Maximal rate and magnitude of augmentation was determined at baseline and 14 weeks.

Results: Treatment was well tolerated with only one withdrawal after the second infusion due to a non life-threatening allergic reaction. Mean BASDAI improved significantly from baseline (6.2) to 14 weeks (2.6)(p=0.005) with 7 patients demonstrating at least 50% improvement (range 0-99.6%).Significant improvement in BASFI (p=0.003), BASGI(p=0.003), Hb(p=0.008), CRP(p=0.004), and ESR(p=0.02) was also evident. Complete remission of peripheral joint disease was evident in 5 patients. Maximal rate of gadolinium augmentation was significantly decreased after treatment (p=0.04).

Conclusion: Infliximab is effective and well tolerated for both axial and peripheral joint disease in AS unresponsive to conventional therapies. Previous studies have examined a 5mg/kg dose. Our work suggests that a lower dose may be equally effective.

T103

THE CHARACTERISTIC SHOULDER LESION IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS) IS AN EROSIVE ENTHESOPATHY OF THE SUPRASPINATUS TENDON

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Purpose: It is often stated that shoulder involvement in Ankylosing Spondylitis is common (25%) and includes primary glenohumeral joint disease although controlled studies are lacking. We have examined the prevalence and characteristics of shoulder involvement in patients with AS in comparison to a control population, adjusted for age and sex, by clinical and radiological assessment.

Methods: Prevalence of shoulder involvement was first ascertained by retrospective chart review of 400 AS patients (M:F=278:122, mean age 43.8 years, mean disease duration 18.4 years). Seventy-three patients were randomly selected for clinical evaluation by the DASH (Disabilities of the arm, shoulder, and head) questionnaire and a standardized physical exam (the Southampton physical exam schedule). Symptomatic patients were evaluated by plain x-ray and magnetic resonance imaging (MRI) with T1 and fat-suppression T2 STIR sequences. Controls were 285 patients (M:F=115:170, mean age 51.2 years) attending a family physician's practice for unrelated complaints. Multiple logistic regression was used to compute odds ratios (OR).

Results: Primary glenohumeral joint involvement was not recorded in any patients. Shoulder involvement by clinical evaluation was noted in 16 (21.9%) of 73 patients versus 12 (4.2%) controls (OR(adjusted for age/sex)=8.17;95%C.I.3.14-21.28;P<0.001). Patient demographics did not differ in those with and without shoulder involvement. Rotator cuff tendinitis (RCT) was significantly more prevalent in patients (15.1%) than controls (3.5%)(OR(age/sex adjusted)=8.17;95%C.I.2.66-25.14;P<0.001). Other clinical diagnoses included acromioclavicular disease (2.7%), bicipital tendinitis (1.4%), and 2(2.7%) were indeterminate. Plain x-ray and MRI were entirely consistent with the clinical evaluation, MRI demonstrating erosive enthesopathy with adjacent bone marrow edema at the insertion of the supraspinatus (3 patients) and at the outer end of the clavicle (1 patient).

Conclusions: The most common shoulder lesion in AS is an enthesopathy at the supraspinatus insertion. Primary glenohumeral joint involvement is rare.

T104

EVALUATION BY DUAL X-RAY ABSORPTIOMETRY (DXA) OF BODY COMPOSITION IN ANKYLOSING SPONDYLITIS(AS) PATIENTS.

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Objective: To evaluate body composition and bone mineral density (BMD) in patients with severe AS of long duration and predominant axial involvement by DXA. Methods : Forty-one AS male patients with mean age 38,9 +- 7,26 years old (23-50 years), and 34 controls matched for age, sex, race, weight, height were studied. Body composition and BMD were measured by DXA (HOLOGIC QDR 2000). BMD was evaluated in two sites: lumbar spine (L1-L4) and femoral neck. Comparisons were performed for the group of patients and controls. Differences were analyzed using x2-test, Student test and Pearson test. Statistical significance was taken at p<0,05.Results: Body-composition indexes as BMD (g/ cm2), BMC (Kg), fat mass (Kg), lean mass (Kg), fat mass percentage (%) were analyzed. Patients with AS had a lower total lean mass (47,72 kg ± 5,82 versus 55,34 kg ± 5,48) and lower total bone mass (1,04 Kg ± 0,96 versus 1,13 Kg ± 1,16) in comparison with controls. The analysis of BMD-lumbar spine and BMD-femoral neck showed low values (0,996 g/cm2 ± 0,20 versus 0,752 ± 0,15) respectively. No difference was found in the fat % regarding AS patients and controls, but a difference was noted as a result of age, in both groups. Additionally, there was a significant correlation between the reduction of lean mass and bone mass and the Schober test, weight and height (p<0,05). Conclusion: Measures of body composition in AS patients can be important to investigate structural severity of the disease. Low values of lean mass was observed in parallel with osteoporosis, that is frequent finding in male patients with AS. This analysis showed a positively correlation between lower total lean / bone mass and anthropometrical measures, probably secondary to the pathologic loss of mobility in the spine and rizomelic joints.

T105

DEVELOPMENT OF THE DIAGNOSIS OF SAPHO SYNDROME IN HUNGARY

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SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is an acronym proposed by Chamot to define a rare syndrome comprising specific bone lesions associated with dermatologic disease. There are more than 50 synonyms in the literature. All over the world these synonyms had been used after the first described SAPHO syndrome by Chamot, too. The usage of SAPHO syndrome diagnosis became widespread only in the latest years.

Authors studied the scientific publications in Hungary examining the appearance and extending of SAPHO syndrome diagnosis: the first review was done in 1995, the first case was published as SAPHO syndrome in 1998. Chronic recurrent multifocal osteomyelitis (CRMO) diagnosis is used also nowadays in the pediatric cases corresponding to SAPHO syndrome.

Authors give a review of the SAPHO syndrome cases publicated and/or presented in Hungary. There were 8 cases as acne arthritis, 1 case as SNSA, 5 cases as SAPHO syndrome publicated. There were 31 cases as sternoclavicular involvement in psoriatic arthritis, 3 CRMO cases, 1 SAPHO syndrome presented in Hungarian Congresses, together 49 case reports. The concomitant skin laesions were: acne conglobata, fulminans or psoriasis vulgaris. Mean age: 33,3 (12-60). Male:female ratio was: 29:20. Almost all the patients had peripheral arthritis, most of them had sacroiliitis and/or SCC arthritis.

T106

LONG - TERM TREATMENT OF JUVENILE RHEUMATOID ARTHRITIS WITH CICLOSPORIN A

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Systemic juvenile rheumatoid arthritis (JRA) is characterized by high morbidity. NSAIDs, most of DMARDs do not prevent functional disability and decrease disease activity in the most of cases.

The aim of the study: to assess therapeutic efficacy and toxicity of Ciclosporin A (CiA) in the long-term treatment of systemic destructive JRA.

Fifteen patients with severe systemic JRA entered the study. All of them had active polyarticular joint damage and extraarticular manifestations.

The mean duration of disease was 4 years. All children received CiA in the mean dose 4,75 mg/kg daily (min. - 4,5; max. - 5 mg/kg). The mean duration of treatment was 3 years (min. 2, max.- 5 years).

Before CiA administration all patients were kept on a daily regimen of NSAIDs, 60% were also on prednisone (8,75 mg/ daily, 01-0,5 mg/kg). Mean duration of GC treatment was 5 years (min. 3, max. 10 years). The main side effects of GC treatment were: growth retardation, Cushing syndrome, hypertrichosis, arterial hypertensia.

Long – term CiA treatment caused remission in 5 and clinically important decrease in disease activity in 10 patients Prednisone was withdrawn in 8 and its dose was significantly decreased in 1 patient. NSAIDs were withdrawn in 13 patients and they received monotherapy with CiA. Stabilization in anatomical damage was observed in all patients, regression of joint destruction – in 4 Treatment with CiA was stopped in 2 patients with remission After withdrawal the remission is lasted for 2,5 years

T107

JUVENILE DERMATOMYOSITIS. A REVIEW AND FOLLOWUP STUDY.

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Objective: To describe patients with dermatomyositis and review their demographics, presentation, diagnosis and therapy in Venezuela.

Results: We describe 18 cases of juvenile dermatomyositis that are followed in the rheumatology clinic or in medical private practices; their records were evaluated retrospectively. Nine patients are males and nine are females. The mean age at onset was seven years old (range: 1 to 12). The mean time between onset of disease and diagnosis was six months (range: 0.5 to 29) and the mean time from onset of disease to treatment was 6.5 months (0.5 month to 34 months). Treatment was started after 6.5 months of disease onset in 8 of the patients, four of them have Calcinosis Universalis. All patients met the criteria of Bohan and Peter for juvenile dermatomyositis. 18/18 patients presented with fatigue, taquicardia, skin rash, peri-articular erythema, Groton's papules, severe proximal muscle pain and weakness and elevated Creatinine phosphokinase. 17/18 had electromyograms with a myopathic pattern. 10/18 patients had muscular biopsies done for diagnosis. 18/18 received prednisone and/or methylprednisolone, 12/18 also received Methotrexate and in 5/18 one more drug (Immunoglobulins, Interferon, Cyclosporine or Hydroxycloroquine) was added. 5/18 patients have calcinosis, and in 4 the calcinosis is generalized, they have recurrent skin infections and are incapacitated due to the Calcium deposits (grade 3-4 ARA functional incapacity).

Conclusions: Juvenile Dermatomyositis appears to have similar clinical features in Venezuela. Delay in treatment might be associated with calcinosis, in some patients. Patients with Calcinosis Universalis have incapacity and devastating chronic complications.

T108

SLE RELATED DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS IN CHILDHOOD: TREATMENT WITH INTRAVENOUS PULSE CYCLOPHOSPHAMIDE.

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Objective: To evaluate the safety and efficacy of intravenous pulse cyclophosphamide (IVPC) in pediatric patients with SLE and diffuse proliferative glomerulonephritis (DPGN).

Rationale: IVPC has become the standard of care for SLE related DPGN in adult patients with relatively good efficacy and acceptable though significant toxicity. There has been little literature regarding the use of IVPC in pediatric patients with lupus nephritis especially with regards to toxicity.

Methods: We reviewed the courses of 10 patients with pediatric SLE complicated by DPGN seen between 1989 and 1996 who were treated with IVPC at our pediatric rheumatology center. The average duration of follow-up was 5.0 years (range, 2.3-8.8). Nine children had biopsy proven DPGN. One child could not be biopsied due to personal beliefs but had clinical and laboratory manifestations consistent with DPGN. Therapy consisted of IVPC 0.5-1.0 gm/m^2 at monthly intervals for six months and subsequent doses at three month intervals for two years. All patients received corticosteroids.

Results: Initial renal response was very good to excellent in 8 of 10 children with 2 patients developing mild renal insufficiency. 24-hour urine protein excretion decreased from a mean of 3281 mg/24 hours to 751 mg/24 hours. There was a significant reduction in the mean prednisone dosage from 45.5 mg /day to 6 mg /day. Four patients had relapses, 1 responding to corticosteroids, 2 requiring restarting IVPC, and 1 requiring mycophenolate mofetil.

Adverse events included the following; one child developed a febrile pulmonary illness with negative cultures and recovered; one child developed toxic shock syndrome from cervical adenitis and recovered; mild treatment related nausea. One of the female patients had normal fertility and delivered a full term healthy baby six years after treatment.

Conclusion: IVPC was well tolerated and the initial renal response was good in children with DPGN with no end stage renal disease or deaths. This is significantly better than outcomes of similar groups of patients published in the literature between 1976 and 1992. However, 4 patients developed relapses requiring further immunosuppressive therapy.

T109

PROPYL-THIOURACIL INDUCED LUPUS ERYTHEMATOSUS IN MONOZYGOTIC TRIPLETS WITH HYPERTHYREOIDISM.

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Factors influencing susceptibility to drug-induced autoimmune diseases include genetic polymorphism that influence drug metabolism and immunological reponse. We describe the autoantibody profile of two triplets treated with propyl-thiouracil (PTU) for hyperthyreoidism who developed lupus erythematosus (LE) manifestations.

Patients: The patients were female monozygotic triplets with a mild psychomotoric retardation of unknown cause. Two of them developed severe hyperthyreoidism at the age of 7½ years and were started with PTU with 3 months interval with a good effect on thyroid function. After 18 and 21 months, respectively, both (A and B) developed a macular exanthema on arms and thighs, migratory arthralgia and synovitis of wrists and ankles. Treatment with PTU was stopped and within one month the exanthema and arthritis disappeared. The third triplet, C, became hyperthyroid later but never received PTU and did not develop LE symptoms. During a following period of 6 years none of the triplets developed lupus-like manifestations.

Results: The autoantibody profile revealed a marked rise in p-ANCA from negative to 1:1280 in A and from 1:40 to 1:1280 in B after PTU was introduced, whereas triplet C not treated with PTU never had a titer higher than 1:80. All sera were investigated for MPO, PR3, p28, NGAL, neutrophil elastase, lactoferrin and cathepsin G-ANCA. A and B had a strongly positive elastase-ANCA but only B had a positive p28-/lactoferrin-/cathepsin G-/and lysozyme-ANCA whereas triplet A only had a positive cathepsin G-ANCA. Triplet C was elastase-ANCA negative. Identical HLA phenotypes were DRB1*15, *03; DRB3, DRB5, DQA1 *0102, *0501.

Conclusion: Our results confirm the importance of a genetic factor influencing the susceptibility to drug-induced autoimmune syndromes and further confirm previous findings showing the association between neutrophil elastase-ANCA and vasculitis in patients treated with propyl-thiouracil.

T110

EVALUATION OF DISEASE ACTIVITY, DISABILITY AND QUALITY OF LIFE IN PATIENTS WITH PERSISTENTLY ACTIVE REFRACTORY JUVENILE IDIOPATHIC (CHRONIC) ARTHRITIS (JIA) TREATED WITH MONOCLONAL ANTI-TUMOR NECROSIS FACTOR-α ANTIBODY (INFLIXIMAB)

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An open prospective trial was carried out in a young population affected by severe, refractory, polyarthritic JIA to evaluate the efficacy of Infliximab (Remicade) on disease activity, disability and quality of life. We enrolled 17 females, median age at the start of the therapy 23.8 yrs (8-32.5), median onset age 3 yrs (1-16), median disease duration 15.7 yrs (5-31.4). All patients had still active disease; 14 patients were still on corticosteroids (median 0.1 mg/kg). All patients discontinued any other DMARD aside from s.c. MTX (median weekly dose 15 mg, range 5-25) and continued with previous NSAIDs and corticosteroids. Infliximab was administrated as a single infusion of 3 mg/kg at time 0 and at weeks 2, 6, 14, 22, 30, 38. Since the 1st infusion, all 17 patients achieved a very good response (≥ 50% reduction in number of active joints, ESR, CRP, VAS). The long-term observation in 9 patients who completed a 9 months course of treatment, up to 22 weeks (5 infusions) and 38 weeks (7 infusions) showed a statistically significant improvement of the median number of active joints, of the DAS index, of the physician global evaluation (VAS). HAQ decreased from 1.44 to 1.12, physical DIM SF-36 increased from 41 to 74 and mental DIM SF-36 increased from 60 to 70. One patient withdrew because of a severe adverse event (hypersensitivity reaction at the third infusion). These data suggest that Infliximab can significantly and promptly reduce disease activity and improve the quality of life in patients affected by persistently active and refractory JIA. However more data are needed to evaluate its efficacy and safety as a long-term therapy.

T111

CLINICAL AND TOMOGRAPHIC FEATURES OF THE TEMPOROMANDIBULAR JOINTS (TMJs) IN PATIENTS AFFECTED BY JUVENILE CHRONIC ARTHRITIS (JCA).

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The aim of this study was to evaluate the incidence of the TMJ involvement in the different subtypes of JCA (systemic, polyarticular, and pauciarticular) and to investigate correlations between symptoms, clinical signs and tomographic modifications of the TMJs. Our series included 56 consecutive patients older than 10 years (42 F, 14 M), mean age of 17.3 yrs (range 10-25 yrs), mean onset age 7.0 yrs (range 1-16 yrs), mean disease duration 10.4 yrs (range 2-22 yrs). Each patient was evaluated according to the Helkimo protocol and, when indicated, a tomographic study was performed (32 patients). Tomographic features were assessed according to the Rohlin-Petersson scale. Radiological alterations were observed in 94% of patients (bilateral in 75%). All patients with systemic and polyarticular onset JIA showed a tomographic TMJ involvement, TMJ changes were present also in 84% of pauciarticular subtype. There was no significant correlation between subjective symptomatology and clinical dysfunctional signs in the TMJ, in particular the severity of the symptoms described by patients was generally lower than that of the clinical dysfunctions revealed by direct clinical examinations. Moreover, no correlation was found between clinical dysfunctional signs and morphological alterations shown in the TMJs tomograms: the severity of dysfunctional signs was lower than that of the morphological alterations of the TMJs. In conclusion these results confirm the importance of clinical examination in patients affected by JCA even if they are asymptomatic and the need for tomograms in patients even with only moderate clinical dysfunctions. These screening procedures are essential for an early diagnosis of TMJ modifications in JCA.

T112

DELAYED MENARCHE AND BONE MASS PEAK IN JUVENILE CHRONIC ARTHRITIS (JCA)

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The aim of this study was to determine if girls with JCA present a delay in the menarche age; which factors affect the timing of menarche and if a delayed menarche influence the bone mass peak. Our investigation consisted in a transversal and a longitudinal study. In the first one we considered 63 girls with JIA (26 on long term steroid treatment and 37 never treated with steroids), mean onset age 5.5 yrs, mean disease duration 7.8 yrs. Subtype diagnosis: systemic onset 13 cases, poly 24 cases, pauci 26 cases. We compared the age at menarche of all the patients (mean 13.4 yrs DS ± 1.5) with that of their mothers (mean 12.8 DS ± 1.4) (statistically significant difference: p=0.03), and with that of the Italian healthy population (mean 12.5 DS ± 1.5) (statistically significant difference: p>0.001). The mean age of the systemic group (14.6 yrs) was higher than the poly (13.3 yrs) and the pauci group (13.0 yrs) with statistical significance between systemic and pauci onset group (p=0.03). There was a significant difference difference between the mean age at menarche of patients treated with steroids and that of patients not treated (13.9 yrs vs 13.0 yrs). In the longitudinal study we considered 21 prepubertal females with JCA (6 systemic, 10 poly, 5 pauci). 18/21 cases were on steroids at the beginning of the study. BMD lumbar spine was monitored every 6-12 months in each patient before and after menarche since the bone mass peak was reached. Considering the time of menarche in comparison with the healthy population the menarche age was normal in 12 cases (mean 13.0 yrs) and delayed in 9 cases (mean 14.8 yrs). Taking into account the BMD % annual change (BMD delta) a statistically significant difference was observed between the patients with delayed menarche in comparison with those with normal menarche (p=0.01). Patients with delayed menarche showed lesser absolute delta values and no trend to a puberal spurt. Patients with delayed menarche present a very low annual bone mass increase and can reach bone mass peak several years after puberty.

T113

BONE MINERAL DENSITY IN JUVENILE CHRONIC ARTHRITIS

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OBJECTIVE: The aim of this study was to evaluate bone mineral density (BMD) in patients with Juvenile Chronic Arthritis (JCA) and to assess the effect of disease activity and corticosteroid treatment.
PATIENTS AND METHODS: Twenty-seven (15 female) patients suffering from JCA and 13 healthy controls (5 female) were included. The mean age of the patient and control groups were 10,77±3,82 and 10,23 ±3.26 years respectively. Disease activity was determined by clinical and laboratory evaluation, Articular Disease Severity Score (ADSS) and Juvenile Arthritis Functional Assessment Report (JAFAR). BMD of the lumbar spine was measured by DEXA. Patients were grouped according to steroid use. Sixteen (59,3%) patients had been receiving glucocorticoid therapy for at least 5 months (Steroid group). Eleven (40,7%) patients received only NSAID (Non-steroid group).
RESULTS: The mean BMD results were 0.494±0,15 gr/cm² in steroid group, 0,595±0,85 gr/cm² in non-steroid group and 0,599±0,096 gr/cm² in control group. Steroid group showed significant bone loss compared to the non-steroid and control groups ($p<0.05$). Age, age of onset and ESR were found to be correlated with BMD, but no correlations were detected between BMD and duration of disease, JAFAR, ADSS and CRP.
CONCLUSION: Data obtained from our study suggest that steroid treatment, age of onset and disease activity are important factors in the development of osteoporosis in JCA.

T114

CHANGES IN BONE MASS AND BODY COMPOSITION IN OBESE ADOLESCENTS DURING WEIGHT REDUCTION

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Objective: The increasing prevalence of obesity in childhood and adolescence observed in many countries is currently a major public health concern. The aim of this study is to determine how bone mineral content (BMC), fat mass (FM) and fat free mass (FFM) vary during weight loss in morbidly obese adolescents.
Methods: 33 girls and 22 boys, aged 13.4 ± 3.6 year with BMI = 34.6 ± 3.6 kg/m² were included in a 7.5 ± 3.2 months multidisciplinary weight reduction program including a slight caloric restriction and regular submaximal physical training. Dual X rays absorptiometry (Hologic QDR 1000/W^{TM}) was used to measure body composition before and after weight loss.
Results: Mean weight loss is 23.5 ± 8.9 kg ($p<0.0001$), growth is 2.7 ± 1.8 cm ($p<0.01$). Total BMC decreases less (-0.25 ± 0.13 kg, $p<0.005$) than bone area (-44 ± 12 cm² , $p<0.001$) resulting in an increased BMD (0.003 ± 0.001 g/ cm² , $p<0.01$). BMC Z scores remain higher than in the reference population (2.7 ± 1.2 vs 2.5 ± 1.4). FM decreases 47.6 ± 10.7 % (40.9 ± 14.4 vs 21.4 ± 7.2 kg, $p<0.0001$). FFM does not vary significantly (51.4 ± 9.9 vs 51.3 ± 9.2 kg, $p=0.86$). Changes of BMC and FM are positively correlated ($R^2=0.54$, $p<0.0001$).
Conclusion: Within limits of interpretation of DEXA, this multidisciplinary weight loss program seems to avoid fat free mass loss and to maintain adequate bone mineralization in the critical period of puberty.

T115

SURVEY OF BOW DEFORMITY IN YOUNG IRAQI CHILDREN

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Objective: To survey the possible causes of genu varus deformity in young Iraqi children.

Methods: Seventy-three Iraqi children with genu varus were studied. Both lower extremities in all patients were examined by measuring the distance between the two medial femoral condyles clinically and the tibiofemoral angle roentgenographically. Other investigations done accordingly; serum calcium, serum Alkaline phosphatase...etc. Patients classified to 3 main groups: group 1: physiological bowing, group 2: pathological bowing and group 3: simple severe bowing.

Results: Of the 73 patients , 34 were female and 39 male, mean age was 19.6 months (11-36m), all patients were bilaterally involved. Physiological bowing found in 33/73(45.2%) patients. 29 (39.7%)patients had pathological bowing including: rickets 26/29 (89.6%)patients, Blount's disease 2/29 (6.89%) patients, and one patient had B-Thalassemia. Simple severe bow legs was found in 11/73 (15.1%) patients .

Conclusions: Physiological bowing was the main cause of bow legs in young Iraqi children. Rickets was the second and the main cause of the pathological group ,while Blount's disease was the second cause of pathological bowing. Mean age at independent walking was more significant with the physiological bowing than the pathological. Rapid progression and presence of lateral thrust were more significant with the pathological bowing than the physiological .

T116

SOME CHARACTERISTICS OF MIXED CONNECTIVE TISSUE DISEASE IN CHILDREN

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We observed 7 children with mixed connective tissue disease (MCTD):3 boys 13-14 years old,4 girls 8-14 years old. In clinical features there were odema of hand fingers and malmobility of big joints (4), Raynaud's syndrome (4), polyarthritis and myositis (3), myopericarditis with cardiac insufficiency(3), lupus dermatitis (3) and Gottron's syndrome (2).There were no symptoms of lung and kidney disturbance. In all patients there were febrile status, high ESR (30-50 mm/ h), SRP, hypochromic anemia tendency. There were revealed some trends in immune status: presence ANF with titres from 1:80 to 1:1280 (5), Ab to DNA (3), RF (only in boys), decrease of serum complement (5), Ab to n RNP (5), anticardiolipin Ab and lupus anticoagulant (1), high concentration of IgG (5). Under treatment immune status became normal.
MCTD diagnosis was confirmed on 1-2-3 years of diseases instead of previous diagnosis of SLE, JRA and virus myopericarditis. Patients were infected by mixed chlamidia - micoplasmatic infection (3), Cocsaki virusis A2, A3, B1, B2 and herpes 1 and 2 (3), tbc mesadenitis (1)
In the course of treatment CS, NSAIDs, cytostatic immunosupressants, antibacterial and antivirus medicaments were utilised with positiv therapeutic effect.
Conclusions: 1) MCTD in children have polysyndromic clinical picture with traits of SLE, SSP, DM/PM and JRA.
2) Possible start mechanism of MCTD are mixed virus, bacterial, parasital infection.
3) The treatment of MCTD have to be differentiated and include NSAD, CS, immunosupressants, antimicrobial and antivirus drugs.
4) Monitoring of all children with stabile Raynaud's syndrome and heavy myopericarditis must be performed with ablention of possible development of MCTD.

T117

THE KUWAIT EXPERIENCE WITH SPECIAL REFERENCE TO ANTI-PHOSPHOLIPID SYNDROME (APS).

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Objective: To study the pattern and practice of rheumatic diseases in Kuwait with special reference to anti-phospholipid syndrome (APS).

Rationale: Teaching of rheumatology as well as the spectrum of rheumatic diseases could vary between different parts of the world.

Methods: The data were prospectively collected from rheumatology clinic of the main teaching hospital in Kuwait. Special emphasis was given to SLE and APS. This was compared with the data collected from a major teaching hospital in New Delhi during late '80s till 1990.

Results: Institution in New Delhi did not have rheumatology course in the undergraduate curriculum. In contrast, a course co-ordinated by a British-trained rheumatologist was incorporated in the UG-curriculum in Kuwait. Regarding spectrum of the rheumatic diseases in Kuwait, during a period of 6 years a total of 3789 patients were seen. Systemic inflammatory rheumatic diseases predominated (67%) followed by OA (12%); soft-tissue disorders (11%) and miscellaneous (~10%). There were 81 (2.1%) patients with APS, 58% of them were positive for aCL, 21% with clinical manifestations. In contrast in New Delhi 28% of SLE patients showed aCL of whom only 13% showed the clinical features. Over all severity of the disease was much more among Kuwaiti patients including mortality.

Conclusion: Undergraduate teaching of rheumatology was given its due importance in Kuwait compared to that in New Delhi. Systemic inflammatory diseases predominated in the clinical practice of rheumatology in Kuwait. Osteoarthritis and soft-tissue rheumatic diseases followed this. Crystal arthropathies appeared under-represented. APS appeared to be common with more severe manifestations among Arabs.

T118

EXPERIENCE IN THE INDIAN SUBCONTINENT WITH SPECIAL REFERENCE TO ARTHRITIS CAMPS

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Rheumatology is a relatively nascent albeit growing discipline in the Indian Subcontinent. Most of the arthritic patients get treated by orthopaedicians and internists, with a trend favouring rheumatologists.

Towards disseminating rheumatology care to the people, free arthritis camps have been organised each month in India. Of the 6,400 patients treated so far, osteoarthritis (OA) was 34%, soft tissue rheumatism(STR) 32%, rheumatoid arthritis (RA) 22%, seronegative spondylo arthropathies 5%, collagen vascular disorders a mere 2%, arthritis in children 1%, 4% miscellaneous including gout. The greatest beneficiaries were RA patients who hardly received disease modifying drugs, and often steroids. A large number of patients came for repeat camps displaying confidence in the system. The opportunities, economics, potential promise and limitations of such free camps is discussed.

In a house survey of 1997 adults in Northern Pakistan, 15% experienced musculo skeletal pain, OA of the knee was the commonest. A rheumatologist was consulted by just 14% of patients. In a survey of 4,073 patients in Bangladesh, 'mechanical arthropathies' were 50%, inflammatory arthritis 16%, STR 28%.

In order to avoid confusion in such population surveys, it is recommended that ICD-10 classification and coding system is adopted universally.

T119

THE CONTRIBUTION OF COPCORD TO UNDERSTANDING THE BURDEN OF RHEUMATIC DISEASES IN DEVELOPING COUNTRIES – THE PAST, PRESENCE, AND FUTURE OF COPCORD AND ITS IMPLICATION TO THE DEVELOPING COUNTRIES IN THE ASIA PACIFIC REGION.

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The Past: Compared with the West similar age and sex adjusted prevalence rates of the rheumatic diseases, except gout and hyperuricemia, were found in The Philippines, Indonesia, Thailand, Malaysia, China, Pakistan, India, and Australia by WHO-ILAR COPCORD Stage I Epidemiological surveys. Significant high prevalence rates of gout and hyperuricemia were found in the Malayo-Polynesians, Polynesians, and Malayo-Mongoloids, compared with Caucasians and Mongoloids in the Asia Pacific region.

The Presence: Recently, one short-term (2 years) completed WHO-ILAR COPCORD Stage II Education study on control of chronic gout and hyperuricemia by primary health care professionals and patients reveals significantly reduced disability, morbidity rate (flares rate per patient per month) compared with the controls. In another currently completed long-term (10 years) observation it is revealed that not only disability and morbidity rate was reduced significantly but also early mortality was prevented in patients with chronic gout with complications and associated conditions after the second decade of the disease course compared with the outcome of inadequately treated chronic gout with similar complications and associated conditions in the dropouts.

The Future: Publication of the completed WHO-ILAR COPCORD Stage II Education may induce an interest in the extension of similar research projects to existing national primary health care system in other developing countries with Polynesian and Malayo related races in Southeast Asia. When these studies in the future are applied to the existing primary health care system of developing countries it will reduce the burden of rheumatic disease and favorably influence the development of third world countries with populations of Polynesian and Malayo related races in the Asia Pacific region. This will reduce the burden of rheumatic disease in particular chronic gout with complications and associated conditions in the region.

T120

THE SOUTHEAST ASIAN PATTERN AND PRACTICE OF THE RHEUMATIC DISEASES WITH SPECIAL REFERENCE TO GOUT, RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS IN PRIMARY AND TERTIARY HEALTH CARE.

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Patterns of rheumatic disease. Rheumatoid Arthritis is a variable disease in its occurrence and manifestations in time and place. The prevalence and incidence rates of RA in Caucasians are 1% and 0.3%, but in non-Caucasian Asians the prevalence rate is 0.3%. Peak prevalence of RA appears in the 50s in the West, but between the 20-30s in Asia. Caucasians have a more severe disease than non-Caucasian Asian and African populations. Disease severity of Arabs Caucasians populations is between Caucasians and Africans. Contemporary there is a tendency for prevalence rate and severity of disease of RA to decline in the West, but to increase in Asia and Africa. Patterns of systemic lupus erythematosus in Southeast Asia are similar to the West and other regions of the world, although with varying severity, rates of morbidity and mortality. Systemic lupus erythematosus showed incidences of fever, facial rash, and photosensitivity higher in the East compared with the West. The various clinical manifestations expressed as a percentage of all cases are similar. Gout is significantly prevalent in Malayo/Polynesian races.

Patterns of rheumatology practice. Autoimmune inflammatory arthritis such as rheumatoid arthritis, Seronegative Spondyloarthritis, Systemic Lupus Erythematosus, Dermato- and/or Polymyositis, etc., are exceptionally rarely seen in primary health care. Osteoarthritis and Low Back Pain are encountered in very few patients in primary health care in both the West and Southeast Asia. In the West, office-based rheumatologists commonly provide both primary and principal rheumatology care. In Southeast Asia, because of non-existent referral system rheumatologist may also provide direct primary care to patients with a non-rheumatologic disorder. Most of the patients with nonspecific back pain are taken care of by chiropractors in the West, while masseurs have a field day with back pain in developing countries of Southeast Asia. Differences between the patterns of rheumatology practice in Southeast Asia and the West are significant and numerous. Developing countries have a long way to go to reach the current level of rheumatology care as in the West especially gout, RA, and SLE.

T121

EPIDEMIOLOGY OF MYOFASCIAL PAIN SYNDROME IN RURAL THAILAND : A WHO-ILAR COPCORD STUDY.

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Objective: To determine the epidemiological data of Myofascial pain syndrome (MFPS) in Thai rural community.

Rationale: MFPS is a common problem in medical practice that is frequently misdiagnosed and improperly managed.

Methods: Rheumatology Unit, Phramongkutklao Hospital had conducted the study among 2,463 Thai who were 15 years of age and older at Kao Changok, Nakonnayok Province. This study is a part of the Thailand WHO - ILAR COPCORD study of epidemiology study of Rheumatic disease in Thai rural community.

Results: The incidence of MFPS was 6.3% (155 cases),second to osteoarthritis which constitutes 36% of total population surveyed. MFPS was most common among 31-40 and 51-60 age groups; female is 2.4 times more common than male and mostly married. Most common trigger points were lower back (71.2%), trapezius (19.7%),gluteal (16.5%) infraspinous (14.6%). 59.2% have one trigger point, 27.2% have two trigger points, 13.7% have three to seven trigger points and 109 cases (70.3%) have other musculoskeletal problems. Among 46 cases with no associated disease; 73.9% have severe to moderated pain; 39.1% stated that pain interfere with routine activities; 15.2% were unable to work. 45.2% of the patient treated themselves, 43.8% received treatment from physicians.

Conclusion: MFPS is a common medical problem. The physicians should be aware of the importance of this syndrome. Correct diagnosis and effective treatment must be instituted to minimize the economic loss and suffering of the patients.

T122

PAIN IN RHEUMATOLOGY, WHAT IS ITS IMPORTANCE?

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OBJECTIVES: to define the importance and characteristics of the symptom "pain" in the first appointment of Rheumatology in the outpatient department in Portugal.
PATIENTS AND METHODS: it was done an inquiry about the existence of "pain" and its characteristics in the first appointment of Rheumatology in the outpatient department, during a period with a maximum duration of one month.
RESULTS: 192 patients were evaluate, 145 women and 47 men, with a mean age of 53,6 years. Pain was the main motive of appointment in 171 cases (89,1%). The mean duration of pain was 80,8 months. About two thirds of patients had regional or widespread pain. The mean rating of pain intensity using the visual analogue scale was 55,3 mm. We found a significant interference of pain with the quality of live and the activity of the patients. The major diagnostics associated with pain were osteoarthritis and tenosynovitis / bursitis. The women have a mean rate of pain intensity significantly superior comparing with the male patients.
CONCLUSION: pain is the main cause of use of a first appointment of Rheumatology in the outpatient department in Portugal. Rheumatologists have an important role in the evaluation and treatment of a great number of pain clinical cases, which are a source of suffering and significant social and economic costs.

T123

OSTEOARTHRITIS IN MOROCCO.

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In clinical practice, OA localizations seem different in our patients when compared to Euro-american data. However, no epidemiological data were available to confirm that clinical observation.
Objective : to identify the main localizations of limbs or spine OA and their incidence in our country.
Patients et Methods : Type of the study : transversal, prospective, multicentric.
Criteria for inclusion : ACR criteria .Collected data : sex, age, weight, height, duration of the disease, clinical and radiological manifestations in 41 articular sites. Statistical analysis used PCSM software. The first step consisted in defining OA involvement in the evaluated sites. Variations in interpreting clinical manifestations made diagnosis difficult when data for limbs or spine OA, and clinical manifestations in localizations as hands. For the second step uni or bilateral site was precised and a descriptive analysis of the so defined OA localizations was made.
Results : 1000 patients were included by 26 rheumatologists. 59.6 % were examined in public heath departments wether universitary or not and 40.4% in liberal practice. They were 216 men (21.6 %) and 784 women (78.4 %). The mean age was: 57.5y±11.5 [17-95]. Duration of the disease was 67.6 months ± 70.9 [0.06-600]. The mean weight was 73.8 kgs ± 12.6[38 ;117] for a height of 1.61m ± 0.09[1.38 ;1.90]. Our results were then compared to euro-american data. OA of the hands, as well as the spine is less frequent (men age : 52y vs 70y). Mostly OA involves the knee: femoro-tibial OA 64.6% for (vs 39.7%) with 48.8% for the internal compartment. Femoropatellar OA : 35.7% of the patients (vs 34.8%). Hip OA : 3,1 % vs 21.1%.
Discussion : Our results probably add some arguments to the different OA localizations according to the ethnics in limbs OA . The involvement of the knee (internal compartment) is very frequent and severe. Hip OA is rare.

T124

DECLINING INCIDENCE OF RHEUMATOID ARTHRITIS MAY BE PRIMARILY IN THE ELDERLY

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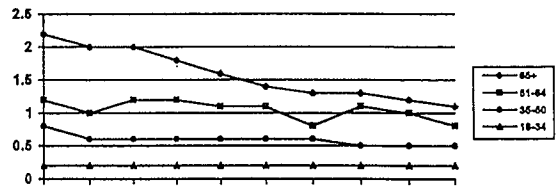
Recent studies have suggested that the incidence of rheumatoid arthritis (RA) is declining. We had previously used a provincial administrative healthcare database to establish the prevalence of RA. Data from the administrative database was also computer linked to a tertiary care clinical database of over 2200 rheumatology patients to examine the accuracy of the administrative diagnoses.
Methods: We used a large administrative healthcare database, linked to a clinical database, to examine the incidence and prevalence of RA over a 12 year period (1984/85-1995/96) in a stable population of over 800,000 adults. The 'International classification of diseases' (ICD-9) code 714 for RA was used to define RA. Prevalent cases were defined as ≥ 1 RA claim per fiscal year. For incident cases, only individuals with ≥ 3 RA claims were included, and the year of the first RA claim was defined as the incident year.
Results: The prevalence rate for RA was increased minimally from 5.4 to 5.8/1000 adults. The overall annual incidence rate declined slightly from 0.8/1000 adults in 1986/87 to 0.5 in 1995/96. The >65 year age group showed a significant decline in the annual incidence rate (p=0.01), while the remaining age groups showed a stable incidence rate.

Incidence of Rheumatoid Arthritis in Manitoba by Age Group-. Case definition: At least 3 714 claims ever. Fiscal Years 1986-1996. (Rates/1000 population)



Conclusions: While the overall annual incidence of RA declined slightly from 1986/87 to 1995/96, the incidence in the elderly decreased by 50%, from 2.2/1000 to 1.1/1000 during the study period. The previously reported declining incidence of RA may be due to a preferential decline in elderly onset RA. Such a trend would have a significant impact on future health care policy given the aging demographics of our population.

T125

RHEUMATOID ARTHRITIS IN CANADIAN ALGONKIAN INDIANS: EARLIER ONSET BUT COMPARABLE OUTCOME.

