23rd–25th September 2010, Sopron, Hungary

Exclusive major sponsors of the CECR 2010

Welcome address

Dear Colleagues and Friends,

On behalf of the organizers I'd like to welcome most cordially all of you to the 8th Central European Congress of Rheumatology (CECR) in Sopron, Hungary.
Not only rheumatologists from the six organizing countries (Austria, Czech Republic, Hungary, Poland, Slovakia, Slovenia) but also specialists and general practitioners interested in musculoskeletal conditions from different parts of Europe will be active participants of this meeting.

The story of the CECR started in Pieštany where the first congress took place in 1996. It was followed by Warsaw (1998), Bratislava (2000), Baden bei Wien (2002), Budapest (2004), Bled (2006), and Prague (2008). The passed 14 years, the number of attendees and the scientific level of the events justified the importance of this biennial congress. Beside the regional scientific collaboration the event has always been an ideal opportunity for the experience of Central European feeling and creative activity.

This year the charming, historical, Western Hungarian town, Sopron acts as host to the congress. In the scientific programme distinguished specialists present state of the art lectures and other oral papers. More than 150 abstracts have been submitted from 25 countries in order to discuss hot topics of molecular and clinical rheumatology. Leading pharmaceutical companies are present with their exhibition booth and six of them (Abbott, Amgen & GlaxoSmithKline, Eli Lilly, MSD, Pfizer and Roche) have the possibility to organize satellite symposia. The social programmes, the special atmosphere of the town and the delicious Hungarian wines and foods will also help us to make this meeting a memorable event. Many thanks the major sponsors for their support making possible the high-standard conditions.

The organizers have spared no time to ensure that this meeting will be an exciting and useful experience for all of you. Your attendance and precious contribution to the success of the meeting are highly appreciated.
We wish you a pleasant stay in Sopron.

Best personal regards

Sopron, September 23, 2010.

Prof. Dr. Gyula Poór

Chairman of the Congress
President, Hungarian Association of Rheumatologists

Scientific programme of the 8th Central European Congress of Rheumatology

September 23rd (Thursday)

8.30–09.00 Opening ceremony

9.00–10.00 Pathogenesis of rheumatoid arthritis
Chairmen: Wlodzimierz Maslinski and Zoltán Szekanecz

O1 Synovial biopsy for the assessment of rheumatoid arthritis and the action of biologics (15')
Paul Peter Tak
University of Amsterdam, The Netherlands

O2 Bone marrow in the pathogenesis of rheumatoid arthritis (15')
Wlodzimierz Maslinski
Institute of Rheumatology, Warsaw, Poland

O3 Cytokine activities in rheumatoid arthritis pathogenesis (15')
Iain McInnes
University of Glasgow, Scotland

O4 B-cells and their targeting in rheumatoid arthritis (10')
Péter Szodoray
University of Oslo, Norway

Discussion

10.00–10.30 Coffee break

10.30–11.30 New treatment modalities in systemic inflammatory rheumatic diseases
Chairmen: Steffen Gay and Jiří Vencovský

O5 Novel strategies for the treatment of arthritis (15')
Steffen Gay
University Hospital, Zurich, Switzerland

O6 Advances in the therapy of myositis (15')
Jiří Vencovský
Institute of Rheumatology, Prague, Czech Republic

O7 New possibilities in the treatment of vasculitis (12')
Vladimir Tesar
Charles University, Prague, Czech Republic

O8 New prospective biologicals in the treatment of rheumatoid arthritis (12')
Ladislav Šenolt
Institute of Rheumatology, Prague, Czech Republic

Discussion

11.30–12.30 Perspectives in rheumatoid arthritis and spondyloarthritis – Treatment needs and therapeutic options
Satellite symposium: MSD
Chairman: László Hodinka

OS1 Rapid radiographic progression and therapy choice in rheumatoid arthritis
Peter C. Taylor
Imperial College London, United Kingdom

OS2 Golimumab: An effective and convenient therapy to address the needs of patients with rheumatoid arthritis
Iain McInnes
University of Glasgow, Scotland

OS3 Spondyloarthritis: Many manifestations of one disease – a multidisciplinary approach to management
Joachim Sieper
Charité University Berlin, Germany

Discussion

12.30–13.30 Lunch-time

13.30–14.30 New trends in spondylarthropathies
Chairmen: Karel Pavelka and Pál Géher

O9 Pathogenetic background of spondylarthritis (15')
Joachim Sieper
Charité University Berlin, Germany

O10 New approaches in the diagnostics and monitoring of spondyloarthritis (15')
Maxime Dougados
René Descartes University, Paris, France

O11 Long-term efficacy and safety of anti-TNF-therapies in ankylosing spondylitis; experiences from nation-wide registry ATTRA (15')
Karel Pavelka
Institute of Rheumatology, Prague, Czech Republic

O12 Vascular diseases in ankylosing spondylitis (10')
Sándor Szántó, Nóra Bodnár, Rudolf Gesztelyi, Ádám Kemény-Beke, Zoltán Szekanecz
University of Debrecen, Hungary

Discussion

Awarding of the honorary membership of the Hungarian Association of Rheumatologists

14.30–15.30 Treating ankylosing spondylitis as soon as possible
Satellite symposium: Pfizer
Chairman: Gyula Poór

OS4 The need for early intervention in spondyloarthritis
Maxime Dougados
René Descartes University, Paris, France

OS5 Efficacy of etanercept in the treatment of ankylosing spondylitis
Tamás Palotai
Special Hospital for Rheumatology of the Regional Health Insurance of Lower Austria, Baden, Austria

OS6 Evaluation of radiological progression in the management of ankylosing spondylitis
Joachim Sieper
Charité University Berlin, Germany

Discussion

15.30–16.00 Coffee break

16.00–17.00 Traditional DMARDs versus biologics in the management of rheumatoid arthritis
Chairmen: Josef Smolen and Witold Tlustochowicz

O13 Do we need traditional DMARDs in the biologic era? (15')
Witold Tlustochowicz
Military Institute of Medicine, Warsaw, Poland

O14 How to use different biologicals for optimal treatment of patients with RA? (15')
Josef Smolen
Medical University, Vienna, Austria

O15 DMARD and biological treatment modalities in childhood (15')
Emese Kiss
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

O16 Enthesitis: Evolving concepts and sonographic evaluation (10')
Péter Bálint, Péter Mandl, Katalin Ács, Éva Ruzicska
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

September 24th (Friday)

08.30–09.30 News in progressive systemic sclerosis
Chairmen: Boris Lestan and László Czirják

O17 Incidence of scleroderma spectrum disorders in Slovenia (15')
Alenka Šipek-Dolničar
University Medical Centre, Ljubljana, Slovenia

O18 Clinical importance of nailfold capillaroscopy in the early diagnosis of systemic sclerosis (15')
Maurizio Cutolo
University of Genoa, Italy

O19 Lung involvement in systemic sclerosis (12')
Nemanja Damjanov
Institute of Rheumatology Belgrade, Serbia