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Introduction: We have previously shown that rheumatoid arthritis (RA) has an earlier age of onset in an Algonkian Indian population (AI) compared with Caucasians (CA), and has features potentially suggesting a more aggressive disease course. This study compared the outcome of RA in a cohort of AI patients with that of CA patients followed over a 5-10 year period.

Methods: Patients meeting ACR criteria for RA were followed in an outpatient rheumatology clinic. Information was collected on demographics (age, gender), joint counts (total affected, tender, swollen, Lansbury articular index, and involvement of individual large joints- hips, knees, shoulders), patient self reported functional status (modified Health Assessment Questionnaire [mHAQ], VAS scores for pain, fatigue), laboratory features (ESR, RF) and markers of socioeconomic status (education, household size). Univariate analyses were performed using Mann-Whitney U tests or Students T tests as appropriate. Multivariate analysis was used to determine predictors of functional outcome.

Results: Baseline data was available on 103 AI and 470 CA patients with RA. AI patients had onset of RA 9 years earlier than CA patients (36 vs 45 years), had higher titers of RF (649 vs 359IU/ml) but significantly fewer tender joints (11 vs 13.5) and affected joints (14 vs 18). No differences were seen in the distribution of affected joints, Lansbury indices, mHAQ scores, a.m. stiffness, VAS scores, gender, or disease duration prior to presentation. AI patients had larger household size and fewer years of education. 21 AI and 99 CA patients were followed for 5-10 years. Length of follow-up and disease duration was no different between AI and CA patients. There were no differences in total joint counts (tender, swollen, affected, Lansbury, or extent of large joint involvement), in mHAQ scores, a.m. stiffness, ESR or VAS scales for pain or fatigue after 5-10 years of disease. Multivariate analysis indicated affected joint count and, in particular, hip involvement predicted functional disability as determined by mHAQ score.

Conclusion: Age of onset of RA was 9.2 years earlier on average in AI compared to CA patients, but the burden of joint disease and functional status are similar with long term follow-up. Hip involvement and total affected joint count are the best predictors of functional status.

T126

ARE OILS USED AS LAXATIVES, IN COSMETICS OR SKIN CARE AN ENVIRONMENTAL TRIGGER FOR ARTHRITIS?

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Objective: To assess the pathogenic potential of oils, used cosmetically/taken internally, by their capacity to induce chronic polyarthritis in rats.

Methods: Arthritis development was quantified 11-15 days after a single tailbase inoculation of admixtures of test oils with either an (a) auto-antigen = collagen type II (C-II), emulsified with oil and 2.5% Arlacel, or (b) exogenous arthritigen = heat-killed *Mycobact.tuberculosis* (MT). Accompanying gastropathy was assessed by mucosal bleeding from oral/parenteral NSAIDs at doses not gastrotoxic in normal fasted animals.

Results: Significant polyarthritis was induced by admixtures of oil with arthritigen: oils or arthritigen alone being non-toxic. Administering MT (in saline) and oil alone at separate sites in the tail also induced arthritis. Combinations of C-II and MT were synergistic when admixed with cosmetic oils. Oils damaging both stomach and joints included products sold as 'baby'/bath oils (mineral oil, apricot kernel), 'facial'/'skin'/'body' oils (soya bean, persic, macademia nut), up-market cosmetics (jojoba bean, avocado) and 'moisturisers' eg Sorbolene (mineral oil-water emulsion).
By contrast, oils used externally in two cultures with low incidence of rheumatoid arthritis, namely emu and goanna oils (Australian Aborigines), ngali nut oil (Solomon Islanders) were non-toxic.

Conclusions: Oils accepted as harmless may become toxic when external barriers (gut, skin) are breached, allowing undigested oils to stimulate Langerhans (skin) and other immunoreactive cells. Rheumatoid arthritis, a relatively modern disease, may be associated with (i) increasing use of oily emollients applied to skin, scalp; (ii) consumption of mineral oil laxatives and (iii) using mineral (baby) oils for infants' nappy rash.

T127

RHEUMATIC DISORDERS IN ANCIENT EGYPT

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Objective: To study the Rheumatic Diseases and its management in Ancient Egypt.

Rationale: Rheumatic Diseases were well known in Ancient Egypt 3000 B.C.

Methods: Studying the data from:

- -Egyptian Papyri.
- -Cairo Museum collections of statues and mummies.
- -Illustrations on temples and mastaba.
- -Cairo University Faculty of medicine of old splints.
- -Manchester mummy 1770.
- -X-Ray of the mummies.

Results: Different diseases were well known including diseases of the spine and peripheral joints as A.S. and O.S.

Conclusion: Methods of treatment were well known including manipulation, massage, exercise and different drug prescriptions e.g. Mertyle which contains Salicylates was used to treat pain and stiffness

T128

THE PREVALENCE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN ALQASIM REGION OF SAUDI ARABIA.

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Objective: To find out the prevalence of SLE in a community study of AlQasim region of Saudi Arabia.

Methods: The AlQasim province has a population of 660,000 based on 1992 census with an expected yearly population growth rate of 5%. This region was divided into 3 strata according to population density; large (>20,000 inhabitants), medium (5000-20,000) and small (<5,000). Random samples proportionate to size were selected from each. The survey was divided into 3 phases. During 1st phase, a GP and 2 nurses personally interviewed all inhabitants of the randomly selected households about signs and symptoms of rheumatic diseases. The 2nd phase involved trained nurse administering detailed questionnaires to those identified in 1st phase as having symptoms and signs of SLE. In the 3rd phase, a consultant rheumatologist interviewed and examined those patients selected in phase 2. Parallel step of determination of ANA (using indirect immunofluorescence) was carried out during phase 2. The ACR 1982 criteria were applied for diagnosis of SLE.

Results: A total of 10,372 individuals were screened -their age were between 1 and 85 years. There were 5,035 males (48.5%) and 5,337 females (51.5%) Out of these, 1,567 entered the 2nd phase and 180 went on to the 3rd phase. Only 2 cases satisfied the diagnosis of SLE (both females-25 and 31 years old). Accordingly, the estimate prevalence is 19.3 per 100,000.

Conclusion: The prevalence of SLE in one large region of Saudi Arabia is estimated to be 19.3 per 100,000. These figures fall within the range of prevalence in other parts of the world, albeit at the lower end.

T129

Low back pain in a cohort of 622 Tunisian School children and adolescents : an epidemiological study

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A study was undertaken to analyse the prevalence, severity, consequences and risk factors for low back pain (LBP) in two preparatory schools in the city of Monastir (Tunisia) in April 2000.
A Total of 622 children and adolescents, 326 females and 296 males, with a mean age of 14 (11 to 19 years old) were included in the study. They completed the questionnaire with the presence of the physician and only the first 201 children and adolescents underwent a spine medical examination with evaluation of pain by visual analogue scale if LBP was present.
The results showed that 28.4% of the subjects had a cumulative life-time prevalence of LBP and 8% suffered from chronic LBP.
LBP was responsible for 23% of school absenteeism and 29% of sports absenteeism. The use of the health system was seen in 32% and the psychological symptoms in 75%.
Stepwise regression logistic analysis showed that 3 factors were associated with LBP:

1) School failure OR=2.6 (95%.CI, 1,96-3,44)
2) Family history of LBP OR=3.80 (95%.CI, 2.94-5.92)
3) Dissatisfaction with school chair OR=3.40 (95%.CI, 2.24-5.29)

There were 2 factors associated with chronic LBP :

1) Dissatisfaction with school chair OR=3.40 (95%.CI, 2.24-5.29)
2) Practice of football OR=3.07 (95%.CI, 2.15-5.10)

Conclusion: the prevalence of LBP among Tunisian school children and adolescents is too high, which requires urgent preventive measures.

T130

THE BURDEN OF MUSCULOSKELETAL CONDITIONS: THE BONE AND JOINT MONITOR PROJECT.

Symmons DPM[1], Pattison DJ[2], Woolf AD[2], Åkesson K[3], Hazes JMW[4], Guillemin F[5], Cimmino MA[6], Shewan C[7] van der Linden S[8]; Balint G[9] and The Bone and Joint Monitor Project Group.
Manchester, UK[1]; Truro, UK[2]; Malmö, Sweden[3]; Rotterdam, Netherlands[4]; Nancy, France[5]; Genoa, Italy[6]; AAOS, USA[7]; Maastricht, Netherlands[8]; Budapest, Hungary[9].

Background: Musculoskeletal conditions have an enormous and growing impact worldwide but this has not been well quantified. The Bone and Joint Monitor Project (BJMP) is a global health needs assessment for musculoskeletal conditions that is a core activity of the Bone and Joint Decade initiative.
Rationale: The initial phase of the BJMP is identifying the global burden of these conditions in collaboration with the WHO Global Burden of Disease 2000 Project and with an international network of collaborators.
Methods: The COPCORD studies and other datasets from throughout the world have been identified which give information on the incidence, prevalence and health, social and economic impact on both the individual and society from rheumatoid arthritis, osteoarthritis, osteoporosis, back pain, major limb trauma and other musculoskeletal conditions. Age and sex related incidence and prevalence rates, using agreed definitions of the conditions, have been estimated for different global regions defined by the WHO (based on geography and mortality rates).
Results: The results show considerable variation in the occurrence of RA, osteoporosis and OA hip. Allowing for differences in methodology, case definition and sampling frames the prevalence of back pain and OA knee is more uniform.
Conclusion: These results demonstrate the importance of musculoskeletal conditions but also show the paucity of data in many areas where the impact is likely to increase due to demographic changes. A greater understanding of the global burden of the various musculoskeletal conditions will enable the development of effective strategies towards its reduction.

T131

EPIDEMIOLOGY OF RHEUMATIC DISEASES AND RHEUMATIC FEVER IN CHILDREN IN LATVIA.

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Objective: Epidemiology of rheumatic diseases in children and adolescents aged 1 – 18 years was researched in order to obtain comparative data with those of other countries. During the last ten years morbidity rate of rheumatic fever and rheumatic heart diseases has been increased.
Methods: In determining incidence and prevalence we used children's rheumatic diseases register data obtained by Jan 1 2001. The goal of the retrospective study rheumatic fever case history in time period from 1991 –2001 was to investigate epidemiology, course and results of disease.
Results: 1251 children and adolescents aged 1 – 18 years have rheumatic diseases. 70,4% have been diagnosed juvenile idiopathic arthritis (JIA) with prevalence 165,1/100 000 and incidence 34,3/100 000. 36% have registered oligoarthritis, 61% polyarthritis (RF+ 5,2%), 2% systemic form arthritis, 0,5% psoriasis with arthritis. Eye injuries in JIA patients occur in 2,4% cases. Collagenoses prevalence 11,1/100 000 and incidence 2,1/100 000. Recent years show an increase of sclerodermia with prevalence 4,5/100 000. Since 1993 rheumatic fever cases tend to grove, reaching incidence 7,5/100 000 in 1998. During the last ten years in Centre of Rheumatology were treated 107 patients, among them 49 were girls, 58 – boys. At age up to 7 years were 10,3%, from 7 – 16 years 86%, from 16 – 18 years 3,74%. 56% have endocarditis.
Conclusion: Epidemiological data in children and adolescents with JIA and collagenoses are similar to those of the developed countries, except for a lesser occurrence of eye injuries. By acute rheumatic fever in 31,8% as result of acute disease was diagnosed mitral, in 9,35% combined mitral and aortal, and 15% aortal insufficiency. The risk group is school age children.

T132

THE EPIDEMIOLOGY OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS IN THE URBAN POPULATION OF ANTALYA, TURKEY

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Objective: To estimate the prevalence of rheumatoid arthritis (RA) and osteoarthritis (OA) in the urban population of Antalya, Turkey.
Rationale: Antalya is a touristic center in the Southwestern Turkey attracting the people for settlement from all over the country. Its rapidly growing urban population is 508.840 according to the 1997 national census. Thus, a prevalence study which will be performed in Antalya can be an indication for the whole country.
Methods: This prevalence study, as part of a continuing larger study, aimed to evaluate the prevalence of RA in the population aged 16 or over, and symptomatic knee and distal interphalangeal joint (DIP) OA in the population aged 50 or over. By random cluster sampling, 1521 individuals (of these, 267 were aged 50 or over) were interviewed at their homes by 20 trained medical students and 10 accompanying physicians. A questionnaire was directed to the individuals, and those suspected of having had inflammatory joint disease or those who had knee pain worsening on exertion and gelling phenomenon and/or swelling in their DIP joints were invited to the hospital for further evaluation by physical examination ,and x-ray and/or laboratory studies were done, if necessary.
Results: Of subjects, 7(0,46%) were diagnosed as RA. The prevalence of symptomatic knee OA was determined as 26,4% and 6,2% in women and men, respectively. The prevalence of DIP OA was 26,3% and 3,8% in women and men, respectively.
Conclusion: Preliminary data suggests that OA is a major health problem in elderly population, especially in women and the prevalence of RA is about 0,5% in Antalya.

T133

PREVALENCE OF MUSCULOSKELETAL COMPLAINTS AND DISABILITY IN CUBA. A COMMUNITY RURAL-BASED STUDY USING THE COPCORD CORE QUESTIONNAIRE.

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INTRODUCTION. Rheumatic diseases are prevalent conditions in the adult population and represent an important cause of morbidity and disability in developed countries. They are not usually included in the list of health priorities by policy markers.

OBJECTIVE.The aim of this study was to evaluate the prevalence of musculoskeletal complaints in the rural community in Cuba using the ILAR-COPCORD core questionnaire .

METHODS. The COPCORD questionnaire (Community Oriented Program for the Control of Rheumatic Diseases) consist of nine sections, including an explanatory introduction , demographic data, pain in the last 7 days , pain in the past, disability and subject evaluation of the questionnaire. This was administered in the form of a home survey to 300 adult subjects.Case defined as those with present pain and no trauma, underwent a physical examination and selected laboratory or Xray evaluations.

RESULTS. The questionnaire was filled out in a mean time of 8 minutes . Patients who presented musculoskeletal pain no related trauma were158 (52.6%).The most frecuently affected regions were the lower back 32(24.4%), cervical spine 24 (18.3%),knee 39(29.7%).and shoulders 24(18.3%). Osteoarthritis was the most common diagnosis with 51(17%) and Rheumatoid Arthritis with a low frecuency 2patients (0.6%). A total of 158 patients sought professional help and only 9(6.5%) were treated by a rheumatologist.

CONCLUSIONS. Rheumatic diseases are prevalent conditions in the adult rural Cuban´s population..Osteoarthritis was the more frecuent disease and Rheumatoid Arthritis the diagnosis with a low prevalence.The majority of subjects were treated by a general practitioner and only 6.5% by rheumatologist.

T134

SCHOLAR TRAYECTORIES (SchT) IN RHEUMATIC PATIENTS (RP). D. Bañuelos-Ramírez, A. González-Martínez. M.M. Ramírez-Palma. Hospital de Especialidades. IMSS y Escuela de Ciencias de la Comunicación UAP. Puebla, Pue., México. CP 7200.

Background: The SchT are the academic behavior of an individual and their analisis it implies the continuous observation of a student population. Carrying a chronic illness as the rheumatic diseases can affect the yield of the fellows and it constitutes an independent variable.

Objective: to know those SchT in a sample or RP assisted in our service.

Methods: We appliying to 36 outpatients inscribed in some school level, copies of its qualifications and to answer a questionnaire that included items as: attributable interference to the illnes, degree of satisfaction and other attitudes related with the acting, and probably attributable to its rheumatic diseases.

Results: 28 completed the criteria inclusion, age 6-26 yeard old; female: 22 (78%) distributed following: elemental school 4 (ARJ) secondary school 4(2APS, 2RA), high school 6(RA and SLE) universitary school: 2 (SA). The average of qualifications was bigger in the female group with 9.0 global and males was 8.2. The students didn't have any school backwardness and in the males there were two repetears. As for the careers 6 of the women were located in communication areas and languages (75%) and none of the males. In areas of the health: 2 women medicine, 1 varon dentistry, 1 lawyer. According to the questionnaire all aspired to continue posgrades and to feel little interference in their attributable school yield to the rheumatic diseases for tose of high school and university level. Those located in secondary and primary had similar answers.

Conclusion: The rheumatic diseases seems to affect little them SchT.

T135

EDUCATION OF PATIENTS WITH RHEUMATIC DISEASES

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Objective:To determine the level of information the patients had about their illness.

Methods:This 4-week study took place in two REHA-Centers in Croatia. 80 patients under therapy for the most frequent diseases (osteoarthritis,RA,lumbago, osteoporosis) were given an anonymous survey. The length of disease in the greatest number of patients (67%) was 4 years.Among those included in the survey, there were more women - 63% (average age 49) and 37% men (average age 46).The majority of patients (58%) only had an 8-year education, 26% had secondary and only 16% had college level education.

Results: The majority of patients (64%) had received information from their specialist physician.Each visit to the specialist lasted, for the majority of patients (86%), about 15 minutes.In assessing their level of information on a scale from 1 (insufficient) to 5 (fully informed), the patients claimed to know most about pain killers (average mark 4) and symptoms (3), while the poorest information was related to the prognosis (1.4) and causes of illness (2.2.). The patients were extremely disciplined in taking the prescribed medication (4.6) but were significantly less willing to adopt the life style advised by the physician (2.5).

Conclusion: In spite of sophisticated means of communication and frequent attempts at educating the patients, the information that patients have on their disease is not satisfactory. The specialist physician continues to play a significant role in educating the patients.

T136

DIFFERENCES IN PERSONALITY OF PATIENTS WITH PSORIATIC ARTHRITIS AND SLE

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Objective: Aim of this perspective review between patients with SLE and those with psoriatic arthritis is to point out differences in their personality.

Rationale: It is well known that different psychotraumatic events most of the time are responsible for the occurrence of exacerbation of many rheumatic diseases.According to different sources psychological factors are involved in the pathophysiology of these diseases.

Methods: Group of 22 patients with P.A., 22 with SLE and 30 control subjects. All patients were hospitalized in the Rheumatology department. Common questionnaire used and included: a) HDHQ (Hostility and Directions of Hostility) which shows the direction of hostility b) The SCL-90 (symptom checklist -90) which counts the psychosomatic expression and c) The DSSI -SAD (Delusion Symptoms States Invectory/ state of anxiety and depression) which expresses levels of stress and depression.Non parametric statistical method (Mann-Whitney test) was used for the analysis of the results.

Results: Those two groups of patients came in comparison with control subjects and appeared with higher levels of psychopathology and especially self oriented hostility ($p=0.000$ for P.A. and $p=0.002$ for SLE).Comparison of two groups of patients showed, that those with SLE appear with higher levels of self oriented hostility($p=0.012$) and general hostility ($p=0.042$) in comparison with patients suffer from P.A.

Conclusion: Differenced in psychologic parameters between patients and control subjects were noted as well as between two groups of patients checked. In international literature there are no publications concerning, consequently the causative agent and the role of declinations concerning each disease is not yet known.

T137

CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS IN THE PRODUCT MONOGRAPHS OF COX-II INHIBITORS: A CANADIAN REGULATORY PERSPECTIVE

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The Contraindications, Warnings and Precautions sections of the Product Monograph alert physicians to serious and unavoidable or avoidable adverse effects associated with the use of a medication. For example, aspirin may provoke an asthmatic episode in certain individuals with asthma, as may certain NSAIDs. The likelihood of such reactions correlates with the potency of an NSAID to inhibit cyclooxygenase however the actual mechanism of such reactions is not fully established. The Product Monograph specifies that use of a particular NSAID is contraindicated in patients who have experienced such reactions with aspirin and/or other NSAIDs. A Warning/Precaution is issued to alert physicians to be cautious in patients with asthma regardless of whether they have a history of such reactions or not.

This presentation will discuss the extent of data required to remove or modify the wording regarding concerns from the Contraindications and Warning/Precautions sections of the Product Monograph of current and future products.

T138

A SURVEY OF A RHEUMATOLOGY TELEPHONE HELPLINE. WHO CALLS AND WHY

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Objective: To establish the number, nature of calls and the identity of the caller to a rheumatology telephone helpline.

Rationale: Rheumatology nurse practitioners provide advice, support and information via a telephone helpline for patients, carers and health professionals. The service operates from 8.30 am to 5.30 pm Monday to Friday and an answering machine records calls outside these hours.

Methods: A retrospective survey of all telephone helpline calls logged over a three-month period was analysed. All calls are recorded on a specially designed form, data collection included, initiator and nature of call and advice given.

Results: 393 calls were received over a three-month period. Of these 122 (31 %) were medication queries, 67 (17 %) treatment inquires, 8(2 %) requests for a sooner appointment, 74(19%) questions regarding outpatient appointment, 28 (7%) required advice about disease flare up, 35 (9%) test results, 24 (6%) received reassurance and support. There were 4 (1%) enquires about Disability Living Allowance and 31 (8%) miscellaneous queries. The main users were patients and carers 358 (91%), with 22 (6%) nurse enquires and 13 (3%) calls from general practitioners.

Conclusion: The telephone helpline is a vital link for patients and is an effective method of communication. It is responsive to the needs of patients and is used as an adjunct therapy to existing management strategies.

T139

RHEUMATOLOGY NURSE OUTREACH CLINICS: OUTCOME AND PATIENT SATISFACTION

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Objective: To establish the nature of rheumatology nurse outreach clinics, evaluate patient satisfaction and views of these clinics.

Rationale: In 1995 nurse outreach clinics were established in primary care in Norfolk. Hospital based specialist nurses extended their traditional service into the community. To assess, educate and follow up patients with rheumatological disorders.

Methods: The outcome of the clinics was evaluated by a retrospective review of the patient's notes over a one-year period. Attendance pattern at hospital, referrals, admission to day unit / ward and reason for visit was noted. A postal questionnaire was used to assess patient views and satisfaction.

Results: Over a one year period 144 (44 %) had reduced hospital visits, 17(5%) more often and 167 (51 %) the same. 73 (22%) referred to physiotherapy, 68 (21%) occupational therapy, 4 (1%) biomechanics, 90 (27%) to the general practitioner and 93 (28%) to the hospital consultant. There were 42 (13%) admissions to the day unit and 13(4%) ward admissions. Reason for attendance included: 60 (18%) patient education, 150 (46%) blood monitoring, 164 (50%) routine follow up, 49 (15%) requests for an earlier appointment and 95 (29%) had disease flare up.
A total of 329 questionnaires sent, 268 returned (81.5%) response rate. 97 % of patients were extremely satisfied and 3 % satisfied with the clinics. 93 % patients found it convenient, all received information regarding disease management and 97 % had a management plan. Patient's views of the service were positive, 100% with the courtesy and 100% with the consultation time.

Conclusion: These clinics are popular with patients and enhance quality of care. Benefits to patients are reduced travelling, less hospital follow up, convenience and continuity of care. Nurse outreach clinics can bridge the gap between primary and secondary care with the transfer of specialist nursing skills to a community setting.

T140

THE SOCIAL SITUATION OF YOUNG PEOPLE WITH ARTHRITIS IN EUROPE

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Objective: The International Organisation of Youth with Rheumatism (IOYR) has, as one of its aims, to raise awareness and change attitudes of both the public and professionals, in relation to the situation of young people with arthritis. However, there have been few research studies conducted that examine the social situation of young people with arthritis in Europe. Therefore IOYR commissioned a pilot research project which would begin to examine this subject.
Method: Every three years IOYR organises and hosts an International Youth Congress for young people with arthritis. The most recent of these, held in Berlin in July 1998, provided the opportunity for data to be collected from the 50 participants who came from 16 European countries. A questionnaire was designed which covered the following areas: Employment, Education, Housing and the Environment and Health Care. Thirty two young people with arthritis (age range 18-38) completed questionnaires, which were included in the analysis. These represented 15 European countries (including eastern and southern Europe). The data was analysed using both quantitative and qualitative methods.
Results and Discussion: A wide range of experiences were recorded in the data. Analysis of the data demonstrates that, for each of the four areas examined (education, employment, housing and the environment, and health care) most of the participants had experienced some disadvantage as a result of having arthritis. For these young people, irrespective of nationality, the biggest problems, which cut across all four areas, were access to buildings and public transport, and the difficulty of managing life with a chronic, unpredictable medical condition. These results will inform the future work of IOYR in the areas of information exchange, self-help and policy influence.

T141

AN EVALUATION OF TELEHEALTH TECHNOLOGY IN PROVISION OF DISTANT AND GLOBAL RHEUMATOLOGY CONSULTS

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Background: Rheumatology consultations are less readily available in many parts of the world, the principal barriers being either geographical or absence of suitably trained specialists. One way by which these can be overcome is by taking the consultant to the patient through utilization the of telehealth technology.
Objectives: This project was undertaken to evaluate the practicality and acceptability of telehealth consults to a remote area where traditional consults are not available.
Methods: A University urban-based rheumatologist has been linked to a family physician in a remote area 750 km from the consultant's location through satellite transmission for two hours on a monthly basis. During each time period a minimum of 6 patients are reviewed. The physician presents the reason for the consultation, which is supplemented by the patient. Appropriate examination is undertaken by the referring physician under observation and direction from the consultant. Issues relating to diagnosis and management of the problem are dealt through 3-way communication between the referring physician, the consultant and the patient. Each of the 3 parties fills in an evaluation form as to the perceived effectiveness and acceptability of the process. A cost/benefit analysis has been undertaken.
Results: Over 100 patient consultations are available for evaluation. The distribution of diagnoses in the telehealth clinics does not differ from those in the referral center. All medical issues were appropriately dealt with through the telehealth consultation. All 3 parties felt that the process was an effective and acceptable alternative to the traditional consultation. A time and cost benefit analysis showed that there was savings in time, both for the specialist and/or the patient and that there are potential cost savings using the telehealth rather than the traditional consultation. Additional benefits were seen to be the enhanced 3-way communication between the referring physician, the specialist and the patient, and a significant continuing professional development activity for the referring physician. The disadvantage of not being able to have direct physical contact with the patient was largely overcome assuming appropriate clinical skill of the referring physician.
Conclusion: Telehealth technology has not been evaluated in Rheumatology. We conclude that this technology is both feasible, practical and acceptable as a means of delivery of Rheumatology consultations and could facilitate access to rheumatologists on a global scale particularly to remote areas were the subspecialty is not now available.

T142

ECONOMIC COST AND WORK STATUS IMPACT OF RHEUMATOID ARTHRITIS: A STUDY OF 146 PATIENTS.

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Objectives: To determine the annual direct costs for the patients and work disability in RA.

Rationale: The impact of rheumatoid arthritis (RA) in work status and loss of economic status is not yet fully quantified.

Methods: 146 patients with RA (female = 88.4%; mean age = 56 years; mean disease duration = 13.9 years; RF positive = 73.8%), completed questionnaires on employment history and health care costs and also AIMS2.

Results: 38.4% of the patients were currently employed and 58.7% were retired. 84.5% of retired patients had stopped working due to RA. From all patients, 83.1% had to take at least one leave due to RA. The mean total time on leave during the RA course was 659 days. AIMS2 scores from good (0 points) to poor status (10 points). In the AIMS2 work scale, 31.9% of the employed patients scored above 7. Mean annual income was 6084 € (euros). The mean total annual spending with RA medical care was 1151 €. This amounts to 21.7% of the patient's mean annual income.

Conclusion: RA has a major impact on work status and health care costs consume a sizable amount of the patient's income.

T143

CLINICAL GUIDELINES IN RHEUMATOLOGY: EVIDENCE BASED?

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Clinical guidelines are a tool that could potentially summarize and deliver the best medical evidence to practitioners, resulting in better patient care and outcomes. There has been a proliferation of practice guideline development in all fields of medicine, including rheumatology.

We have performed a systematic review of clinical practice guidelines in rheumatology in order to determine face validity, external validity and the quality of evidence used. We searched the electronic database MEDLINE, as well as numerous online medical sites for lists of guidelines. Guidelines were then retrieved and examined for evidence regarding a systematic review of the literature, critical appraisal of study design, quality grading of the evidence and some declaration of which evidence backs up particular recommendations.

We identified 27 guidelines published by national or international organizations. These included guidelines regarding rheumatoid arthritis, osteoarthritis, juvenile arthritis, osteoporosis, low back pain and systemic lupus erythematosus. Only ten of the published guidelines provided extensive evidence from the literature to support their recommendations. One guideline was truly evidence-based. Many were unclear as to how they used the literature and some relied on review papers and expert opinion to support their recommendations. We could only identify one guideline that had been validated in a clinical setting.

Further work remains to be done in the field of guideline development to ensure the use of best medical evidence. Guideline validation in clinical scenarios would increase the impact on practicing physicians.

T144

CAN WE MODIFY THE UTILIZATION OF DIAGNOSTIC TESTS WITH CONTINUING MEDICAL EDUCATION?

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Most rheumatologic disorders are best diagnosed by a thorough history and physical examination and not by the use of screening diagnostic tests. Diagnostic tests are overutilized by referring physicians leading to increasing medical costs and unnecessary referrals to rheumatologists to rule out nonexistent disease.

We have conducted a prospective evaluation of a medical education program and its impact on the ordering of diagnostic tests by family physicians. Physicians were asked to complete a problem-based questionnaire, featuring clinical scenarios in rheumatology, prior to the medical education program. After a series of lectures on the use of diagnostic tests, as well as workshops on clinical examination, the questionnaire was re-administered. The data regarding patterns of diagnostic test utilization was analyzed using paired T test analysis. The physicians were 65% male and equally distributed between urban and rural centres. Anti-nuclear antibody testing (ANA) and sedimentation rates (ESR) were among the most frequently requested test across most patient scenarios. After the intervention, the total number of tests requested was reduced by 50% ($p<.001$). Specific tests that were significantly reduced are listed in the following table. The percentage of physicians ordering a test is listed as mean (pre or post). Rheumatoid factor is RA.

SCENARIO	DIAGNOSTIC TEST	MEAN(PRE)	MEAN(POST)
Rheumatoid arthritis	ANA	72%	11%
Osteoarthritis	ANA	59%	24%
Osteoarthritis	ESR	74%	37%
Fibromyalgia	RF	56%	6%
Fibromyalgia	ANA	59%	6%
Fibromyalgia	ESR	89%	16%

It is possible to influence physicians regarding the appropriate utilization of diagnostic tests through medical education programs. Further research is required to determine the most effective methods of long-term influence on actual practice patterns.

W1

GENOME-WIDE SCREENING OF GENETIC FACTORS IN JAPANESE RA: TENTATIVELY ASSIGNED 5 GENES, TIRA1-5.

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Objective: The genome-wide screening of susceptibility genes of rheumatoid arthritis (RA) has been carried out to clarify the contribution of genetic factors of Japanese RA.

Methods: Genetic linkages were studied using micro-satellites (MS) polymorphism (ABI-PRISM LMS-10 ver.1) by affected sib-pair method. HLA-DR was also examined As sample, 59 RA families with more than 2 affected sibs were used. We also have investigated allele frequencies of MS of Japanese control. For analysis, MAPMAKER/SIB programs were used.

Results: MS polymorphisms in Japanese were different from those in Caucasian and 18% of MS showed heterozygosity less than 0.7. Preliminary data showed increases of Maximum LOD Score more than 1.5 in 5 lesions, tentatively identified as TIRA1 - 5. The frequency of the DR shared epitope was not significantly increased in the familial RA comparing to that of in non-familial RA The shared epitope seemed to contribute dominantly to RA

Conclusion: Genome wide screening of Japanese RA susceptibility gene tentatively showed 5 candidate areas as TIRA1-5

W2

HIGHER INCIDENCE OF OSTEOPOROSIS IN RHEUMATOID ARTHRITIS ACCORDING TO THE SHARED EPITOPE

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Objective: To investigate the association of HLA-DRB alleles encoding the shared epitope (SE) and the occurence of osteoporosis in patients with rheumatoid arthritis.

Rationale: Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology. The most-well established genetic susceptibility factor for RA and disease progression is the HLA-DRB-locus. DNA sequencing studies have identified a similar amino acid sequence at residues 70-74 of the third hypervariable region of the DRB1 gene shared by RA associated alleles which is called the shared epitope.

Methods: 148 RA patients (mean age 61.2 years, 122 women/26 men) were HLA-DRB genotyped applying SSP-PCR and reverse hybridisation. Bone mineral density was measured by dexa-scan (Hologic QDR 4500W) at the lumbar spine and femoral neck.

Results: 108 out of 148 patients (73%) were typed HLA-DRB*04 or *01 in at least one allel. The number of patients with osteoporosis was elevated in the group with at least one SE positive allel compared to the SE negative group (48.1% vs. 30%). Especially in a subgroup of 49 patients with HLA-DRB1*01 more frequently osteoporosis was diagnosed (55.1%).

Conclusion: This results provide evidence that HLA-DRB locus influences the course of RA. The presence of the shared epitope seems to be associated with a higher risk to develop osteoporosis in RA.

W3

ELEVATED PLASMA MMP-3 LEVELS ARE ASSOCIATED WITH THE PRESENCE OF THE SHARED EPITOPE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To determine whether there exists an association between plasma MMP-3 levels and the presence of the shared epitope (SE) in patients with rheumatoid arthritis (RA).

Rationale: RA is characterized by an overexpression of proinflammatory cytokines such as IL-1 and TNFα, which are known to stimulate the production of matrix degrading enzymes. One of the most abundant matrix metalloproteinase (MMP) found in RA is MMP-3. It is well established that high plasma levels of MMP-3 account for an early erosive form of RA.

Methods: HLA-DRB genotyping of 45 RA patients was performed applying SSP-PCR and reverse hybridisation (AID GmbH Strassberg). Plasma MMP-3 levels were determined applying the MMP-3 ELISA by Amersham Pharmacia Biotech.

Results: Significantly elevated plasma MMP-3 levels were observed in the SE positive compared to the SE negative group (99.50±13.74 ng/ml vs. 43.02±9.23 ng/ml, mean±SEM, p=0.012). The highest MMP-3 levels (139.99±27.25 ng/ml) were found in patients with the allels *0101, *0102, *0404 or *0405 encoding QRRAA at the position 70-74 in the third hypervariable region of the HLA-DRB1 molecule. The MMP-3 levels in this group were significantly higher compared not only to the SE negative group (p=0.011) but also compared to the group with the amino acid sequence QKRAA (p=0.032).

Conclusion: Our data indicate that plasma MMP-3 levels may vary according to the presence of the SE. This result may explain the association of early erosive RA with the presence of SE.

W4

TRANSCRIPTOME ANALYSIS IN RHEUMATOID ARTHRITIS FOLLOWING ANTI-TNF-ALPHA (ENBREL®) THERAPY

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Objective: To gain insight into the complex mechanisms which occur after neutralisation of TNF-alpha in rheumatoid arthritis (RA) at the transcriptome level.

Rationale: Oligonucleotide arrays can provide a broad picture of the state of cells by monitoring the expression levels of thousands of genes at the same time.

Methods: DNA array technology (Affymetrix) was used to cover changes in the expression levels under etanercept treatment. Total RNA for analysis was isolated from mononuclear cells (PBMC) and neutrophils (PMN) from peripheral blood and synovial fluid (SF) cells at different time points in the course of treatment.

Results: The expression level of 5600 transcripts was analysed. The most expressed genes were found in SF-cells. About 3.3%, 2.4% and 0.2% of the assessed genes in PBMC, PMN and SF-cells, respectively, showed significant changes in gene expression in either direction. In cells from peripheral blood most changes in expression levels were due to an increase of transcripts.

Conclusion: The group of genes which are up- or downregulated included a number of genes which are known to be involved in transcription, cell adhesion as well as genes not previously examined in the context of RA. The results have to be considered preliminary and confirmed in further experiments.

W5

THE INFLUENCE OF HLA-DR/DQ CODING AND QBP PROMOTER ALLELIC POLYMORPHISM ON THE ANTIPHOSPHOLIPID ANTIBODY RESPONSE IN SLE

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Objective: To ascertain if the polymorphism of HLA-DR, DQA and DQB alleles and QAP and QBP promoters influences the production of aCL and anti-ß2-GPI in SLE.

Rationale: While the role of HLA-antigens in directing various autoantibody responses is relatively well known, the effect of promoters is less established.

Methods: 65 consecutive unrelated Slovenian SLE patients (all female, mean age±SD 36±8.3 years, mean follow-up 93 months) and 74 unrelated healthy adults were investigated. aCL and anti-ß2-GPI were determined by ELISA. The patients and controls were typed for DRB1, DQB1, QAP and QBP alleles by PCR-SSO, using the 12th IHW primers, probes and protocols. The subtyping of DQB1 alleles as well as DQA1 typing were carried out with selected Dynal SSP primers. Allelic and deduced haplotypic frequencies in patients and controls were compared using Fisher's exact test.

Results: 32 (49%) and 16 (25%) of 65 SLE patients were positive for IgG, IgM and/or IgA aCL and anti-ß2-GPI, respectively. The DQB1*0301 allele and its promoter QBP3.1 were significantly more common in the aCL negative patients, while both these alleles were underepresented in the anti-ß2-GPI negative patients compared with controls. The frequency of the DQB1*0202 allele was significantly higher in the anti-ß2-GPI negative patients than in controls.

Conclusion: The structural variability of the QBP 3.1 promoter between W and X1 boxes (TG dinucleotide deletion) may account for the high level of expression of the DQB1*0301 molecules on the antigen presenting cells, as we have already observed for the anti-Ro alone antibody response in the same group of SLE patients. A high level of expression of the DQB1*0301 molecules could protect from escape aCL-antigen specific autoreactive T-cell clones during the thymic selection period in SLE with subsequent absence of the production of aCL. These two alleles did not seem to protect the SLE patients against anti-ß2-GPI antibody production. On the contrary, the DQB1*0202 allele may have a preventive role in provoking autoimmune response against ß2-GPI.

W6

POLYMORPHISM OF NITRIC OXIDE SYNTHASE GENE IN SYSTEMIC SCLEROSIS

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Objective: To assess the contribution of endothelial nitric oxide synthase (eNOS) gene polymorphism in systemic sclerosis (SSc).

Rationale: NO constitutively produced by endothelial cells is believed to protect the microvasculature. A eNOS gene polymorphism (894 G→T) has recently been implicated in coronary artery disease.

Methods: We studied 31 SSc patients, 11 with the diffuse form (dSSc) and 20 with the limited form (lSSc). One hundred twenty three healty subjects served as controls.

Results: The table shows that the frequency of G/G was significantly reduced in dSSc vs controls (9 vs 29%; $p<0.05$).
Moreover, the frequency of G/G could distiguish between dSSc and lSSc (9 vs 55%; $p<0.05$)

Genotype	Controls	dSSc	lSSc
G/G	36	1	11
G/T	73	6	7
T/T	14	4	2

Conclusion: 1) eNOS may be a susceptible factor for SSc and 2) dSSc and lSSc may have different backgrounds.