O20 Emergency states in systemic sclerosis (12')
Luc Mouthon
Hopital Cochin, Rene Descartes University, Paris, France

Discussion

Awarding of the honorary membership of the Hungarian Association of Rheumatologists

09.30–10.30 Optimising patient pathways in rheumatoid arthritis
Satellite symposium: Pfizer
Chairman: Karel Pavelka

OS7 Towards optimal management of the rheumatoid arthritis patient
Paul Peter Tak
University of Amsterdam, The Netherlands

OS8 Clinical results with etanercept in early rheumatoid arthritis
Tom Huizinga
Leiden University Medical Center, The Netherlands

OS9 Ten years of TNF-blockers for treating rheumatoid arthritis: What have the registries taught us?
Emilio Martin Mola
Hospital University La Paz, Madrid, Spain

Discussion

10.30–11.00 Coffee break

11.00–12.00 Anti-TNFs in the forefront of biologic treatment in rheumatoid arthritis
Satellite symposium: Abbott
Chairman: Gyula Poór

OS10 Access to innovative rheumatoid arthritis treatments in EU
Gyula Poór
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

OS11 Classification and management of rheumatoid arthritis
– the 2010 news
Josef Smolen
Medical University, Vienna, Austria

OS12 Treat to target – implement today for tomorrow
Karel Pavelka
Institute of Rheumatology, Prague, Czech Republic

OS13 Importance of ultrasonography in early detection and monitoring of rheumatoid arthritis patients
Walter Grassi
University of Ancona, Italy

Discussion

12.00–13.00 Lunch-time

13.00–14.00 Disease activity and functional measurements in rheumatology
Chairmen: Piet van Riel and Burkhard Leeb

O21 Composite measures (15')
Piet van Riel
Radboud University Nijmegen Medical Centre, The Netherlands

O22 Patient related outcomes in routine monitoring of rheumatoid arthritis patients (15')
Burkhard F. Leeb
Center for Rheumatology, Stockerau, Austria

O23 Development of remission and minimal disease activity cut-points for the juvenile arthritis disease activity score (JADAS) (12')
Angelo Ravelli, Consolaro Alessandro
University of Genoa, Italy

O24 Outcome measures in the rehabilitation of musculoskeletal conditions (12')
Ernst Wagner, Tamás Palotai
Special Hospital for Rheumatology of the Regional Health Insurance of Lower Austria, Baden, Austria

Discussion

14.00–15.00 The RANK ligand inhibitor – fracture protection throughout the skeleton
Satellite symposium: Amgen & GlaxoSmithKline
Chairmen: Socrates Papapoulos and Gyula Poór

OS14 The diverse role of the RANK/RANKL/OPG system
Gyula Poór
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

OS15 Bone strength – role of trabecular and cortical bone
Péter Lakatos
Semmelweis University, Budapest, Hungary

OS16 Effect of denosumab treatment of bone turnover markers and BMD
Pavel Horak
Palacky University, Olomouc, Czech Republic

OS17 Clinical evidence for antifracture protection of denosumab
Socrates Papapoulos
Leiden University Medical Center, The Netherlands

15.00–15.30 Coffee break

15.30–16.30 Endrocrine parameters in rheumatic diseases
Chairmen: Maurizio Cutolo and Jozef Rovensky

O25 Neuroendrocrine-immune network in rheumatic diseases (15')
Maurizio Cutolo
University of Genoa, Italy

O26 Klinefelter's syndrome, Turner syndrome and rheumatic diseases (15')
Jozef Rovenský, Richard Imrich, Elene Košková, I. Lazúrová, J. Payer
National Institute of Rheumatic Diseases, Pieštany, Slovakia

O27 Hypothalamic-pituitary-adrenal function in rheumatoid arthritis (15')
Richard Imrich
Center for Molecular Medicine, Bratislava, Slovakia

O28 The presence and function of nicotinic acetylcholine receptors on osteoclasts, and their effect on osteoclastogenesis (10')
Péter Mandl[1,2], Silvia Hayer[2], Despoina Sykoutri[2], Gyula Poór[1], Josef Smolen[2], Kurt Redlich[2]
[1]National Institute of Rheumatology, Budapest, Hungary, [2]University of Vienna, Austria

Discussion

September 25th (Saturday)

08.30–09.30 Poster session – authors at posters

P1 Major histocompatibility complex class I. chain-related gene A: Risk and protective alleles in systemic lupus erythematosus pathogenesis
Marketa Fojtíková[1], Peter Novota[1], Pavlina Cejkova[2], Dana Tegzova[1], Satu Pesickova[1], Karel Pavelka[1], Marie Cerna[2]
[1]Institute of Rheumatology, [2]Charles University, Prague, Czech Republic

P2 Rheumatoid arthritis and prolactin: Association with disease activity and joint damage
Marketa Fojtíková[1], Jana Tomasová Studýnková[1], Maria Filková[1], Zdeňka Lacinová[2], Jindřiška Gatterová[1], Karel Pavelka[1], Jiří Vencovský[1], Ladislav Šenolt[1]
[1]Institute of Rheumatology, [2]Charles University and General University Hospital in Prague, Czech Republic

P3 Lipid peroxidation and antioxidant enzyme activities in patients with systemic lupus erythematosus
Attila Kovács[1], Do Huy Quai[2], Aranka László[2], Ilona Varga[2]
[1]Hospital of Hungarian State Railways, Szolnok, [2]University of Szeged, Hungary

P4 Lupus nephritis: The therapeutic aspects
Teuta Backa, Alma Idrizi, Myftar Barbullushi, Argjend Tafaj, Alketa Koroshi
UHC Mother Teresa, Tirana, Albania

P5 Flaccide hypokalemic paralysis in a patient with primary Sjögren's syndrome
Teuta Backa, Alma Idrizi, Myftar Barbullushi, Kliti Hoti
UHC Mother Teresa, Tirana, Albania

P6 Vascular endothelial growth factor and basic fibroblast growth factor in systemic lupus erythematosus with Jaccoud´s arthropathy
Zbynek Hrncir, Marcela Drahosova, Ctirad Andrys, Petr Bradna, Tomas Soukup, Jan Toms
University Hospital, Hradec Králové, Czech Republic

P7 Vascular endothelial growth factor and epidermal growth factor in patients with systemic sclerosis and systemic lupus erythematosus
Radim Becvar[1], Ivana Putova[1], Michal Tomcik[1], Simona Skacelova[1], Dana Tegzova[1], Radka Svobodova[1], Jiri Stork[2], Petr Zatloukal[3], Alena Zatloukalova[3]
[1]Institute of Rheumatology, [2]General Teaching Hospital, [3]Clinic of Pneumology and Thoracic Surgery, Prague, Czech Republic

P8 Prevalence, incidence and survival of diffuse systemic sclerosis in Dalmatia county, Croatia
Mislav Radić, Dušanka Martinović Kaliterna, Josipa Radić, Damir Fabijanić, Vedran Kovačić
University Hospital Split, Croatia

P9 Impact of metacarpophalangeal and proximal interphalangeal joints flexion contractures on disability and health-related quality of life in systemic sclerosis
Mislav Radić, Dušanka Martinović Kaliterna, Josipa Radić
University Hospital Split, Croatia

P10 Peripheral neuropathy in systemic sclerosis patients
Diana Vučina, Dušanka Martinović Kaliterna, Mislav Radić
University Hospital Split, Croatia

P11 Systemic sclerosis – clinical and immunological features of 211 patients of Slovak population
Jozef Lukáč, Oľga Lukáčová, Jozef Rovenský, František Máliš, Peter Poprac, Alena Tuchyňová, Roman Stančík, Darina Kozáková, Karol Bitter
National Institute of Rheumatic Diseases, Piešťany, Slovakia

P12 Altered cellular immunity in diffuse cutaneous systemic sclerosis
Gábor Papp[1], Ildikó Fanny Horváth[1], Sándor Baráth[1], Edit Gyimesi[1], Péter Szodoray[2], Margit Zeher[1]
[1]University of Debrecen, Hungary, [2]Rikshospitalet University of Oslo, Norway

P13 Evaluation of the cardiopulmonary status in systemic sclerosis patients with ergospirometry and stress echocardiography
Daniella Hulló[1], Gergely Ágoston[1], János Varga[1], Imre Lajkó[1], Ágnes Milassin[1], Attila Somfay[1], Albert Varga[1], Attila Pálinkás[2], László Kovács[1]
[1]University of Szeged, [2]Erzsébet Hospital, Hódmezővásárhely, Hungary

P14 Selected risk factors for coronary heart disease in patients with psoriatic arthritis, who were treated in the rheumatology clinic in Wroclaw between 2008–2009
Renata Sokolik, Dominik Samotij, Agata Sebastian, Arkadiusz Chlebicki, Piotr Wiland
Rheumatology Clinic, Wroclaw, Poland

P15 ^{166}Holmium-phytate-radiosynoviorthesis in rheumatoid arthritis. Five years clinical results. Phase III. prospective study
Margit Szentesi, Pál Géher
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

P16 Regulation of CD3 expression on human T-lymphocytes
György Nagy, Barbara Érsek, Zoltán Wiener, Melinda Rácz, Edit Buzás, Viktor Molnár, Pál Géher, András Falus
Semmelweis University, Budapest, Hungary

P17 The impact of the anti-cyclic-citrullinated peptide antibody status in the management of patients with early rheumatoid arthritis in Hungary: Results from an interim analysis
Péter Juhász[1], Katalin Dankó[2], Katalin Fazekas[3], Ramóna Gaál[1], Judit Korda[1], Hajnalka Laczkó[4], Nóra Nusser[5], Katalin Seregély[6], János Szász[7], Eszter Tóvári[8], Edit Vereckei[1], Orsolya Nagy[9], Gyula Poór[1]
[1]National Institute of Rheumatology and Physiotherapy, Budapest, [2]University of Debrecen, [3]Szent Ferenc Hospital, Miskolc, [4]Vaszary Kolos Hospital, Esztergom, [5]Zsigmondy Vilmos Hospital, Harkány, [6]Bács-Kiskun County Hospital, Kecskemét, [7]I. Rheumatology Clinic, Székesfehérvár, [8]Integrated Health Care Institution of Pécs, [9]Abbott Laboraties (Hungary) Ltd., Budapest, Hungary

P18 Correlation between clinical manifestation and immune-genetic determinants at patients with psoriatic arthritis in Republic of Moldova
Liliana Groppa, Liudmila Gonta, Eugeniu Russu
State Medical and Pharmaceutical University “Nicolae Testemitanu”, Kishinau, Moldova

P19 Assessment of clinical efficiency of tocilizumab in disease evolution of patients from Moldova with rheumatoid arthritis
Liliana Groppa, Daniela Cepoi-Bulgac, Eugeniu Russu, Laura Vremis, Hellis Osama
State Medical and Pharmaceutical University “Nicolae Testemitanu”, Kishinau, Moldova

P20 Influence of glucose level control in blood on evolution of inflammatory joint syndrome at patients with a diabetes mellitus type 2.
Liliana Groppa, Lia Chislari, Eugeniu Russu, Zinaida Anestiadi
State Medical and Pharmaceutical University “Nicolae Testemitanu”, Kishinau, Moldova

P21 Research of a bone metabolism at patients with diabetes mellitus type 2.
Liliana Groppa, Lia Chislari, Eugeniu Russu, Zinaida Anestiadi
State Medical and Pharmaceutical University “Nicolae Testemitanu”, Kishinau, Moldova

P22 The role of Th17 cells in spondylitis ankylopoetica
Attila Balog[1], Balázs Szalay[2], László Kovács[1], Daniella Hulló[1], Barna Vásárhelyi[2]
[1]University of Szeged, [2]Semmelweis University, Budapest, Hungary

P23 Frequency of myostitis-specific and myositis-associated autoantibodies in the serum of patients with idiopathic inflammatory myopathies
Katalin Dankó[1], Melinda Vincze[1], Judit Tumpek[1], Lászlóné Szőllősi[1], Peter J. Charles[2]
[1]University of Debrecen, Hungary, [2]Kennedy Institute, Imperial College London, United Kingdom

P24 Anti-Pm-Scl autoantibody positivity in patients with idiopathic inflammatory myopathy
Andrea Váncsa[1], Peter J. Charles[2], Júlia Németh[3], Andrea Ponyi[4], Judit Tumpek[1], Melinda Vincze[1], Katalin Dankó[1]
[1]University of Debrecen, Hungary, [2]Kennedy Institute, Imperial College London, United Kingdom, [3]National Institute of Health, Budapest, [4]Semmelweis University, Budapest, Hungary

P25 Association of idiopathic inflammatory myositis and myasthenia gravis
Anna Bazsó[1], Anna Polgár[1], Edit Vereckei[1], Mária Judit Molnár[2], Gyula Poór[1], Emese Kiss[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Semmelweis University, Budapest, Hungary

P26 Anti muscarinic receptor-3 autoantibodies in secondary Sjögren's syndrome
Magdolna Deák, Nóra Árgyelán, Attila Balog, Daniella Hulló, Gyula Pokorny, Mária Kiss, Gábor Tóth, László Kovács
University of Szeged, Hungary

P27 The immune-modulating role of vitamin A, D and E in the pathogenesis of primary Sjögren's syndrome
Ildikó Fanny Horváth, Gábor Papp, Sándor Baráth, Péter Szodoray, Margit Zeher
University of Debrecen, Hungary

P28 Thalidomide in the treatment of Behcet´s syndrome in a 16 year old girl
Elena Koskova[1], Daniela Salatová[2], Stanislava Blažíčková[1], Vladimír Bošák[1], Jozef Rovenský[1]
[1]National Institute of Rheumatic Diseases, Piešťany, [2]Pediatric Rheumatology Outpatient´s Department, Žilina, Slovakia

P29 Investigation of connective tissue diseases depending on serologic markers in young women who have somatisation disorders order and carried out systemic interrogation in details
Ozgur Tanriverdi
Safak Health Group Goztepe Hospital, Istanbul, Turkey