W7

ASSOCIATION OF HLA-DRB1*02 AND *06 WITH OSTEOARTHRITIS IN A COHORT OF 59 PATIENTS

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Objective: We have previously shown that the inflammatory cytokines TNFα and IL-6 or IL-1β are upregulated in chondrocytes of Osteoarthritis (OA) patients. However, the inflammatory responses associated with OA are low grade and restricted. To investigate an involvement of the immune sytem in the pathogenesis of OA we here analyzed patients for their HLA-DRB1 haplotypes.

Methods: Combining SSO or SSP typing procedures, 59 OA patients and 139 randomly selected controls were typed for their HLA-DRB1 alleles.

Results: A global test for the comparison of DRB1 allele frequencies between OA patients and controls yielded a statistically significant difference with a P-value of 0.0176. The difference resulted from elevated frequencies of DR2 and DR6 in the OA patients compared to the controls. The odds ratios conferred by the DR2 and DR6 alleles are 1.76 and 1.95 with confidence bounds of 1.05 – 2.96 and 1.14 – 3.34, respectively.

Conclusion: The association of DR2 and DR6 with OA might hint at a linkage disequilibrium between HLA-DRB1 genes and genes involved in the pathogenesis of OA. Alternatively, DR2 and DR6 may directly play a role in restricting immunological responses to the low grade inflammation characteristic of OA.

W8

INTERFERON GAMMA GENE POLYMORPHISM: RELATIONSHIP TO SUSCEPTIBILITY AND SEVERITY OF RHEUMATOID ARTHRITIS.

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Background: Interferon gamma (IFNg) gene is a potential candidate as marker of rheumatoid arthritis (RA) susceptibility and severity.

Objectives: In this prospective longitudinal study we have investigated the association between a variable length CA repeat in the first intron of the IFNg gene and RA susceptibility and severity.

Methods: One hundred and three early RA patients were evaluated clinically, serologically and radiographically (modified Sharp / van der Heijde method) yearly for 4 years. The total radiological damage score was used to quantify RA severity. One hundred thirty healthy individuals were used as controls. The microsatellite region in the first intron of the IFNg gene was analysed by PCR and electrophoresis in a DNA sequencer.

Results: Twelve CA repeat (12R) and 13 CA repeat (13R) alleles were the most common in RA patients (41.7% and 48.5%) and healthy controls (45.3% and 45.7%). 12R/12R, 12R/13R and 13R/13R genotypes were the most common in RA patients (15.6%, 44.1% and 21.6%) and healthy controls (22.4%, 38.0% and 21.7%). No association has been observed between the IFNg gene polymorphism and RA susceptibility. No association has been observed between the IFNg gene polymorphism and RA severity, by comparing at the end of the 4 year follow-up period the radiological scores of carriers of the different alleles and genotypes.

Conclusion: The present study fails to reveal any association between this particular IFNg gene polymorphism and RA.

W9

ASSOCIATION ANALYSIS OF MATRILIN-1 ALLELIC AND GENOTYPIC FREQUENCIES IN ARGENTINIAN PATIENTS WITH OSTEOARTHRITIS.

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Rationale: It has been suggested that genotypic variation in the gene which encodes the matrilin-1 protein may be involved in the development of hip osteoarthritis (OA).
Objectives: We compared allelic and genotypic frequencies of the matrilin-1 (CRTM, 1p35) gene in patients with peripheral and/or axial OA to determine if there was any association between them.
Patients and methods: 71 unrelated subjects from a rheumatology ambulatory office with clinical and radiographic OA were studied. They were classified as having axial involvement (n=15), peripheral OA (n=34) or both (n=22). They came from hyspanic ethnic background. The CRTM microsatellite polymorphism in the 3' untranslated region was amplified. After PCR was performed, the alleles were separated in a 8% polyacrilamide gel, stained with ethidium bromide and analyzed by UV light.
Results: We identified 3 alleles according to their basepair (bp) length: A1= 106 bp; A2= 104 bp and A3=102 bp. 5 genotypes were found, with an heterozygosity of 0.45. Overall, the most frequent genotype was A1/A1 (46.5%). No significant correlation among any of the OA groups and the CRTM allelic or genotypic frequencies was found (X^2 test: p=ns).
Conclusion: These results do not support a role of the CRTM alleles in the ocurrence of these types of OA. A study with a much larger sample size would nonetheless be valuable to confirm or negate this association.

W10

LOCAL CELL PROLIFERATION DETECTED WITH CYCLIN A IN RHEUMATOID SYNOVIAL TISSUE

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Objective: To evaluate cell proliferation in the synovial tissue of patients with rheumatoid arthritis (RA).
Materials: Synovial specimens from the knee joints of 16 with RA, 6 with osteoarthritis (OA), and 4 with trauma were examined. Samples were obtained during total knee arthroplasty or arthroscopic examination. Average age was 63 (RA), 71 (OA), and 58 (trauma).
Methods: Immunohistochemical staining with antibodies for cell cycle marker PCNA, cyclin A, and cyclin B1 was done to count positive cells in the lining (synoviocytes) and sublining (lymphoid and non-lymphoid cells) in at least 10 areas (X200) randomly selected from each sample by two examiners. Moreover, the relationship with preoperative CRP levels was statistically analyzed.
Results: The average number of cyclin A-positive cells in the lining was 3.1 in RA, 1.6 in OA, and 0.4 in trauma. In the sublining, positive lymphoid cells totaled 5.4 in RA, 0.6 in OA, and 0 in trauma, while positive non-lymphoid cells totaled 1.6 in RA, 0.2 in OA, and 0.2 in trauma. A significant relationship was observed between CRP level and cyclin A-positive cells in the lining ($p=0.008$), as well as non-lymphoid cells in the sublining ($p=0.002$). PCNA staining did not show any significant relationship or cyclin B1.
Conclusions: Our data showed that cyclin A is a more suitable marker of cell proliferation in RA synovium, and that clinical RA activity was related to the proliferation of synoviocytes in the lining layer and non-lymphoid cells in sublining.

W11

COMPREHENSIVE GENE EXPRESSION ANALYSIS OF SYNOVIAL FIBROBLAST CULTURES DERIVED FROM RHEUMATOID ARTHRITIS(RA) USING cDNA ARRAY TECHNOLOGY

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Purpose: Elucidation of specific gene expression profile in RA synoviocytes as compared with control synoviocytes.

Methods: Synovial fibroblasts were obtained from five RA patients (at active disease phase) and five control patients of menisectomy or ACL tear upon arthroscopy. Polyadenylated mRNA was purified from these synovial cell cultures and cDNA probes were synthesized by reverse transcription. Hybridization was performed with human cDNA macroarray (Clontech). The amounts of transcripts were quantitatively compared by ArrayGauge Ver.1.0 (Fujifilm). RT-PCR and real time PCR were performed for specifically genes in RA.

Results:Among 588 different human transcripts compared, we identified a group of genes constitutively in RA synoviocytes: for example, PDGF-alpha-receptor and PAI-1. Expressions of these genes were confirmed by RT-PCR and more guarantively by real time RT-PCR. In fact, we confirmed that growth stimulatory effect of PDGF was significantly augmented in RA synoviocytes. We also compared gene expression profile upon TNF-alpha stimulation. Although induction of IL-6 was equally induced, some genes (MMP-11, CyclinB1, Jagged2, Notch1 and Notch4) were preferentially induced in RA synoviocytes.

Conclusions: These findings suggest that RA synoviocytes have a distinct gene expression profile as compared from normal counterpart, which may contribute pathophysiology of RA.

W12

THE LEVELS OF SERUM SOLUBLE FAS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC SCLEROSIS

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Objective: To determine whether elevated serum soluble Fas (sFas) levels are associated with rheumatoid arthritis (RA) or systemic sclerosis (SSc), and evidence of disease activity.
Rationale: It has been suggested that rheumatic diseases may result from a deficit in Fas-mediated T-cell apoptosis. Recent studies have demonstrated increased serum sFas in patients with rheumatic diseases, especially systemic lupus erythematosus.
Methods: Soluble Fas levels were assayed using a sandwich ELISA in serum from 37 RA patients, 28 SSc patients and 20 healthy subjects. The RA patients were classified according to disease activity, functional status, Larsen score reflecting anatomical joint damage, and the presence of pulmonary involvement.
Results: The mean serum sFas levels were similar in the study groups (8498 ± 4013 pg/ml in RA, 8436 ± 3237 pg/ml in SSc, and 7493 ± 3449 pg/ml in healthy subjects; $p>0.05$). Serum sFas levels in the active RA patients were significantly higher than those of the inactive patients (respectively 9241 ± 3843 and 6186 ± 3832 pg/ml, $p<0.05$). Serum sFas levels did not correlate with functional status or the presence of pulmonary involvement in RA patients. However, there were significant relations between sFas levels and Larsen's score, hematocrit, rheumatoid factor and CRP levels, and erythrocyte sedimentation rate in RA patients. Serum sFas levels did not correlate with the presence of pulmonary fibrosis and DLCO in patients with SSc.
Conclusion: These findings suggest that the Fas-mediated apoptosis may play a role in the pathogenesis of RA.

W13

ALTERATIONS OF CD8+CD28- T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND RHEUMATOID ARTHRITIS (RA).

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Aim: To determine the relative population size of CD8+CD28± T subsets in peripheral blood (PB) samples from controls and patients with RA and SLE, and to determine the immuno-regulator function of these two T subsets through their ability to release IFN-γ, IL-4 and IL-10.
Method: PB samples were stained for CD3, CD8 and CD28 molecules for flowcytometric analysis. For intracellular cytokine assay, CD8+ T cells were isolated using Dynabead. After stimulation with phorbol myristate and ionomycin, CD8+ T cells were surface-stained with conjugated anti-CD28 and anti-CD16 and subsequently stained intracellularly with conjugated anti-IFN-γ, anti-IL-4 or anti-IL-10 in the presence of 0.1% of saponin. CD16- cells were gated and examined by flowcytometry.
Results: Shifts in CD8+ T cell population were observed, with increased proportion of CD3+CD8+ population in SLE group (57.9% vs 35.8% in controls, $p<0.001$) and CD3+CD8+CD28- population in both SLE (62% vs 32.7% in controls, $p<0.0001$) and RA (54.7%, vs 32.7% in controls $p<0.001$) groups as compared with controls. In control subjects, significantly more CD8+CD28+ T cells were positive for IL-4 and IL-10 (15% & 14% respectively) than the CD8+CD28- T counterpart (4.1% and 2.9% respectively). In contrast, more CD8+CD28- T cells (58%) were positive for IFN-γ than CD8+CD28+ T cells (30%). Furthermore, expression of IFN-γ in CD8+CD28- T subset was significantly reduced in both SLE and RA groups (36% & 23% respectively vs 56% in control; $p<0.005$ both). However, increased expression of IL-10 in CD8+CD28- T cells was found in SLE group (7.1% vs 2.9% in control, $p<0.01$).
Conclusions: CD8+CD28± cells are distinct T cell subsets in terms of cytokine production. The general increase in CD28- fraction of CD8+ T cells in systemic autoimmune disorders merits further investigation to delineate its contribution in these disorders.

W14

SURVIVIN IN SYNOVIUM OF DBA/1 MICE WITH TYPE Ⅱ COLLAGEN- INDUCED ARTHRITIS.

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Objective: Impaired apoptosis has been reported to contribute to an extended lifespan of synoviocytes invading the cartirage in RA, we investigated the survivin, anti-apoptotic molecule, in synovial tissue of collagen-induced arthritis.
Methods: Thirty five DBA/1 mice were immunized with bovine type Ⅱ collagen emulsified with Freund's incomplete adjuvant., Macroscopicaly, swelling and reddish of paws evaluated with arthritis index (AI). Synovium in the knees were evaluated immunohistochemically using anti-survivin polyclonal serum with avidin-biotin glucose oxidase complex method(Vectastain ABC-GO kit and glucose oxidase substrate kit, Vector Laboratories, Inc., CA, USA).
Results: AI of mice was elevated significantly at 5 weeks after the immunization (5.1 ± 9, $n=5$)($p<0.05$). Survivin was expressed in the synovial cells and chondrocytes from 3 weeks after the immunization. Survivin was positive in $8.6\pm3.9\%$ of synovial cells in knees of mice at 3weeks and it increased to $23.4\pm1.8\%$ at 6 weeks.
Conclusion: These findings suggest that transcription of survivin is expressed not only in tumor cells but in synovial fibroblasts. Inhibitory apoptosis of inflammatory synoviocyte might mediate joint destruction in DBA/1 mice immunized with type Ⅱ collagen.

W15

IRON ENHANCED TNFα-INDUCED APOPTOSIS OF U937 CELLS (A MONOCYTE-LINEAGE CELL LINE).

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Objective: We have examined the effect of iron on immune cell functions based on the fact that a large amount of iron deposition is found in rheumatoid arthritis synovial tissue. In this study, we investigated whether iron can induce the apoptosis of U937 cells (a monocyte-lineage cell line).

Methods: U937 cells were maintained in RPMI medium with 10 % FCS. The cells were stimulated by human recombinant TNFα at the concentration of 200 U/ml for 5 - 48 hours with or without ferric citrate (Fe-citrate) at the final concetrations of 0.1 - 0.5 mM. The expression of annexin V on the cells as a marker for apoptotic cells was checked by flow cytometry analysis. Simultaneously propidium iodide staining for detecting dead cells was performed.

Results: TNFα induced the apoptosis of U937 cells after 5 hour-incubation. Fe-citrate by itself did not induce the apoptosis of cells. However, Fe-citrate (0.5 mM) significantly enhanced TNFα-induced apoptosis after 48 hours.

Conclusion: Iron enhanced TNFα-induced apoptosis of U937 cells in vitro. These results indicate the possibility that iron could regulate apoptosis of monocytes in RA synovial tissue.

W16

IRON SUPPRESSED CONCANAVALIN-A-INDUCED GENERATION OF MULTINUCLEATED GIANT CELL BY HUMAN MONOCYTE.

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Objective: A large amount of iron deposition is found in rheumatoid arthritis synovial tissue. To examine the effect of iron on the generation of multinucleated giant cell (MGC) by human monocytes in vitro.
Methods: Human monocytes were isolated from venous blood of healthy adult volunteers and cultured in RPMI medium supplemented with 10% FCS. Monocytes were stimulated by Concanavalin-A (Con-A) with or without ferric citrate (Fe-citrate) at the final concentrations of 0.1 - 1 mM or desferrioxamine (DFX). The fusion rate (% Fusion) of monocytes was determined by counting the number of nuclei within MGC divided by that of nuclei in whole cells × 100.
Results: The Con-A-induced MGC generation was increased in dose-dependent manner and reached a plateau after 3 days of incubation. % Fusion was decreased when monocytes were incubated with Fe-citrate or DFX in dose dependent manner. Using flow cytometry, the Con-A-induced CD18 (β2 Integrin) and CD54 (ICAM-1) expression on monocytes was suppressed by addition of Fe-citrate.
Conclusion: Iron supressed the generation of MGC by human monocytes in vitro. It is suspected that iron affected the MGC generation by supprressing the expression of adhesion molecules on monocytes.

W17

LYMPHOCYTES SUBPOPULATIONS AND INTERLEUKIN-II IN PATIENTS WITH RHEUMATIC CARDITIS

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Objective: To evaluate the lymphocytes-subpopulation and interluekin-2 (IL-2) levels in patients with rheumatic carditis before and after therapy with either salicylates or corticosteroids.

Rationale: Acute rheumatic fever (ARF) has the characteristics of autoimmune disease; the delay in manifestations of ARF following streptococcal infections, presence of infiltrates of T helper lymphocytes & macrophages in valvulitis and B cells in Aschoff nodules suggest the important role of immune system in its pathogenesis.

Methods: The study included 40 patients (18 males & 22 females) who were subdivided according to drug therapy into 2 groups (group I; treated with salicylates, and group II; treated with corticosteroids) the study included also 10 patients with quiescent rheumatic valvular diseases (group III) and 10 healthy subjects as controls (group IV). Clinical assessments included presence of arthritis, or active carditis (by auscultation, ECG & echocardiography) and laboratory assessments included ESR, CRP, ASOT, lymphocytes subsets counts in peripheral blood (CD3, CD4, CD8 and B lymphocytes) and serum level of IL-2 assay.

Results: On admission the means of CD4 & B-lymphocytes counts were significantly higher while the CD8 counts were significantly lower in patients (group I & II) than groups III & IV. After 6 weeks of therapy the means of CD4 & B lymphocytes counts were still significantly higher & CD8 mean counts significantly lower than controls, there were no significant differences in mean counts of CD4, CD8 and B-lymphocytes between patients treated with either salicylates or corticosteroids. In addition, serum IL-2 showed significant decrease and there were no significant differences in its mean levels before and after treatment.

Conclusion: Abnormalities in lymphocytes subpopulations occur in ARF. IL-2 is increased with rheumatic activity. Treatment by salicylates or corticosteroids do not normalize these abnormalities after 6 weeks from therapy in spite of the significant fall in mean IL-2 level and prolonged time may be needed. IL-2 can be considered as an index of activity in ARF.

W18

CD1D ALTERNATIVE SPLICING FORMS IN MONONUCLEAR CELLS FROM PATIENTS WITH AUTOIMMUNE DISEASES.

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【Objective】 Our previous study on T cell receptor (TCR) of $CD4^-$ and $CD8^-$ (double negative, DN) T cells in autoimmune diseases showed that DN NKT cells are selectively reduced in the peripheral blood and in the arthritic regions compared to controls. Therefore, we speculated that DN NKT cells might function as regulatory T cells in patients with autoimmune diseases. Our recent studies showed the dysfunction of NKT cells by themselves in α-Galactosylceramide (α-GalCer) non-responders of patients with autoimmune diseases and the lower activity of antigen presentation on APC. To clarify the lower presentation of antigen on APC in patients, we focused on the expression and the alternative splicing of CD1d molecule that strongly associate with NKT cell differentiation and activation.

【Methods】 (1) PBMC from nine α-GalCer responder (RA:3, SLE:4 , SSc:1 ,SS:1), eight non-responder (RA:2, SLE:1 , SSc:2 , SS:1), and three healthy donors were stained with anti-human CD1d mAb, and CD1d positive monocyte were calculated by flowcytemetry. (2) Total RNA was prepared from fresh PBMC from three healthy subjects and copied into cDNA. Oligonucleotide primers were designed to amplify the entire CD1d cDNA, and CD1d mRNA structure was analyzed by nested PCR, Southern blot analysis and sequencing method.

【Results】 (1) There was no difference for the expression of the CD1d on peripheral blood monocytes between α-GalCer responder patients, non-responder patients and healthy donors. (2) Nine forms of CD1d mRNA were detected by gel electrophoresis and Southern blot analysis. Two types of splicing variants of CD1d were thought to be functional. One is soluble form of CD1d, because the deletion of TM and CY sites. The other is the lack form of β_2-microglobulin binding domain, suggesting the instability of antigen presentation.

【Conclusion】 These findings suggest that alternatively spliced CD1d transcripts may function as inhibitor of CD1d-ligand-NKT cell interaction in patients with autoimmune diseases. At present, the quantity of each alternative splicing variant in patients is being determined by TaqMan PCR method.

W19

CONCENTRATIONS OF CIRCULATING INTERSTITIAL COLLAGENASE, STROMELYSIN-1, TIMP-1 AND TIMP-2 IN MORPHOLOGICAL VARIANTS OF RHEUMATOID ARTHRITIS.

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Objective: The aim of this study was to explore whether the serum levels of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) are associated with the morphological appearance of rheumatoid arthritis (RA).

Methods: Tissue and serum samples were obtained from 37 patients with clinically active RA and 30 with osteoarthritis (OA). After the histological analysis, RA synovial specimens were divided into two distinct types. In 22 samples only diffuse infiltrates of mononuclear cells without any further microanatomical organization were observed. Lymphocytic conglomerates with germinal center-like structures formation were found in 15 specimens. The measurement of serum concentrations of interstitial collagenase (MMP-1), stromelysin-1 (MMP-3), TIMP-1 and TIMP-2 was based on ELISA technique.

Results: The serum concentrations of MMP-1 and MMP-3 were higher in RA patients than in OA patients used as a control group (in both cases $p<0.001$). These MMPs dominated in the serum of RA patients with follicular synovitis compared to those with diffuse ($p<0.05$ and $p<0.01$ respectively). The analysis of the serum concentrations of TIMP-1 and TIMP-2 showed that their levels were also elevated in RA patients in contrast to OA patients ($p<0.001$ and $p<0.01$ respectively). But only TIMP-1 was found in a significantly higher amount in the serum of RA patients with follicular synovitis than in those with diffuse ($p<0.05$). The serum concentrations of MMPs and TIMP-1 could clearly identify patients with two different histological types of rheumatoid synovitis and with OA. Additionally, the analysis of clinical data showed that the rheumatoid disease in patients with follicular synovitis seems to be more active than in those with diffuse.

Conclusion: The correlations between different morphological appearance of rheumatoid synovitis and serum MMPs or TIMP-1 profile, and varied clinical activity of the disease confirm RA heterogeneity.

W20

EXPRESSION OF MEMBRANE TYPE MATRIX METALLOPROTEINASES IN THE SYNOVIAL TISSUE FROM PATIENTS WITH PHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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Objective: To investigate the expression of membrane type matrix metalloproteinases(MT-MMPs) and matrix metalloproteinases(MMPs) in the synovial tissues from patients with rheumatoid arthritis(RA) and osteoarthritis (OA)

Rationale: MT1-MMP, MT3-MMP, and probably MT2-MMP, may be involved in joint destruction of RA and OA.

Method: Expression of MT-MMPs and MMPs was examined using reverse transcription-polymerase chain reaction(RT-PCR) with degenerate oligonucleotide primers and northern blot analysis.

Result: MT-MMP, MT3-MMP, MMP-1, MMP-8, MMP-13, MMP-3, MMP-10, MMP-7 and MMP-12 were detected in RA by RT-PCR. Northern analysis demonstrated strong expression of MT1-MMP, MT3-MMP, MMP-1 and MMP-3 and weak expression of MT2-MMP and MMP-8 in RA and OA. MT4-MMP was not detected. No significant difference was demonstrated in the expression of MT-MMPs between RA and OA.

Conclusion: Synovial tissues of RA and OA expression MT-MMPs as well as MMPs. These results indicate that, in addition to MMPs, MT1-MMP, MT3-MMP, and probably MT2-MMP, may play a role in the degradation of bone and cartilage matrix in RA and OA.

W21

THROMBIN INDUCES CHEMOKINE RANTES PRODUCTION VIA PROTEASE-ACTIVATED RECEPTOR-1 IN SYNOVIAL CELLS FROM PATIENTS WITH RHEUMATOID ARTHRITIS.

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Objective: To examine the effect of thrombin on RANTES production in synovial cells from patients with rheumatoid arthritis (RA).

Rationale: RANTES has been shown to be a chemotactic factor for T lymphocytes and macrophages and to be presented in synovial lining cells of patients with RA. Clotting factors such as thrombin are increased in synovial fluids of patients with RA. Recently we have reported thrombin induces synovial cell proliferation via protease-activated receptor (PAR)-1, which is one of the thrombin receptors. Little is, however, known about the effects of thrombin / PARs on RANTES production in RA synovial cells.

Methods: We performed semiquantitative RT-PCR analysis for the expression of RANTES, PAR-1, PAR-3 and PAR-4 using synovial cells from patients with RA. In addition we studied transcriptional effect of thrombin on RANTES gene expression using a reporter plasmid of RANTES promoter driving the luciferase gene and expression vectors of PAR-1 and PAR-3 in HeLa cells, since PARs were not expressed in HeLa cells.

Results: PAR-1 and PAR-3, but not PAR-4 were expressed in RA synovial cells. 50 U/ml of thrombin up-regulated mRNA levels of RANTES at 6 h after treatment. Moreover, thrombin dose-dependently transactivated RANTES gene expression in HeLa cells expressed PAR-1, but not PAR-3, possibly indicating that thrombin induces RANTES production via PAR-1 in RA synovial cells.

Conclusion: We found that thrombin promotes RANTES gene expression through PAR-1 in synovial cells from patients with RA, suggesting that thrombin might play a pivotal role in the pathogenesis of RA.

W22

PPARγ ACTIVATORS INHIBIT IL-1ß-INDUCED NITRIC OXIDE AND MMP-13 PRODUCTION IN HUMAN CHONDROCYTES

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Evidence suggests that peroxisome proliferator-activated receptor γ (PPARγ) agonists not only regulate lipid and glucose homeostasis, but may also be important antiinflammatory agents. Since chondrocytes are key players in arthritis through the elaboration of multiple proinflammatory mediators such as NO and MMP, the role of PPARγ in their activation by IL-1ß was investigated.

By RT-PCR and immunohistochemical analysis, we showed that PPARγ is expressed and synthesized in human articular chondrocytes. Treatment of chondrocytes with PPARγ ligands BRL 49653 and 15d-PGJ_2, but not with PPARα ligand, dose-dependently decreased the expression and synthesis of IL-1ß-induced NO and MMP-13. The inhibitory effect of PPARγ activation was not restricted to IL-1ß, as TNF-α- and IL-17-induced NO and MMP-13 production were also inhibited by 15d-PGJ_2. In transient transfection experiments, we showed that a constitutively active form of MEKK1 induces the MMP-13 and iNOS human promoter activity. This process was reduced by 15d-PGJ_2 and abolished with cotransfection with a PPARγ expression vector. Similarly, in a PPARγ-dependent-manner, 15d-PGJ_2 inhibits ΔMEKK1-induced AP-1 and NF-κB-luciferase reporter plasmid activation.

These findings demonstrate that PPARγ agonists inhibit proinflammatory cytokine induction of both NO and MMP-13 in human chondrocytes at the transcriptional level through a PPARγ dependent pathway. In view of the crucial role that proinflammatory cytokines play in arthritis, our data point to the fact that the PPARγ system may represent a therapeutic target in arthritis.

W23

INHIBITORY EFFECT OF BUCILLAMINE ON THE VASCULAR ENDOTHELIAL GROWTH FACTOR IN CULTURED SYNOVIAL CELLS FROM PATIENTS WITH RHEUMATOID ARTHRITIS.

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Objective: To evaluate whether disease-modifying anti-rheumatic drugs (DMARDs), including bucillamine (BUC), gold sodium thiomalate (GST), methotrexate (MTX), salazosulfapiridine (SASP) and dexamethasone (DEX; a steroid), act by inhibiting the production of vascular endothelial growth factor (VEGF) by cultured synovial cells of patients with RA, and to determine the molecular mechanism of the VEGF inhibition.

Methods: The synovial cells from patients with RA were used at the 3rd or 4th passage for the experiments. They were stimulated with lipoplysaccharide (LPS), interleukin-1beta (IL-1beta) or hypoxia and cultured with DMARDs and DEX in 1% FCS containing medium. The production of VEGF in the supernatants was measured by ELISA. Total RNA was extracted from the cells using Isogen, VEGF mRNA levels were measuring by RT-PCR analysis.

Results: BUC, GST and DEX significantly inhibited VEGF production induced by each stimulus in cultured syonovial cells in a concentration dependent manner. Furthermore, BUC also inhibited the expression of VEGF mRNA in synovial cells.

Conclusion: These findings suggest that BUC may act as an anti-antigenic agent, producing clinical improvement in patient with RA.

W24

SALAZOSULFAPYRIDINE SUPPRESS THE DELAYED-TYPE HYPERSENSITIVITY AND NORMALIZE TH1 / TH2 BALANCE

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Objective: To examine the effect of salazosulfapyridine (SASP) for delayed-type hypersensitivity (DTH), and its mechanism of the suppression of DTH.

Methods: DTH was induced with chicken lyzozyme in C57BL/6 mice. SASP or its metabolites, sulfapyridine (SP) and 5-aminosalitylic acid (5-ASA) were treated into the DTH mice. The footpad swelling, serum concentration of some cytokines produced from Th1 or Th2 cells, and mRNA contents of cytokines in lymph node were measured.

Results: SASP suppressed the footpad swelling in DTH dose dependently, but SP or 5-ASA did not. The imbalance of Th1 / Th2 cytokine in DTH was improved after SASP treatment.

Conclusion: SASP itself, not its metabolites, suppresses DTH. The suppressive mechanism seems to normalize the balance of Th1 / Th2 cytokines.

W25

LYSOZYME AND ITS BIOLOGICAL VALUE IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS OF THE KNEE

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Lysozyme or muramidase catalyzes the hydrolysis of 1,4-beta-linkages between N-acetylmuramic acid and N-acetyl-D-glucosamine residues in peptidoglycan. It functions as an antibacterial agent. Lysozyme is well known for the ability to hydrolize the cell wall of bacteria.
Objective:The aim of the study was to measure and compare the concentration of lysozyme in synovial fluid in RA and OA patients.
Methods : We measured the lytic activity of lysozyme towards micrococcus lysodeikticus, bacteria which are highly susceptible to lysis by lysozyme by the turbidometric method 30 synovial fluid of RA patients and 30 synovial fluid of OA patients.
Results: IN all our RA and OA synovial fluid we observed increased level of lysozyme: in RA patients it ranges between 7.1 to 20.9 ug/ml /mean range 11.76+-3.41 ug/ml/, in OA patients it ranges between 1.5 to 4.9 ug/ml /mean range 2.96+-1.1 ug/ml/. We observed higher level of lysozyme /p<0.001/ in RA synovial fluid and the correlation between the level oflysozyme in synovial fluid and disease activity /p<0.039/.
Conclusion: The increased levels of lysozyme in synovial fluid in RA could indicate monocyte/macrofage activity and might be used to study disease activity in RA.

W26

DO ELEVATED LEVELS OF TRANSFORMING GROWTH FACTOR ß (TGFß) PROVIDE PROTECTION AGAINST OSTEOPOROSIS IN RHEUMATOID ARTHRITIS?

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Objective: It was the aim of this study to determine the role of TGFß for bone metabolism in rheumatoid arthritis (RA).

Rationale: TGFß in bone has been described to provide a protective effect against matrix degradation. TGFß induces synthesis of matrix proteins and inhibits matrix degradation by downregulation of MMPs. In RA elevated TGFß plasma levels have been described.

Methods: Total TGFß in plasma samples and bone extracts from 36 RA patients and 55 patients with osteoarthritis (OA) was determined after transient acidification applying three isoform specific ELISAs. Bone mineral density was measured by dexa-scan (Hologic QDR 4500W) at the lumbar spine and femoral neck.

Results: The concentrations of TGFß1 in bone were slightly elevated in the RA group compared to the OA group, no significant differences were found for neither of the three isoforms. No association was found for TGFß levels in peripheral blood and in the corresponding bone extracts. A strong negative correlation was found between bone TGFß1 levels and T-score values (r=-0.479, p=0.002).

Conclusion: The finding of elevated TGFß1 concentrations in bone in RA patients with reduced BMD suggest that in RA TGFß does not protect against matrix degradation. It seems likely that more proinflammatory features of TGFß are important in bone metabolism in RA.

W27

CD13/AMINOPEPTIDASE N IS A NOVEL LYMPHOCYTE CHEMOATTRACTANT IN RHEUMATOID ARTHRITIS

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Objective: To examine the role of CD13/aminopeptidase N in lymphocyte involvement of rheumatoid arthritis (RA).

Rationale: CD13/aminopeptidase N induces chemotactic migration of T lymphocytes by its enzymatic activity.

Methods: Studies were made on 27 patients with RA and 6 patients with osteoarthritis (OA). Synovial tissue specimens were obtained from 3 patients with RA and 3 patients with OA. Protease activity of aminopeptidase was assayed fluorometrically by L-leucine-AMC. Immunohistochemistry, flow cytometry analyses and Western blot were performed using anti-human CD13 antibody.

Results: The mean value of aminopeptidase activity in the synovial fluids from RA patients was significantly higher than that of OA patients. Increased enzymatic activity of aminopeptidase was detected on synovial fibroblasts from RA patients when compared with that from OA patients. Flow cytometry showed that the expression of CD13 on syonovial fibroblasts from RA patients was higher than that from OA patients. Western blotting showed that the lysate protein of synovial fibroblasts from RA patients contained higher amount of CD13/aminopeptidase N significantly correlated with lymphocyte counts in synovial fluid. Synovial fluids from RA patients in which high aminopeptidase activity was detected contained considerable chemotactic activity for lymphocytes and bestatin inhibited chemotactic activity for lymphocytes of synovial fluid from RA patients.

Conclusion: CD13/aminopeptidase N may participate in the mechanism of lymphocyte involvement in RA as a lymphocyte chemoattractant.

W28

CD13/AMINOPEPTIDASE N, A USEFUL MARKER FOR DISEASE ACTIVITY OF COLLAGEN VASCULAR DISEASES

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Objective: To examine whether CD13/aminopeptidase N is a useful marker for disease activity of collagen vascular diseases (CVD).

Rationale: Aminopeptidase N is a membrane-bound metalloprotease, and was shown to be identical to CD13, a 150-kDa cell surface glycoprotein, and was recently shown to have the in vitro chemotactic activity for T lymphocytes.

Methods: Patients with CVD consisted of 29 systemic lupus erythematosus (SLE), 10 systemic sclerosis (SSc), 8 polymyositis (PM), and 6 Sjogren's syndrome (SjS). The activity of aminopeptidase in serum, pleural effusion, bronchoalveolar lavage fluid (BALF) and alveolar macrophages was assayed fluorometrically with L leucine-7-amino-4-methyl-coumarine as a substrate.

Results: Serum aminopeptidase activity from patients with SLE, SSc and PM was significantly higher than that of control subjects. Significantly increased aminopeptidase activity in BALF was detected from patients with SSc, PM and SjS-related interstitial lung diseases. Higher activity and expression of CD13/aminopeptidase N protein were found in alveolar macrophages from patients with SSc, PM and SjS. The level of aminopeptidase activity was significantly higher in pleural effusion from SLE patients than that of transudate effusion.

Conclusion: This study suggests that serum CD13/aminopeptidase N is derived from lesions of CVD and its activity is a useful marker to determine the disease activity of CVD.

W29

UP-REGULATION OF PROSTAGLANDIN E2 RECEPTOR SUBTYPES IN RATS WITH ADJUVANT ARTHRITIS

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Objective : To evaluate the role of PGE receptor(EP) subtypes in the development of inflammatory synovitis.

Rationale:PGE2 regulate the development of synovitis via some different EP subtypes in rats with adjuvant arthritis.

Methods: We used RT-PCR and *in situ hybridization* analyses to measure the EP subtype(EP1,EP2,EP3,EP4)mRNA expression levels of synovial tissues and cultured synovial cells from arthritic joints of rats. RT-PCR and ELISA were to analyze the effects of three selective EP agonists on IL-6 production by cultured rat synovial cells.

Results:EP2 and EP4 mRNA expression in inflamed synovial tissues was upregulated. Of two rat EP3 isoforms, rEP3B mRNA but not rEP3A mRNA was expressed in rat synovial cells. EP2, rEP3B and EP4 mRNA were co-expressed in synovial macrophages and fibroblasts in inflamed tissues. EP2 and EP4 agonists both inhibited IL-1-induced IL-6 production. On the other hand, selectiveEP3 agonist induced IL-6 production by rat synovial cells in a time- and dose-dependent manner.

Conclusion :Our results suggest that PGE2 regulates the functions of synovial macrophages and fibroblasts through EP2 and EP4, which are induced by inflammatory stimuli in rats with adjuvant arthritis.

W30

OSTEOPONTIN IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITS.

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Objectives: Osteopontin (OPN) is a sialic acid-rich, adhesive, extracellular matrix (ECM) protein with Arg-Gly-Asp cell-binding sequence that interacts with several integrins, including $\alpha v\beta 3$. OPN plays important roles in immunity, infection, inflammation and cancer. We sought to investigate the expression of OPN in rheumatoid arthritis (RA) and OA synovial tissue.

Methods: The expression of OPN mRNA and protein in synovia from 10 RA and 15 OA patients was examined by in situ hybridization and immunohistochemistry, flow cytometry, ELISA and RT-PCR. Regulation of OPN expression was investigated by treatment of cultured fibroblasts with IL-1β, IL-10 and TNF-α.

Results: In all RA and OA patients studied, we observed an expression of OPN mRNA and protein. OPN was present in synovial lining and sublining layer. Double labeling revealed that the majority of OPN expressing cells in RA synovial tissue were CD4+ lymphocytes. In contrast, the majority of OPN expressing cells in OA synovial tissue were fibroblasts. Expression of OPN by epithelial, endothelial, smooth muscle cells and fibroblasts was observed in both RA and OA patients. Interestingly, OPN was not detectable in cultured fibroblasts from RA or OA but it could be induced by IL-1β and TNF-α in a dose- and time-dependent manner. Furthermore, the increased OPN expression was specifically inhibited by p38 mitogen-activated protein (MAP) inhibitor SB203580.

Conclusion: These results demonstrated for the first time that OPN was produced by various cells in OA as well as RA patients. The TNF-α and IL-1β induced upregulation of OPN is possibly mediated through the p38 MAP kinase pathway.

W31

INTERLEUKIN-10 (IL-10) AND MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) PROMOTE PHAGOCYTOSIS OF APOPTOTIC NEUTROPHILS.

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Objectives: Phagocyte recognition, uptake and degradation of neutrophils undergoing apoptosis promote the resolution of inflammation. This study assessed the effects of anti-inflammatory cytokine IL-10 compared with pro-inflammatory cytokine MIF on neutrophil clearance mechanism.

Results: Pretreatment of human monocyte-derived macrophages for 24 hours with IL-10 and MIF increased the proportion of macrophage up-taking of apoptotic neutrophils in a concentration-dependent fashion by up to ~ 200%. This effect was rapid and was detectable by 6h. It was also specific in that only macrophages but not neutrophils were affected. IL-10 and MIF also increased the number of apoptotic neutrophils taken up by each macrophage. The enchanced phagocytosis of apoptotic neutrophils by MIF and IL-10 was specifically inhibited by MIF and IL-10 antibodies respectively. Furthermore, MIF enchanced phagocytosis can be specifically inhibited by anti-IL-10 mAb. MIF and IL-10 also expanded phagocytic subpopulations that employed the thrombospondin and $\alpha v\beta 3$ integrin dependent recognition mechanism. Moreover, increased phagocytic capacity by IL-10 is anti-inflammtory since IL-10 did decrease the release of pro-cytokines IL-6, IFN-γ, IL-2 and IL-12 by macrophages. In contrast, MIF enhanced phagocytosis is phlogistic as MIF triggered the macrophage release of large amount of pro-inflammtory cytokines.

Conclusions: These data showed for the first time, that IL-10 and MIF can potentiate macrophage phagocytosis of apoptotic neutrophils. Furthermore, MIF mediated enchancement of uptake of apoptotic neutrophils is probably mediated by IL-10, which is increased by MIF and in turn enhances phagocytosis.

W32

ROLE OF SOLUBLE FORM OF CD44 IN SYNOVIAL FLUID OF PATIENTS WITH RHEUMATOID ARTHRITIS

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[Objective] To investigate the role of soluble form of CD44 (sCD44) in synovial fluid of patients with rheumatoid arthritis (RA).