P30 The effect of the different doses of alfacalcidol on regulatory T-cells in patients with undifferentiated connective tissue disease
Éva Zöld, Sándor Baráth, János Kappelmayer, László Csáthy, Edit Gyimesi, Ágota Hajas, Margit Zeher, Gyula Szegedi, Edit Bodolay
University of Debrecen, Hungary

P31 What is the minimum duration of symptoms to suspect undifferentiated arthritis?
Burkhard F. Leeb[1], Pia M. Haindl[1], Klaus P. Machold[2], Bernhard Rintelen[1], Manfred Herold[3]
[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Universitätsklinik III AKH Wien, [3]Universitätsklinik Innsbruck, Austria

P32 Initial therapy in patients with undifferentiated peripheral inflammatory arthritis: A systematic literature review
Burkhard F. Leeb[1], Pia M. Haindl[1], Hans Peter Brezinschek[2], Bernhard Rintelen[1], Gabriele Eberl[3]
[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Universitätsklinik Graz, Rheumaklinikum Malcherhof, Baden, Austria

P33 Optimal time to start disease modifying therapy in patients with undifferentiated peripheral arthritis: A systematic literature review and expert consensus
Burkhard F. Leeb[1], Pia M. Haindl[1], Gabriele Eberl[2], Manfred Herold[3], Bernhard Rintelen[1]
[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Rheumaklinikum Malcherhof, Baden, [3]Universitätsklinik Innsbruck, Austria

P34 A comparison of patient questionnaires and composite indexes in routine care of rheumatoid arthritis patients
Burkhard F. Leeb, Judith Sautner, Harsono T. Mai, Pia M. Haindl, Bernhard Rintelen
Lower Austrian State Hospital Weinviertel Stockerau, Austria

P35 Usefulness of procalcitonin measurement in differentiating between activity of systemic autoimmune disease and bacterial infection
Olga Sleglova[1], Helena Dejmková[1], Jana Uhrova[2], Jaromir Belacek[3]
[1]Institute of Rheumatology, [2]Institute of Clinical Biochemistry, [3]Charles University, Prague, Czech Republic

P36 Measurement of interleukin-1-receptor antagonist in patients with systemic lupus erythematosus could predict renal manifestation of the disease
Boglárka Brúgós[1], Emese Kiss[2], Gyula Szegedi[1], Sándor Sipka[1], Margit Zeher[1]
[1]University of Debrecen, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P37 Involvement of specific types of laminin in glomerulal basement membrane of patients with lupus nephritis and monitoring of serum levels of laminin as possible marker of organ damage
Hana Ciferska[1], Pavel Horak[1], Josef Zadrazil[1], Zuzana Hermanova[2], Yrjo Konttinen[3], Martin Tichy[1]
[1]University of Olomouc, [2]Faculty Hospital, Olomouc, Czech Republic, [3]University of Helsinki, Finland

P38 Challenges and experiences of teaching courses of the modified Rodnan skin score assessment in systemic sclerosis
Tünde Minier[1], Ruxandra Ionescu[2], Simona Rednic[3], Nemanja Damjanov[4], Cecília Varjú[1], Zoltán Nagy[5], László Czirják[1]
[1]University of Pécs, Hungary, [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, [3]University of Medicine and Pharmacy Iuliu Hatieganu, Cluj-Napoca, Romania, [4]Institute of Rheumatology Belgrade, Serbia, [5]Szatmár-Bereg Hospital and Medical Bath, Fehérgyarmat, Hungary

P39 Construct validity evaluation of the European Scleroderma Study Group activity index, and investigation of possible new disease activity markers in systemic sclerosis
Tünde Minier[1], Zoltán Nagy[2], Zsófia Bálint[1], Helka Farkas[1], Gábor Kumánovics[1], Diána Simon[1], Cecília Varjú[1], Péter Németh[1], László Czirják[1]
[1]University of Pécs, [2]Szatmár-Bereg Hospital and Medical Bath, Fehérgyarmat, Hungary

P40 Patient and physicians global assessment on disease activity of rheumatoid arthritis
Bernadette Rojkovich[1], András Inotai[2], Ágnes Mészáros[2], Emese Jászay[1], Katalin Imre[1], Györgyi Mészáros[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]Semmelweis University, Budapest, Hungary

P41 The rheumatoid arthritis EULAR response criteria compared to the RADAI-5 response in daily routine
Bernhard Rintelen, Pia M. Haindl, Judith Sautner, Barbara A. Leeb, Christiane Kaspar, Burkhard F. Leeb
Lower Austrian State Hospital Weinviertel Stockerau, Austria

P42 Proposals for thresholds to express improvement and deterioration in rheumatoid arthritis patients according to the RADAI-5
Bernhard Rintelen, Judith Sautner, Christiane Kaspar, Pia M. Haindl, Barbara A. Leeb, Burkhard F. Leeb
Lower Austrian State Hospital Weinviertel Stockerau, Austria

P43 Summary findings of a systematic review of global ultrasound scores for the assessment of synovitis in rheumatoid arthritis
Péter Mandl[1], Péter V. Bálint[1], Esperanza Naredo[2], Richard J. Wakefield[3], Maria-Antonietta D'Agostino[5], on behalf of the OMERACT-EULAR Ultrasound Group
[1]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary, [2]Hospital Severo Ochoa, Madrid, Spain, [3]University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom, [4]Paris-Ouest-Versailles Saint Quentin en Yvelines University, Paris, France

P44 Ultrasound for detecting abnormal effusion and synovial proliferation in the knee – which knee position is the best?
Péter Mandl[1], Lene Terslev[2], Wolfgang A. Schmidt[3], Myriam Brossard[4], Péter V. Bálint[1], Esperanza Naredo[5], Richard J. Wakefield[6], Maria-Antonietta D'Agostino[7] on behalf of the OMERACT-EULAR Ultrasound Group
[1]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary, [2]University of Copenhagen Hospitals at Hvidovre and Glostrup, Denmark, [3]Medical Centre for Rheumatology Berlin-Buch, Immanuel Krankenhaus, Berlin, Germany, [4]Versailles-Saint Quentin en Yvelines University; APHP, Ambroise-Paré Hospital, Boulogne-Billancourt, France, [5]Hospital Severo Ochoa, Madrid, Spain, [6]University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom, [7]Paris-Ouest-Versailles Saint Quentin en Yvelines University, Paris, France

P45 Tumor necrosis factor alpha and soluble tumor necrosis factor receptor type 1 levels comparison in blood serum in rheumathoid arthritis and ankylosing spondylitis patients
Inita Bulina[1], Daina Andersone[1], Vladimirs Lavrentjevs[2], Janis Arajs[2], Ineta Astica[2], Julija Zepa[2], Evita Sikora[2], Sarmite Abelite[2], Inta Jaunalksne[2]
[1]Latvian University, [2]Pauls Stradins Clinical University Hospital, Riga, Latvia