[Materials and Methods] Synovial fluid were obtained from 26 knees with RA and from 18 knees with osteoarthritis (OA). SCD44, tumor necrosis factor α (TNFα) in synovial fluid were measured using enzyme linked immunosorbent assay (ELISA).

[Results] SCD44 was detected in synovial fluid in 19 out of 26 rheumatoid patients and in 12 of 18 osteoarthritis (OA) patients. Levels of sCD44 in synovial fluid were significantly higher in RA patients than in OA (RA: 135.6 ± 30.3 ng/ml, OA: 46.8 ± 10.5 ng/ml, $p<0.05$). TNFα was detected in synovial fluid in 17 of 26 RA and in 7 of 18 OA patients. Levels of TNFα in synovial fluid was significantly higher in RA than in OA (RA: 1.25 ± 0.20 ng/ml, OA: 0.61 ± 0.19 ng/ml, $p<0.05$).

[Conclusion] These findings suggest that sCD44 may play an important role in RA synovial fluid.

W33

IL-1β-induced upregulation of OPG in human endothelial cells and synovial cells.

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Osteoprotegerin (OPG) is a secreated cytokine that belongs to TNF receptor supergene families. We examined in the present study the possible role of OPG in the pathologic process of rheuamtoid arthritis (RA). OPG protein expression was determined by a specific ELISA in the rheumatoid synovial fluid, and its concentration was positively correlated with that of IL-1β. OPG expression was not determined by either RT-PCR or western blot analysis in unstimulated human umbilical vein endothelial cells (HUVECs), however, the expressions were markedly induced in IL-1β-stimulated HUVECs *in vitro* in a dose- and time-dependent manner. Furthermore, OPG expression in cultured synovial cells, isolated from RA patients, was also significantly augmented by IL-1β. Since recent investigation has revealed that OPG acts as a decoy receptor for TRAIL, our present study may suggest an anti-apoptotic function of OPG expressed in endothelial cells and synovial cells, leading to the synovial hyperplasia found in patients with RA.

W34

EFFECT OF PRO-INFLAMMATORY CYTOKINES (IL-12, IL-15, IL-17 AND IL-18) ON RESPIRATORY BURST OF NEUTROPHILS

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Objective: To evaluate the effect of pro-inflammatory cytokines, important in the pathogenesis of rheumatoid arthritis, on oxidative metabolism of human neutrophils.
Methods: Neutrophils were isolated from heparinized peripheral blood collected from healthy donors and patients with classical rheumatoid arthritis by using Gradisol G density gradient centrifugation. Neutrophils were incubated with cytokines and subsequently stimulated with FMLP, PMA or opsonised zymosan. Luminol-enhanced chemiluminescence was measured using Bio-Orbit 1251 luminometer.
Results: IL-12, IL-15 and IL-17 did not induce chemiluminescence in neutrophils but stimulated neutrophils for an enhanced response to receptor (opsonised zymosan, FMLP) or non-receptor activation. The stimulating effect depends on the functional status of neutrophils. The production of reactive oxygen species by blood neutrophils from RA patients („primed" *in vivo*) and neutrophils from healthy donors „primed" *in vitro* by non-stimulatory doses of FMLP, was greater than that of resting neutrophils. In contrast resting neutrophils responded to IL-18 significantly by generation reactive metabolities.
Conclusion: These findinds suggest that IL-12, Il-15 and IL-17 stimulated oxygen radicals production in „primed" neutrophils, Il-18 in resting neutrophils and therefore these cytokines may play an important role in inflammation.

W35

HISTAMINE IN CHONDROCYTES OF RHEUMATOID ARTHRITIS (RA) CARTILAGE

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Objective: To evaluate the distribution of mast cells and histamine in RA joints.
Rationale: Mast cells are belived to be a main source of histamine in the inflamed joints. Binding of histamine to its specific chondrocyte receptors may contribute to some pathological changes observed in the cartilage of RA joints.

Methods: Tissue samples were dissected from the RA knee joints undergoing orthopedic replacement. Tissue was fixed in 1-ethyl-3(3-dimethylaminopropyl) carbodiimide (ECDI, Sigma) or formaldehyde and frozen or embedded in plastic (Epon). Histamine and mast cells were examined by means of immunohistochemistry using specific antibodies against histamine, tryptase and chymase (Chemicon, USA).

Results: Mast cells were found scattered in the inflamed synovioum and beneath the pannus cells. No mast cells were present outside of these areas and among chondrons of the cartilage.Histamine was localized in the cytoplasm of numerous pannus cells and in extracellular matrix surrounding some of these cells. In the catrilage, histamine was found only in cytoplasm of chondrocytes but no immunoreactivity was localized outside of chondrons.

Conclusions: It is shown for the first time that in RA joints histamine is present not only in mast cells but also in chondrocytes as a result of its production within these cells and/or the uptake from extracellular matrix

W36

INDUCTION OF THE TRANSCRIPTION FACTOR AP-1 IN THE MOUSE AIR POUCH BY LIPOPOLYSACCHARIDE

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【Objective】 To investigate the induction of AP-1 in the mouse air pouch model of inflammation.

【Methods】 20 DBA/1J mice were used. Sterilised air was injected subcutaneously into the back to form a pouch. Intra-air-pouch injection of 10 μ g/ml lipopolysaccharide (LPS) orPBS was performed 7 days after the formation of the pouch. Mice were sacrificed at 2h and 24h after injection of LPS and the pouch tissue was excised. The tissue were stained with HE and evaluated immunohistochemicaly using sheep polyclonal anti-c-fos / c-jun antibodies.(Genosys Biotechnologies,inc)

【Results】 Hyperplasia of lining cells was observed in all mice 2h and 24h after the injection (N=5). Immunohistochemically c-fos and c-jun was observed in the lining and sublining of the air pouch. Percentage of c-fos and c-jun positive lining cells at 2h and 24h were 47.5±5.0 and 64.7±2.7% respectively. Percentage Ratio of c-fos and c-jun positive sublining cells were 40.6±6.0 and 67.0±5.1% respectively.

【Conclusion】 The transcription factor AP-1 in the mouse air pouch was induced by LPS and it increased for 24hours.

W37

Vaccination and Autoimmunity -"Vaccinosis":A Dangerous Liaison?

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The question of a connection between vaccination and autoimmune illness (or phenomena) is surrounded by controversy.

A heated debate is going on regarding the causality between vaccines, such as measles and anti-hepatits B virus (HBV), and multiple sclerosis (MS). Brain antibodies as well as clinical symptoms have been found in patients vaccinated against those diseases.

Other autoimmune illnesses have been associated with vaccinations. Tetanus toxoid, influenza vaccines, polio vaccine, and others, have been related to phenomena ranging from autoantibodies production to full-blown illness (such as rheumatoid arthritis (RA)). Conflicting data exists regarding also the connection between autism and vaccination with measles vaccine.

So far only one controlled study of an experimental animal model has been published, in which the possible causal relation between vaccines and autoimmune findings has been examined: in healthy puppies immunized with a variety of commonly given vaccines, a variety of autoantibodies have been documented but no frank autoimmune illness was recorded. The findings could also represent a polyclonal activation (adjuvant reaction).

The mechanism (or mechanisms) of autoimmune reactions following immunization has not yet been elucidated. One of the possibilities is molecular mimicry; when a structural similarity exists between some viral antigen (or other component of the vaccine) and a self-antigen. This similarity may be the trigger to the autoimmune reaction. Other possible mechanisms are discussed.

Even though the data regarding the relation between vaccination and autoimmune disease is conflicting, it seems that some autoimmune phenomena are clearly related to immunization (e.g. Guillain Barre syndrome).

We will present 4 cases of autoimmune phenomena following BCG vaccination.

The issue of the risk of vaccination remains a philosophical one, since to date the advantages of this policy have not been refuted, while the risk for autoimmune disease has not been irrevocably proved. We discuss the pros and cons of this issue (although the temporal relationship (i.e. always 2-3 months following immunization) is impressive).

References:

1) Shoenfeld Y, Aron-Maor A. Vaccination and autoimmunity -'Vaccinosis': a dangerous liaison? J Autoimmunity. 14 1-10, 2000.

2) Aharon-Maor A, Shoenfeld Y. The good, the bad and the ugly of vaccination. IMAJ 2: 225-227, 2000.

3) Shoenfeld Y, Aharon-Maor A, Sherer Y. Vaccination as an additional player in the mosaic of autoimmunity. Clin Exp Rheumatol 18: 1-4, 2000.

4) Shoenfeld Y. Vaccination and arthritis revisited. http www.rheuma21st.com/archives/apls_shoenfeld..vaccination_ revisited_html . 11.9.2000 pp: 1-6.

W38

TISSUE-FACTOR(TF) EXPRESSION BY ENDOTHELIAL CELLS UPON EXPOSURE TO ANTI-ENDOTHELIAL CELL ANTIBODIES DIRECTED TO DIFFERENT TARGET ANTIGENS.

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TF is the most potent activator of coagulation, we analyzed the potential of anti-endothelial cell antibodies (AECA) mAbs to induce the expression of TF by ECs. All the AECA induced TF release by EC in a dose dependent manner and reached the pick at 8 hrs after exposure to the AECA. Kinetic studies revealed an increase of 12.5-15.3 fold with 6ug/ml mAECA and 24.8-34.3 fold in the presence of 25ug/ml mAECA. Similar increase in TF production was accomplished by AECA $F(ab)_2$ and not by Fc portion of the immunoglobulin. The increase in TF expression by EC was associated with a significant upregulation of adhesion molecule expression (E-selectin, VCAM-I and ICAM-I). Furthermore, augmentation in TF mRNA transcription was detected already 60 min after exposure to the AECA. Our data show the possible pathogenic role of AECA in activation of coagulation cascade via induction of a potent TF, leading to thrombus formation.

W39

RELATIONSHIP BETWEEN RHEUMATOID FACTOR ACTIVITY AND GLYCOSYLATION IN IGG FROM RA PATIENTS.

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Objective: To elucidate the mechanisms of IgG-IgG complex formation and the pathogenicity of these complexes in RA patients.

Rationale: It has been shown that galactose-free oligosaccharides are significantly increased in total serum IgG of RA patients and the high incidence of galactose-free oligosaccharides in serum IgG is related to disease activity and progression to erosive articular changes.

Methods: Three IgG fractions with RF activity (IgGRFs) and an IgG fraction without RF activity (non-RF IgG) were prepared from sera of RA patients using an IgG-Sepharose column, and their oligosaccharide structures were characterized.

Results: All the IgG samples were shown to contain a series of biantennary complex-type oligosaccharides. The incidence of galactose-free oligosaccharides was significantly higher in both IgGRFs and non-RF IgG from RA patients compared with IgG from healthy individuals. The levels of sialylation and galactosylation of all IgGRFs were lower than those of non-RF IgG from RA patients, but the level of sialylation of non-RF IgG was the same as that of IgG from healthy individuals. In addition, the decrease in galactosylation and sialylation of oligosaccharides in IgGRF well correlated with the increase in RF activity.

Conclusion: These data suggest that the lower the level of galactosylation and sialylation of IgGRF oligosaccharides, the higher the RF activity.

W40

CHARACTERIZATION OF RF IMMUNE COMPLEX FORMATION BY SURFACE PLASMON RESONANCE.

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Objective: To biochemically and biophysically characterize the formation of IgGRF-IgG immune complexes.

Rationale: It has been shown that IgGRF contributes to immune complex formation, complement consumption, and chronic tissue damage in the rheumatoid synovium.

Methods: IgGRF was isolated from sera of RA patients using an IgG-Sepharose column, and the interaction of IgGRF with immobilized IgG was analyzed by means of surface plasmon resonance (SPR).

Results: The IgGRF eluted as a single peak corresponding to IgG on gel filtration, hence excluding the possibility of forming self-associating IgGRF complexes in solution. Sensorgrams of interaction of the IgGRF with immobilized IgG by SPR revealed that it clearly bound to IgG at 6°C, but did not bind at 30°C. The degree of interaction decreased inversely with a rise in temperature, suggesting that IgGRF is much more reactive at lower temperatures. The association rate constant (*ka*) of IgGRF was decreased with a rise in temperature, while the dissociation rate constant (*kd*) of IgGRF was greatly reduced at 25°C. This nature was different from those of the other RF (IgM RF and IgA RF).

Conclusion: The kinetic properties of IgGRF-IgG interaction suggest that IgGRF forms immune complexes more rapidly at lower temperature and the resulting immune complexes are more stable at higher temperature.

W41

AUTOANTIBODIES AGAINST CALPASTATIN IN RHEUMATIC AND OTHER DISEASES

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Objective: To evaluate the anti-calpastatin ELISA in patients with rheumatoid arthritis, other collagenosis, and autoimmune liver diseases.

Rationale: Calpastatin is an inhibitor of the protease calpain. The physiological and pathological role of the autoantibodies is not clear.

Methods: We used the anti-calpastatin ELISA (PROGEN Biotechnik GmbH Heidelberg) as described by Schlosser et al. Clin. Chem. 42, 1996, 1250-1256. Values below 30 units were judged as negative.
Patients were grouped into three categories of autoimmune diseases (see below) and a control group of patients with several degenerative diseases (rheumatic diseases excluded).

Results: We observed the following frequencies of the occurence of anti-calpastatin autoantibodies: Rheumatoid arthitis 14 of 235 investigated patients, other collagenosis including lupus erythematodes 3 of 43, autoimmune liver diseases 12 of 161, control groups 0 of 101 patients. The frequency of autoantibodies specific to calpastatin in patients with rheumatic and autoimmune liver diseases was statistically elevated compared to nonrheumatic patients ($p < 0.05$).

Conclusion: The results prove that anti-calpastatin antibodies are associated with rheumatic and autoimmune liver diseases. Furthermore, they suggest, that a relation exist to the disease activity and severity.

W42

ANTI-APOLIPOPROTEIN A-I AUTOANTIBODY: CHARACTERIZATION OF MONOCLONAL AUTOANTIBODIES ESTABLISHED FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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Objective: To investigate reactivity of the autoantibody to apoA-I, we have established a series of monoclonal anti-apoA-I antibodies (MAAI) from two patients with systemic lupus erythemotosus (SLE). ***Methods:*** Six MAAI reactive with human apoA-I , originating in peripheral blood B cells from patients with SLE, in both ELISA and immunoblotting analysis were established. The reactivities of MAAI with HDL, single-stranded DNA (ssDNA) and double-stranded DNA (dsDNA), phospholipids such as cardiolipin (CL), and coagulation factors were examined by ELISA. ***Results:*** Although all of MAAI bound effectively to apoA-I after the protein had been denatured and transferred to the filter membrane (in immunoblotting analyses), they bound less effectively to apoA-I present in HDL. Both oxidation of HDL in the presence of Mn^{2+} and an association of apoA-I with autoxidized trilinolein strongly enhanced the binding of MAAI to apoA-I. MAAI showed a functional heterogeneity in their cross-reactivity with self components: some of MAAI were shown to cross-react with anionic substances such as CL and ssDNA, and one MAAI was shown to bind effectively to thrombin. ***Conclusion:*** In this study we identified a novel family of anti-apoAI antibodies which show a preferential binding to apoA-I in oxidatively modified HDL. These MAAI are comprised of antibodies with heterogeneous cross-reactivities to various self components such as anionic phospholipids, ssDNA, and thrombin.

W43

WITHDRAWN

W44

IDENTIFICATION AND CHARACTERIZATION OF TWO AUTOANTIBODY-SYSTEMS TARGETTING THE ENDOCYTIC COMPARTMENT OF THE CELL.

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Objective: To characterize human autoantibody systems associated with the cytoplasmic discrete speckled (CDS) pattern.

Methods: Indirect immunofluoresce (IIF), immunoblot (IB), immunoelectron microscopy and mass spectrometry were used to analyze 19 sera displaying IIF CDS pattern.

Results: Two distinct CDS patterns were identified: CDS-I was characterized by 3-20 discrete bright speckles and CDS-II depicted over 30 speckles spread throughout the cytoplasm. CDS-II speckles were slightly smaller and less bright than those in CDS-I pattern. There were 14 CDS-I sera and 5 CDS-II sera. Clinical data were obtained for 5 CDS-I patients (3 SLE; 1 SLE+ Hashimoto´s tiroiditis; 1 osteoporosis + myalgia) and 2 CDS-II patients (systemic vasculitis; kidney lithiasis). CDS-II sera recognized a double band with a relative mobility of 170-185 kDa. Affinity-purified antibodies from the 170-185 kDa IB region reproduced both the IIF pattern and the IB reactivity of the original serum. No consistent IB reactivity could be demonstrated in CDS-I sera. Affinity-purified anti-CDS-II antibodies colocalized with monoclonal antibodies against Lysosomal Associated Membrane Protein 2 (LAMP-2) and Early Endosomal Antigen 1 (EEA-1) in HEp-2 cells as shown by confocal microscopy. In contrast, anti-CDS-I antibodies depicted poor colocalization with LAMP-2 and EEA-1. Immunoelectron microscopy of HEp-2 cells labeled with anti-CDS-I antibodies and affinity-purified anti-CDS-II antibodies followed by protein A-gold showed that both patterns decorated multivesicular bodies in the cytoplasm. Lipid extraction with organic solvents did not affect CDS-II characteristic pattern but resulted in severe impairment of CDS-I reactivity. Mass spectrometry findings showed that CDI-I sera reacted strongly with the phospholipid phosphatidilethanolamine.

Conclusion: CDS-I and CDS-II patterns seem to correspond to different sets of the cellular vesicular systems and are distinct in biochemical nature. Our results suggest that CDS-I pattern is associated with lipid moieties and that the target antigen of anti-CDS-II antibodies seems to be a protein present in the endosome-lysosome system.

W45

LONGITUDINAL OSCILLATION OF AUTOANTIBODIES (AA) TO EXTRACTABLE NUCLEAR ANTIGENS (ENA) IN SLE PATIENTS.

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Objective: To determine the frequency of longitudinal oscillation of anti- native DNA and anti-ENA AA in SLE patients.

Material and Methods: A hundred and seventeen SLE patients were retrospectively selected from the registration book of the Immuno-Rheumatology Laboratory at the Federal University of São Paulo. All patients had annual AA profile test (anti-native DNA, anti-Sm, anti-U1-RNP, anti-SS-A/Ro, and anti-SS-B/La) for at least five consecutive years (5 to 12, mean 7 years), between 1987 and 1999. Anti-DNA AA were determined by immunofluorescence in Crithidia luciliae and anti-ENA AA by double immunodiffusion. The average number of tests per patient was 17 (5 to 76). At least two different results (positive or negative) in relation to the majority of tests were required in order to define the presence of oscillation of AA. An AA was considered positive in one patient if detected at least in two occasions.

Results: Table 1 shows the frequency of each AA as well as rate of oscillation. Depending upon the AA considered oscillation ranged from 52 to 93%. Anti-native DNA, anti-Sm, and anti-SS-B/La AA depicted higher oscillation rates. Anti-U1-RNP and anti-SS-A/Ro oscillated in half of the positive patients.

Table 1. Oscillation frequency in autoantibodies of SLE patients.

	AUTOANTIBODIES				
	a-nDNA	a-Sm	a-U1-RNP	a-SS-A/Ro	a-SS-B/La
NEGATIVE	52%	76%	61%	62%	96%
POSITIVE	48%	24%	39%	38%	04%
Oscillation present	91%	93%	52%	52%	80%
Oscillation absent	09%	07%	48%	48%	20%

Conclusion: We conclude that AA oscillation is a common feature in long-term follow-up of SLE, not only for anti-DNA but also for anti-ENA AA. Further studies are warranted in order to determinate possible clinical associations with such AA oscillations

W46

DETECTION OF ANTI-U1 RNP AUTOANTIBODIES BY ELISA USING RECOMBINANT U1 RNP AND U1 RNA COMPLEX AS AN ANTIGEN.

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Objective: Recombinant U1 RNP proteins (70 kDa, A and C protein) have been used as an antigen for our previous Anti-RNP antibody ELISA kit. This previous kit is less sensitive than DID (double immuno diffusion) because of lack of U1 RNA molecule as an antigen. In order to improve sensitivity of the ELISA, U1 RNA-RNP complex was used as an antigen for our new ELSIA.

Methods: Recombinant U1 RNP-70kDa, A, and C proteins were mixed with in vitro transcribed U1 RNA to construct U1 snRNP molecule. This reconstituted antigen was used as a substrate for improved ELISA. Reconstituted U1 snRNP antigen was evaluated by immunoprecipitation assay (IPP). Among DID positive sera, false negative sera (DID positive and our old version of the ELISA negative) were measured by improved ELISA.

Results: By IPP analysis, it was confirmed that recombinant U1 RNP-70k and U1 RNP-A proteins were directly assembled with U1 RNA, whereas U1 RNP-C was not. Epitopes of autoantibodies reactive to U1 RNA-RNP complex were mainly induced by a binding of U1 RNP-70kDa to U1 RNA. The sera reacted to U1 RNA itself were merely observed. The increased reactivity of anti-U1 RNP autoantibodies in the false negative sera depended on a quantity of added U1 RNA to recombinant RNP in ELISA and our improved ELISA was able to detect all false negative sera that measured. The sensitivity against DID positive sera increased from 92% to 100 % by using U1 RNA-RNP complex as an antigen. The correlation coefficients was 0.895 and p value was < 0.001 between current and improved ELISA.

Conclusion: Some of anti-U1 RNP autoantibodies recognized U1 RNA-RNP complex as well as RNP proteins and naked U1 RNA. The results of U1 RNA+RNP ELISA system was well correlated with DID. Recombinant RNP proteins and U1 RNA complex enabled our ELSIA to detect anti-U1 RNP antibodies specifically with high sensitivity.

W47

NAIVE B CELLS IN SLE PREFERENTIALLY UTILIZE DIVERSITY GENE SEGMENTS IN READING FRAMES ENCODING HYDROPHOBIC AMINO ACIDS

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Objektive: We examined the CDR3 composition in individually sorted peripheral blood naive B-cells, memory B-cells and plasma cells obtained from an SLE patient.

Rationale: It has been suggested that in SLE the main antigen binding site of an antibody, i.e. the complementarity determining region (CDR) 3, is different from that found in normals.

Methods: Peripheral blood B-lymphocytes were individually sorted according to their surface expression of CD 27 and IgD. A total of 12 (CD 27-/IgD+) naive B cells, 13 (CD 27+/IgD+) memory B cells and 12 (CD 27+/IgD-) plasma cells were obtained. Amplified VH gene segments were directly sequenced and analyzed using the V BASE Sequence Directory and GeneWorks software (Intelligenics, Inc.) to identify the respective diversity (D) segment.

Results: The majority of naive B-cells are using D segments encoding hydrophobic amino acids (aa; 6/9). In contrast, memory B-cells and plasma cells hardly utilized D segments encoding hydrophobic aa (2/7 and 0/5 , respectively). Furthermore, there was a significant increase in D segments encoding hydrophilic aa in the latter B-cell subsets compared to the naive B-cell population (5/7 and 4/5 vs 1/9, respectively; $p<0.01$).

Conclusion: Our data suggest that in SLE the majority of B-cells generated in the bone marrow utilize D segments encoding hydrophobic aa either because of selection or recombinational bias. Surprisingly these cells seem to be negatively selected in the periphery, since the majority of memory B-cells and plasma cells express D segments encoding hydrophilic aa.

W48

THE PHYTOESTROGEN COUMESTROL DELAYS THE ONSET OF AUTOANTIBODIES IN MURINE LUPUS.

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Environmental agents and xenobiotics are known to induce autoimmune features that include the expression of autoantibodies. Reproductive hormones modulate autoimmune diseases, particularly systemic lupus erythematosus (SLE). Objective: To determine whether the phytoestrogen coumestrol can influence disease expression in the NZB/W murine model of SLE.

Methods: Seventy female NZB/W F1 mice, 5-6 weeks of age were fed a soy-free, casein-based diet with or without coumestrol (0.01%). Groups of ten animals were sacrificed at pre-determined intervals. Anti-nuclear antibodies (ANA) were detected by indirect immunofluorescence on HEp-2 cells. *Crithidia luciliae* substrate was to test for anti-dsDNA.

Results: None of the ten baseline mice (5-6 weeks) had a positive ANA; 20% (2/10) were positive for anti-dsDNA. At 16 weeks, 10% of the treatment (n=10) and 10% of the control (n=10) groups had positive ANAs; 10% of the treatment group and none of the controls had antibodies to dsDNA. By 24 weeks, 30% of the treatment group (n=10) vs. 60% of the controls (n=10) had ANA (p= 0.37); none of the treatment group had anti-dsDNA, but 40% of the controls did (p=0.07). By 36 weeks, this difference was no longer apparent; ANAs were positive in 89% and 100% of the treatment (n=9) and control (n=10) groups respectively; anti-dsDNA was positive in 56% and 50% respectively. No significant differences in proteinuria or survival were noted. Analyses of other outcomes including renal histology, proteinuria, and cytokine profiles are currently underway.

Conclusion: Coumestrol seems to have a transient effect on autoantibody expression in NZB/W mice.

W49

ROFECOXIB INHIBITS IL-1β STIMULATED NITRIC OXIDE AND STROMELYSIN PRODUCTION BY HUMAN SYNOVIAL TISSUE AND REVERSES IL-1β INHIBITION OF OSTEOARTRITIC ARTICULAR CARTILAGE SYNTHESIS

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Objective : To evaluate rofecoxib effects on nitric oxide (NO) and stromelysin (MMP-3) production by IL-1β stimulated human synovial tissue and synthesis of osteoarthritic cartilage in culture
Rationale : Rofecoxib, a specific COX-2 inhibitor is now widely used in the management of symptomatic osteoarthritic patients. Additional rofecoxib effects on function of human synovial tissue and articular cartilage may predict its potential value or side effects for articular structures, beyond COX-2 inhibition.
Methods: Synovial tissue and cartilage were obtained in the operation theater from patients undergoing total knee replacement for osteoarthritis put into small pieces and cultured in the presence or absence of IL-1β and rofecoxib. NO in culture media was measured with the Griess reagent, MMP-3 by ELISA and cartilage synthesis by ^{35}S incorporation.
Results: Rofecoxib (0.1μg/ml, 0.3μg/ml, 1.3μg/ml) ibhibited IL-1β (1ng/ml) stimulated NO production by synovial tissue cultures in a dose dependent manner reaching statistical significance ($P<0.05$) at 0.1 μg/ml. Rofecoxib also inhibited IL-1β stimulated MMP-3 production by synovial tissue cultures in a dose dependent manner reaching statistical significance ($P<0.05$) at 0.1 μg/ml and reversed IL-1β inhibition of cartilage synthesis ($P<0.05$ at rofecoxib 0.4μg/ml).
Conclusions : Rofecoxib may have a chondroprotective effect by inhibiting NO and MMP-3 production by IL-1 stimulated synovial tissue and by reversing IL-1 inhibition of articular cartilage synthesis.

W50

TGF-ß-INDUCED MMP-13 PRODUCTION IN HUMAN OSTEOARTHRITIC CHONDROCYTES IS TRIGGERED BY SMAD PROTEINS: COOPERATION BETWEEN AP-1 AND PEA-3 BINDING SITES

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Metalloprotease (MMP) genes are expressed in cartilage, and their transcription is induced by various factors. We reported that TGF-ß treatment of normal human cartilage increased the expression of MMP-13 by chondrocytes, and mimicked the *in situ* distribution of this enzyme in OA cartilage. We examined the signaling pathways of TGF-ß-induced MMP-13 production in human OA chondrocytes, as well as the transcription factors and their binding sites involved in the transcriptional control of this gene.
The primary target of TGF-ß-induced MMP-13 in OA chondrocytes was the Smad2 protein. Contrasting with the Smad2, the untreated OA chondrocytes had already detectable levels of the phosphorylated forms of p38 and p44/42 MAPK. Electromobility shift revealed that TGF-ß-treated OA chondrocyte proteins bound only to the AP-1 and PEA-3. Supershifts with the AP-1 oligonucleotide showed the presence of the Jun and Fos proteins in the untreated and TGF-ß-treated OA chondrocytes, whereas Smad proteins (Smad2, 3, and 4) were present in the AP-1-binding proteins only from the TGF-ß-treated chondrocytes. The AP-1 expression vector mutation decreased both the basal (95%) and TGF-ß-induced (99%) MMP-13 production, whereas the PEA-3 mutation decreased the basal (15%) but more significantly (50%) the TGF-ß-induced transcription.
In conclusion, Smad proteins are the main cytoplasmic signaling pathways in TGF-ß-stimulated MMP-13 in OA chondrocytes. The AP-1 site appears critical, but also requires PEA-3 sites for optimal response.

W51

HYALURONIC ACID INHIBITS CARTILAGE DEGRADATION IN RHEUMATOID ARTHRITIS

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Objective: We reported that intraarticular injection of huarulonic acid (HA) provided symptomatic relief in rheumatoid arthritis(RA). However, there is limited information on the effects that this treatment may have on articular cartilage. The inhibitory effect of hyaluronic acid on cartilage degradation was examined.

Methods: Synovial membrane and articular cartilage samples were collected from patients with RA at the time of joint replacement. Lymphocytes and fibroblasts were isolated from the synovium, and the articular cartilage was prepared as discs. Synovial lymphocytes or fibloblasts were incubated with cartilage discs, and the amount of glycosaminoglycan(GAG) in the supernatant and the cartilage discs were determined. Then, the inhibitory effect of HA with molecular wight 900 or 1800 kilodaltons on GAG release from cartilage discs was examined.

Results: Synovial lymphocytes and fibroblasts-mediated GAG release from cartilage discs was higher than spontaneous GAG release. HA showed no significant effect on spontaneous GAG release. However, synovial lymphocyte or fibloblast-mediated GAG release was suppressed by HA. The inhibitory effect of 1800 kilodalton HA was more dominant than 900 kilodalton HA.

Conclusion .: These findings suggest that intraarticular injection of HA is beneficial therapeutic use for RA by suppressive effect on lymphocyte or fibloblast-mediated cartilage degradation.

W52

ASSOCIATION OF GENOTYPES AFFECTING THE EXPRESSION OF IL-1β OR IL-1RA WITH OSTEOARTHRITIS

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Objective: We have previously shown that the majority of cytokines and growth factors known to be involved in cartilage metabolism are synthesized by the chondrocytes themselves. They are up-regulated in osteoarthritic cartilage resulting in two opposite phenotypes called TNFαHi and TNFαLo characterized by an elevated number of TNFα positive and IL-1β positive chondrocytes, respectively. To establish a hierarchy among cytokines and growth factors expressed in articular chondrocytes, we here investigate cytokine genes for known polymorphisms which may contribute to the deregulated expression.
Methods: Performing PCR-techniques either in a Thermal Cycler using standard methods or in a Light Cycler, we analyzed the frequencies of the TNFα (-308), IL-1ra (intron 2), IL-1β (exon 5) and IL-6 (-174) polymorphisms in 61 OA-patients and 254 randomly chosen controls.
Results: For the TNFαLo–phenotype we found a statistically significant association with the less frequent allele of IL-1β which carrys a single base pair substitution in exon 5 and may contribute to the characteristic increase in IL-1β positive chondrocytes. In contrast, the TNFαHi –phenotype was significantly associated with the less frequent allele of IL-1ra which carries two 86bp repeats in the 2nd intron and is assumed to lead to an elevated expression of the antagonist.
Conclusion: Our results point at an association of the IL-1β polymorphism with the TNFαHi- and the IL-1ra polymorphism with the TNFαLo-phenotypes found in OA. Both associations suggest that IL-1β may be more important than TNFα for the regulation of cytokine and growth factor expression in articular chondrocytes.

W53

JOINT COLLAGEN DESTRUCTION VERIFIED BY PYRIDINIUM CROSS-LINK MEASUREMENT IN SYNOVIAL TISSUE AND URINE IS STRONGLY RELATED TO DISEASE-ACTIVITY IN RHEUMATOID ARTHRITIS.

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Objective: To know more about the source of urinary collagen crosslinks Pyr (pyridinoline) and Dpyr (deoxypyridinoline) in inflammatory joint destruction we quantified these in synovial tissue(ST), -fluid(SF), serum(S) and urine(U) of RA and OA.

Rationale: A few reports estimate the increased urinary excretion of Pyr (collagen I and II from bone and cartilage) and Dpyr (collagen I, bone and dentin) as markers of collagen destruction. But the exact origin of the crosslinks remains unclear because disease-related osteoporosis or steroid treatment may contribute to their excretion.

Methods: Simultaneously collection of ST and SF of knee joint, S and U from 12 aRA patients (active RA; CrP>=28mg/l), 10 iRA (inactive RA; CrP<28mg/dl) and 21 OA. Pyr and Dpyr determination: simultaneous gradient ion-paired reversed-phase HPLC. Histomorphological activity was expressed as low (grade 1) and high (grade 2) actual and basic activity (AA; BA) and divided into the synovialitis-types I (non-destructive course with low disease progression) and II (aggressive course of disease with rapid bone destruction).

Results: In aRA vs. iRA/OA we found significantly elevated levels for Pyr and Pyr/Dpyr ratio in ST (Pyr: 1.32 vs. 0.39/0.84 mol/mol Collagen; Pyr/Dpyr: 33.0 vs. 13.0/12.0) and U (Pyr: 78.3 vs. 54.5/55.0 nmol/mol Creatinine; Pyr/Dpyr 4.7 vs. 3.5/3.4) and correlation of Pyr/Dpyr in ST and urine ($p<0.05$). Pyr/Dpyr was elevated in ST of RA with high actual activity (AA2), n=11, 24.2(SD7.6) vs. AA1 n=9, 17.5(3.7); $p<0.025$. Significant increased Pyr/Dpyr ratio was also found for higher basic activity (BA2>BA1) and synovialitis type (II>I). A significant correlation between Pyr/Dpyr in ST and both ESR and CrP ($p<0.05$) was observed.

Conclusion: Pyr and Dpyr levels in ST and U estimate increased destruction of collagen II vs. collagen I, indicating ST as important source of the urinary excreted Pyr. Because of correlation between elevated Pyr/Dpyr ratio and serological and histomorphological inflammation parameters we conclude, that high activity of synovialitis is related to an increased collagen II destruction of ST and cartilage compared to those of bone-related collagen I. Increased Pyr/Dpyr ratio in type II-synovialtis (with rapid joint destruction) will be discussed as prognostic marker in RA.

W54

THE FEATURES OF CURRENT RHEUMATOID ARTHRITIS DURING ONSET DEPENDING FROM SEX

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Objective: the comparison of the clinical signs and of hormonal status parameters in men and women with rheumatoid arthritis during a onset.

Rationality: it is proved, that the clinic of rheumatoid arthritis and the parameters of hormonal status essentially differ in the men in comparison with the women.

Methods: the research consited of 15 men and 20 women with the duration of disease till 1 year, we investigated articular sindrom, extraarticular injuries, the presence of rheumatoid factor and some parameters of rheumatic status (thyreoid hormons, prolactin, cortizol).

Results: we noted the following differences in articular sindrom: in men the illness more often affected the humeral joints (men=26,2%, women=11,2%) and ankle joints (men=53,4%, women=23,4%) and more often affected the cervical spine (men=26,2%, women=11,2%). At the study of extraarticular injuries we noted, in men less visceritis (men=7,2%, women=11,0%), anemia (men=14,4%, women=45,1%) injury of kidneys (men=8,9%, women=25,2%). The seronegative variant often more were met in the men (men=41,8%, women=27,3%).
The research of hormonal status, found the hypothirosis more often: in the women (men=11,3%, women=24,6%), hipoprolactinemia was marked only in 7% of the women the raised level of the cortizol equally often is met in the men and in the women (men=4,2%, women=4,15%).

Conclusion: the received data shows essential differences of rheumatoid arthritis in the men in comparison with the women as in clinical, paraclinical signs, and in hormonal status, that confirms the role of endocryne system in occurrence and development of the rheumatoid arthritis.

W55

WITHDRAWN

W56

WITHDRAWN

W57

INTERLEUKIN-2 LEVELS ARE ELEVATED IN THE BONE MARROW SERUM OF PATIENTS WITH MUTILANS-TYPE RHEUMATOID ARTHRITIS

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Objective:To investigate the pathogenesis of mutilans-type rheumatoid arthritis (RA), cytokine levels in the bone marrow serum of patients with RA were measured.

Patients and Methods: We studied 35 patients with non-mutilans RA, 19 with mutilans RA, and 20 patients with osteoarthritis (OA) undergoing joint surgery. Iliac bone marrow and blood were sampled from all 74 patients and cytokine levels were measured. The levels of 5 cytokines (IL-1b, IL-2, IL-3, IL-6, and GM-CSF) were measured by ELISA.

Results: Levels of IL-2, IL-6, and GM-CSF in bone marrow serum were significantly higher in all RA patients than in those with OA. Mean (±SD) IL-2 levels were significantly higher in patients with mutilans-type RA (309.8±686.3 pg/mL) than in patients with other types of RA (66.5±173.1 pg/mL; P<0.01). IL-2 was detected significantly more often in patients with mutilans-type RA than in patients with other types of RA (P<0.01). Inflammatory factors were higher in all RA groups than in OA patients. However, the hematologic and immunologic variables were not different between mutilans RA and other types of RA. No correlations were observed between IL-1b, IL-2, IL-3, IL-6, and GM-CSF levels and these laboratory variables.

Conclusion: In patients with mutilans-type RA, IL-2 levels in the bone marrow serum are significantly higher than in patients with other types of RA and with OA.

W58

ANALYSIS OF PROSTAGLANDIN E RECEPTOR EP4 SUBTYPE mRNA EXPRESSION IN SYNOVIAL TISSUES OF PATIENTS WITH RHEUMATOID ARTHRITIS.

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Objective: PGE2 appears to play an important role in the pathogenesis of rheumatoid arthritis (RA). PGE2 is recognized cellular effects specifically by interacting with PGE receptor (EP) subtypes designated four subtypes EP1, EP2, EP3 and EP4. We investigated the distribution of specific EP subtypes mRNA in synovial tissues isolated from RA patients.

Methods: Twenty-seven patients with RA, 6 patients with osteoarthritis(OA) were included. Synovial membranes in this study were obtained after informed concent was obtained during the process of total knee replacement or endoscopic synovectomy. Detection of EPs mRNA performed using reverse transcriptase chain reaction (RT-PCR) and In situ hybridization(ISH).

Results: EP4 was detected in synovial tissues by RT-PCR. ISH in synovial tissues revealed signals to multilayered synovial lining cells. EP4 was also highly expressed in the macrophages, fibroblast, and endothelial cells. EP4 expression was parallel with the pathological synovial tissue inflammatory activity index.

Conclusion: This study will facilitate the better understanding of the regulatory mechanisms for EP4 subtype gene expression in the inflammatory arthritis such as RA.