P46 Radiological particularities of joint involves in women with ankylosing spondylitis in correlation with HLA-B27 antigen
Oxana Sirbu, Liliana Groppa, Eugeniu Russu
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

P47 Experience with the use of Quantiferon test, a novel method to detect tuberculosis, in two arthritis centers in Budapest, Hungary
István Á. Juhász[1], Judit Korda[2], Bernadette Rojkovich[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P48 Experiences with tumour necrosis factor alpha inhibitors in patients with juvenile idiopathic arthritis. Hungarian data from the National Institute of Rheumatology and Physiotherapy registry
Krisztina Sevcic[1], Ilonka Orbán[1], Valentin Brodszky[2], Anna Bazsó[1], Zsolt Balogh[1], Emese Kiss[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Corvinus University, Budapest, Hungary

P49 Treatment of adult juvenile idiopathic arthritis patients with TNF-blockers and effect of switching to a second anti-TNF agent. Data from the Czech National Registry
Katerina Jarosova[1], Karel Chroust[2], Lucie Burešová[2], Jiří Vencovský[1]
[1]Charles University Prague, [2]Institute of Biostatistics and Analyses, Brno, Czech Republic

P50 Biological therapy in patients with rheumatoid arthritis (observation for longer time)
Oľga Lukáčová, Jozef Lukáč, Jozef Rovenský
National Institute of Rheumatic Diseases, Piešťany, Slovakia

P51 A long-term follow up in the Czech National Registry ATTRA: Efficacy of anti-TNF-alpha inhibitors on the quality of life in rheumatoid arthritis and ankylosing spondylitis patients
Katarína Hviščová[1], Liliana Šedová[1], Karel Chroust[2], Lucie Burešová[2], Karel Pavelka[1]
[1]Institute of Rheumatology Prague, [2]Masaryk University, Brno, Czech Republic

P52 Assessment of fatigue in patients with ankylosing spondylitis receiving biological TNF antagonist therapy
Secil Demirdal, Fatıma Yaman, Hasan Toktas, Vural Kavuncu
Afyon Kocatepe University, School of Medicine, Afyonkarahisar, Turkey

P53 Methotrexate-naive psoriatic arthritis patients respond rapidly to infliximab plus methotrexate therapy – results from the RESPOND trial
Helena Raffayova[1], N. Kungurov[2], A. Kubanova[3], A. Baranaskaite[4], A. Venalis[5], L. Helmle[6], E. Nasonov[7]
[1]National Institute of Rheumatic Diseases, Piešťany, Slovakia, [2]Ural Dermatovenerology Institute, Jekaterinburg, Russia, [3]Centra DermatoVenerology Institute, Moscow, Russia, [4]Kaunas MedicalUniversity Hospital, Lithuania, [5]Vilnius University Hospital, Lithuania, [6]Schering-Plough Corp., Budapest, Hungary, [7]Central Rheumatology Institute, Moscow, Russia

P54 Biologic therapy and pregnancy
Ilona Ujfalussy[1], Bernadette Rojkovich[2], Éva Koó[2], László Czirják[3], Cecília Varjú[3], Zoltán Szekanecz[4], Katalin Nagy[5], Ilonka Orbán[6]
[1]Ministry of Defence, State Medical Centre, Budapest, [2] Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, [3]University of Pécs, [4]University of Debrecen, [5]Markhot Ferenc Hospital, Eger, [6]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P55 TNF-alpha antagonist treatment of renal amyloidosis complicating rheumatoid arthritis. A five-year follow-up of two patients
Györgyi Mészáros[1], Kálmán Polner[2], Bernadette Rojkovich[1], István Á. Juhász[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]St. Margit Hospital, Budapest, Hungary

P56 HLA-DRB1*15 is associated with very high levels of anti-cyclic citrullinated peptide antibodies and non response to infliximab in rheumatoid arthritis
Judit Laki [1,2], Emeli Lundström[2], Omri Snir[2], Johan Rönnelid[3], Sædis Sævarsdottír[2], Marius Wick[2], Lars Alfredsson[3], Lars Klareskog[2], Leonid Padyukov[2]
[1]Ministry of Defence, State Medical Centre, Budapest, Hungary, [2]Karolinska Institutet, Stockholm, [3]Uppsala University, Sweden

P57 On the occurrence of compelling reasons for the interruption of treatment with TNF-alpha inhibitors
Éva Lányi, Pál Géher
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

P58 Difficulties in the management of patients with biological therapy
Katalin Nagy, Judit Jász, Mária Pelsőczy, Eszter Deák
Markhot Ferenc Hospital, Eger, Hungary

P59 Tocilizumab induced Tako-Tsubo cardiomyopathy in a patient with rheumatoid arthritis
Angéla Tóth[1], Ilona Márkus[1], Klára Barabás[2], László Krivanek[2], Gyula Poór[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Health Service of First District of Budapest, Hungary

P60 Comparison of occurrence of adverse events in patients with rheumatoid arthritis and ankylosing spondylitis treated with biologic therapy in Czech National Registry ATTRA
Šárka Forejtová[1], Hermann Mann[1], Karel Chroust[2], Lucie Burešová[2], Karel Pavelka[1]
[1]Institute of Rheumatology, Prague, [2]Institute of Biostatistics and Analyses, Brno, Czech Republic

P61 Acquired inhibitor to factor VIII in patient with rheumatoid arthritis previously on biologics
Katalin Imre[1], László Nemes[2], Bernadette Rojkovich[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]Ministry of Defence, State Medical Centre, Budapest, Hungary

P62 Effectiveness of leflunomide in psoriatic joint and skin disease: Results from a multinational non-interventional study of psoriatic arthritis treated with leflunomide
F. Behrens[1,2], K. Pavelka[3], J. Štolfa[3], A. Sipek-Dolnicar[4], H. Burkhardt[1,2], On behalf of the OSPAL-Study Group
[1]Johann Wolfgang Goethe University, Frankfurt am Main, Germany, [2]Rheumazentrum Rhein-Main, Germany, [3]Institute of Rheumatology, Prague, Czech Republic, [4]University Medical Center Ljubljana, Slovenia

P63 Association of methotrexate treatment and serum levels of Dickkopf-1 and cartilage oligomeric matrix protein in rheumatoid arthritis patients
Jerzy Swierkot, Katarzyna Gruszecka Marczynska, Agnieszka Matuszewska, Piotr Wiland
Wroclaw Medical University, Poland

P64 Life-threatening leucopenia during methotrexate therapy of rheumatoid arthritis
Petr Bradna, Jaroslav Maly, Tomas Soukup, Alzbeta Zavrelova, Jan Toms, Oldrich Siroky, Miroslav Pecka, Dalibor Milka
Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Czech Republic

P65 Retrospective study of polymyalgia rheumatica treated with glucocorticoids plus methotrexate
Zsuzsa Schmidt, György Hittner, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P66 Sympathoneural and adrenomedullary responses to orthostasis in female patients with rheumatoid arthritis
Jozef Rovenský, Miroslav Vlcek, Adela Penesova, Martin Zlnay, Anna Scipova, Zofia Radikova, Richard Imrich
Institute of Experimental Endocrinology, Bratislava, Slovakia