W59

CHARACTERIZATION OF FIBRINOLYTIC PATTERN OF SYNOVIOCYTES FROM RHEUMATOID ARTHRITIS (RA)

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Background: in RA, the fibrinolytic cascade is involved in the generation of cartilage damage and in the genesis and maintenance of synovitis.

Aim: to evaluate the fibrinolytic pattern in synoviocytes from RA patients and healthy donors (H) in order to establish the role of each component of the fibrinolytic cascade in the genesis and progression of the RA synovitis.

Materials and methods: the production of plasminogen activators and their inhibitors was studied in vitro on synoviocytes (SY) obtained from 4 H and 4 RA subjects undergoing joint surgery. SY monolayers were used within the 7th passage in culture. Cells were seeded on to 6 multiwell plates (20.000 cells/plate) with RPMI 1640 supplemented with 10% fetal calf serum and incubated for 48 h. Then, the serum concentration was reduced to 0.1% for additional 48 h. At the end of incubation, the supernatants were removed, centrifugated and stocked at -20C° until the determination of urokinase-Plasminogen Activator (u-PA) and Plasminogen Activator Inhibitor-1 (PAI-1). Cells were detached, counted and lysed. The lysates were stocked at -20°C until the determination of urokinase Plasminogen Activator Receptor (u-PAR). The levels of u-PA, u-PAR and PAI-1 were assayed by ELISA.

Results: SY from RA, in respect to SY from H, showed significantly higher levels of PAI-1 [(6.34 µg/million cells ± 1.13 standard deviation (SD) vs 2.9 µg/million cells ± 0.7 SD, p= 0.01], minor levels of u-PA (2.58 ng/million cells ± 1.4 SD vs 10.94 ng/million cells ± 2.1 SD, p=0.01), and more u-PAR on their surface (28.5 ng/million cells ± 4.8 SD vs 13 ng/million cells ± 3.0 SD, p<0.05).

Conclusions: These data show that RA SY present the typical fibrinolytic pattern of the invasive cells. Fibrinolytic system provide an extracellular proteolysis required for the invasion of articular tissues from SY and for the first steps of synovitis. The components of this system may be a future target for new RA therapies.

W60

ALTERATION OF SUBSETS OF T-LYMPHOCYTES IN RHEUMATOID ARTHRITIS

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The role of T-lymphocytes (TL) in the pathogenesis of rheumatoid arthritis (RA) has already been demonstrated, but the site of T-cell activation is still unknown. The differentiation and maturation of TL takes place either on the peripheral blood (PB) or in the synovial fluid (SF). Using monoclonal antibodies labelled with fluorochromes and the flow-cytometry technique we tried to assess the most important alterations of lymphocyte subtypes both in PB and in SF.

The study involved 29 patients: 19 with RA in stage II, 8 with ankylosing spondylitis and 2 with knee osteoarthritis (used as controls). A higher per cent of CD14+, CD19+ and CD3+ was isolated from the SF than from the PB. According to the data in literature, a higher rate CD4/CD8 was found in SF than in PB, and many of the CD3+ and CD8+ cells showed a cytotoxic phenotype. The TL showed a "memory" or activated phenotype as defined by the CD45 RO expression and a high HLA-DR class II. Following stimulation, naive TL cells lose CD45 RA and gain CD45 RO expression. To locate the site of this change in phenotype, the per cent of TL positivity for CD45 RA, CD45 RO, HLA-DR and CD3 in the PB and SF in patients with chronic arthritis was compared. The expression of CD45 isoforms on CD3+ cells could not indicate the site of activation, but in the SI double positive CD45 RA, CD45 RO and HLA-DR cells were identified.

The TL are in a most activated state both in the SF and in the Pb of RA patients, and the positivity for HLA-DR is associated with a phenotype of "memory cells.

W61

DIFFERENCES IN DISEASE EXPRESSION IN ADJUVANT ARTHRITIS OF LEWIS RATS INDUCED BY MYCOBACTERIA OR LIPOIDAL AMINE

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Marked polyarthritis is induced in male Lewis rats by injection of either heat-killed *Mycobacterium tuberculosis* (H37Ra, Difco; 10mg/ml) in mineral oil (AdA) or lipoidal amine (50 mg/ml) in complete Freund's adjuvant (LA/CFA). For both models, paw swelling and body weight loss occur in all rats by 10 to 12 days after immunization. Interestingly, however, the present study demonstrates that the morphologic and densitometric changes of each condition are distinguishable. We induced AdA or LA/CFA in male Lewis rats (180g) and evaluated both clinical (body and spleen weight, volume of the tibiotarsal [hock] joints) and morphologic changes (bone mineral density [BMD] by DEXA; histopathologic lesions in the hock and femorotibial [knee] joints). Readings were obtained at the day of onset (as determined by initial paw swelling) as well as 5 (see Table), 10 and 25 days after onset.

Endpoint	Control	AdA**	LA/CFA**
Paw Volume ± SD [ml]	1.80 ± 0.08	3.05 ± 0.36	3.08 ± 0.36
Body Weight ± SD [gram]	301 ± 15g	247 ± 21g	242 ± 11g
Spleen Weight (Onset + 10)*	100%	217%	203%
Hock BMD *	100%	87.5%	99.9%
Hock Inflammation Score ± SD	0	3.2 ± 0.4	2.5 ± 1.4
Hock Erosion Score ± SD	0	3.0 ± 1.9	2.2 ± 1.5
Hock Cartilage Score ± SD	0	3.2 ± 0.8	2.2 ± 1.8
Knee BMD *	100%	72.9%	80.6%
Knee Inflammation Score ± SD	0	3.3 ± 0.5	2.2 ± 0.4***
Knee Erosion Score ± SD	0	3.2 ± 1.2	1.7 ± 1.0***

* Values given represent the percent change relative to the control group
** Bolded values are statistically equivalent, and unbolded values different, from controls
*** Significantly different from AdA, $p < 0.05$ (Newman Keuls *post hoc* test)

Inflammatory and skeletal changes for AdA and LA/CFA were similar by clinical and histopathologic measures 10 days after onset, while inflammation receded by Onset + 25 days in LA/CFA more than it did in AdA. These data indicate that bone densitometry and morphology can distinguish these two models of adjuvant arthritis despite their similar clinical presentations.

W62

ANTI-INFLAMMATORY AND BONE-PRESERVING EFFECTS OF IL-1Ra AND PEG sTNF-RI ARE WELL CORRELATED IN LEWIS RATS WITH ADJUVANT ARTHRITIS.

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Marked inflammation and joint destruction affecting many joints are the hallmarks of mycobacterial-induced adjuvant arthritis (AdA) in Lewis rats. Our group has shown that skeletal dissolution may be reduced – even in the presence of severe inflammation – by preventing osteoclast production (*Nature* 402: 304, 1999), and that inhibiting inflammation is an effective means of ameliorating bone loss (*Cell. Mol. Life Sci.* 57:1457, 2000). In this study, we examined whether the bone-sparing effects of the cytokine inhibitors interleukin-1 receptor antagonist (IL-1ra) and pegylated soluble tumor necrosis factor receptor type I (PEG sTNF-RI) act by modifying osteoclast numbers in arthritic joints. Male Lewis rats with AdA (n = 6/group) were treated with IL-1ra or PEG sTNF-RI, given alone or in combinations, s.c. for 7 days beginning at the onset of paw swelling (day 9 after adjuvant inoculation) at the following doses: IL-1ra, 0.2, 1.0 or 5.0 mg/kg/hr (by infusion); PEG sTNF-RI, 0.25, 1.0 or 4.0 mg/kg/day (by bolus). Assessments were made of inflammation (hind paw volume, days 9 to 16; histopathology, day 16), skeletal integrity (bone mineral density [BMD] by DEXA, histopathology, both on day 16), and osteoclast numbers (a histopathologic score based on detection of multinucleated cells labeled immunohistochemically with the osteoclast marker cathepsin K). Measures of paw volume and loss of BMD were quantitative, while the histopathology scores were acquired in a blinded fashion using semi-quantitative grading scales. Dose-dependent reductions in inflammation, joint destruction, and osteoclast scores were noted for IL-1ra and PEG sTNF-RI, whether given alone or together. Correlations between inhibition of inflammation and reduction of loss of BMD (r^2 = 0.6292), bone erosion (r^2 = 0.90), and osteoclast numbers (r^2 = 0.85) were independent of whether IL-1ra, PEG sTNF-RI, or both had been used as the therapeutic agent. These data indicate that the anti-inflammatory proteins IL-1ra and PEG sTNF-RI protect skeletal integrity in adjuvant arthritis by regulating osteoclast numbers.

W63

KINETICS OF BONE PROTECTION BY THERAPY WITH RECOMBINANT OSTEOPROTEGERIN (OPG) IN LEWIS RATS WITH ADJUVANT ARTHRITIS.

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Our group has shown that daily therapy with recombinant human osteoprotegerin (rhOPG) starting at the onset of clinical arthritis significantly reduces the severity of joint destruction in male Lewis rats with mycobacteria-induced adjuvant arthritis (AdA) (*Nature* 402: 304, 1999). The current study was performed to assess the kinetics associated with rhOPG-mediated bone preservation. AdA was induced in 8-week-old rats (n = 6/group) on Day 0; arthritis (indicated by hind paw swelling) developed on Day 9. Arthritic animals received 4 mg rhOPG/kg (daily s.c. bolus) by one of five schedules: no rhOPG (Group 1, control for AdA induction); daily rHOPG, Days 9 to 15 (Group 2, control for rhOPG efficacy); early intervention, Days 9 to 11 (Group 3); late intervention, Days 13 to 15 (Group 4); or single-dose intervention, Day 9 (Group 5). Rats were necropsied on Day 16 to evaluate bone mineral density (BMD, assessed by dual X-ray absorptiometry; DEXA), as well as erosion and osteoclast scores (acquired by microscopic evaluation using tiered, semi-quantitative grading scales) in the tibiotarsal (ankle) region. Vehicle-treated arthritic rats (Group 1) lost BMD and had myriad erosions and osteoclasts. A 7-day course of rhOPG (Group 2) preserved BMD and significantly decreased both erosions (by 73%) and osteoclastogenesis (by 80%). Early initiation of rhOPG (Group 3) preserved BMD and inhibited erosions (by 73%), while delayed rhOPG therapy (Group 4) protected BMD but was significantly poorer at lowering erosions (45%). A single rhOPG dose on Day 9 (Group 5) prevented exacerbation of the erosion score until Day 13. The degree to which rhOPG prevented bone damage was correlated to osteoclast numbers (r^2 = 0.91). Our data show that therapy with rhOPG should be initiated early during the course of clinical disease to achieve the greatest benefit with respect to protecting skeletal integrity in arthritic joints.

W64

INHIBITORY EFFECT OF ENZYME THERAPY AND COMBINATION THERAPY WITH CYCLOSPORIN A ON COLLAGEN-INDUCED ARTHRITIS

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Objective: There is increasing interest in the use of combination therapy for rheumatoid arthritis and in the possibility of combining the conventional drug approach with newer antirheumatic therapy. This study investigates the efficacy of long-term prophylactic treatment with enzyme therapy, and combined therapy with cyclosporin A in rats with collagen-induced arthritis.
Methods: Rats with collagen-induced arthritis were administered the following drugs: cyclosporin (5 and 10 mg/kg/day orally); a mixture of enzymes containing pure substances (bromelain, trypsin, rutin) in the same ratio as in Phlogenzym® (PHL, 150 mg/kg, twice daily intrarectally); and a combination of 5 mg cyclosporin A + 300 mg PHL for a period of 50 days from immunization. Levels of serum albumin, serum nitrit/nitrate concentrations, changes in hind paw swelling and bone erosions were measured in rats as variables of inflammation and destructive arthritis - associated.
Results: Treatment with 10 mg of cyclosporin A, as well as with the combination therapy with half dose of cyclosporin A (5 mg) plus PHL, significantly inhibited both inflammation and destructive arthritis-associated changes. However, 5 mg of cyclosporin A or PHL alone reduced these disease markers, although to a lesser extent and in the case of enzyme therapy at a later stage of arthritis development.
Conclusion: Our results show the inhibitory effect of enzyme therapy on collagen-induced arthritis in rats, as well as the efficacy of low dose of cyclosporin A given in combination with enzyme therapy, which may be useful in the treatment of rheumatoid arthritis.

W65

ELECTRIC MOXIBUSTION INDUCES IMMUNE RESPONSES AGAINST HSP(HEAT SHOCK PROTEIN) THEREBY SUPPRESSING COLLAGEN-INDUCED ARTHRITIS IN MICE.

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Objective : To study the mechanism for the effect of moxibustion on murine collagen-induced arthritis(CA), an experimental model of human rheumatoid arthritis(RA).

Rationale : Moxibustion, one of the alternative medicine has been known to have therapeutic effect on RA. However, the mechanism for it remains to be studied. Recently, it has been reported that moxibustion activates the immune systems. In this presentation, we studied the possibility that HSP (heat-shock protein) produced in the site of moxibustion induces immune responses as an immunogen.

Methods : Female DBA/1 mice, 7 wks old were used for induction of CA and for moxibustion with pencil-typed electric device originally developed by us. Moxibustion was done in the back or bilateral footpads everyday for 6 weeks. Anti-type II collagen(CII) and anti-HSP antibody responses were determined by ELISA. In vitro antigen-induced proliferative response was measured using (^{3}H)-thymidine. Skin in the site of moxibustion was solubilized with lysis buffer containing 3%NP-40 for SDS-PAGE and western-blotting.

Results : Moxibustion suppressed the development of CA and increased the number of lymphocytes of the spleen and lymphnode lymphocytes but had no effect on adrenal weight or on the number of peripheral lymphocytes. Mice treated with moxibustion demonstrated higher level of anti-HSP 70 antibody titer and lower anti-CII antibody titer as compared with those of control mice. Lysates of the local skin treated with moxibustion showed increased band of HSP-70 in the mice as compared with the control ones as revealed by western blotting.

Conclusion : These results suggest that the effect of moxibustion is associated with immunological activation with endogenously-induced substances such as HSP-70, resulting in immune tolerance against arthritogen, CII, thereby causing suppression of CA.

W66

SUPPRESSION OF AUTOIMMUNE RESPONSES AND INFLAMMATORY EVENTS BY A NEWLY DISCOVERED ANTI-ARTHRITIC COMPOUND SX-5452, 2-[(2,6-DIPHENYLPYRIMIDIN-4-YL)AMINO]ACETAMIDE DERIVATIVE IN ANIMAL MODELS FOR RHEUMATOID ARTHRITIS

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Objective: To investigate the effectiveness of SX-5452 in preventing the development of arthritis /autoimmune diseases.

Rationale: Newly discovered diphenylpyrimidine amino acetamide derivatives reduce anti-CII antibody production.

Methods: The effects of treatment with SX-5452 (2-[[5-chloro-6-phenyl-2-(4-trifluoromethylphenyl)pyrimidine-4-yl]amino]-N-cyclopropyl-N-methylacetamide) on the development of CIA were evaluated clinically and histologically. The inhibitory effect on the antibody formation was evaluated in vivo and in vitro. In addition to CIA, the effect of SX-5452 on the lymphoproliferation and anti-DNA antibody production in MRL/lpr/lpr mice were also evaluated.

Results: Oral administration of SX-5452 (0.03mg/kg/day-10mg/kg/day) from the day of immunization with CII strongly and dose-dependently suppressed the development of arthritis. SX-5452 at the dose of 10mg/kg prevented completely the development of arthritis in both arthritic score and histological changes. SX-5452 also ameliorated the lymphoproliferation and autoimmunne responses in MRL/lpr/lpr at the dose of 10mg/kg-30mg/kg. These effects were at least three-fold more potent than those of leflunomide. Studies are on going to elucidate the possible molecular mechanisms for these anti-arthritic effect.

Conclusion: The development of CIA in DBA/1 mice and lymphoproliferation and autoimmune response in MRL/lpr/lpr mice were markedly suppressed by SX-5452, possibly via inhibition of anti-CII/anti-DNA antibodies production. Since SX-5452 exerts no overt toxicity after repeated administration for 2 weeks in mice, it is an interesting candidate for therapeutic use in rheumatoid arthritis.

W67

PLASMID ENCODING IL-4 AMELIORATES MURINE COLLAGEN-INDUCED ARTHRITIS.

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Rationale: IL-4 acts as a suppressive agent on collagen-induced arthritis (CIA) development and has an ability to induce Th2 cytokine shift and regulates Th1 cytokine production.

Methods: Control plasmid vectors, pCAGGS (pCont), and plasmid encoding full-length IL-4 cDNA, pCAGGS IL-4 (pIL-4) were administered to DBA/1 mice in CIA model by gene gun (g.g.) delivery and intradermal (i.d.) injection.The signs of arthritis and the date of the disease onset was recorded in combination with severity of arthritis. The levels of serum Abs to CII were measured by ELISA.

Results: The incidence of arthritis was 64.3% in pCont i.d. injection group and 27.3% in i.d. pIL-4 injection group (p=0.0093). In gene gun delivery, the incidence of CIA onset in pIL-4 group showed a significantly lower incidence (8.7%) of arthritis onset compared with that in pCont group (60.7%) (p=0.0001). In both g.g. and i.d. administration of pIL-4, CII-specific-IgG2a, IgG2b, and IgG3 levels were lower compared with those with pCont treatment. Among IgG subclasses analyzed in g.g. delivery, IgG1 levels were increased in pIL-4 treatment group compared with pCont group.

Conclusion: In this study, the plasmid encoding IL-4 cDNA had a markedly regulatory effect on CIA, reducing the incidence and severity of arthritis.

W68

PREVENTION AND TREATMENT OF ANTIGEN-INDUCED ARTHRITIS BY $ISA_{TX}247$, A NOVEL CALCINEURIN INHIBITOR.

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Objective: To examine the efficacy and toxicity of $ISA_{TX}247$, a novel calcineurin (CN) inhibitor, in comparison to cyclosporine (CsA) and placebo in the prevention and treatment of antigen-induced arthritis in rabbits. $ISA_{TX}247$ is substantially more potent than CsA in an *in vitro* CN inhibition assay and demonstrates superior potency in *in vivo* allograft rejection and autoimmune disease models. Animal toxicity studies and Phase I clinical trials show no discernable nephrotoxicity.

Methods: New Zealand White rabbits were immunized with ovalbumin followed by two daily intra-articular injections of ovalbumin and human transforming growth factor. Treatment interventions (placebo, $ISA_{TX}247$ (2.5, 5.0 , 10 mg/kg), CsA (5, 10, 15 mg/kg)), were administered daily either for 28 days from the first intra-articular injection (prevention protocol) or for 14 days once arthritis had been established for 14 days (treatment protocol).

Results: A significant decrease in synovial histopathological scores was observed in $ISA_{TX}247$ (P=0.006) and CsA (P=0.018) animals after 28 days of therapy (prevention protocol) compared to vehicle control animals. This was accompanied by significant reductions in synovial fluid counts ($ISA_{TX}247$-P=0.003; CsA-P<0.001). Significant amelioration in synovial histopathological scores was also evident in $ISA_{TX}247$ (P=0.02) and CsA (P=0.005) animals with established arthritis treated for 14 days compared to vehicle controls (treatment protocol). A significant reduction in macroscopic arthritis score was evident in $ISA_{TX}247$ (P=0.01) but not in CsA treated animals. Treatment was well tolerated with no significant toxicity on analysis by either serum creatinine or post-mortem histology.

Conclusion: $ISA_{TX}247$ demonstrates efficacy and safety in the prevention and treatment of antigen-induced arthritis. In view of its superior nephrotoxicity profile in comparison to CsA, this agent warrants further examination for its therapeutic potential in autoimmune disease.

W69

AMELIORATION OF ESTABLISHED COLLAGEN-INDUCED ARTHRITIS BY $ISA_{TX}247$, A NOVEL CALCINEURIN INHIBITOR.

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Objective: To examine the efficacy and toxicity of $ISA_{TX}247$, a novel calcineurin (CN) inhibitor, in comparison to cyclosporine (CsA) and placebo in established collagen-induced arthritis. $ISA_{TX}247$ has up to a 3 fold greater potency than cyclosporine (CsA) in an *in vitro* CN inhibition assay and in *in vivo* solid organ and cell transplantation models. Phase 1 clinical trials show no discernable nephrotoxicity.

Methods: Type II collagen-immunized DBA/Lac J mice with established arthritis were treated with $ISA_{TX}247$ (125/250/500 ug/mouse), CsA (250/500 ug/mouse), or vehicle for 10 days.

Results: A significant dose-dependent reduction in clinical severity as well as paw swelling was observed in $ISA_{TX}247$, but not in CsA treated animals at 10 days. Significant improvement in synovial histology and articular cartilage damage scores was also noted in $ISA_{TX}247$ treated animals, even in the 125 ug dose group. $ISA_{TX}247$ (500 ug dose group) was the only agent to significantly decrease the development of proximal interphalangeal joint erosions. A significant reduction in Type II collagen antibody titre was noted in $ISA_{TX}247$ animals in both 250 ug ($p<0.01$) and 500 ug ($p<0.001$) dosage groups. Treatment was well tolerated with no significant toxicity in $ISA_{TX}247$ treated groups.

Conclusions: $ISA_{TX}247$ demonstrates efficacy and safety in the treatment of established collagen induced arthritis. Together with its improved potency and nephrotoxicity profile in comparison to CsA, this agent warrants further clinical investigation in autoimmune disease. Phase II studies in RA will commence in 2001.

W70

THE COMPARATIVE VALUE OF THE DIFFERENT FUNCTIONAL STATUS TESTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To assess the correlation of Steinbrocker's functional classification (SFC) and Health Assessment Questionnaire (HAQ) with Complex Functional Test (CFT).
Methods: In a prospective study, functional status of 58 pts. with rheumatoid arthritis (49 F and 9 M; mean age 50,8 yrs; mean duration of the disease 7,42 yrs) was assessed during a six months period of treatment with immunomodulatory drug Leflunomide. Functional capacity was assessed by three different tests: SFC, HAQ and CFT which was designed at the Institute of Rheumatology, Belgrade. CFT is composed of 17 parameters concerning activities of daily living and mobility. Wilcoxon matched pair test and Spearman's rang correlation was used for statistical analysis.
Results: On study entry, SFC was 2,25, HAQ index was 2,04 and CFT total score was 21,16, showing highly significant positive correlation with each other ($p<0,01$). After 6 months of treatment with Leflunomide, SFC was 1,81, HAQ index was 1,75 and CFT total score was 15,45, showing again highly significant positive correlation between tests ($p<0,001$). All 3 tests demonstrated a significant improvement in functional capacity of patients after 6 months of treatment with Leflunomide.
Conclusion: All 3 used tests were similarly valid for the assessment of functional capacity of patients with rheumatoid arthritis. New developed Complex Functional Test showed high correlation with Steinbrocker's functional class and Health Assessment Questionnaire.

W71

PERCEPTIONS OF CONTROL IN RHEUMATOID ARTHRITIS.

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Objective: To identify influences on control perceptions in patients with rheumatoid arthritis (RA).
Rationale: The individual with RA faces a chronic and unpredictable condition. One of the objectives of treatment is to enable the patient to cope with this unpredictability. An internal locus of control (i.e. the belief that the individual can influence events) has been shown to positively impact on adjustment in RA.
Methods: Forty patients with a diagnosis of RA were randomly selected from an outpatient population attending a RA follow up clinic over a four month period. All patients completed the Health Assessment Questionnaire (HAQ), the Rheumatology Attitude Index (RAI), demographic profile and engaged in a semi-structured interview to ascertain influences on control perception.
Results: Demographic profile of the sample revealed 28 women and 12 men, age range 21-75 years, disease duration 8 months-30 years, HAQ mean 1.68 and RAI mean 36. Five main categories emerged that positively influenced patients' perception of control.

1. The reduction of physical symptoms e.g. pain and stiffness.
2. Social support equating with perceived need.
3. The nature of the clinical consultation.
4. Treatment interventions to match patients' expectations.
5. The provision of information to enable understanding.

Conclusion: By addressing the identified factors a patient's loci of control can be influenced to aid adaptation.

W72

THE PATHOLOGY OF THE THYROID GLAND AND RHEUMATOID ARTHRITIS IN THE PERIOD OF A ONSET

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Objective: the research of the frequency of the thyroid gland involvement in rheumatoid arthritis during a onset and correlation between thyroid gland function and clinical-paraclinical features, efficiency of treatment of the patients with rheumatoid arthritis.

Rationality: there are messages about the role of thyreoid hormons in the development and progress of rheumatoid arthritis.

Methods: 95 medical cards of the patients with rheumatoid arthritis were investigated during a onset from the different regions of Moldova. The average duration of the disease was 9,8 months, the relation between women and men was 3,3: 1 (73 women and 22 men), the average age was 36,8 years (from 18 till 64 years).

Results: it was revealed, that 13 patients had thireoiditis autoimmun (13,5 %), 11 of them were with hypothyreozis (11,5 %) and 2 with hyperthyreozis (2,1 %), in 2 patients was diagnosed hyperplasia of thyroid gland (2,1 %) of I-II degree (endemic struma) and in 2 patients rheumatoid arthritis developed on a background of existing pathology of thyroid gland (in both cases was nodular struma, operated on by the method of hemistrumectomia with development of hypothyreozis after the operation).
The essential differences in a clinical picture, degree of activity noted of the disease, efficiency of treatment in the patients with rheumatoid arthritis and associated with hypo - or hyperthyreozis. Were noted in the patients with the lowered function of thyroid gland the arthritis was moderate (articular index 5-8, inflammatory index 4-6, activity of disease of I-II degree, good answer to treatment with basic drugs) and on the contrary in patients with the (increased) function of thyroid gland (articular index 10 and more, inflammatory index 8-10, visceral lesion (endomiocarditis, nephritis, hepatitis, autoimmun anemia) activity of illness of II-III degree, more (limited) answer to treatment with basic drugs).

Conclusion: the raised frequency (by 17,5% of patients) of thyroid gland pathology in patients with rheumatoid arthritis in onset and the dependence of the course of the rheumatoid arthritis from the function of the thiroid gland, allows to recommend research of its function in all patients with rheumatoid arthritis in the onset with the purpose to recomend the appropriate treatment of the found changes, that will allow to improve the prognosis of the disease.

W73

IDENTIFYING GENERATIVE FACTORS BEHIND SUBAXIAL SUBLUXATION IN RHEUMATOID ARTHRITIS

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Objective: To detect the mechanism of subaxial subluxation progression in Rheumatoid Arthritis.

Rationale: Mechanical factors such as bony ankylosis in other cervical spine are one of the most critical causative agents in subaxial subluxation progression as well as the severity of the disease itself in RA.

Method: Seventy patients with subaxial subluxation(SAS) who had either objective neurological symptoms or persistent pain were evaluated both clinically and radiologically. One hundred and twenty patients with atlanto axial subluxation(AAS) were also examined as a control study. An additional retospective study was performed in 32 patients from 5-12 years (mean7.2 years).

Results: A significant difference was found between SAS and AAS in the incidence of bony ankylosis of adjacent areas of the cervical spine ($p<0.001$). An additional retrospective study showed the similar results;11 cases out of 18 with bony ankylosis progressed, while 11 out of 14 without bony ankylosis did not progress. Other clinical markers such as age, long term corticosteroid use , and major joint lesions; NS, $p<0.01$, 0.05, respectively.

Conclusion: We conclude that generative factors behind SAS in RA is not only the disease severity but also mechanical factors. With this in mind, those engaged in diagnostics should be aware of the comprehensive causes of SAS.

W74

THE RELATION OF PLASMA LEPTIN TO BODY FAT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To study the relation between fat mass and serum leptin in patients with rheumatoid arthritis (RA).

Rationale: Low body mass and anorexia are common in patients with RA. Cytokines increase the secretion of anorectic hormone - leptin which was found in both experimental and clinical studies in chronic inflammatory states.

Methods: 53 non-diabetic and non-obese patients were studied (39F, 14 M; mean age 56±11 years; mean body mass index (BMI) 24.6±4 kg/m^2). The disease activity score (DAS) was 3.9±1.4; range 1.4±7.4 and disease duration 8.1±6.7 years. Serum leptin was measured by ELISA and body composition by double X-ray densitometry .

Results: Mean serum leptin was 2.8±1.4 ng/ml. In a simple regression analysis leptin did not correlate with BMI ($r=0.02$), C-reactive protein ($r=-0.16$), total fat mass ($r=0.09$), trunk fat ($r=0.07$), limb fat ($r=0.11$) and DAS ($r=-0.11$), respectively. This relation was also not influenced by gender or type of immunosuppressive therapy. In a multiple regression model none of the independent variables explained the significant portion of the variance of serum leptin.

Conclusion: The physiologic relation of serum leptin to body fat stores is not present in patients with RA

W75

RENAL INVOLVEMENT IN RHEUMATOID ARTHRITIS: ANALYSIS OF RENAL BIOPSY SPECIMENS FROM 100 PATIENTS

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Objective: To evaluate the characteristics of renal involvement in patients with rheumatoid arthritis (RA).

Rationale: No inherent renal lesions are known in RA, but the prevalence of urinary abnormality and renal dysfunction are not rare.

Methods: We analysed the renal biopsy specimens from 100 patients, 20 men and 80 wemen with a mean age of 53.1 years. Renal histopathology was evaluated by light microscopy, immunofluorescence and electron microscopy.

Results: Membranous nephropathy was the most common renal histological pattern (31%), followed by mesangial proliferative glomerulonephritis (21%), minor change (17%), renal amyloidosis (11%), and interstitial nephritis (9%). Most of membranous nephropathy was induced by disease-modifying antirheumatic drugs. Mesangial proliferative glomerulonephritis presented high grade hematuria. Amyloidosis was associated with long duration of RA, half of them presented nephrotic syndrome, and 82% of them fell into renal failure. Interstitial nephritis without glomerular abnormality was in 9%, but 82% of all showed some tubulointerstitial changes.

Conclusion: The renal lesions in RA are very diverse, and some of them have poor prognosis. For these reasons, histological examinations by renal biopsy should be done in the cases with continuing urinary abnormality or worsening of renal function.

W76

CLINICAL LONGTERM UPDATEABLE EVALUATION (CLUE) ONE-PAGE PHYSICIAN FORMS TO MONITOR CLINICAL FEATURES AND MEDICATIONS IN RHEUMATOID ARTHRITIS

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Objective: To develop standard, one-page clinical longterm updateable evaluation (CLUE) forms for completion at the first visit of patients with rheumatoid arthritis (RA), to be kept at the front of the medical record for reference and updating clinical features and medications.

Rationale: Rheumatologists collect similar data in the care of patients with RA, but generally in non-standard formats, so that most data are not easily accessible for clinical care and/or clinical research.

Methods: Two one page CLUE forms: clinical features - extra-articular disease, comorbidities, classification criteria, family history, joint surgeries, radiographs; medication review - all DMARDs and NSAIDs.

Results: CLUE forms in 102 patients with RA indicated that 86% took methotrexate, 28% hydroxycholoroquine, 10% leflunomide, 8% cyclosporine, 8% etanercept, 8% infliximab. Extra-articular disease included dry mouth in 46%, dry eyes in 35%, and carpal tunnel syndrome in 37%. Comorbities included chronic back pain in 36%, hypertension in 31%, peptic ulcer in 27%, esophageal symptoms in 25%, cataracts in 20%, cancer in 10%, diabetes mellitus in 4%.

Conclusion: Two simple one-page clinical longterm updateable evaluation (CLUE) forms are easily completed at the first visit in usual clinical care to characterize patients with RA, complemented by a patient questionnaire and joint count form to provide simple, standard measures of RA clinical care, clinical research, and clinical outcomes.

W77

RENAL DISEASE IN RHEUMATOID ARTHRITIS. A STUDY OF URINARY N-ACETYL-β-D-GLUCOSAMINIDASE EXCRETION

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Objective: To evaluate the frequency of tubular dysfunction in patients with rheumatoid arthritis (RA) using the urinary excretion N-acetyl-β-D-glucosaminidase (NAG) and to estimate the influence of clinical features of RA and drug therapy on proximal renal tubular cells.

Rationale: Frequent renal dysfunction in RA patients remains often subclinical. It requires use of sensitive parameters of renal function other than serum creatinine level or proteinuria. At present NAG activity seems to be the suitable marker of tubular dysfunction.

Methods: Urine samples from 181 patients with RA were assessed to determine urinary NAG excretion. No patients had received DMARDs other than sulphasalazine in the preceding 3 months. The majority of patients were taking NSAIDs.The first control group included 44 patients with osteoarthritis, the second control group included 33 healthy subjects. None of the patients of control groups were suspected of having renal diseases.

Results: The NAG activity in the urine of 33 healthy control subjects was 26,8 ± 17,7 (3,4 - 71,3 nmoles /mg of creatinine). Abnormal urinary NAG/creatinine activities of more than 70 nmoles/mg cr. were found in 58,6 % of the urine samples of RA patients. Our data demonstrate that urinary NAG to creatinine ratios were higher in a group of patients with RA than in the OA patients and healthy controls (median: 93,8 vs 37,4 vs 24,1nmol/mg of cr.); the normal (<70 nmol/mg cr.), slightly increased (70-140 nmol/mg cr.) and markedly increased (>140 nmol/mg cr.) NAG activities. were found in 75 (41,4 %), 40 (22,1%) and 66 (36,5%) RA patients. Abnormal serum creatinine (≥ 1,4 mg%) was found in 10 RA patients. 24-hour urinary protein higher than 0,15 g were found in 16 patients. Higher NAG values were observed in RA patients with more active disease characterising by the presence of erosions in hand radiographs and laboratory indices of inflammation like ESR. Concurrent use of NSAIDs does not influence distinctly on NAG values.

Conclusion: Renal proximal dysfunction estimated by NAG activity in urine occurs more often than glomerular changes in patients with RA and high urinary NAG excretion reflects active feature of RA.

W78

EVALUATION OF CA-RF AND NTX VALUES IN RHEUMATOID ARTHRITIS.

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Objective: To evaluate immunological values using the anti-galactosyl IgG antibody (CARF) and to measure bone absorptional activities using the type 1 collagen cross-linked N-telopeptides (NTx) from patients with rheumatoid arthritis (RA).

Rational: RA causes joint destruction. We suppose the CARF play an immunological marker which correlate with RA activity and values of the NTx were able to control for RA activities.

Methods: The CARF and other parameters were measured in 60 outcome RA patients (male 14, female 46. age 29 - 78. stage 1:11, 2:12, 3:10, 4:27) in Sakai Hospital at first time and 6 month later. The NTx was measured in 31 of above 60 RA patients at same time.

Results: The CARF detected in 50 of 60 RA at first time and 43 of 48 RA at 2nd period. The values of CA-RF correlated with RA activities (CRP, Lansbury index). Significant positive correlations were observed between CARF and NTx ($r2=0.211$, $p=0.01$).

Conclusion: These results suggest that CARF has a potentiality as the RA activity marker, reflecting not only the immunological marker but also joint destruction.

W79

MARKERS(SP-D & KL-6) OF INTERSTITIAL PNEUMONITIS IN RHEUMATOID ARTHRITIS.

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Objective: Aims of this study are to evaluate whether assays for hydrophilic surfactant protein SP-D and mucin like glycoprotein KL-6 in sera from rheumatoid arthritis(RA) patients are diagnostically useful tools for detecting interstitial pneumonitis (IP) and whether these assays are superior to chest plain radiography or CT scanning and other laboratory parameters such as lactate dehydrogenase (LDH).

Rationale: Serun level of SP-D and KL-6 were known to increase when the type II pneumocytes were damaged in any way. Recently, these markers have been used to detect IP in some lung diseases.

Methods: The level of SP-D and KL-6 in sera from patients with RA were measured. Then, patients were divided into 3 groups (A,B and C) according to the level of SP-D and KL-6. Group A includes patients with both high SP-D and KL-6 (5 patients), group B includes patients with high SP-D and normal KL-6 (8 patients) and group C includes normal SP-D and high KL-6 (15 patients). Chest X-ray and CT scan films were examined whether there were IP findings or not. Detection of SP-D or KL-6 was performed by the method of sandwich enzyme immunoassay. Monoclonal antibody to SP-D or KL-6 coated EIA plate was placed. Then,sample serum was added,incubated each time. Next add POD-conjugated monoclonal antibody followed by incubation. After adding substrate, the absorbance was measured at 450 or 405 nm, respectively.

Results: Hundred percent of the patients in group A showed IP by CT scan. Patients in group B showed IP at 12.5% by X-ray and 50% by CT scan. Patients in group C showed IP at 46.7% by X-ray and 60% by CT scan.

Conclusion: 1. High level of both SP-D and KL-6 in serum showed IP at 100% level. 2. High level of SP-D and normal of KL-6 showed the possibility of slight or early phase IP. 3. Because most patients with high level of KL-6 showed IP, detection of the high level of KL-6 is a very useful tool to diagnose IP in RA patients.

W80

ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY AND KL-6 IN PATIENTS WITH RHEUMATOID ARTHRITIS.

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Objective: TO study the character of anti-glomerular basement membrane (GBM) antibody inpatients with rheumatoid arthritis (RA).

Methods: Sera from 123RA patients (22men; 101 women: age 61.0 ± 12.4 yrs.) were studied for anti-GBM antibody, KL-6 and other laboratory parameters. ELISA was employed for anti-GBM antibody, KL-6 measurement. Every studied patient was examined for the interstitial pneumonia (IP) by chest X-ray, chest CT and/or clinical symptom.Results: 8 sera (6.5%) were anti-GBM positive among 123. Those with positive anti-GBM antibody were more frequently complicated with IP than those without the antibody ($p<0.05$). The mean levels of serum KL-6 for anti-GBM antibody positive subjects was significantly ($p<0.05$) elevated compared to negative subjects. As for other parameter concomitantly studied, i. e. IgG rheumatoid factor (RF), erythrocyte sedimentation rate, C-reactive protein and urinary protein, any significant difference was not detected between anti-GBM positive patients and negative patients.

Conclusion: It is suggested that anti-GBM antibody in patients with RA originate from pulmonary alveoli, which are damaged by the rheumatoid disease process and provided GBM as the antigen.

W81

IMPACT OF FORESTIER'S DISEASE (DISH) ON THE COURSE OF RHEUMATOID ARTHRITIS.

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Introduction: In the last time diffuse idiopathic skeltal hyperostosis (DISH) is supposed to be a metabolic disease often accopanied with disorder of glycide, purine and lipid metabolizm, including hyperretinolemia. Rheumatoid arthritis (RA) coincidental with DISH is rather rare.

Material and methods: During the last five years we could observe and study a group of 11 (eleven) patients, 9 females and 2 males with definite diagnosis of RA established according to ARA criteria. The average duration of RA was 10,7 years. In the same patients the definite diagnosis of DISH according to Utsinger's criteria was proved.