P67 Age peculiarities of bone loss in women with rheumatoid arthritis
Vladyslav Povoroznyuk, Tetyana Karasevska
Institute of Gerontology AMS, Kiev, Ukraine

P68 Osteoporosis in patients of different age with ankylosing spondylitis
Vladyslav Povoroznyuk
Institute of Gerontology AMS, Kiev, Ukraine

P69 Vitamin-D deficiency and insufficiency in Ukrainian population
Vladyslav Povoroznyuk, Nataliya I. Balatska, Victor Y. Muts, Tetiana Y. Solonenko, Volodymyr Vayda
Institute of Gerontology AMS, Kiev, Ukraine

P70 Effect of zolendronic acid in treatment of postmenopausal women with osteoporosis
Vladyslav V. Povoroznyuk, Nataliia Grygorieva, Volodymyr Vayda, Nataliia Dzerovych, Nataliya I. Balatska
Institute of Gerontology AMS, Kiev, Ukraine

P71 Prevention of osteoporosis in Northern youth
Milana Petrova N.
North-Eastern Federal University, Yakutsk, Russia

P72 The role of Vitamin-D and calcium in prevention of postmenopausal osteoporosis
Nikolov Tatjana[1], Vladimir Bobic[2], Branislav Bobic[1]
[1]Institute for Rheumatology Novi Sad, [2]Pfizer H.C.P, Corporation Beograd, Serbia

P73 A ten year study of clinical fractures, changes in density, risk factors and FRAX in normal and osteopenic postmenopausal women
Csaba Kiss, Éva Ruzicska, Gyula Poór
National Institute of Rheumatology and Phisiotherapy, Budapest, Hungary

P74 Evaluation of Achilles tendon and plantar fascia in diffuse idiopathic skeletal hyperostosis by ultrasound and X-ray
Csaba Kiss, Ádám Mester, Péter Mandl, Éva Ruzicska, Péter Bálint, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P75 Quantifying of serum concentration of beta crosslaps as a factor of estimate in efficacy bisphosphonate therapy in postmenopausal women with osteoporosis
Aleksandar Jovanovski[1], Olgica Rankovic[1], Jadranka Bozovic-Jelic[1], Zoran Grujic[2]
[1]Regional Hospital Sabac, [2]Special Hospital for rheumatology Banja Koviljaca, Serbia

P76 Proposition for a national training program in musculoskeletal ultrasound in Hungary, based on available programs in Europe and in the United States
Katalin Áts, Péter Mandl, Éva Ruzicska, György Hittner, László Hodinka, Péter Bálint, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P77 Psychosomatic status in patients with gout
Larisa Rotaru, Liliana Groppa, Elena Deseatnicova, Mircea Revenco
State Medical and Pharmaceutical University, Kishinau, Moldova

P78 Cognitive dysfunction in the Czech population of patients with systemic lupus erythematosus
Radka Svobodova[1], Marie Posmurova[1], Vera Peterova[2], Petr Kozelek[2], Ivana Putova[1], Marketa Fojtíková[1], Ctibor Dostal[1], Marta Olejarova[1]
[1]Institute of Rheumatology, [2]Faculty Hospital of Charles University, Prague, Czech Republic

P79 Rehabilitation in rheumatology in the era of biological therapy
Márta Király, Judit Ortutay
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P80 Inpatient rehabilitation of musculoskeletal diseases in centres of the Austrian Pension Insurance Institution – data of outcome measurement
Werner Kullich[1], Rudolf Müller[2]
[1]LBG, Institute for Rehabilitation, Cluster Rheumatology, Balneology, Rehabilitation, Saalfelden, [2]PVA – Pension Insurance Institution, Vienna, Austria

P81 Clinical characteristics of 97 patients with inflammatory myopathy
Cecília Varjú, Tünde Minier, Mónika Péter, Krisztina Parti, Gábor Kumánovics, Dániel Kehl, Tímea Berki, Diána Simon, László Czirják
University of Pécs, Hungary

P82 Clinical characteristics of patients with immunodeficiency syndromes
Dóra Niedermayer, Gábor Kumánovics, László Czirják, Tímea Berki, Gábor Sütő
University of Pécs, Pécs, Hungary

P83 Distinct phenotypes in mixed connective tissue disease: Subgroups and survival
Ágota Hajas[1], Péter Szodoray[2], Éva Zöld[1], István Csípő[1], Margit Zeher[1], Gyula Szegedi[1], Edit Bodolay[1]
[1]University of Debrecen, Hungary, [2]University of Oslo, Norway

P84 About Wegener's granulomatosis: Results from a single centre
Anna Polgár, Gyula Poór, Emese Kiss
National Institute of Rheumatology and Physioterapy, Budapest, Hungary

P85 Formal pathogenesis of AA amyloidosis in rheumatoid arthritis
Miklós Bély [1], Ágnes Apáthy[2]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P86 High prevalence of amyloidosis AA in patients with adult onset Still's disease
Arkadiusz Chlebicki[1], Bożena Kowalewska[1], Eliza Roszkowska[1], Renata Wojtala[2], Piotr Wiland[1]
[1]Academic Clinical Hospital Wrocław, [2]Medical University, Wrocław, Poland

P87 Pregnancy in patients with systemic connective tissue diseases. Results of two-years study
Dana Tegzova[1], Katerina Andelova[2], Ivana Kucerova[2]
[1]Charles University, [2]Institute for the Care of Mother and Child, Prague, Czech Republic

P88 Primary Sjögren's syndrome associated liver involvement
Gábor Sütő, Tímea Berki, László Pálinkás, Péter Németh, László Czirják
University of Pécs, Hungary

P89 Muckle Wells syndrome in a Hungarian girl
Ilonka Orbán, Krisztina Sevcic, Emese Kiss
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P90 Subcutan calcinosis: Case history
Angéla Fülöp, Bernadette Rojkovich
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

P91 Diagnostic difficulties and therapeutic success in a case with primary central nervous system vasculitis
Edit Vereckei, Anna Bazsó, Gyula Poór, Emese Kiss
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P92 Scintigraphic, biochemical and clinical response to zoledronic acid treatment in patients with Paget's disease of bone
Judith Donáth, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

P93 Undenaturated collagen type I. in the treatment of painful osteoarthritis of the knee
Roman Stančík[1], Jozef Rovenský[1], Jozef Zvarka[1], Maria Stancikova[1], Marian Hlavac[2], Vladimir Kubinec[2]
[1]National Institute of Rheumatic Diseases, Piešťany, [2]FDR Hospital, Banska Bystrica, Slovakia

P94 Effect of virgin olive oil phonophoresis on exercise-induced chondromalacia
Babak Nakhostin-Roohi[1], S. Bohlooli[2], F. Khoshkhahesh[3]
[1]Islamic Azad University-Ardabil Branch, [2]Ardabil University of Medical Sciences, [3]The University of Mohaghegh-Ardabili, Iran

P95 Significance of some oxidant and antioxidant enzymes in fibromyalgia
Daniela Cepoi-Bulgac
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