Results: As for RA, in most of patients the typical polyartikular onset was seenwith presence of rheumatoid nodules and middle inflammatory synovial fluid, oligoarticular affection was rare. Skiagraphically the finding of subchondral erosion and /or cystoid changes were observed and the destructive changes were found to be rather eburnated with proliferation about osseous erosions and osteophytosis. The formation of marked exostotic periostoses, especially on the processus styloideus ulnae as well as on proximal and distal phalanges and higher rate of evolution of joints ankylosis, are typical for coincidental RA and DISH. In the region of the spine the variable hyperostotic ossifications were found with extensive enthesopathic changes on the spina iliaca anterior, as well as in the suprnacetabular and trochanteric region.

Conclusion: Our results prove that DISH can modify the course of RA, slow down evolution of its destructive chnages by means of formation osteoplastic perifocal changes with marked eburnation of focal defects associated often with erosion recalcification. Exostotic formation on the processus staloideus ulnae and sometimes ankyloses of joints may occur. The autors assume that genetic predisposition and metabolic abnormalitie of DISH are responsible for this peculiar coincidence of RA and DISH.

W82

JOINT DAMAGE DOES NOT EXPLAIN FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS PATIENTS: A CROSS-SECTIONAL STUDY OF 146 PATIENTS.

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Objective: to evaluate the impact of joint damage on functional disability in rheumatoid arthritis (RA) patients.

Rationale: the contribution of joint damage to functional disability in RA is not fully quantified.

Methods: 146 RA patients (female=88.4%, mean age=56 years; mean disease duration=13.9±8.1years; RF positive = 73.8%) fulfilling ACR criteria, were submitted to a cross-sectional evaluation including X-ray of hands, wrist, elbow, shoulder, hip, knee and feet (scored using Larsen's method). Simultaneously they completed AIMS2 questionnaire.

Results: mean total Larsen score of hands and feet was 42.4+/-16.8. Average Larsen score for upper limbs was 5.1+/-3.5 and 4.8+/-3.2 for lower limbs. Mean score for physical category (PC) of AIMS2 was 7.0+/-1.7. We found a correlation between PC and Larsen score for large joints of upper and lower limbs (r=0.327, p=0.009) but not with the score for small joints of hands and feet. AIMS2 mobility scale correlated with Larsen score for lower limb joints (r=0.3, p=0.017) but not with the score for feet. We found no correlation between Larsen score for hands and the AIMS2 hand and finger function scale.

Conclusion: Joint destruction contributes to functional disability in RA, however cannot fully explain by itself the degree of impairment.

W83

THE SOCIAL AND PSYCHOLOGICAL IMPACT OF RHEUMATOID ARTHRITIS: A STUDY OF 146 PATIENTS.

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Objectives: To evaluate the social and psychological impact of RA.

Rationale: Social and psychological impact of rheumatoid arthritis (RA) is not yet fully quantified.

Methods: 146 RA patients, fulfilling 1987 ACR criteria, followed in a hospital-based outpatient rheumatology clinic (female=88.4%; mean age=56 years; disease duration=13.9+/-8.1years), completed questionnaires on social support network and psychological status, including AIMS2.

Results: 81.4% of the patients were married, 7.9% single, 2.8% divorced or separated and 7.9% widowed. The major providers of social support were the spouse (48.8%) and first grade relatives (50.4%). In the AIMS2 level of tension scale, 5.8% scored up to 5 and 77.9% scored above 7. In the mood scale, 10.1% scored up to 5 and 52.7% scored above 7. There was a correlation between the social interaction dimension of AIMS2 (social activity + family support scales) and the affect / psychological dimension (level of tension + mood) (p=0.002).

Conclusion: RA patients have a major impairment of social activity and develop high levels of psychological stress. Family relatives provide generally good social support, which nonetheless is not enough to compensate for RA social and psychological impact.

W84

HEALTH STATUS AND DISABILITY MEASURES DO NOT PREDICT INDIVIDUAL QUALITY OF LIFE IN RHEUMATIC PATIENTS.

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Objective: To evaluate the correlation between measures of health status and disability, and individual quality of life (QOL) in rheumatic patients.

Rationale: Recent evidence suggests that individual perception of QOL is not reliably reflected by health status and disability questionnaires.

Methods: 312 patients with miscellaneous rheumatic diseases (255 F and 55 M, mean age 52.2±14.1 yr) completed the HAQ Functional Disability Index (FDI), the MOS SF36 and EQ5D questionnaires, and an individual QOL index, the Patient Generated Index (PGI).

Results: The mean PGI score in the whole population was 3.4±2.0, and was not significantly affected by demographic variables and comorbidity (ANOVA, $p>0.05$). Spearman correlation with the PGI score was highest for SF36 physical functioning, EQ5D usual activities, and FDI scales ($r=0.47$, 0.43, and 0.41 respectively), and lowest for SF36 general health ($r=0.10$) scale. All SF36 and EQ5D scales, the FDI, the presence of fibromyalgia, patient and physician assessment of disease activity, and patient assessment of pain, were entered as independent variables on the PGI score in a generalized linear model. Only SF36 physical functioning, EQ5D usual activities and VAS, and patient assessment of activity were retained in the final model, explaining 30% of PGI score variability ($R^2=0.298$, $p<0.0001$).

Conclusion: Our results suggest that measures different from conventional health status and disability questionnaires should be adopted to assess individual quality of life in rheumatic patients.

W85

THE EVALUATION OF RADIOGRAPHIC DAMAGE BY 4 DIFFERENT METHODS IN HAND X-RAYS AND THE CORRELATION OF RADIOLOGIC CHANGES WITH CLINICAL AND LABORATORY ABNORMALITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: The aim of this study is to compare the scores of 4 different quantitative radiological methods by each other and physical measures of functional status, clinical and laboratory variables as well as indexes of disability in RA patients.

Methods: Thirty-three patients with a mean age of 47.5±10.3 years were included to the study. Demographic data, laboratory and clinical activity parameters including pain by VAS, erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), rheumatoid factor (RF) were recorded and HAQ and Ritchie articular index (RAI) were used to assess disability and disease activity respectively. The degree of destruction in hand x-rays was analysed according to Sharp, modified Larsen, Kaye and Rau methods.

Results: There was a significant correlation between the mean score of each radiographic method. All the radiographic scores were highly correlated with duration of disease ($p<0.01$). The scores were also correlated with age and ESR at lower levels. None of the radiographic scores are correlated with VAS, CRP, RAI and HAQ scores. The highest correlation coefficients were observed between disease activity parameters and the radiographic scores of modified Larsen method. The patients with short disease duration had also high scores according to the joint space narrowing and erosion. All the radiological total scores were higher in sero-positive than in sero-negative patients, but the differences were not statistically significant ($p>0.05$).

Conclusion: These different radiologic scoring methods provide similar data and various clinial activity measures in patients with RA may be correlated only at modest levels with radiographic damage. Further longitidunal studies are needed to develop a scoring system that estimate minimally detectable changes to assess severity and decrease management accordingly.

W86

COMPARISON OF SELF-REPORTING MEASURES OF FUNCTIONAL DISABILITY AND CLINICAL VARIABLES IN RHEUMATOID ARTHRITIS IN A TURKISH POPULATION

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Objective: Self report measures of functional disability in rheumatoid arthritis (RA) have become increasingly important over the past decade. The aim of this study was to evaluate the relationship between clinical variables and the scores of functional disability assessed by 3 different self-report questionnaires of functional status in Turkish RA patients and to assess if the simple self-report questionnaires provides information similar to many traditional measures in RA.
Methods: Fifty RA patients with a mean age of 47.7±11.1 years were recruited. Data about the demographical and clinical characteristics were obtained. Health assessment questionnaire (HAQ) disability index, AIMS and Duruoz Hand Index (DHI) were used to assess functional status in RA patients.
Results: The self-reported functional indexes had high correlation between each other and between the subscales of AIMS. The HAQ and DHI had their closest correlation with clinical activity parameters of RA such as Ritchie articular index (RAI), pain by VAS and erythrocyte sedimentation rate. Radiological scores had the strongest correlation with disease duration. The sex and rheumatoid factor were not significantly correlated with DHI whereas RF correlated with functional disability assessed by HAQ. The psychological scales of AIMS correlated highly with RAI and swollen joint counts. An association between the mean disease duration and scores of functional status could not be demonstrated. Disability was slightly but not significantly higher in sero (+) than in sero (-) patients. The difference of functional disability scores in patients with long and short disease duration was not statistically significant ($p>0.05$).
Conclusion: The self-report questionnaire scores can reflect accurate information about clinical and functional status in a cost-effective way. Using these self-report measures of functional disability that have been previously studied in different populations, we conclude that the patterns of interaction with disease activity measures and functional disability scores in a group of Turkish RA patients share similar relationships with other RA patients reported from different countries.

W87

CLINICAL SIGNIFICANCE OF THE IMMUNOLOGICAL TESTS IN RHEUMATOID ARTHRITIS

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Objective: To determine the clinical significance of the immunological tests in diagnosis and evaluation of rheumatoid arthritis (RA).
Rationale: The synovial tissues in rheumatoid arthritis display a number of immunological abnormalities associated with inflammatory processes.
Methods: In order to clarify the clinical significance of the imunological tests in RA, we studied immunoglobulins, rheumatoid factors (RF) and complement levels in sera and synovial fluid (SF) in 112 RA patients and in control group of 53 patients with seronegative arthropaties (SA) and 46 with osteoarthrosis (OA). SF and serum levels of C3, C4 complement, IgA, IgG and IgM were determined simultaneously using radial immunodifussion method (Mancini et al). The complement levels for C3 and C4 were expressed by the ratio C3SF/C3S and C4SF/C4S respectively.
Results: The levels of immunoglobulins were elevated in both serum and SF in patients with RA. IgM levels in SF and sera were more increased in the cases with RA (1,57+1,6) than in SA (0,7 +0,8) and OA (0,7+0,2), and more prominent in the seropositive than the seronegative cases ($p<0,001$). The levels of C3 and C4 were lower in SF in RA (C3 0,487+0,6 gr/l) than in SA (C3 1,03+1 gr/l) and OA (C3 0,92+1g/l, C4 0,40+0,4gr/l). C4 was significantly decreased in SF than C3 ($p<001$) and they were more decreased in seropositive than in seronegative cases ($p<0,001$). C3 and C4 in SF were significantly lower in RA than in SA and OA. The activity of C4 was significantly decreased in SF than C3. Lower complement levels implicate complement consummation in cases with RA. The patients with RA were seropositive in 65%, but RF was positive in 69% of SF. 19,5% seronegative patients had positive RF in SF, especially cases in early stadium of the disease.
Conclusion: Imunological tests such as immunoglobulins, RF and complement levels, specially in SF, has clinical significance and relationship can be find between studied parameters and activity of the disease.

W88

CLINICAL ASSESSMENT OF DMARDs CHANGE IN PATIENTS WITH RHEUMATOID ARTHRITIS BY MEASUREMENT OF THE SERUM CHONDREX.

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Objective: We studied the usefulness of serum chondrex as the index of clinical evaluation of DMARDs change in patients with rheumatoid arthritis (RA).

Rationale: Chondrex has been used as a biochemical marker of the cartilage metabolism.

Methods: We measured serum chondrex by ELISA in 15 patients with RA at the 2 points (pre-, and post 3 months of the DMARDs change). The disease activity of RA was assessed by serum CRP and a Lansbury index (LI). The RA group were divided into two subgroups according to the ACR criteria of the 20 % clinical improvement in RA (effective group; fulfilled the 20 % improvement, non-effective group; failed to the 20 % improvement).

Results: Chondrex showed the positive correlation with the both CRP and LI in RA. At the post 3 months of the DMARDs change, the effective group (n=9) showed lower level of CRP, LI, and chondrex than the non effective group (n=6) unless there were no differences of these parameters between 2 groups at the study entry.

Conclusion: Serum chondrex reflects the RA disease activity. Furthermore, it may be useful for the clinical assessment of DMARDs change in RA.

W89

THE CARPAL X-RAY CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELATION TO THE CERVICAL SUBLUXATIONS AND/OR THE EXPERIENCE OF TOTAL HIP/KNEE ARTHROPLASTY

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Objective: To study the radiological changes of the carpal and the cervical spine in rheumatoid arthritis (RA) patients with or without the experience of total hip/knee arthroplasty (THA/TKA).
Methods: After the carpal X-ray evaluation on 136 female RA patients, those with severe, intermediate or mild changes in the carpal were classified respectively into Category A, B or C. On the cervical X-ray from 70 subjects, atlanto-axial, or sub-axial subluxation (AAS/SAS) was checked to divide the patients into 4 Groups. Group V contained 30 cases with AAS/SAS and with 1 or more experiences of THA/TKA. Group W patients were 7 with AAS/SAS but without THA/TKA. Group X, or Group Y was comprised respectively by 23 without AAS/SAS but with THA/TKA, or by 10 without AAS/SAS nor THA/TKA. 66 patients who had no cervical X-ray nor orthopedic operations provided a cotrol Group Z.
Results: Group V, W, or X showed significantly longer duration of RA than Group Y or Z, despite the similarity of mean ages among the Groups. Mean grip power was weakest in the hands of Group V patients, and Group Z (strongest), Y, X or W patients had stronger grip power in this order. Upper extremity function was more deteriorated in Group V, W, or X than Group Z. Group V or X showed severer damages in the lower extremity than Group Y or Z. Better quality of life (QOL) was suggested among Group Z than Group V patients. Combined Groups V, W and X contained 55 Category A, 4 B and 1 C carpi, while Groups Y and Z with 28 Category A, 21 B and 27 C carpi suggested changes milder than the former Groups.
Conclusion: The longer duration of RA, which parallels with the severer radiological carpal damages, brings the more AAS/SAS and the more THA/TKA occasions.

W90

RELIABITY AND VALIDITY OF THE SLOVAK VERSION OF THE STANFORD HEALTH ASSESSMENT QUESTIONNAIRE - FUNCTIONAL DISABILITY INDEX (HAQ) IN PATIENT WITH RHEUMATOID ARTHRITIS (RA).

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Objective: To evaluate reliability and validity of the Slovak version of the HAQ in patients with RA.

Rationale: Functional disability is one of the most important consequences of RA in the patient's daily life. The HAQ has been widely used in its self administered form for the assessment of disability.. A sensitive and valid instrument is needed for a Slovak population with RA.

Methods: In preparing the Slovak version of the HAQ careful attention has been paid to the translation, in terms of linguistic and conceptual equivalence.. The sample consisted of 160 RA-patients. To analyse the data t-test, correlations, one-way analysis of variance (ANOVA) with corrections for multiple comparisons with Scheffe procedure ($p<.05$) and principal component analysis (PCA) available in the SPSS/PC+ statistical package were used.

Results: The Cronbach's coefficient of reliability alpha for the HAQ total scale was 0.94. The results of PCA showed that the 20 HAQ items loaded on four components for which the eigen values were greater than 1, accounting for 70% of overall interpersonal variability. Orthogonal varimax rotation of the PCA is provided factor loadings reflecting the eight dimensions within the HAQ. Validity of the HAQ was examined further by means of known-groups technique. The HAQ was found to be sensitive to differentiate between the Steinbrocker's functional capacity groups, as well as between males and females. Significant correlations ($p<.01$) were found between the HAQ and the C-reactive protein, the ESR, the NHP-pain, the Ritchie articular index, the Steinbrocker's functional capacity) and disease duration ($p<.05$).

Conclusion. The results of the current investigation provide support for reliability and construct validity of the Slovak version of the HAQ in patients with RA

W91

RESPONSE OF THE IMMUNE SYSTEM TO ACUTE PSYCHOLOGICAL STRESS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS.

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Objective: To evaluate an influence of experimentally-induced psycho - social stress on blood lymphocytes' number in women with early RA.
Methods: The total lymphocytes' number and CD3, CD4, CD8, CD16, CD19 % in the blood of 4 women with early RA and 4 female age-matched controls were compared two times. At baseline (after resting for 30 min. in sitting position and listening to a calm music) and after 15 min.-lasting experiment. Each of the person under examination had to play a role of an employee, called for a talk with his company's chief, who was going to limit the number of his workers. All the obtained results were subsequently analysed with respect to some psychological variables, which are regarded to be responsible, at least in part, for individual differences in stress response.
Results: A significant difference between arthritics and healthy controls was found, when changes(after stress - baseline) of CD16 and CD19 were taken into consideration. Both parameters tended to increase in healthy controls, but decrease in arthritics. Furthermore, the change in CD16 cells' numbercorrelated positively with perception of stressful situation as a chalenge and negatively - with it's perception as a threat, difficulties to describe emotions and level of anxiety. In all these psychological dimensions the RA patients were significantly different from healthy controls ($p<0.05$), and experienced more anxiety and difficulties to depict their own feelings and perceived stress as a loss or threat rather than as a challenge.
Conclusion: Preliminary data suggests that the stress response of the immune system in rheumatoid arthriticxs may be different than in healthy controls and may depend - at least in part - on their psychological characteristic. These findings may contribute to the explanation of mechanisms responsible for rheumatoid disease exacerbation after a psychological stress.

W92

PERSONALITY DISORDERS AND RHEUMATOID ARTHRITIS
GUILT AND FEARS

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Objective: The possible handicap which could be caused from Rheumatoid Arthritis (R.A.), is well perceived not only to the affected person and his family but also to the whole society.Pshychologic reactions especially guilt for their disease and autocritisism worsen their situation.

Retionale: It is well known that R.A due to it's long duration and relapses can interfere with psychic sphere of those suffer from it.

Methods: We studied 50 patients with R.A. due to criteria of American Society of Rheumatology and equal number of control subjects who did not needed medical or pshycologic interference. The psychometric instruments measuring the structure and expression of hostility, anxiety and depression are; a) HDHQ measures non physical aggressiveness, b) DSSI-SAD and SCL-90R measures somatisation and psychiatric symptomatology. Non parametric statistical method (Mann-Whitney test) was used for the analysis of the results.

Results: Group of patients includes 17 men (34%) and 33 women (66%) with mean age 57,38±13,75 years of age and mean disease duration 104±127,12 months. Depressive idealism with characteristic ideas of guilt autocritism is remarkably increased in patients with R.A.(p=0,0017).Depressive idealism with characteristic ideas of guilt and autocritisism is remarkably increased in patients with R.A. (p=0.017).

Conclusion: Patients with R.A. appear with increased levels of somatization, guilty and fears than the control subjects because they are protracted and suffered and havens development our defensive mechanisms.

W93

OTO-LARYNGEAL INVOLVEMENT IN RHEUMATOID ARTHRITIS

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Objective: To study the effect of rheumatoid arthritis on larynx, middle ear conducting system and the inner ear transmitting system.
Rationale: Joints of middle ear (incudomalleolar, incudostapedial) and larynx (cricoartenoid) are synovial joints subjected to rheumatoid arthritis involvement and extra-articular manifestations of the disease (rheumatoid nodular vasculitis) can affect the inner ear.
Methods: Patients included 30 rheumatoid arthritis patients (18 females and 12 males) and 20 controls. Clinical assessment included musculoskelatal examination, audiological evaluation (pure tone air and bone conduction, speech reception and discrimination thresholds, threshold bone decay, auditory brain stem response audiometry), complete laryngeal examination (indirect laryngoscopy, fibreoptic direct laryngoscopy, stroboscopy), laboratory investigations (ESR, complete blood picture, rheumatoid factor), and radiological examination of hands.
Results: A significant increase in pure tone average, speech receptor threshold and acoustic reflex threshold was observed in patients group. Audiologicaly 43.33% of rheumatoid arthritis patients had sensorineural hearing loss of cochlear type, 13.33% had conductive deafness and 43.33% were with normal hearing. Laryngeal evaluation revealed that 50% of rheumatoid arthritis patients had laryngeal symptoms (symptomatic group), and 20% of them showed signs of laryngeal affection by indirect and fibreoptic laryngoscopy. Stroboscopic study showed positive findings in both symptomatic and asymptomatic group. There was a significant relation between laryngeal affection and the presence of subcutaneous nodules.
Conclusion: These results suggests that rheumatoid arthritis could affect middle ear and or inner ear as well as the larynx.

W94

EFFECT OF WEATHER ON PAIN IN RHEUMATIC PATIENTS.

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Rationale: The widespread accepted belief that weather influences arthritic pain has been previously studied with controversial results.
Objectives:1) Evaluate the influence of weather on onset of articular pain in people with and without rheumatic pathology. 2) Correlate different climate variables with the patients' impression of weather sensitivity. 3) Assess correlation between pain and 5-days preceeding and following climate conditions in Córdoba city, Argentina.
Methods: Self-reported questionnaires to assess the presence and features of spontaneous daily pain during one year (1998) were completed by 151 out-patients with osteoarthritis (OA) (n=52), rheumatoid arthritis (RA) (n=83), fibromyalgia (FM) (n=16) and 33 healthy subjects. Data were correlated with daily temperature, atmospheric pressure and relative humidity obtained during the same period. p values <0.001 were considered significant.
Results: 1) Low temperature, high atmospheric pressure and high humidity were significantly correlated with pain in RA ($r=-0.30$, $r=0.34$, $r=0.23$; $p<0.001$); in OA, pain correlated with low temperature and high humidity ($r=-0.23$, $r=0.24$; $p<0.001$), in FM, with low temperature ($r=-0.29$; $p<0.001$) and no correlation was found in controls. 2) Patients self-described as being weather sensitive, only correlated with high humidity ($r=0.45$; $p<0.0001$). 3) There was no correlation with climate variables 5 days before or after the episode of pain.
Conclusion: These results support the belief that weather influences on articular pain, albeit in different ways depending on the subyacent pathology and subjective weather sensitivity. This influence would not depend on weather conditions of the previous or following days.

W95

AZATHIOPRINE AND METHOTREXATE AS COMBINATION CHEMOTHERAPY IN RHUEMATOID VASCULITIS

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Objective: To compare the efficacy and toxicity of azathioprine (AZA) or AZA and methotrexate (MTX) in rheumatoid vasculitis.

Rationale: Low dose combination therapy for complicated rheumatoid arthritis might contribute to better results and tolerance.

Methods: A six months randomized trial including 31 patients with classic rheumatoid arthritis who met clinical and laboratory criteria for vasculitis. Treatment with 150 mg/24 h AZA (16 patients) or 50 mg/24 h AZA and 7,5 mg/week MTX (15 patients). Clinical and laboratory assessments (ulcerations, splinter hemorrhages, gangrene, peripheral neuropathy, serositis, visceral arteritis as well as serum rheumatoid factors, antineutrophil cytoplasmic antibodies (ANCA), complement fraction 3 (C3), immune complexes and cryoglobulins) were carried out at 0, 1, 2, 3 and 6 months.

Results: All variables improved significantly with time. There was no statistically significant difference between the combination treatment and AZA alone. Three patients on AZA were excluded from the study because of major side effects. The majority of patients in each treatment group experienced one or more minor toxic reactions during the follow-up period.

Conclusion: For the treatment of rheumatoid vasculitis the combination of low-dose MTX and AZA is at least as effective as high-dose AZA but seems to be better tolerated.

W96

Clinical Efficacy and Safety of Sinomenine in the Treatment of RA Patients

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Objective:To evaluate efficacy and safety of Sinomenine in the treatment of rheumatoid arthritis (RA) patients.
Rationale: Sinomenine could inhibit PGE_2, reduce inflammatory reaction and might have immunosuppressive effect.
Method: This is a double blind, double dummy control trial. The testing drug is Sinomenine and MTX is the control. They appear the same with the placebo. Each patient took the same amount of drugs. They took drugs according to the sequence number.
Morning stiffness, grip strength, joint swelling index, joint tenderness index were recorded every month, and evaluated by physicians and patients before and after the trial. laboratory parameters (blood routine, ESR, CRP, RF, urine routine, liver and renal function) were tested before and after treatment.
The efficiency, toxicity and adverse effects were recorded every month.
Results: The difference of total effective rate of Sinomenine and MTX on month 3 and 6 are statistically insignificant (65.62% vs 65%; 87.5% vs 91.7% respectively). Joint swelling, joint tenderness, morning stiffness, grip strength of the hand, ESR, RF were all improved in every group. Both patients' and physicians' evaluation showed that these two drug were similar. There are no significant difference between these 2 drugs.
Conclusion: Sinomenine is the extract of natural Chinese herbs. According to the record of traditional medicine, it could be used in treating joint pain and arthritis. Our clinical trial demonstrated that the efficacy of Sinomenine and MTX in treating RA is similar in 6 month. This suggested indirectly that this drug might have immunosuppressive effect, therefore it could be used as one of DMARD in treating RA. Another advantage of this drug is that it has mild adverse effect.

W97

Clinical Observation of Jingzhu Rheumatism Capsule in the Treatment of 162 cases Rheumatism Symptoms of Numbness

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Objective: To evaluate efficacy and Safety of Jingzhu rheumatism capsule in the treatment of rheumatism symptoms of numbness

Rationale: Jingzhu rheumatism capsule can reduce pain and protect Joint and muscle function

Method: this is a open trial 162 patients all follow the criteria of rheumatism Symptoms of numbness

Drug regimen

Oral Jingzhu rheumatism capsule 3 tablets tid after meal, the duration is 90 days.

Clinical and Laboratory parameters:

Joint pain joint swelling

Joint function

ESR. RF.

Result: There is obvious improvement after treatment with statistically difference compared with pre-treatment (P<0.01) in joint swelling and joint function. total effectiveness : 88.27% .

Conclusion: Jingzhu Rheumatism capsule is a good medicine in treating symptoms of numbness, it has satisfied efficiency in relieving pain getting rid of swelling and improving joint function .Another advantage of this drug is that it has mild adverse effect.

W98

Clinical Efficacy and Safety of Jinzhu Rheumatism Capsule in the Treatment of RA Patients.

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Objective: To evaluate efficacy and safety of Jingzhu Rheumatism Capsule in the treatment of rheumatoid arthritis (RA) patients.

Rationale: Jingzhu Rheumatism Capsule can increase the power of muscles and skeleton, inhibit inflammation and relieve pain, tonify blood.

Method: This is an open trial. 63 Patients all follow the ACR RA diagnostic Criteria in 1987.

Drug regimen: Oral Jingzhu Rheumatism Capsule 3 tablets tid after meal, the duration is 90 days. Clinical and Laboratory Parameters werepecorded. Joint pain,Joint swelling,Joint function. ESR. RF.

Result: there is statistically difference between Pretreatment and post treatment in Joint tenderness and Joint function, the total effective rate is 90.48%

Conclusion: "Symptoms of numbness" are results of invasion ofthe body by external pathogenic factors such as wind, cold, damp and heat. Numbness and pain occur in bones, tendons, muscles and Joints. Jing-zhu Rheumatism Capsule is a kind of modern Tibetan medicine. Our clinical trial showed indirectly that this drug could inhibit PGE, and might have immunosuppressive effect. It's another advantage is that it has mild adverse effect.

W99

CEMENTED BIOCERAMIC YMCK TOTAL KNEE ARTHROPLASTY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To investigate the clinical results of total knee arthroplasty using YMCK prosthesis (ceramic femoral and tibial components, cemented without screw fixation, posterior cruciate ligament retained).

Rationale: Cemented total knee arthroplasty using ceramic knee prosthesis is of low friction and useful for rheumatoid patients.

Methods: Eighty-seven knees of 65 rheumatoid patients were evaluated using the knee score system of the Knee Society and radiographically. There were 5 men (5 knees) and 60 women (82 knees) with a mean age of 58.6±9.9 years, excluding one knee with the prostheses retrieved. The mean follow-up duration was 39.1±10.1 months ranging from 24 to 64.

Results: The greater part of the patients obtained relief of pain and improvement of walking ability. The knee score improved from 34.5 ±18.2 points preoperatively to 79.6±12.9 points postoperatively, and the function score improved from 28.4±20.8 points to 52.5±31.1 points. The arc of motion improved from 100.8±32.1 degrees to 106.9±18.1 degrees. The flexion contracture improved from 12.8± 14.5 degrees to 1.4±5.1 degrees. The standing femoro-tibial angle was 172.1 ± 8.6 degrees before and 171.8 ± 5.2 degrees after arthroplasty. A radiolucent line with a thick of two millimeters was identified ajacent to tibial component in one knee. Complication was a fracture of the femoral condyle during surgery in one knee.

Conclusion: These results showed that the clinical evaluations at three years were satisfactory after cemented total knee arthroplasty using YMCK prosthesis.

W100

TREATMENT OF SINOVITIS RESISTANT IN RHEUMATIC DISEASES TO OTHER THERAPIES WITH INTRAARTICULAR METOTREXATE (Mtx).

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Objective: To prove the effectiveness and security of the Mtx applied in intraarticular form in patient with sinovitis and spill to articular with previous flaw to the infiltration steroid.

Background: Mtx can any action over local production of sinovitis by several mechnism.

Methods: 40 outpatiens were included; with punction, synovial fluid was aspired. In the tird part of patient sinovial biopsy we performed. The Mtx was aplicatted to the 10 and 20% weekly up to 7-10 infiltrations. When concluding the treatment we effectued a new biopsy in the selected subjects. The protocol was approbed for our ethic comité and informed consent was signature.

Results: The 40 outpatients concluded the treatment: 24 female and 16 male; age average 27 y±12. Diagnosis were: OA (26 patients); RA 6, Spondiloartrhopathies 4 and the 4 remaining had reactive artritis. The sinovial fluid in excess disappared to the 3ª applicattion. The biopsy show decrease of the one infiltrated and edema. 5% of the patient refer to fatigue sensation to the folowing day of the application. T test show statistical significance in before and last state; using visual scale for pain, leucos count, proteins in sinovial fluid and linfocites, leucos in biopsy were decreased.

Conclusion: according to the obtained results, the Mtx in IAA aplication improves in objective form to the patients, with histologic demonstration and statistic significance according to the used methodology.

W101

ANTIBODIES ANTI-TNF ((INFLIXIMAB) + METOTREXATE IN THE TREATMENT OF RESISTANT RA. A OPEN MULTICENTRIC STUDY. D.Bañuelos-Ramírez, J. Rojas-Rodríguez, I.G. Holguín-Dorador, S. Salinas-Saldívar. Hospital de Especialidades de Puebla, Hospital ISSSTEP, Clinica de Prevención y Diagnóstico. IMSS. Puebla, Pue., México. CP 72000.

Objective: To describe the effectiveness of the Infliximab in a study open of patient with RA and resistance to the treatment combined with DMARD.
Methodology: we make an open study applying Infliximab iv at 3mg/kg for dose in weeks 0-2 and 6 and later on every 2-3 months in patient with resistant RA. Additionally oral metotrexate to weekly dose of 10mgs. The study variables were: time evolution, age, functional, anatomical state, visceral affection, flaw, complications, quality of life according to reference and HAQ, used medications. The patient were their own controls (pre and postreatment) .The final data is analyzed with paired t, X2 and descriptive statistic.
Results: 72 patients to the date the Infliximab receives, completing all the approaches. Comparing their initial mensurations with the current state lower figures is observed in holding of antibodies, not affection of leuco-linfocites figures. The visceral affection, number and dose of medications are smaller as the treatment advances and you increment the functional capacity starting from the 3era application.
Conclussion: The coadministration of Infliximab+metotrexate seems to play a favorable paper and sinergic in the treatment of the resistant RA. Even lack to value their paper in the long term.

W102

APPLYING HYDROSYLPHATE WATER BATHS IN REHABILITATION AFTER KNEE SYNOVECTOMY IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)
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Objective: To study and evaluate the effectiveness of natural hydroxylphate water baths in rehabilitation after knee synovectomy, in patients with RA.
Rationale: Hydrosylphate water baths possess anti-inflammatory factors, improving reparative processes in patients with RA.
Methods: Twenty-four patients (20 women, 4 men at the age from 20-60 years old) had treatment after knee synovectomy. With this purpose natural thermal hydrosylphate balneosource was applied with medium saturation of free H_2S (water should be 37C°). The application of hydrosylphate water baths (10-12 baths) for the courses of treatment were made in 2 months after synovectomy. Nineteen patients had seropositive and 5 patients seronegative form of RA. Seventeen patients had X-Ray I-II stage, 7 patients had X-Ray I-II stage in synovectomy joint. These patients along with balneotherapy also received nonsteroid anti-inflammatory therapy. Balneotherapy was used once a year and long-term results were observed from 1-3 years. After balneotherapy in the dynamics of these patients clinical-laboratory indicators and character of general inflammatory process were studied.
Results: The results of elaborated balneotherapy were graded with special criteria prepared by us. The frequency of acuteness, tension of the laboratory inflammatory indicators, cell and humoral immunological indicators, character of drug therapy after and before balneotherapy, were considered. Hydrosylphatic factor, possessing anti-inflammatory, immune-modulating secretor, sedative qualities considerably improved conditions of patients with knee synovectomy. Statistically, the frequency of activity of general inflammatory process was decreased. The doses and quantities of drug laboratory indicators of inflammatory process were decreased, functions of the operating joint were improved. Only 4 patients-in the nearest 4 months had acuteness of RA. Most of the patients after treatment with hydrosylphate baths had improvements in general rheumatoid arthritis and synovectomy knee joint.
Conclusion: Our research performed the right choice of tactics; hydrosylphate water baths are good additional treatment factors for rehabilitation of the patients after surgery. Most likely, general desensitizing effect of the synovectomy of large joints such as knee joint with extracting of damaged tissues, combining with anti-inflammatory effects of balneofactors, perform considerable treatment influence on patients with RA.

W103

A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO EVALUATE THE SAFETY AND PRELIMINARY CLINICAL ACTIVITY OF MULTIPLE DOSES OF CTLA4Ig AND LEA29Y ADMINISTERED INTRAVENOUSLY TO SUBJECTS WITH RHEUMATOID ARTHRITIS. P. Emery, L. Moreland, R. Alten, M. Leon, T. Appelboom, V. Manna, K. Natarajan, D. Hagerty, I. Nuamah, S. Carr, L. Prince, R. Cohen and J. Becker. Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08540

Objective: CTLA4Ig and LEA29Y bind to B7 receptors on antigen presenting cells, thereby preventing T-cell proliferation and cytokine production. This study assessed the safety and preliminary efficacy of these medications in subjects with rheumatoid arthritis.

Method: CTLA4Ig, LEA29Y (0.5, 2, or 10 mg/kg doses) or placebo were administered intravenously to 214 subjects (25-32 per treatment group). Subjects received four infusions of study medication on days 1, 15, 29, and 57 and were evaluated on day 85. The primary endpoint was the proportion of subjects meeting the ACR20 criteria. All subjects were monitored for peri-infusional adverse events and global safety. Subjects at baseline had a mean disease duration of 3.4(±2.0) years and had failed at least one DMARD. Stable NSAIDS or steroids (≤10mg/day) were permitted and concomitant DMARDS were prohibited.

Results: CTLA4Ig and LEA29Y were generally well-tolerated at all dose-levels. Peri-infusional adverse events were similar across all dose groups with the exception of headaches. ACR20 responses on day 85 increased dose-dependently 23%, 44%, 53% in CTLA4Ig-treated subjects, and 34%, 45%, 61% in LEA29Y-treated subjects at 0.5, 2.0, 10 mg/kg, respectively -- vs 31% for placebo. The incidence of discontinuations due to RA flares for the CTLA4Ig-treated subjects was 19%, 12%, and 9% at 0.5, 2, and 10 mg/kg, respectively; and 3%, 3%, and 6% for LEA29Y-treated subjects at 0.5, 2, and 10 mg/kg, respectively -- vs 31% for the placebo group. Mean % change from baseline for IL-2R and CRP levels were dose-dependent in both treatment groups (IL-2R: -2%, -10%, -22% for CTLA4Ig and -4%, -18%, -32% for LEA29Y at 0.5, 2, and 10 mg/kg, respectively -- vs +3% for placebo; CRP: +12%, -15 %, -32% for CTLA4Ig and +47%, -33%, -47% for LEA29Y-- vs +20% for placebo at 0.5, 2, & 10 mg/kg, respectively).

Conclusion: CTLA4Ig and LEA29Y were well-tolerated and demonstrated clinical activity in patients with RA.

W104

A LONG-TERM, OPEN-LABEL TRIAL OF THE SAFETY AND EFFICACY OF ETANERCEPT (25 MG TWICE WEEKLY) IN PATIENTS WITH RHEUMATOID ARTHRITIS (INTERIM ANALYSIS).
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Background: Several double-blind, placebo-controlled studies previously demonstrated that etanercept was safe and efficacious in treating rheumatoid arthritis (RA) patients who had an inadequate response to disease-modifying antirheumatic drugs (DMARDs).
Objective: To evaluate the long-term safety and efficacy of etanercept in patients who completed prior double-blind clinical studies comparing etanercept to placebo.
Methods: As reported in previous updates, 549 patients entered this 4-year, open-label study and began treatment with etanercept 25 mg twice weekly at 58 centers in Europe following completion of double-blind clinical studies. All patients previously had inadequate responses to DMARDs. Safety assessments were performed at regular intervals to determine the incidence of treatment emergent adverse events including malignancies and serious infections (those associated with hospitalisation and/or the administration of intravenous antibiotics). The numbers of painful and swollen joints were predefined as primary efficacy endpoints; other efficacy measures included ACR response rates and acute phase reactants. Efficacy was analyzed with the last observation carried forward (LOCF).
Results: Of the 549 patients initially enrolled, 437 (80%) are currently active, 479 (87%) completed 1 year, and 94 (17%) completed 2 years. A total exposure of 927 patient-years has been accrued. The rate of withdrawal from the study was similar for efficacy- and tolerance-related reasons (7% and 8%, respectively). Adjusted for patient exposure, the most frequent adverse events were injection site reactions and upper respiratory infections. Rates of serious infections and malignancies have remained unchanged over the course of the study. Maintained efficacy was observed as demonstrated by a mean 71% and 72% reduction in painful and swollen joint counts, respectively. Similar to results measured at the early timepoints of this open-label trial, ACR 20, 50, and 70 response rates were determined to be 79%, 47%, and 25%, respectively, as patients approached two years of treatment.
Conclusion: Following the accumulation of substantial exposure in patients with RA, etanercept demonstrates an acceptable safety profile and continues to provide significant and maintained clinical benefit.

W105

TEN YEARS FOLLOW UP OF RHEUMATOID ARTHRITIS PATIENTS IN INDONESIA, TREATED WITH AGGRESSIVE IMMUNOSUPPRESSIVE COMBINATION THERAPY.

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Objective. To describe the course of disease and outcome of 3 groups of patients with Rheumatoid Factor Positive Rheumatoid Arthritis with different disease duration at the start of the study.

Materials and Methods. Group I, II, and III comprised 87, 12, and 89 consecutive subjects with disease duration at presentation of less than 4 months, 4-24 months, and 25-135 months respectively. Group I had a mean age of 28± 4.7 standard deviation (SD), Group II of 29 ± 6.3 SD, and Group III of 29±3.7 SD years. The male to female ratio was 1:3 in all groups. All Rheumatoid Factor Positive Rheumatoid Arthritis patients were treated with combinations of low dose pulse intravenous Methylprednisolone + Methotrexate + Cyclophosphamide and oral Cyclosporine A and the last three years also Mycophenolate mofetil in a prospective study. The World Health Organization - International League of Associations for Rheumatology (WHO-ILAR) RA outcome criteria were applied in a completed 10-years observation in cases, dropouts, and withdrawals.

Results. In Group I 88.5% and in Group II 31.2% of patients achieved treatment-free control during a cumulative treatment period of mean 21±1.9 SD and 87±3.1 SD months, while the rest obtained control under maintenance therapy. In the cases under control progression of destruction as seen on x-ray was prevented, while it developed in the dropouts and withdrawals. Of the withdrawals 6 could be traced as well as 21 of the dropouts. Long-term adverse effects were substantial in the dropouts and withdrawals, ascribe to selfmedication with NSAID's and prednisone.

Conclusion. The majority of patients with Rheumatoid Factor Positive Rheumatoid Arthritis with a disease course of < 4 months without or with grade I erosions acquired treatment-free control by therapy with a combination of 4-5 immunosuppressants.

W106

THE EFFECT OF COMBINED DRUG TREATMENT USING CHLOROQUINE AND METHOTREXATE ON THE STATUS OF ANTIOXIDANT CAPACITY OF PLASMA IN RHEUMATOID ARTHRITIS.

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INTRODUCTION: Oxygen free radicals that are generated mainly through the phagocytic activity of the polymorphonuclear leucocytes have been implicated as mediators of tissue damage in patients with rheumatoid arthritis (RA). Accordingly low levels of antioxidants, which increase free radical activity, are clearly associated with an increased risk of RA.

METHODS: Of 24 patients who entered the study 14 patients were excluded because they failed regular follow up. The analysis was done on 10 patients who fulfilled the ACR criteria for RA. They were all on chloroquine and methotrexate plus low dose prednisolon. The patients were evaluated at zero, 6, and 12 months. The clinical (general symptom, morning stiffness, index of swelling, pain and limitation of joints) and laboratory (ESR, RF, CRP, CBC, endogenous antioxidant such as lipid profile, uric acid, bilirubin, plasma ceruloplasmin) finding and the status of antioxidant capacity of plasma by FRAP were evaluated at each control.

RESULTS: The mean age of onset of RA in our patients was 36.8± 8.20. The mean age at the beginning of combination therapy was 41.8± 8.94. Reduction of morning stiffness and improvement of general symptoms were statically significant after 6 months ($p< 0.021$). Index of swollen, painful and limited joints were decrease after 12 months of the initiation of combined therapy ($p<0.002$). The effect of combined therapy on laboratory tests was statistically significant only for ESR ($p<0.05$). Combined treatment had not any results on endogenous antioxidant except for high-density lipoprotein (HDL). The increase of HDL was statistically significant after 6 and 12 months.The level of cereloplasmin did not change during the treatment. Antioxidant status of plasma increased after the initiation of combination therapy but it was not statistically significant. Its maximum level was 682.6 mmol/lit after 6 months.

CONCLUSION: Although combination therapy had good results on clinical symptoms, it had no effect on the status of antioxidant capacity of plasma in RA.

W107

THE EFFECTIVENESS OF WOBENZYM AS THE BASIC TREATMENT OF THE RHEUMATOID ARTHRITIS

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Objective: To study the effectiveness of Wobenzym (Mucos Pharma) – a drug of sistemic enzymotherapy used as basic treatment of seropozitive RA.

The target: To demonstrate in a comparative study the effectiveness of Wobenzym as the basic treatment of RA.

Methods: This study consists of 30 patients (3 males, 27 females) with seropositive rheumatoid arthritis with mild evolution and minimal activity that were divided in 2 series. The first sery consisted of 15 patients that took Wobenzym according to the following program: 7 tablets 3 times per day 10 days, 5 tablets 3 times per day 10 days, 3 tablets 3 times per day 10 days tablets 3 times per day day till 12 monthes. The second sery consisted of 15 patients and were treated with Methotrexat 5mg one time per week 12 months. The effectiveness of the treatment was evaluated by clinic methods (intensity of the pain, duration of the morning stiffnes, the number of affected joints, the force of the hand), laboratory methods evaluated eache 3 months, radiology, schintigraphy.

Results: After the treatment in both series were noted the duration of morning stiffness (-68,7±8,6 and –70,3±6,9),Ritchie Articular Index(-8±2,3 and -7±3,1) and were changes in the laboratory tests such as the diminuation of ESR (-13,2±0,3; -15,1±0,2), rheumatoid factor (-8,7±0,7 and –6,9±0,5) but in the first sery the chages were less and in a longer period of time in comparation with the second sery. During the treatment with Wobenzym were not found any intolerations, side effects and complications.

Conclusion: The Wobenzym is of benefic effect in the long treatment of rheumatoid arthritis, has a good toleration and can be used as basic treatment of rheumatoid arthritis with mild activity.

W108

CEMENTLESS TOTAL HIP ARTHROPLASTY WITH MORSELIZED BONE GRAFTING IN PROTRUSIO ACETABULI OF RHEUMATOID ARTHRITIS

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Objective: To assess the outcome of cementless total hip arthroplasty (THA) in rheumatic patient with respect to the acetabular grafted morselized bones.

Rationale: Impaction morselized bone grafting is useful method for the treatment of acetabular large bone defect during revision THA.

Methods: Sixty-one THA procedures were performed from 1988 in 50 rheumatic patients with severe protruded acetabulum. Follow up period range 5 to 11 years with an average of 8 years 5 months. A Mollory/Head prosthesis with porous coated socket was used in 43 hips and other types in 18 hips. In all cases, autogenous morselized bones were packed into the acetabulum.

Results: The clinical improvement in pain was the most apparent. X-ray findings of the grafted bone in the acetabulum showed a homogenous pattern in most cases (90.2%) at 6 months. A radiolucent zone appeared in 20 hips (32.7%) at a non-weight-bearing zone between the grafted bone and socket up to 3 years. This clear zone tended to gradually disappear and changed to sclerotic zone. Collapse or absorption of the grafted bone was observed in 3 hips in more osteoporotic or active disease cases.

Conclusion: THA in which the morselized bones are packed into the acetabulum and a porous coated socket is used is a simple and useful procedure for treating rheumatic protruded acetabulum.

W109

THE EFFECT OF ACTIVITY AND TYPE OF RHEUMATOID ARTHRITIS ON THE FLEXIBLE IMPLANT ARTHROPLASTY OF THE METACARPOPHALANGEAL JOINT.

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Objective: To investigate the influence of systemic factors on the clinical and radiological results of the flexible implant arthroplasty of the metacarpophalangeal (MP) joint.

Methods: A retrospective study was performed on 184 Swanson flexible implant arthroplasties of the MP joint in 76 hands with rheumatoid arthritis (RA). The factors included the mean postoperative serum C-reactive protein (CRP) level (<2.0mg/dl: n=76, ≧2.0mg/dl: n=108) and the type of RA (the mutilating type: n=17, the non-mutilating type: n=167), and the mean follow-up period was 5.9 years.

Results: The mean CRP level was found to affect postoperative pain, and in the mutilating type, the clinical and radiological results were inferior to those in the non-mutilating type, in regard to postoperative pain, extension lag, subsidence of the implant, and revision rate.

Conclusions: Maintaining the patients under low disease activity and in the non-mutilating type is important to maintain favorable results in flexible implant arthroplasty of the MP joint. The operation is indicated in patients who are well informed, highly motivated and cooperative with the medical treatment required for RA.

W110

EFFECTIVE AND APPARENTLY SAFE LONG-TERM PREDNISONE IN 94% OF PATIENTS WITH RHEUMATOID ARTHRITIS, USING DOSES OF ≤5MG IN MOST PATIENTS.

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Objective: To analyze results of long-term low-dose prednisone in 102 patients with rheumatoid arthritis (RA) seen in a weekly academic clinic from 1982 to 1999, with a mean starting dose of 4.3 mg/day.

Rationale: Corticosteroids may be disease-modifying and have low levels of toxicities over long-periods if used in does of 5mg or less.

Methods: 102 consecutive patients in 1999 were analyzed for drugs taken, changes on a multidimensional health assessment questionnaire (MDHAQ) over 0.1-17 years, and possible toxicities of corticosteroids.

Results: 96 of the 102 patients (94%) were taking low dose prednisone over a median of 6.1 consecutive years; 94% were also taking disease-modifying antirheumatic drugs (86% methotrexate). The mean starting dose in 74 patients begun at this clinic was 4.3 mg/day (median 5mg), compared to 13.1 (median 10mg) in 22 patients begun elsewhere. At the most recent visit, 76% were taking ≤ 5 mg/day, 55% ≤4, 46% ≤3, and 4 11-20 mg/day. MDHAQ scores were improved >0.25 units from baseline in 40% of patients, unchanged in 39%, and worse by 0.25 units in 21%. The prevalence of hypertension was 32%, diabetes mellitus - 4%, cataracts - 20%, similar to published reports of patients with RA.

Conclusion: Long-term low-dose prednisone with a starting and maintenance dose of <5mg/day may be a safe therapy in RA, in contrast to high-dose prednisone, although further studies are needed to characterize risks and benefits of long-term corticosteroids.

W111

FOLINIC ACID SUPPLEMENTATION REVERSES MACROCYTOSIS WITHOUT ALTERING EFFICACY OF METHOTREXATE IN PATIENTS WITH ARTHRITIS.

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Objective: To determine if daily folinic acid supplementation reverses macrocytosis noted in some patients with arthritis treated with low dose methotrexate (MTX) and folic acid (FA) and if it alters the disease modifying activity of this drug.
Rationale: Methotrexate is known to cause folate deficiency, which in turn increases drug toxicity. Macrocytosis is a clue to folate depletion.
Method: Patients included 20 women and 8 men. Twenty-four had rheumatoid arthritis and 4 had psoriatic arthritis (PsA). All were treated with MTX between 5-15mg weekly, FA 2mg daily and a nonsteriodal anti-inflammatory drug. Macrocytosis developed in 23 patients after being on MTX and FA for 3-4 years. Two patients reversed their macrocytosis when their FA dose was increased to 3mg. For the other 21 patients the FA was replaced with 5mg of folinic acid daily.
Result: Patients were followed for 3-7 years. Of the 21 patients on folinic acid supplementation 20 (95%) had a reversal of their macrocytosis in 12-15 months. The 1 non-respondent had active PsA. When the folinic acid was stopped, macrocytosis recurred in 2 – 3 years in 5 patients and responded to another course of folinic acid. Eight patients who had active disease from the onset continued to have active disease and 6 were subsequently given etanercept injections. The remaining 13 patients continued to show improvement of all parameters of disease activity.
Conclusion: These observations suggest that reversal of macrocytosis can be accomplished with 5mg of folinic acid daily without diminishing the effectiveness of low dose MTX in patients with arthritis.

W112

MORE THAN 15 YEARS FOLLOW-UP STUDY OF KINEMATIC TOTAL KNEE ARTHROPLASTIES FOR THE RHEUMATOID PATIENTS.

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Objective: To evaluate the long term results of Kinematic total knee arthroplasties in the patients with rheumatoid arthritis.

Methods: We evaluated 22 rheumatoid knees of 15 patients following over 15 years of total knee arthroplasty without patellar replacement. Fourteen patients were women. Fifteen knees were replaced with anteriorly joined type and seven knees were replaced with posterior cruciate retention type of the Kinematic prosthesis. The average age at surgery was 48.8 years (range, 39 to 62). The average follow-up periods was 16.1 years (range, 15 to 18). Knee functions were evaluated according to the criteria of the Japanese Orthopaedic Association (JOA score). Standing FTA (femoro-tibial angle) and clear zone were measured on roentgenograms.

Results: The average range of motion was 26.8°–107.1° preoperatively and 4.2°–102.9° postoperatively. The mean total JOA score was 38.9 preoperatively and 80.1 postoperatively. The total scores improved from none of excellent (100-90 points) cases preoperatively to 3 of excellent cases postoperatively; none of good (89-70 points) cases preoperatively to 16 of excellent cases postoperatively. The pain score was improved a mean of 19.1 preoperatively to a mean of 36.8 postoperatively. The patella was resurfaced in 6 knees. Standing FTA was improved from 164° to 175.1°. Radiolucent line (>2mm) was observed in one knee.

Conclusion: The results suggested that knee function was well maintained over 15 years of surgery.

W113

THE EFFECT OF INTRAARTICULAR METHOTREXATE OF INTERLEUKIN 8 SYNTHESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Methods: 5 patients with definite rheumatoid arthritis and knee effusions under the constant doses of DMARD were treated up 6 i.a. injections of 10 mg MTX every week for 13 weeks. The control group with 5 patients who received a single i.a., injection of 40 mg triamcinolone hexacetonide (TC) was monitored according to the same protocol.

Results: The intraarticular granulocyte counts and IL-8 levels decreases in MTX treated patients on day 10-13 and stayed low in those patients who could be re-evaluated after 13 weeks. The other tested cytokine levels (like IL1, IL2, TNF Alpha, etc.) showed only minor changes on day 10-13. The other control group was no need for re-injection in the TC-group during 13 week study phase.

Conclusion: Our data confirm that interleukin 8 is an independent parameter of serological, clinical and radiological findings by time course observation during the i.a. MTX therapy. However in our study the decrease of interleukin 8 levels did not seem to be associated with an improvement of the knee measured by clinical parameters.

W114

LONG-TERM USE OF ENBREL® (ETANERCEPT) IN PATIENTS WITH DMARD-REFRACTORY RHEUMATOID ARTHRITIS

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Background: Results from an ongoing long-term safety trial of ENBREL as monotherapy in adults with RA who had failed at least 1 DMARD have been reported. This report summarizes safety and efficacy in 628 patients treated for up to 4.3 years (median = 2.4 years) for a total of 1336 patient-years.

Methods: Efficacy was evaluated using ACR criteria. Adverse event rates were compared with data from controlled studies.

Results: Of the 628 adult RA patients, 479 have received ENBREL monotherapy for over 1 year, 420 for over 2 years, 164 for over 3 years, and 12 for over 4 years. Response has been sustained for the duration of therapy. At baseline, the median tender and swollen joint counts were 31 and 25, respectively. At 3.5 years, the median tender and swollen joint counts were 3 each. ACR 20, ACR 50, and ACR 70 response rates were 69%, 50%, and 25%, respectively. Also at 3.5 years, 24% of patients had zero tender joints, 26% had zero swollen joints, and 15% had disability scores of zero. 59% have decreased steroid doses (by a mean of 71%); 29% have discontinued steroids. Only 5% have increased steroid doses. Compared to controlled trials, no significant differences in rate or type of adverse events occurred in patients treated long-term with ENBREL. In open-label studies of RA patients receiving ENBREL, serious adverse events occurred at a rate of 0.13 per patient-year, compared to 0.13 in ENBREL-treated patients and 0.20 in placebo patients. Serious infections occurred at a rate of 0.05 per patient-year in open-label trials, compared to 0.04 in ENBREL patients and 0.05 in placebo patients in controlled studies. No opportunistic infections have been observed. The number of malignancies in ENBREL patients was similar to that predicted using the National Cancer Institute SEER database (9 reported vs. 12.7 expected).

Conclusion: ENBREL as monotherapy continues to be safe and effective in patients with DMARD-refractory RA for over 4 years.

W115

CLINICAL AND RADIOLOGICAL OUTCOME AFTER LONG-TERM TREATMENT FOR RHEUMATOID ARTHRITIS: COMPARISON BETWEEN 5-YEAR PERIODS IN 1980'S AND 1990'S.

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Objective: To investigate probable superiority of more recent treatment for RA during 1990's over that during 1980's. Methods: 405 RA patients were divided into 18 men with 178 women who received treatment for 5 years from the first clinical visits between 1980 and 1984 (Group 80's), and 30 men 179 women who were treated for 5 years from the first visits between 1990 and 1994 (Group 90's). There was no significant difference of age or mean duration of RA, between the two Groups. Difference were investigated between the Groups as for administered DMARDs, the disease progression in terms of Stage (Stinbrocker) of wrist-carpal X ray, along with several other parameters of disease activity changes and the rate of cases who underwent orthopedic operations during 5 years designed for each Group. Results: Stage IV wrist-carpal X-ray was more often found among those from Group 80's (106/196 vs. 89/209, $p<0.005$). Tiopronin (49/196 vs. 5/209, $p<0.0001$), gold sodium thiomalate (29/196 vs. 12/209, $p<0.005$), or D-penicillamine (22/196 vs. 11/209, $p<0.05$) was DMARD used predominantly among Group 80's. On the other hand, MTX (8/196 vs. 47/209, $p<0.0001$), SASP (9/196 vs. 38/209, $p<0.0001$), or bucillamine (11/196 vs. 57/209, $p<0.0001$) was more frequently employed for Group 90's than for Group 80's patients. There was no significant difference between the Groups, as for other parameters. Conclusion: The more recent and surmisably more potent DMARDs seem to have brought quite small beneficial addition, suggested from the less severe wrist-carpal X-ray changes among Group 90's patients, for inhibiting the disease progression of RA. More effective anti-rheumatic agents or therapeutic regimens should be sought for.

W116

PREVENTING EFFECT OF ORAL TYPE2 COLLAGEN TREATMENT ON CARTILAGE DISTRACTION IN MRL/l MICE.

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Objective: To evaluate the preventing effect of oral type2 collagen (C2) treatment on cartilage/bone distraction in murine model of rheumatoid arthritis (RA) and to determine whether low dose or high dose is more effective.

Methods: Forty of 6 week-age MRL/l male mice were divided in 4 groups. Treated with oral bovine C2 at 80 μ g/day in 1% citric acid, 20 μ g/day, 5 μ g/day or with placebo (1% citric acid only) for 12 weeks. At 18th week, knee joints were histopathologically examined. The degree of changes on synovium, cartilage, bone and artery were scored at each joint.

Results: Significant improvements are observed in pannus formation ($p<0.05$), replacement of bone and cartilage with connective tissues, edema under synovial tissues, and formation of multiple layer with synovial cells ($p<0.01$) between highest dosage of C2 and placebo.

Conclusion: In spontaneous arthritis murine model (MRL/l), cartilage and bone distraction are prevented by high dosage of oral C2 treatment.

W117

OPEN-LABEL EVALUATION OF THE EFFICACY AND SAFETY OF ETANERCEPT IN COMMON RHEUMATOLOGY USAGE.

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Objective: Etanercept, a dimeric fusion protein of two p75/sTNFR molecules linked to the Fc portion of IgG_1, is approved in Europe for reducing signs and symptoms of moderate to severe RA or for treating active RA in adults where DMARDs are insufficient. The objective was to assess the clinical efficacy and safety of etanercept 25 mg administered twice-weekly for 16 wks in patients with active RA for whom DMARD therapy is insufficient or inappropriate, in a naturalistic setting.

Methods: Data are presented for males and females from Austria or Portugal who received a twice-weekly subcutaneous injection of etanercept 25 mg for 16 wks (N=85). Patients could receive concomitant methotrexate but not other DMARDs, cytotoxic drugs, or opioid analgesics. The primary efficacy endpoint was the proportion of patients achieving a 20% improvement in symptoms according to the ACR response criteria at 16 wks.

Results: Preliminary data indicate that 81% of patients achieved a 20% improvement at 16 wks (median response time: 57 d). Furthermore, 49% and 10% of patients achieved a 50% and 70% improvement, respectively (50% response median time: 109 d). There was a clinically significant improvement (-0.65 units) in patient assessment of physical function (HAQ) at 16 wks. 56% of patients reported a total of 347 AEs. Of patients with a probably- or definitely-related AE (32%), the AE was usually (63% of patients) an injection site reaction, most of which were mild.

Conclusions: Preliminary data from a less restrictive setting than previously evaluated suggest that etanercept is at least as efficacious and well tolerated in Austrian and Portuguese RA patients, for whom DMARDs are insufficient or inappropriate, as was previously reported for US and EU controlled clinical trials.

W118

COMBINATION THERAPY OF LEFLUNOMIDE (LEF) & METHOTREXATE (MTX) IS EFFECTIVE & WELL TOLERATED IN RA PATIENTS INADEQUATELY RESPONDING TO MTX ALONE

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Objectives: To investigate the efficacy and tolerability of adding LEF to an existing MTX regimen on efficacy and tolerability in patients with active RA in a 24-week multi-center, randomized, double-blind, placebo (PLC)-controlled trial. Methods: Patients with active RA receiving MTX (15–20mg/week) ≥ 6 months were randomized to receive LEF 100mg QD x 2 days followed by 10mg QD thereafter (n=130) or matching PLC (n=133). Mean doses of MTX were 16.7mg/week and 16.2mg/week for LEF+MTX and PLC+MTX, respectively. The primary efficacy endpoint was ACR 20 responder rate at 24 weeks. ACR 20, 50 and 70 response rates, as well as safety monitoring, were assessed every 2 weeks up to week 8, and every 4 weeks thereafter. Results: At week 24, ACR 20 responder rates were LEF+MTX = 46.2% *vs* PLC+MTX = 19.5% ($p \leq 0.0001$). The ACR 20, 50 and 70 rates using LOCF were LEF+MTX =51.5%, 26.2% and 10.0% *vs* PLC+MTX =23.3%, 6.0% and 2.3% ($p \leq 0.0001$, $p \leq 0.0001$, and $p \leq 0.02$). Reported AEs included diarrhea (LEF+MTX=25.4% *vs* PLC+MTX=13.5%), upper respiratory infections (LEF+MTX=22.3% *vs* PLC+MTX=24.1%), nausea (LEF+MTX=16.2% *vs* PLC+MTX=11.3%) and dizziness (LEF+MTX=7.7% *vs* PLC+MTX= 5.3%). Increases in LFTs of >3xULN at any time during the 24-week treatment period for ALT and AST for LEF+MTX were 3.8% and 1.5%, respectively, compared to 0.8% on both for PLC+MTX. Conclusion: LEF combined with MTX is well tolerated and confers significant therapeutic advantages in patients with active RA inadequately responding to treatment with MTX alone.

W119

COMBINATION THERAPY OF LEFLUNOMIDE (LEF) AND METHOTREXATE (MTX) IMPROVES PHYSICAL FUNCTION AN HRQOL IN RA PATIENTS INADEQUATELY RESPONDING TO MTX ALONE

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Objectives: To investigate the effects of adding LEF to an existing MTX regimen on physical function and HRQOL in active RA patients in a 24-week multi-center, randomized, double-blind placebo (PLC)-controlled trial. Methods: Patients receiving MTX (15–20mg/week) for ≥6 months were randomized to receive LEF 100mg QD x 2 days followed by 10mg QD thereafter (n=130) or matching PLC (n=133). Mean doses of MTX were 16.7mg/week and 16.2mg/week for LEF+MTX and PLC+MTX, respectively. Mean improvements from baseline in HAQ and SF-36 components were compared at week 24 for both treatment groups. Results: Mean baseline values for the disability index (DI) derived from the HAQ were LEF+MTX=1.6 *vs* PLC+MTX=1.5 (NS). At 24 weeks, mean changes from baseline in HAQ DI were LEF+MTX=-0.42 *vs* PLC+MTX=-0.09 ($p \leq 0.0001$); representing mean improvements of 29% and 5%, respectively. Mean baseline values for the physical component summary scale (PCS) derived from the SF-36 were LEF+MTX=28.4 *vs* PLC+MTX=29.0 (NS). At 24 weeks, mean changes from baseline in the PCS were LEF+MTX=6.8 *vs* PLC+MTX=0.3 ($p \leq 0.0001$); representing mean improvements of 29% and 3%, respectively. Conclusions: LEF combined with MTX provides significant improvements in physical function and HRQOL over 24 weeks in patients with active RA inadequately responding to MTX alone.

W120

EFFICACY OF AND PREDISPOSING FACTORS FOR RESPONSE TO LEFLUNOMIDE (LEF) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Objectives: To evaluate the efficacy of, and predisposing factors for response to LEF in a large multinational, open-label cohort study at week 24. Methods: Patients with active RA classified by a disease activity score (DAS >3.2) were enrolled (n=966), treated with LEF 20mg daily after 100mg for 3 days and studied at week 24 for their response status according to DAS 28, ACR 20%, 50% and 70%. In order to investigate the predisposing factors of response to LEF, patients found to be responders at week 24 were compared for their baseline data to patients that were non-responders. Results: Mean duration of previous RA was 7.5 years, with 62% of patients with disease duration >2 years. Thirty-five percent and 50% were responders at week 4 and 8, respectively, and maintained efficacy through week 24. Eleven percent of patients withdrew due to an AE and 3% due to lack of efficacy. ARA functional class 1 and RA duration >2 years were identified as predisposing factors for treatment response.

	DAS 28	ACR20%	ACR50%	ACR70%	DAS 28 ≤3.2†	DAS 28 <2.6 (remission)
Wk 24*	78	67	36	10	27	13

*% responders, † low disease activity

Conclusions: This study confirms the efficacy of LEF in patients with RA. Further evaluation may suggest the clinical relevance of the identified predisposing factors.

W121

RECOMBINANT HUMAN INTERLEUKIN-1 RECEPTOR ANTAGONIST REDUCES RADIOLOGIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A MULTICENTER, DOUBLE-BLIND, DOSE-RANGING, RANDOMIZED AND PLACEBO CONTROLLED STUDY

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Objective: To evaluate radiographic progression and the relation between the Genant and Larsen radiologic scoring methods in a clinical trial of recombinant human interleukin-1 receptor antagonist (IL-1ra).

Methods: Patients with rheumatoid arthritis (RA) were randomized into 4 groups: placebo (n = 121), IL-1ra 30 mg (n = 119), 75 mg (n = 116), or 150 mg (n = 116) daily. Hand radiographs obtained at baseline, 24- and 48-week follow-up were scored using both methods.

Results: At 24-weeks, Genant scoring detected significant reduction of progression in joint space narrowing (JSN) and Total (a combination of erosion and JSN) in all treatment arms. Least squares mean changes of Genant erosion score from baseline to 24-weeks were significantly reduced after treatment with IL-1ra at 30 mg and when all dose groups were pooled. The changes corresponded to a reduction of 38% in erosion, 58% in JSN, and 47% in Total score. The Larsen erosive joint count (LEJC) showed a significant reduction at 75 mg, and all groups receiving doses combined together showed a 45% reduction. Correlations between Genant Total and Larsen score were 0.84 for baseline, 0.83 for week 24, and 0.83 for week 48 ($p<0.0001$); between Genant erosion and LEJC were 0.83 ($p < 0.0001$) for all visits; between Genant Total and Larsen score were 0.32 and 0.49 ($p<0.0001$) for progression from baseline to week 24 and to week 48, respectively; between Genant erosion and LEJC were 0.36, and 0.41 ($p<0.0001$) for progression to weeks 24 and 48, respectively.

Conclusion: IL-1ra reduced RA radiologic progression. The two methods correlated strongly for scores at each individual time point, but much less strongly for disease progression.

W122

ENBREL® (ETANERCEPT) IN ADDITION TO METHOTREXATE (MTX) IN RHEUMATOID ARTHRITIS (RA): LONG-TERM OBSERVATIONS

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Background: Results have been previously presented from an ongoing, long-term trial of ENBREL as additional therapy in 79 patients with persistent RA despite treatment with MTX. Patients have now received therapy for a median of 32 months (max. 37).

Methods: Disease activity was evaluated using ACR criteria. Adverse events were compared with data from a previous controlled study.

Results: Of 79 patients who entered this long-term trial, 9 have withdrawn: 3 for lack of efficacy, 2 for adverse events, 1 prior to knee surgery, 2 who planned to conceive, and 1 who began commercial ENBREL. Compared to the initial study, no differences in the type or rate of adverse events have been observed over time. In the initial 6-month blinded study of ENBREL plus MTX, 2 of 59 patients were hospitalized for infections; in the extension study, 2 of 79 patients had a similar event. One malignancy was observed in the initial trial, compared to 2 in the extension study. Both the latter patients recovered and resumed ENBREL therapy. At baseline, the mean MTX dose was 18 mg. 54 (68%) of patients have reduced their MTX dose (by a mean of 63%) and 22 (28%) have discontinued MTX. In 45 patients initially taking corticosteroids, the mean prednisone dose was 6.3 mg. 30 (67%) patients have reduced their steroid dose (by a mean of 78%), and 19 (42%) patients have discontinued steroids. Improvement of disease activity has been sustained despite these changes in therapy. At the most recent visit, ACR 20, ACR 50, and ACR 70 responses were achieved by 69%, 51%, and 27%, respectively. Also, 19 patients had no tender joints, 10 had no swollen joints, and 12 patients had a zero HAQ score.

Conclusion: ENBREL plus MTX remains safe and well tolerated. Improvement of disease activity is sustained even with reduced or discontinued doses of MTX and/or steroids.

W123

IMPROVEMENT OF DISABILITY IN RA PATIENTS WITH EARLY VS ESTABLISHED DISEASE AFTER TREATMENT WITH ENBREL® (ETANERCEPT)

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Background: Functional health status declines and disability increases early in patients with RA, with half of affected patients developing moderate loss of functional ability within 2 years of diagnosis (Wolfe A&R 43:2751-61 2000). Early aggressive treatment may improve long-term outcomes.

Methods: We compared the improvement in Health Assessment Questionnaire (HAQ) disability scores over 2 years in 207 RA patients with early (mean duration 1 year) disease to 563 RA patients with long-standing (mean duration 12 years) disease who were treated with 25 mg ENBREL SC twice weekly. Mean baseline patient characteristics in the early vs. late groups were similar, including HAQ (1.5 vs 1.6), number of tender (31 vs 32) and swollen (24 vs 26) joints, CRP (3.3 vs 4.4 mg/dL), presence of RF (87% vs 81%), and age (51 vs 53 years). Patients with early disease had been treated with fewer DMARDS (0.5 vs 3.3).

Results: Patients with both early and late RA achieved rapid and sustained clinical responses and improvement in HAQ scores, but the magnitude of improvement in HAQ was greater in patients with early disease. At 2 years, mean HAQ scores declined from 1.5 to 0.6 in the early RA group and from 1.6 to 1.0 in patients with established disease. The proportion of patients who achieved zero HAQ scores was greater for patients with early disease (29%) compared to patients with late disease (14%) ($p<0.001$).

Conclusion: While patients with early or long-standing disease had significant improvement in disability with ENBREL therapy, patients with early disease had greater benefit. Aggressive therapy in patients with early RA has greater potential to improve disability as measured by HAQ than in patients with more established disease who have failed multiple DMARDs.

W124

ENBREL® (ETANERCEPT) VS. METHOTREXATE (MTX) IN EARLY RHEUMATOID ARTHRITIS (ERA TRIAL): TWO-YEAR FOLLOW-UP.

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Background: The first year of this 2-year study of patients with early erosive RA (mean disease duration 1 year) demonstrated that ENBREL 25 mg twice weekly gave a more rapid clinical response and was more effective in preventing erosions than high dose (median 20 mg/wk) oral MTX (Bathon NEJM 343:1586-93 2000).

Methods: Patients continued to receive open-label therapy with the treatment to which they had been randomized after the study was unblinded (at a mean of 17.3 months). The 2-year endpoints were ACR responses (using last on-drug observation carried forward) and change in Sharp score. Readers were blinded to treatment and chronological order of the x-rays.

Results: 154 of 207 patients (74%) who received ENBREL 25 mg completed 2 years of treatment, compared to 129 of 217 patients (59%) who received MTX. Twice as many patients (12%) discontinued MTX for adverse events as did those taking ENBREL. The ACR 20 response at 2 years was 72% in those randomized to ENBREL and 59% in those randomized to MTX ($p = 0.005$). ENBREL 25 mg was superior to MTX in arresting radiographic progression. Mean (median) changes in total Sharp score were 1.3 (0) and 3.2 (0.5) units in the ENBREL 25 mg and MTX groups, respectively ($p = 0.001$), and changes in erosion score were 0.7 (0) and 1.9 (0) units, respectively ($p = 0.001$). Radiographic progression was prevented in 63% of ENBREL 25 mg patients compared to 51% of MTX patients ($p = 0.017$). Significantly more ENBREL 25 mg patients than MTX patients had a meaningful (≥ 0.5 units) improvement from baseline in HAQ disability score. ENBREL was well tolerated and rates of adverse events were similar to that seen with MTX.

Conclusion: Over 2 years ENBREL was superior to MTX in reducing disease activity and inhibiting radiographic progression.

W125

ACETABULAR RECONSTRUCTION OF RHEUMATOID HIP USING AUTOGRAFT OF FEMORAL HEAD IN CEMENTLESS TOTAL HIP ARTHROPLASTY.
— MORE THAN 5 YEARS FOLLOW-UP RESULTS

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Objective: To report the more than 5 years follow-up results of cementless total hip arthroplasty (THA) with the autograft of block bone using femoral head resected at surgery.

Patients and Methods: Acetabular reconstruction using autograft of block bone was performed in 24 hips of 16 rheumatoid patients from 1988 to 1995. Average age at surgery was 48 years (23-66yrs). All patients were ladies (right hip: 11, left hip: 13). Femoral head was grasped by Allo-grip, shaped using acetabular reamer of which size was same as that of artificial cup and fixed with cup by several screws simultaneously.

Results: The grafted bones were incorporated to the acetabulum in all hips except one which was revised using resected femoral head of opposite hip. Post-operative JOA hip score was improved in all cases by 42 points by average. The width of reconstructed acetabulum at one year after surgery was maintained at the follow-up. Clear zone surrounding cup was found in 8 hips, however less than 1mm.

Conclusion: Reconstruction of thin acetabulum using autograft of block bone using femoral head is useful for rheumatoid hip at cementless THA.

W126

FOREFOOT RECONSTRUCTION FOR RHEUMATOID PATIENTS BY METATARSAL OBLIQUE OSTEOTOMY

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Objective: Since 1998, we have been performing metatarsal oblique osteotomy for rheumatoid patients with forefoot deformities. The purpose of this study is to evaluate our patients treated by this procedure.
Patients and Methods: Between 1998 and 2000, we performed 26 forefoot reconstructions for 15 patients. In lateral toes, an oblique osteotomy was performed at the metatarsal neck, starting proximally on the dorsum and proceeding distally and plantarward at an angle of 45 degrees, and resected five to ten millimeters in width. Then the dislocated base of the proximal phalanx was corrected. After this procedure, the osteotomized bones were transfixed longitudinally by Kirschner wires from the distal phalanx to the metatarsal base.
Results: All 15 patients were women, whose mean age at the operation was 60.4 years (range, 45-74). The mean duration from onset of rheumatoid arthritis to operation was 18.1 years (7-36). Patients were followed for 3 to 25 months (mean, 13.1). Among the 26 feet, 19 underwent arthroplasty with a Swanson implant in the metatarsophalangeal joints of the great toe, and Mitchell's osteotomy was performed on the remaining 7 feet. All patients had reduced pain, callosity and deformity. Overall results were classified as excellent in 22 feet and good in 4 feet by our grading system.
Conclusion: In the current study, almost all of our patients had no pain in the operated feet at the time of their last followup. Because of the improvement in pain, deformities, function and cosmetic appearance, patient satisfaction was very high.

W127

TRIALS OF SUPPRESSION THE PROGRESSING OF RHEUMATOID ARTHRITIS BY INTRAARTICULAR SYNOVIAL MEMBRANE INACTIVATION.

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Objective: To elaborate local more selective intraarticular (i/a) procedures for interruption at main target areas immune-driven inflammation and to prevent progressing of rheumatoid arthritis (RA) and early appearance of joint destructions resulting severe disability.

Rationale: Local i/a procedures investigated (artifical lubricants, laser, chemical, electromagnetic and combined influences) inhibit aggressive course in RA, supress chronic inflammation in the joints.

Methods: For experimental i/a therapy immune synovitis was reproduced in 60 rabbits by immunisation with extract of active, RF positive RA patients. Artificial lubricants (AL) elaborated from polyvinylpyrrolidone solutions. 250 RA patients received different i/a procedures (i/a AL, laser, electrotherapy, light, chemical synovectomy, gas therapy).

Results: After i/a AL 4-6 injections into affected joints an impprovement in many value of joint function and laboratory indices has been revealed, including normalising of permeability of the synovial membrane, suppression of RF, elimination of metabolites. More effectives was combined i/a procedures: light synoviophotocytolisis after porphyrins i/a and following red laser (630 nm) irradiation, chemical synovectomy and i/a gas mixtures use.

Conclusion: Preliminary data suggests that i/a combined procedures in RA may possess suppression of progressing and preventing early destruction in the joints.

W128

EFFECTS OF TRIPTOLIDE, AN ACTIVE INGREDIENT OF TRYPTERYGIUM WILFORDII HOOK F (THUNDER GOD VINE, A TRADITIONAL CHINESE HERB), ON RHEUMATOID SYNOVIAL FIBROBLAST FUNCTION.

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Background and Purpose: Triptolide (Tr) is an active ingredient of a Chinese herb, Trypterygium Wilfordii hook f also known as Thunder God Vine, that is widely used in China as an anti-rheumatic drug. We have previously shown Tr has suppressive (at concentrations >7.5 nM) as well as cytotoxic effects (at concentrations >20 nM) on peripheral immune cells. In this study, we investigated the effects of Tr on the growth, survival and interleukin (IL)-6 production of rheumatoid fibroblast-like synoviocytes (FLSs).
Methods: Synovial tissues were obtained from rheumatoid arthritis patients at the time of synovectomy or total knee replacement. Tr, at various concentrations, were added. FLSs proliferation was determined by crystal violet staining. Survival of FLSs was determined using the MTT assay. IL-1β (1ng/ml) was used to stimulate IL-6 synthesis of FLSs. The supernatant was removed at the end of day 2 and the concentration of IL-6 in the supernatant was measured by ELISA.
Results: Tr caused a dose dependent inhibition of rheumatoid FLS proliferation (IC50 = 30 nM). Tr, at concentrations above 1 nM, produced a dose dependent inhibitory effect on IL-1β induced synthesis of IL-6 by rheumatoid FLSs. The IC50 for inhibition of IL-6 synthesis was 5 nM. The above effects did not appear to be mediated through cell killing as no demonstrable cytotoxicity of Tr on rheumatoid FLSs was observed at concentrations below 75 nM.
Conclusions: This study further confirmed that Tr has potential therapeutic values on rheumatoid arthritis with direct effects on FLS function. Further studies will focus on the mechanism of action of Tr e.g. its effects on the signal transduction pathway of IL-6 synthesis.

W129

HOW IMPORTANT IS FLARE IN THE DESIGN OF NSAID TRIALS IN THE TREATMENT OF RHEUMATOID ARTHRITIS (RA)?

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Objective: Evaluate the relationship between response to a trial non-steroidal anti-inflammatory drug (NSAID) and the flare induced by withdrawal of a previous NSAID to assess the value of requiring patients to flare prior to initiation of therapy and the impact of how flare is defined.