P96 Direct costs of chronic low back pain in Austria
Ernst Wagner
RSKA der NOEGKK, Baden, Austria

P97 National Health Service, insurance companies – from medical expert point of view
Krisztina Baraczka
Semmelweis University Budapest, Hungary

P98 Self help groups for patients with arthritis/rheumatism in Hungary
Judit Ortutay
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

09.30–10.30 Efficacy of teriparatide in the treatment of severe osteoporosis
Satellite symposium: Eli Lilly
Chairman: Juraj Payer

Welcome and objectives of the symposium
Juraj Payer
Comenius University, Bratislava, Slovakia

OS18 Anabolic therapy in the severely osteoporotic patient
Astrid Fahrleitner-Pammer
Medical University of Graz, Austria

OS19 Clinical presentation and treatment of glucocorticoid-induced osteoporosis
Willem F. Lems
Vrije Universty Medical Centre Amsterdam, The Netherlands

Discussion

10.30–11.00 Coffee break

11.00–12.00 New worlds in rheumatoid arthritis management
Satellite symposium: Roche
Chairman: Gyula Poór

OS20 B-cell therapy: A “positive” direction to personalized healthcare in rheumatoid arthritis
Zoltán Szekanecz
University of Debrecen, Hungary

OS21 Tocilizumab efficacy: The science of IL-6R inhibition
László Czirják
University of Pécs, Hungary

OS22 Safety of tocilizumab in patients with rheumatoid arthritis: Analysis of long-term extension studies
Ronald van Vollenhoven
Karolinska University Stockholm, Sweden

Discussion

12.00 Closing of the CECR

12.00-13.00 Lunch-time

13.00 Opening of the Congress of the Hungarian Association of Rheumatologists

Abstracts of the 8th Central European Congress of Rheumatology 23rd–25th September 2010, Sopron, Hungary

The list of the abstracts is not complete since the organizers have not received all of them until the deadline given. The authors not the organizers are responsible for the content of the abstracts.

Oral presentations of scientific sections (O)

O1

Synovial biopsy for the assessment of rheumatoid arthritis and the action of biologics

Paul Peter Tak
Academic Medical Center, University of Amsterdam, The Netherlands

Examination of serial synovial biopsies has been instrumental in the evaluation of novel targeted therapies in rheumatoid arthritis (RA). This approach, which is generally well-tolerated by the patients, has been used in various ways to provide insight into the pathogenesis of the disease and the mechanism of action of the therapy (for instance, TNF blockade and rituximab treatment), as well as for selection purposes during early drug development (e.g. chemokine and chemokine receptor antagonists). For the latter objective, three types of data are obtained: (1) clinical data (e.g. the DAS28); (2) synovial biomarkers specifically related to the mechanism of action of the therapy, for example, CCR1-positive cells in the synovium and peripheral blood after anti-CCR1 therapy or B cells and plasma cells after rituximab treatment; and (3) biomarkers that are related to changes in clinical signs and symptoms independent of the primary mechanism of action (thus far, most of the data are available for CD68-positive macrophages in RA). Based on these data, we recommend a rethinking of the therapeutic strategy to large clinical trials when there is no change in DAS28, no specific effects related to the mechanism of action and no change in macrophage numbers after treatment: the drug might not hit the target effectively or the concept behind the role of the target in the pathogenesis might be wrong. When there is a signal in at least one of the variables, the next step would be to test the drug in conventional studies to determine whether the biological effect translates into clinically relevant improvement. Such proof-of-concept studies can also help to optimize the range of dosages to be tested in the phase II/III trials. Taken together, analysis of molecular markers in synovial tissue is increasingly used in clinical trials on targeted therapies. With this approach, tissue specificity is not a problem and examination of serial biopsy samples can be used to monitor the response in individual patients and screen for interesting biological effects at the site of inflammation. It can be anticipated that future development will include the use of more extensive markers of joint degradation – in addition to the available markers of inflammation – as well as the use of panels of biomarkers in synovial tissue samples combined with other biomarkers.

O2

Bone marrow in the pathogenesis of rheumatoid arthritis

Wlodzimierz Maslinski, Weronika Rudnicka, Ewa Warnawin, Anna Radzikowska, Monika Prochorec, Tomasz Burakowski, Magdalena Chorazy-Massalska, Ewa Kontny, Paweł Małdyk
Institute of Rheumatology, Warsaw, Poland

Despite intensive research and great progress in understanding mechanisms contributing to chronic inflammation and joint destruction in rheumatoid arthritis (RA), the pathogenesis of this disease still remains unknown. Recent data indicate that beside affected joints, lymphoid organs, and especially the bone marrow (BM) compartment may actively participate in the initiation and perpetuation of the autoimmune-inflammatory processes in RA. BM edema, reflecting true inflammation, is often seen both in early as well as in advanced RA. Recent analysis of RA bone marrow confirms ongoing abnormal immune processes in this compartment. Comparison of RA and osteoarthritis (OA) clearly document overproduction of proinflammatory cytokines: IL-1, IL-6, TNF-α, IL-15 and IL-17, and osteoclastogenic RANKL in RA bone marrow. Moreover, activated, memory type CD4+ and CD8+, and Th17 T-cells are present in situ in higher numbers in RA. Higher ratio of CD4+/CD8+ T cells expressing early activation marker CD69 in RA bone marrow suggest their activation in situ. In addition, reduced number of forkhead box P3 (FOXP3) positive regulatory T-cells is present in RA, in comparison to OA indicates lower capacity of immunoregulation in RA bone marrow. Histological analysis of RA bone marrow, obtained by trephine biopsies, revealing the presence of germinal centers with higher proportions of CD4+ T-cells, not only in advanced RA but also in the early stages of RA, confirms involvement of this compartment in the autoimmune immune processes from the beginning

of the disease. Although at present it is not entirely clear what triggers the inflammation in RA BM, our data indicate higher frequency and levels of eubacterial DNA than in OA BM. Functional TLR9, responding to bacterial DNA by increased proinflammatory cytokine production (TNF-α, IL-6), overexpression of costimulatory molecules (CD86), proliferation and differentiation toward plasma cells, are gained by BM B-cells at pre-B/immature B-cell stages of their maturation in BM. These effects are enhanced in the presence of IL-15. Freshly isolated RA BM CD20+ B-cells exert higher CD86 expression than OA bone marrow cells, suggesting their activation in situ. Taken together these data indicate important role of BM compartment in the initiation and/or propagation of inflammation in RA that should be considered for successful targeted therapies in RA.

O3

Cytokine activities in rheumatoid arthritis pathogenesis

Iain McInnes
University of Glasgow, Scotland

Cytokines are central to the initiation and perpetuation of the synovial inflammatory response in rheumatoid arthritis (RA). We have recently been exploring those pathways that perpetuate cytokine production including cellular interactions, lipid interactions and epigenetic regulatory pathways. It remains our contention that unraveling these interactions will lead to increased pathogenetic understanding and in due course to refined therapeutic interventions.