Methods: A total of 894 patients were randomized and treated in a 12-week double-blind, double-dummy, parallel group trial comparing daily oral meloxicam doses of 7.5, 15 and 22.5 mg to placebo and diclofenac 75 mg twice a day. Upon discontinuation of their previous NSAID, patients were required to flare. Flare was defined in terms of worsening in at least 3 of the following: patient overall pain (POP), patient global assessment (PtGA), physician global assessment of disease activity (PhGA), painful joint count (PJ), and swollen joint count (SJ). The relationship between flare and subsequent response to therapy was evaluated by covariance and subgroup analysis. Linear covariates were assessed in analyses of models including the baseline and flare covariates, treatment, center, and second-line therapy. The study population was divided at the 'median' flare and each subgroup was analyzed separately.

Results: The extent of flare was a significant covariate, with greater flare associated with greater response. For PtGA, POP, PJ and SJ, flare was significant ($p<0.001$). For PhGA, flare was less significant due in part to 72% of patients having a flare of 1 unit (Likert scale). As the table illustrates for painful joints, flare is associated with ability to distinguish between active drug and placebo. In the subgroup of N=430 patients, differences between placebo and active drug are significant for patients with flare of more than 6 joints.

Painful Joints	Flare ≤6 joints (N=458)		Flare >6 joints (N=430)	
Treatment group	Adjusted Mean Change	p-value vs placebo	Adjusted Mean Change	p-value vs placebo
Placebo	-5.53		-6.29	
Meloxicam 7.5mg	-6.89	0.12	-8.56	0.02
Meloxicam 15 mg	-5.81	0.75	-8.66	0.01
Meloxicam 22.5 mg	-7.26	0.053	-8.51	0.02
Diclofenac 150 mg	-7.11	0.077	-9.47	0.001

Conclusions: The results of this study indicate that a rigorous definition of flare will make a trial more sensitive to the difference between placebo and active drug.

W130

Classification Criteria % Predictors for "Apparent Cure" of Classical RA (82 Patients) in an Open Case – Controlled Study (380 Patients) of Gold + MTX Versus Gold Alone Pulses T. Bitter, Lausanne University, Lausanne, Switzerland

Introduction: We have assessed and compared the effectiveness of 2 regimes of remittive therapy in rheumatoid arthritis patients: high dose gold thiopropanol (200 mg allochrysine/injection, ie. 60 mg atomic gold) alone or in combination with weekly parenteral methotrexate (20 mg).

Methods: Patients with ACR criteria positive RA presenting to the clinic between 1984 and 1994 were alternately assigned to one of the above regimes. Patients on systemic steroids were weaned off over a maxiumum of 4 months.

In order to search for predictors of outcome, 20 initial variable were available on every single patient, including late appearing nodules or ulcers. In patients improving by ACR 20%, or even 70%, injections (dosage unchanged) could be spaced to bimonthly or every 2 months.

Results: After 10 months of completely NSAID-free, pain-free remission with zero swollen, zero tender joint count and normal CRP throughout, 108 out of 320 patients could completely discontinue all DMARDS. During the 4 years of follow up 18 patients were lost, 8 experienced mild relapse. Two predictors of adverse outcome were: a) delay of DMARD therapy; b) previous steroids. "Apparent cure" (for 4 years or more off DMARDS) was seen in 82 patients.

W131

META-ANALYSIS OF ANTI TNF THERAPIES IN RHEUMATOID ARTHRITIS

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Objective: To conduct a systematic review of anti TNF therapies for rheumatoid arthritis (RA) in order to get a overview of the clinical effectiveness of these therapies.

Methods: A number of databases, Medline, Embase, Cochrane Controlled Trials register, DARE and Science Citation Index were searched for randomised controlled trials of all published anti TNF therapies till November 2000. Only fully published trials were considered for the main analysis although abstracts and longer term data from previously published trials were analysed separately. Data was abstracted independently by two reviewers who assessed the methodological quality of trials using the Jadad scale. A pooled analysis performed using the ACR 20% or Paulus 20% criteria as end points.

Results: There were 10 studies identified, dealing with either Infliximab or Etanercept; one of which is a long term follow up of a previously published trial and the other was a direct comparison with Methotrexate in early RA. The rest were of 6 months duration or less and formed the basis of our main analysis and summary relative risk (RR),defined as patients who attained a 20% response was 3.5 (CI 2.7 to 4.5). We preferred the RR to odds ratio in the absence of heterogeneity. There were no differences in the frequency of adverse events occuring in treatment and control patients.

Conclusion: This overview confirms the effectiveness of the several anti TNF agents both in the short and long term.

W132

EFFECT OF FOLIC VERSUS FOLINIC ACID SUPPLEMENTATION IN PLASMA HOMOCYSTEINE LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH METHOTREXATE

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A sensitive inverse relationship between plasma homocysteine concentration and folate status has been demonstrated. Hiperhomocysteinemia is an established independent risk factor for cardiovascular diseases. Methotrexate (MTX) is an antifolate that has been in use for the treatment of rheumatoid arthritis (RA) since the early 1980s. In the present study we investigated: 1. if homocysteine concentrations are elevated in the plasma of patients with RA treated with MTX without folate supplementation in comparison with healthy subjects and patients with RA who had never received MTX treatment. 2. the influence of folate supplementation on the plasma homocysteine concentration. **Patients and Methods:** 83 patients with a diagnosis of RA according to the ACR criteria who received low to intermediate dose MTX as the sole second-line agent for at least 6 months. No patients received supplementation with folate. 53 healthy subjects and 28 RA patients who had never received MTX treatment constituted the control groups. Patients were randomly assigned to either 5 mg/day of folic acid or 15 mg of folinic acid in a single weekly dose 24 hours after MTX administration. The plasma homocysteine and folate levels were measured before and 3 months after treatment with folate. **Results:** Patients with AR treated with MTX before folate supplementation had significantly higher homocysteine concentrations (mean 15.3 +/- 5.2 micromol/l) compared to AR patients and to healthy individuals (7.9 +/- 2.3 and 9.6 +/- 4.1 micromol/l, respectively), $p< 0.05$). After 3 month of folate treatment the median plasma homocysteine concentration in RA patients treated with MTX was significantly reduced (10.2+/-7.3 micromol/l), $p<0.05$. There was no significant difference between folic and folinic supplementation. **Conclusions:** Patients with AR treated with MTX without folate supplementation have elevated plasma homocysteine concentrations, but this is significantly reduced after administration of folate supplementation (folic or folinic acid).

W133

$ISA_{TX}247$: PHASE 1 CLINICAL TRIAL RESULTS OF THE NOVEL CALCINEURIN INHIBITOR

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$ISA_{TX}247$ is a novel calcineurin inhibitor which exhibits 3-5 fold more potency and significantly less toxicity than cyclosporine in pre-clinical studies. We report the results of a Phase 1 clinical trial in which the drug was administered to over 150 subjects.
In the single escalating dose study, the drug was administered at doses from 0.75 to 6 mg/kg with no significant adverse events noted. A proportionality was found to exist between dose, Cmax, and AUC. There was no significant change ($p<0.05$) in half-life with increasing dose.
In a multiple dose study, $ISA_{TX}247$ was administered for 7 days at 2, 4 or 6 mg/kg/d with no significant adverse events. There was no change in creatinine clearance. $ISA_{TX}247$ was rapidly absorbed following administration. Pharmacodynamic monitoring as measured by inhibition of calcineurin activity indicated a mean inhibition at peak drug concentrations of 44% at the 1mg/kg dose. This indicates that even at this dose optimal immunosuppression was obtained. There was no significant ($p<0.5$) change in the absorption of the drug between a fasting or fed state.
In summary, no significant side-effects of $ISA_{TX}247$ were noted confirming the safety of this drug for use in transplantation as well as in patients with autoimmune diseases. In addition, these trials indicate that $ISA_{TX}247$ is well absorbed. In addition, Phase 2 trials in renal transplantation, rheumatoid arthritis, and psoriasis are planned for the first half of 2001.

W134

A NOVEL CALCINEURIN INHIBITOR WITH MINIMAL RENAL TOXICITY: $ISA_{TX}247$

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$ISA_{TX}247$ is a novel calcineurin inhibitor. Acute and chronic toxicity studies have been completed in the rabbit, rat, dog, and monkey. Rabbits which received $ISA_{TX}247$ at doses of up to 15 mg/kg/d for 30 days did not exhibit any significant change in renal function as compared to controls. In contrast, rabbits which received cyclosporine (CsA) at a dose of 10 mg/kg/d experienced a 30% increase in serum creatinine. In 2 separate studies, rats received $ISA_{TX}247$ at doses up to 80 mg/kg/d for 28 days with no significant morbidity or mortality even though this dose was greater than 40-fold higher than that required for optimal immunosuppression. Rats receiving CsA had creatinine levels 1.5-fold higher than those receiving $ISA_{TX}247$. Noted in female rats was a 2-fold higher level of both ALT and Alk phos in those receiving CsA as compared to $ISA_{TX}247$. In a 13-week study in rats receiving $ISA_{TX}247$ up to doses of 25mg/kg/d also demonstrated no significant morbidity or mortality. In 14-day and 13-week studies in dogs dosed with $ISA_{TX}247$ up to 50mg/kg/d, no significant side-effects were observed. A 13 week study in the primate at doses up to 300mg/kg/d was recently completed and did not find any outward signs of toxicity.
In summary, $ISA_{TX}247$ was shown to exhibit fewer side-effects than that previously observed for CsA. This suggests that $ISA_{TX}247$ is the first selective calcineurin inhibitor with greatly reduced nephrotoxicity and may have a significant advantage over presently used immunosuppressive drugs.

W135

THE QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD UNDERWENT LOWER LIMB JOINT REPLACEMENT. 9 TO 13 YEAR FOLLOW UP STUDY.

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Objective: The purpose of the present study is to review the quality of life (QOL) of patients with rheumatoid arthritis (RA) who had underwent lower limb joint replacemnt.
Methods: The subjects were 55 patients with RA who had underwent joint replacement (hip and/or knee) at Nagoya National Hospital between January 1987 and April 1992. These patients were consisted of 4 males and 51 females, their ages at the initial operation were ranged from 43 to 82 years (58.4 years in mean),and their duration of disease were ranged from 2 to 31 years (12.4 years in mean). The QOL was evaluated using the Sickness Impact Profile (Bergner 1981) and the scores calculated at preoperative and 1year, 5 year postoperative and the last recently period (9-13 years).
Results: The scores showed a marked improvement ,primarily physical score, at 1year postoperatively compared to the preoperative level ($P<0.01$). At 5 years postoperatively as well ,the scores continued to show a significant improvement, as for physical & psychosocial scores ($P<0.01$). In last recently period (9-13 years postoperatively), 29 patients already had died. The SIP scores of 26 survivors showed a good improvement compared to the preoperative level, but worsened to the 5 years level. Particularly, independent scores (sleep & rest, eating, work, recreation & pastimes) in last period changed worsening compared to the 5 years. But the physical & psychosocial scores maintained good levels to last period postoperatively.
Conclusion: The QOL of patients with RA who had underwent lower limb joint replacement maintained better improvement compared to the preoperative one for long term in not only physical status but also psychosocial conditions.

W136

Advantages of simultaneous joint replacement

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Total endoprosthetic replacement of hip- and knee joints in patients with degenerative or inflammatory disease is a reliable treatment in orthopedic surgery since many years. Also patients with oligo- or polyarticular disease are still a problem because of several operations within repeated periods of hospitalisation. Patients who need multiple joint replacements reject surgical procedures considering long time of suffering and hospitalisation by being treated in following one step after the other. Offering simultaneous surgery in two joints is often a probate opportunity to avoid this problem. To resolve this problem we decided one stage procedure in selected cases.

Between 1.1.99 and 31.12.00 we supplied 17 patients with 2 endoprosthesis (hip or knee) in one single surgical procedure.

In 8 cases we implanted total hip replacement bilateral. 3 patients were female and 5 patients were male. The age differed between 36 an 70 years. One patient got hybridendoprostheses (Muenchner socket/MEM stem). The others got a cementless model (Fiteck socket/Weill stem). The average time of hospitalisation was 24,5 days.

In 9 cases we did total knee alloarthroplasty on both sides. 8 patients received all cemented Wallaby I knees and 1 patient received all cemented PFC knees. 6 of these patients were female and 3 patients were male. The age differed between 37 and 75 years. The average time of hospitalisation was 20,5 days.

In two cases we saw an increase of the inflammatory test results one week postoperative, which we treated with Tavanic 500 1 - 0 – 0 orally. Other complications didn't occur. All patients were able to leave the hospital with full weight bearing.

Simultaneous replacement of two joints is an approbiate procedure in patients suffering from multiple joint destructions which has a high acceptance and provides several advantages which will be discussed from different points of view.
Details of perioperative conditions compared to single joint procedures will be analysed and reported.

W137

DEPOT CORTICOSTEROIDS IN THE TREATMENT OF RHEUMATOID ARTHRITIS (RA)

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Objective: As we reported earlier, since 1995 depot corticosteroid Diprophos® (DPH, mixture of two betamethasone esters – dipropionate and phosphate: 5mg + 2mg in one ml) have been used as bridging therapy of RA until therapeutic efficacy of prescribed DMARDS would be expressed. The aim of study was to evaluate therapeutic and adverse effects of this way corticosteroid administration.
Rationale: Delayed effects of DMARDS demand use of potent anti-inflammatory agents, almost always corticosteroids, whose continuos administration is associated and often limited by severe side effects.
Methods: We have followed up 185 patients (f:m=2.8:1) from the RA diagnosis establishment. All od them fulfilled ACR criteria for RA and RF seropositivity was obtained in 124 (67%) patients. 23%, 56% and 21% of patients belonged to 1, 2 or 3 functional and radiographic stadium of disease, respectively. Combined therapy with methotrexate (MTX) and chlorochine (CC) was started in 47 patients, with MTX and sulfasalazine (SS) in 36, while 38, 41 and 23 patients received monotherapy with MTX, CC and SS. At all of patients DPH have been administered in 3-5 weeks periodic intervals as one i.m. injection during 6-12 months.
Results: Permanent clinical and biochumoral remission and slow radiographic progression of disease were achieved in 91% (168/185) of patients. This way of systemic corticosteroid administration did not expresse any metabolic disturbance, gastrointestinal bleeding, clinically important hormonal or psychiatric impairment as well as any increase of infection frequency. On the other hand, skin and ocular adverse effects were rare.
Conclusions:Our results suggests that systemic DPH administration as bridging therapy is not only effective but on the first place safe.

W138

METHOTREXATE IN RHEUMATOID ARTHRITIS: A 5 YEAR PROSPECTIVE STUDY

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Objective: The aim was to evaluate the efficacy and tolerability of low dose of longterm Methotrexate (MTX) treatment of rheumatoid arthritis (RA).
Methods: This study examines prospectively the response to oral MTX (5-12,5 mg) over a 5 year period of 70 patients (pts) with active RA. 54 pts were female, mean age 53,6 years and mean diseases duration 9,7 years. Clinical evaluation were performed by the same physician-investigator every 3 months for the first year of the study and every 6 months thereafter. Every 4 weeks complete blood cound and every 12 weeks thereafter complete erytrocyte sedimentation (ERS), blood count, serum creatinine and liver blood tests were obtained
Results: 11 (15 %) pts completed the 5 year study, 14 (20%) dropped out because of an adverse event or due to inefficacy. After 3, 6, 12, 24, 36 months of treatment a good clinical response was shown by signifficant clinical improvement in the joint swelling ($p<0,001$), morning siffness ($p<0,001$), as well as in both physicians and patients assessment of the disease activity ($p<0,001$) compared to pretreatment values. The clinical improvement was also associated with a decrease of ERS after 3,6,12 months ($p<0,001$), after 24 and 36 months ($p<0,05$). Although a sustained clinical response was noted in the diseases variables during the 5 year study, there was no significant difference noted in the improvement in the joint swelling after 48 and 60 months, in duration of morning stiffness and in decrease of ERS after 60 months of treatment.
Conclusion: Methotrexate therapy appears to be effective and safe in the treatment of RA in this 5 year prospective study

W139

COMPARATIVE CLINICAL EVALUATION OF SYNOCARE- A NEW POLYHERBAL DISEASE MODIFYING AGENT AND CHLOROQUIN IN RHEUMATOID ARTHRITIS

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OBJECTIVE: To compare the clinical efficacy and the disease modifying activity and safety of Synocare a new poly herbal agent and Chloroquin in patients with rheumatoid arthritis.
METHODS: Study was approved by Institute ethical committee. Written informed consent was taken from the patients. 18 Patients received Chloroquin phosphate 250 mg once daily and 30 patients received Synocare 2 tablets bid for 6 months. Clinical assessment was carried out at entry and at monthly intervals for 6 months. Side effects were recorded. Statistical analysis was done by ANOVA and paired 't' test.
RESULTS: There was a significant reduction in the number of painful joints, pain index, number of swollen joints, swelling index, morning stiffness and PIP loop size at the end of 3 and 6 months in both the groups as compared to baseline ($p<0.001$). There was statistically significant improvement in, onset of fatigue at the end of 3 and 6 months in synocare group and at the end of 6 months in chloroquin group as compared to baseline ($p<0.001$). Grip strength improved significantly in both the groups at the end of 3 and 6 months as compared to baseline ($p<0.01$). ARA functional class improved significantly in both the groups at the end of 6 months as compared to baseline ($p<0.05$). As compared to synocare, chloroquine showed significant reduction in pain index, number of swollen joints, swelling index and rheumatoid factor at the end of 6 months ($p<0.05$ & $p<0.01$). Morning stiffness improved significantly in chloroquin group as compared to synocare at the end of 3 and 6 months ($p<0.05$) and onset of fatigue at the end of 3 months ($p<0.05$). Global evaluation by the patients at the end of study was very good by 15 and 12; good by 11 and 3; fair by 3 and 1 and poor by 1 and 2 in Synocare and chloroquin groups respectively. The investigator's global evaluation was very good for 13 and 12; good for 10 and 2; fair for 6 and 2 and poor for 1 and 2 patients in Synocare and chloroquine groups respectively. 7 and 9 patients on Chloroquin and Synocare had side effects respectively.
CONCLUSION: Synocare and Chloroquin showed good disease modifying action. However, as compared to Synocare, Choloroquin was better.

W140

INFLIXIMAB TREATMENT OF RHEUMATOID ARTHRITIS (RA).

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Objective: To analyze the factors affecting the duration of Infliximab treatment of arthritis.
Method: The clinical course in all patients selected for treatment by 5 rheumatologists, with infliximab since 1/00 are analyzed in a life table format.
Results: 66 RA patients, 44 stage 1, 12 stage 2, and 10 stage 3; 46 females and 20 males age (mean, (std dev)) 63.5 (13.8) yrs with 15.2 (10.6) years duration have been treated. 93% had failed MTX treatment, and 2.4 other demards, and 30% failed triple therapy. The probability of continuing treatment was 71% at 47 weeks with 10 patients still at risk. The most common reason to stop treatment was sepsis, 14% at 27 weeks. 4 developed pneumonia, and 2 had septic arthritis. The risk of stopping due to inefficacy was 10% at 7 weeks. Transfusion reactions (hypotension, hypertension,chills, nausea, vomiting) developed in 3 (risk 6% at 7 weeks), and one stopped due to fear of side effects, and another due to intercurrent rash which was probably unrelated. 2 men, age 86 and 75, with interstitial lung disease, died of pneumonia, and one female, age 78, dued 4 months after her last dose (stopped due to inefficacy) due to congestive heart failure and pulmonary embolism. In those who improved and continued treatment the mean MTX went from 12.0 to 9.8 mg/wk and prednisone from 8.7 to 5.8 mg/day. Sedimentation rate decreased from 54 to 41 mm. in one hour.
Conclusion: Infliximab was effective enough to maintain treatment up to 47 weeks in 71% with demard resistant RA. Avoiding treatment in those with high risk of infection, and pain due mostly to old deformities rather than active inflammation, should result in a longer average duration of treatment.

W141

Treatment of Rheumatoid Vasculitis with Infliximab

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Rheumatoid vasculitis (RV) is a systemic late stage complication in patients with rheumatoid arthritis (RA). Despite cyclophosphamide (CYC) therapy which is the treatment of choice the prognosis is very poor and most patients die within two years.
From our last ten patients with RV who had to be treated by CYC five patients had to stop therapy because of serious complications like infection orcardiac failure. Three patients refractory to CYC were treated with infliximab. A 48 year old male RA patient developed systemic vasculitis with a pericardial effusion, which did not respond to pulse corticosteroids, CYC or even to plasmapheresis. The only way to manage this life threatening condition was to drain the effusion continously. Infliximab therapy at 3 mg/kg was initiated. The pericardial effusion as well as all other signs of the systemic vasculitis resolved within two weeks. The second patient, a 62 year old man who underwent abdominal surgery -retrospectively probably because of vasculitis- developed vasculitic skin ulcers on the scrotum, the lower legs and in the abdominal wound. Since CYC and methotrexate only lead to a partial remission, infliximab infusions were given. Again, the vasculitic lesions healed. The last case is a 58 year old woman with a more classic RV characterized by crural ulcers. After getting panmyelopathy caused by CYC, infliximab was given and the vasculitic features disappeared. No complications of infliximab therapy occured although two patients had superinfected skin ulcers.
Our cases show that infliximab is an effective salvage therapy in patients with RV refractory to even CYC. Given the toxicity and complication rate of CYC in this RA patient subset infliximab may well be considered as a first choice alternative to CYC.

W142

EVALUATION THE QUALITY OF LIFE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH MONOCLONAL ANTIBODIES ANTI-TNFα.

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Objective: As the main cause of disability of patients with early rheumatoid arthritis /RA/ is pain and inflammation of joints, we have studied the influence of treatment with Remicade on the quality of life of patients.
Rationale: The efficacy of monoclonal antibody anti-TNFα in rapid alleviation of inflammatory process in patients with RA has been recently documented though its ability to slow disease progression remains to be proved.
Methods: Two groups of patients with RA were observed for one year. First comprised of 20 patients with good response to methotrexate /Mtx/ treatment and second 10 patients with bad response and then concomitant treatment with Remicade. In both groups clinical and laboratory parameters of disease activity and health assessment questionnaire /HAQ/ were evaluated before, after 6 weeks, 6 months and one year of treatment.
Results: The response to treatment was only slightly better in Mtx+Remicade group as measured with Ritchie index at the end of observation, but the rate of improvement was significantly better and the difference could be observed after 6 weeks of treatment.
The patients global health improved and the degree of disability diminished as measured with HAQ. Three patients from this group have resume the employment 4 months from beginning the treatment.
Conclusion: The long term efficacy of anti-TNFα treatment has to be define in the near future. However, the potent and rapid anti-inflammatory action of this drug significantly improve the quality of life of patients with RA.

W143

Preliminary Study on Diagnosis of Tumor-like Sjogren 's Syndrome

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(Abstract) **Objective** To explore clinical features and diagnosis of tumor-like Sjogren's Syndrome. **Methods** 22 cases with tumor-like Sjogren's Syndrome of parotid gland, 50 cases with pleomorphic adenoma of parotid gland and 25 cases with adenolymphoma of parotid gland were studied retrospectively. **Results** Statistical analysis showed that tumor-like Sjogren's Syndrome is predominantly disease of middle-aged women (40-59y) with a woman to man ratio of 6.33:1. Patients commonly present with salivary gland swelling repeatedly , varying in size, treatment effectively with antibiotic, accompanying dry mouth , dry eyes and aching joints. The mass probably displays medium quality and smooth appearance. The discriminant functions with tumor-like Sjogren's Syndrome, pleomorphic adenoma and adenolymphoma were also established. **Conclusion** The discriminant functions provide a simply and practical method to diagnose tumor-like Sjogren's Syndrome .

(Key words) tumor-like Sjogren's Syndrome: pleomorphic adenoma ; adenolymphoma

W144

Liver damage in primary Sjögren's syndrome

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Objective: To study clinical features of the liver damage in primary Sjögren's syndrome (pSS) and to investigate the nature of their pathological changes.
Rationale: Some cases of the liver damage's group in pSS were similar with primary biliary cirrhosis(PBC) in clinical and pathological aspects.
Method: Clinical data of 56 pSS patients with liver damage and without liver damage were analyzed.
Results: Among 56 patients with pSS, 13(23.2%) showed liver damage. The positive rates of sex, age, duration from symptom appearance to definite diagnosis, ANA, anti-SSA, anti-SSB, RF, IgG and γ-globulin revealed no significant difference between both groups($P>0.05$). Among the 13 patients with liver damage, AKP and γ-GT were raised in 6, and AKP, γ-GT, TBIL and DBIL all elevated in 4. In 8 patients anti-SMA and AMA were detected, and 5 showed AMA positive. Liver biopsy in 6 patients showed 3 with chronic active hepatitis among which 2 were complicated with liver cirrhosis, 1 chronic persistent hepatitis and 2 cholangitis. Of the 6 patients 5 showed different degrees of infiltration of mononuclear cells in the portal tracts.
Conclusion: The occurrence of liver damage in pSS is rather high. The liver damage may be related to PBC. Patients' response to corticosteroid treatment is favourable and their prognosis appears good.

W145

PRIMARY AND SECONDARY SJÖGREN'S SYNDROME - CLINICAL AND SEROLOGICAL FEATURES

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Objective: To compare the extraglandular manifestations and serological abnormalities in patients with primary and secondary to SLE and RA Sjögren's syndrome (SS).

Rationale: SS that occur in the context of distinct rheumatic diseases, in some respects, may be diverse from each other.

Methods: Analysis was based on 3 groups of female patients: SS (n=50), SS+SLE (n=31), SS+RA (n=40). The prevalence of constitutional symptoms, skin features, arthritis, serositis, nefropathy (active urine sediment and proteinuria), neuropathy, adenopathy, hematological and serological abnormalities were assessed.

Results: In SS and SS+RA patients extraglandular manifestations, hematological and serological abnormalities were common but less frequent then in SS+SLE patients. Only in SS+SLE patients antibodies to dsDNA and Sm were present. The SS A/Ro and SS B/La antibodies were detected in all groups with the highest frequency in SS patients (respectively 74% and 30%).

Conclusion: Our data indicate, that only presence of SS A/Ro and SS B/ La antibodies can be considered the serological marker of the primary and secondary Sjögren's syndrome.

W146

ELEVATED LEVELS OF SOLUBLE CD40 LIGAND IN PATIENTS WITH SJÖGREN'S SYNDROME

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Objective:To evaluate the role of the costimulatory molecules, CD40 Ligand (CD40L) in Sjögren's syndrome(SS).

Rationale: The CD40-CD40L interaction would inolve tne polyclonal B cell activation in SS patients.

Methods: (1) Serum samples from 33 primary SS (I°SS) patients, 37 secondary SS (II° SS) patients and 40 healthy controls were tested. We used sCD40L ELISA kits. (2) Detection of CD40L expression on lymphocyte subsets was examined by two-color-flowcytometry. (3) After peripheral blood mononuclear cells were cultured with Ionomycin and PMA, CD40L expression on T cells was detected.

Result: (1) The concentration of serum CD40L was statistically significant higher ($p<0.01$) in both I°SS and II°SS patients than in healthy controls. (2) There were no significant difference between healthy controls and SS patients in the expression of CD40L on both T cells and B cells. (3) Both SS patients and healthy controls showed marked increased expression of CD40L on T cells at 6 hours of culture. Activated T cells from SS patients continued to demonstrate the increased expression of CD40L rather than normal controls at 48 hours.

Conclusion: The activation of CD40-CD40L system may play a role of a pathogenesis of polyclonal B cell activation in Sjögren's syndrome.

W147

MICROCHIMERIZM IN PATIENTS WITY SYSTEMIC SCLEROSIS OR SJÖGREN'S SYNDROME

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Objective: To identify fetal cells in patients with systemic sclerosis (SSc) or Sjögren's syndrome (SS). Rationale: Microchimerism of fetal cells occurs during most pregnancies, and fetal progenitor cells persist in the maternal circulation. SSc and SS have many clinical and pathological features similar to chronic graft-versus-host disease. These findings suggest that anti-maternal graft-versus-host reaction (GVHR) by fetal cells may be involved in the pathogenesis of those diseases. Methods: We examined Y-chromosome (SRY) specific sequence as a marker for fetal cells in peripheral blood cells (PBC) or in minor salivary glands (MSG) from women who had delivered at least one son by a nested PCR. Results: In PBC, SRY sequence was detected in 3 of 23 (13%) women with SSc, 2 of 6 (33%) women with SS and 5 of 20 (25%) healthy women. SRY sequence was amplified in 11 of 20 (55%) MSG from women with SS, but in only one of 8 normal controls. Additionally, Y-chromosome bearing mononuclear cells infiltrating in the MSG was clearly identified in 3 out of 8 women with SS by *in situ* hybridization. Conclusion: It was hard to conclude that circulating fetal cells in peripheral blood directly cause the diseases. The infiltration of Y-chromosome bearing cells in MSG suggests that GVHR initiated by fetal cells may, in part, involved in the pathogenesis of SS.

W148

MORTALITY AND MORBIDITY IN ITALIAN PATIENTS WITH SJÖGREN'S SYNDROME.

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Objective: To evaluate mortality and morbidity of primary (pSS) and secondary (sSS) Sjögren's Syndrome.

Rationale: As reported by the literature, Sjögren's Syndrome is associated with an increased risk of developing lymphoproliferative disorders and may lead to glomerulonephritis and peripheral neuropathy.

Methods: 89 patients (68 with pSS and 21 with sSS) were evaluated in a 10 years follow-up from January 1987 to November 2000.
Survivorship of SS patients was estimated by Kaplan-Meier curve analysis and compared with survivorship of the general population of Padova (Italy), matched for sex and age.

Results: During the follow-up 19 patients died: 10 (14.7%) with pSS and 9 (42.8%) with sSS. Among the latter, 7 were affected by rheumatoid arthritis and 2 by systemic sclerosis.
The whole SS patients group showed an increased mortality compared to the general population. Those with sSS exhibited a significant reduction of survival ($p<0.01$), while pSS patient showed only a slightly decreased survival rate (86.5%) compared to general population (95%). Lymphoproliferative disorders were diagnosed in 5 patients with pSS (7.35%), and in all the cases they resulted late events in the course of the disease.

Conclusion: Our results suggest that 10 years survival in pSS patients is comparable to that of the general population. Mortality was increased only in sSS patients, particularly those with rheumatoid arthritis.

T78B

THE CLINICAL PARTICULARITIES IN THE PATIENTS WITH DIAGNOSIS OF SYSTEMIC SCLERODERMIA WITH BLOCK PHENOMENON OF T LYMPHOCITES.

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Objective: To study the clinical particularities in the patients with Systemic Sclerodermy (SSc) that had increased indices of block lymphocytes.

Methods: Determination of block phenomenon of T lymphocytes in 50 patients with SSc. Was used reaction of rosette formation.

Results: The average age of patients 28,2 years, the duration of illness 1,5 – 7 years. These indices were smaller in comparison with average age and duration of illness in-patients with SSc in absence of block lymphocytes. The clinical changes revealed the Raynaud's Syndrome (RS) predominance over the indurative edema of skin. The livedo reticularis were frequent. Oesophagus was involved in process in the majority of cases among the internal organs. The illness onset is characterised by RS. The presence of localised form of skin affectation is characteristic. Was observed the predominance of A_2, B_{18}, DR_2 from the HLA system. Antiendotelial antobodies were present in the patients with moderate indices of block lymphocytes with variation of 1.14 – 1.8.

Conclusion: The data of the study suggest that presence of localised form of skin affectation is characteristic for the patients with SSc, with block phenomenon of T lymphocytes.

T78C

CHANGES IN MICROCIRCULATION AND REVEAL OF ANTIBODIES TO ENDOTHELIUM AND SKIN IN PATIENTS WITH SISTEMATIC SCLERODERMIS.

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Objective: To examine correlation between disturbances in micro-circulation and presence of antibodies to endothelia and skin in-patients with Systematic Sclerodermis (SSc).

Methods: 175 patients with SSc. Women-87,65%. Average age 42,8 ± 2,34 years. Duration of illness 0,5 -26 years. II stage of SSc - 58% cases, chronic – 81%, with minimal activity – 67%.

Results: In the onset stage Syndrome Raynaud (SR) was localised in wrists-97% cases, in legs-89%, facial–36%. SR was permanent in 68% patients (P), diverse frequency crises–other. Indurative oedema of skin on phalanges in onset-63%, arthralgy-87%. SSc began from allergic reaction in 5 % of P. SR in II stage of illness-94,75% cases, skin affection–93,42%, joints' syndrome–92,11%, affection of alimentary tract–78,95%, heart–68,42%, lungs–34,21%, kidneys–28,95%. Changes in microcirculation on the peripheral were investigated by rheovasography, oscillometry and capillaroscopy. Scintigraphy of lungs revealed reduction of perfusion in the right lung in 40% of P, left lung–in 65%, nonuniform distribution of isotope on the right side-5%, on the left side–30%. In onset of SSc, in 30 P antibodies to endothelia and skin were determined with immunophoresis method. General group (GP)-antibodies to endothelia -53,6%, SR group–69,16%. GP-antibodies to skin-51,7%, in SR group–in 49,8%.

Conclusion: Reveal of antibodies to endothelia and skin in onset of SSc may assist in precision of diagnosis on the earlier stages of SSc.

W94B

PERCULARITIES OF SERUM NEGATIVE RHEUMATOID ARTHRITIS.

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Objective: The complex study during 15-year course of patients with serum negative Rheumatoid Arthritis (RA).

Methods: Examined 200 patients with real RA, from which 150 were serum negative and 50 serum positive by rheumatoid factor. Average age 42, 7 ± 1,64 years, duration of illness 18, 5 ± 1,2 years. All patients repeatedly were examined thoroughly according to clinical, immune, immune and genetic, radiology and morphological data.

Results: Long term comparative examination of patients with serum negative RA revealed essential differences: progressive attraction of wrist joints into the process with earlier transgress of function, domination of ankylosing processes over the erosions; frequent affection of hip joints with development of aseptic necrosis, pronounced amiotrophy, generalised lymphadenopathy, frequent affection of kidneys, including the development of secondary amiloidosis. The level of activity really ($p > 0,05$) correlated with IgA, and weak expression of local immune and morphological manifestations was revealing on the background of activation of fibroblastic elements and changes in vessels.

Conclusion: The depth of established changes confirms opinion about nozologic isolation of serum negative RA.

W94C

THE INFLUENCE OF PHYSICAL THERAPY ON THE RANGE OF JOINT MOTION IN RHEUMATOID ARTHRITITS PATIENTS.

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There is not much information about quantitative effects of physical therapy (PT) on changes of joints in rheumatoid arthritis (RA), because the right model on which examination would be conducted does not exist.

The **aim** of this work was to examine the influence of PT on the range of joint motion (ROM), according to our model.

Material and methods: The examination was conducted on 45 RA patients, with mean age of 58,2 and mean duration of their illness of 13,1 years. Ranges of every joint motion on the extremities are examined. ROM is expressed by number, not by degree. Every joint has its maximum ROM. The limitation was converted from a degree to a percentage and after that to a number, so the limitation of 10% is number 1, of 25% is number 2, of 50% is number 3, of 75% is number 4 and of 100 % (complete disability) is number 5. ROM is measured at the beginning and at the end of PT. Physical therapy lasted for 4 weeks and it included cryotherapy, electric therapy and exercises.

Results: Completely normal ROM was found only by 2,2% before the PT and by 11% pts. after the PT. Statistically significant improvement of ROM of all joints was found after PT, except the ones with ankylose. The best results were achieved on those joints were the limitation was 10 - 50 %. That has significantly improved functional status, which has been measured with HAQ, and it is decreased from 1,62 to 0,94.

Conclusion: The limitation of joint's motion directly influences the physical ability of pts. It is necessary to measure ROM on every rheumatology examination.

W94D

THE INFLUENCE OF SOCIOECONOMIC CONDITIONS ON THE COURSE OF RHEUMATHOID ARTHRITIS

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Treatment of rheumatoid arthritis (RA) is better every day but it is getting more and more expensive.

The aim of this work was to analyze socioeconomic conditions of patients with RA after four years of war and social security crash, as well as to analyze their possibility to use contemporary therapy.

Material and methods: Hundred and forty RA patients were analyzed as well as their profession, level of education, marital status, functional status (HAQ), dependence of other people's help, possibility of drug purchase.

Results: Out of 140 patients 88% are females and 12% were males. Most of them do not work, or work on hard, low paid jobs. 41% of them work as a farmer, 13% as a worker, 22% are housewives. College education have only 4%, high school education 6% and rest of them have lower school degree. 64% of them are financially dependent on other people Examined patients have worse functional status then ones in other areas; 37% of patients have HAQ from1-2, and 36% have from 2-3. Almost 63% depend on other's people physical help. All patients have health insurance, but beside that they have to buy medications which most of them can not afford and they use only NSAIDs.

Conclusion: Obviously hard economic conditions in our country do not go in favor of RA patients. They are not in the position to earn enough money and their illness requires lots of it. For the most of our patients " the therapy for 21st century" is not important because they can not use the one of the 20th century. Rheumatology team has to find means for free treatment of RA patients because it is cheaper to cure the disease in its early stage then when it gets to the phase of complete disability.

W142B

THE USE OF ENCEPHABOL AS A BASIC DRUG IN THE TREATMENT OF RHEUMATOID ARTHRITIS.

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Objective: The aim of this study was to identify the efficiency of the long-lasting treatment with Encephabol in patients with rheumatoid arthritis (RA) by Emerch, Germany.

Methods: A 12-month controlled blind trial with Encephabol has been carried out in 30 patients with serum positive RA. All patients have been separated into two groups: the first one included 20 patients which have been administered Encephabol 600 mg per day, and a second group consisting of 10 patients that have been given placebo. All patients have undergone NSAID treatment. All clinical features have been studied in evolution on a monthly basis (pain assessment by patient and according to a visual analogy scale, the degree of morning stiffness, the number of painful and swelled joints), biochemical parameters (non-specific signs of inflammatory process), immunological (rheumatoid factor titers), and scintigraphy data ($Tc99^{M}$). X-ray investigations have been performed before and one year after the treatment course.

Results: After 12 months of treatment, the Group 1 patients showed a significant statistical decrease in pain intensity assessed by both patient and visual analogy scale, presented a drop in morning stiffness, Richi's joint index and a reduction in the number of swelled joints ($p<0.05$), as well an obvious decrease in non-specific inflammatory indicators and RF titers has been noticed ($p<0.05$). The Group 2 patients displayed no significant statistical decrease in the given indicators; a trend towards decrease in pain intensity by visual analogy scale was mentioned in just 20% of patients ($p<0.1$), as it has been in the number of swelled joints ($p<0.1$); the rest of indicators were practically unchanged. Only two patients from the Group 1 have been left out of trial due to proteinuria (1) and thrombocytopenia (2).

Conclusion: The resulting outcomes suggest that Encephabol can be used as basic treatment in RA.