O4

B-cells and their targeting in rheumatoid arthritis

Péter Szodoray
University of Oslo, Norway

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease that affects primarily the joints and results in their progressive destruction.
Although T-cells greatly outnumber B-cells in RA synovium, synovial tissue is nevertheless an active site of B-cell differentiation. Plasma cells are present and synovial tissue is an antibody-producing organ in RA. Furthermore, in RA joints and synovial membrane, B-cells secrete cytokines (e.g. IL-6, IL-10, TNF-α) and chemokines, and may function as antigen presenting cells. The central function of B-cells identifies them as excellent targets for immunosuppressive therapy. Targeting the B-cell antigen CD20 by Rituximab (RTX) causes rapid and specific B-cell depletion. Following B-cell depletion in patients with RA, a positive clinical response occurred in correlation with a significant drop in the levels of CRP and autoantibodies (IgA-, IgM-, and IgG-class RF, and anti-CCP). Contrary to CD20, CD19 expression can be detected on pro-B cells, as well as on all mature B-cell subsets and even in a fraction of mature plasma cells. Targeting of CD19 is a promising alternative and trials with humanized anti-CD19 antibodies are under development. Another potential, effective B-cell and pre-plasma cell target could be CD79; which in addition to cell-death initiation, also inhibits B-cell receptor (BCR) activation and could contribute to ectopic germinal center depletion.
Interfering with B-cell co-stimulatory molecules/molecular pairs, amongst others CD40, CD40L (CD154), inducible costimulator (ICOS) and its ligand (ICOS-L), can lead to disrupted B-cell activation. Toll-like receptors (TLRs), mainly TLR 7 and 9 can induce B-cell activation upon ligand encounter, and eventually lead to autoantibody production; TLR 9/7 inhibitor is under development for RA. Anti-cytokine (IL-6, IL-17, IL-21, LT, TNF-α and chemokine (CXCL10, 12, 13) therapy can be efficacious in RA by the disruption of B-cell activation and autoantibody production, B-cell synovial migration and ectopic GC formation. Presumably one of the most important molecules in B-cell stimulation is BAFF/BLyS (B-cell activating factor). BAFF and APRIL (a proliferation-inducing ligand) are members of the TNF superfamily. BAFF induces B-cell proliferation and differentiation In vitro, BAFF increases survival of both immature and mature B-cells and serum levels of BAFF have been shown to be elevated in patients with RA. Moreover, BAFF levels correlated positively with RF titers among seropositive RA patients. Anti-BAFF antibodies (Belimumab) or BAFF-R-Ig provide selective BAFF blockade, whereas agents that bind TACI (TACI-Ig; Atacicept) interrupt both BAFF and APRIL-mediated signaling. Targeting BAFF/APRIL has shown clinical promise and safety in a phase 2 study of Belimumab and a phase 1b study of Atacicept. Post-receptor targeting, aiming the effector signal transduction pathways, including the spleen tyrosine kinase (Syk), required for proximal BCR signaling has also been found efficacious in early clinical trials in RA. Finally, the recent identification of regulatory B-cells (B-reg) may warn for cautious B-cell depletion in RA. The better insight in the pathogenic role of B-cells provides opportunities to improve prognosis and therapy of RA.

O5

Novel strategies for the treatment of arthritis

Steffen Gay
University Hospital, Zurich, Switzerland

After the successful implementation of the novel “biologicals” into the treatment regimen of patients with rheumatoid arthritis (RA), over 700 clinical trials have been registered to compare to and even more to improve current therapies. However, none of the therapies in present use and development have resulted so far in an ACR 70 in more than 60% of the treated patients.

Therefore the question to be asked is: Why we can not do better, and why we can not (yet) cure the disease? It is well established that RA is an autoimmune disease characterized by the progressive destruction of the involved joints. Although we target and consequently remove monocytes/macrophages and/or B and T lymphocytes successfully from the affected joints, no therapies have been attacking the synovial fibroblast (SF) in RA. We and others have shown that the RA-SF are endogenously activated, grow invasively and able to migrate in the absence of stimulating cells and cytokines that it appears logically to target these cells. Based on earlier observations that RA-SF express also Toll- and Nod-like receptors which upon stimulation with various exogenous and endogenous ligands express powerful proinflammatory chemokines and cytokines, it is important to target these cells, because these cells appear responsible for the re-attraction of inflammatory immune cells to the involved joints after cell depleting therapies. In the search of factors leading to the state of intrinsic activation of RA-SF we have explored epigenetic processes, including cell regulation mediated by acetylation, methylation, ubiquination and microRNAs . Author demonstrated that RA synovium is hyperacetylated and that RA-SF are demethylated, modified by ubiquination through sumoylation and characterized by specific microRNAs.
These data clearly point to target synovial activation in the pathogenesis of RA by the development of novel drugs beyond current therapeutic strategies.

O6

Advances in the therapy of myositis

Jiří Vencovský
Institute of Rheumatology, Prague, Czech Republic

The most common idiopathic inflammatory myopathies (IMM) comprise dermatomyositis (DM), polymyositis (PM) and sporadic inclusion body myositis (sIBM). The aetiology of these diseases is largely unknown and hence the difficulties in their treatment. There is an evidence for immune pathogenesis of PM and DM, and to a lesser extent for sIBM, which include frequent association with disease specific autoantibodies, occasional combination with other connective tissue diseases, inflammatory infiltrates in the affected muscles, frequent systemic features and visceral involvement, and finally, although variable, the response to immunosuppressive treatment. Consequently, therapeutical approaches have been predominantly aimed at suppression of immune regulations. Treatment of sIBM has been largely unsuccessful; in a recent proof-of-principal study disease progression had been slowed after one series of alemtuzumab infusions. Treatment of PM and DM is usually initiated with glucocorticoids. Medium doses have been used in some uncontrolled studies with diminished frequency of side effects; however, high doses are advocated by most. Slow tapering according to the clinical response should follow. Steroid myopathy may be a complication which can be distinguished from active disease by dose reduction or use of MRI. Clinical experience suggests that addition of immunosuppressive drugs to glucocorticoids is indicated in the majority of patients either to improve outcome or reduce side effects of long-term glucocorticoid treatment. Since the data show that the prognosis is worse if the treatment is delayed, the situation of long and insufficiently suppressed activity should be limited. There have been only few controlled trials in PM and DM performed, usually with relatively low number of patients enrolled. These trials include: i) a double blind trial with azathioprine+prednisolone as initial treatment of 16 PM patients, which showed improvement in functional ability at 1 and 3 years after initiating treatment; ii) trial in 39 patients with plasmapheresis and leukapheresis, which failed to show efficacy; and iii) administration of high i.v. immunoglobulin doses, which demonstrated beneficial effect in 15 DM patients. Combination therapy with azathioprine and methotrexate as well as high dose of intravenous methotrexate with leucovorine rescue showed some effectiveness in a cross over trial. Open studies, case series or clinical experience suggest effectiveness of methotrexate, cyclosporine A, combination of methotrexate+cyclosporine, mycophenolate mofetil, tacrolimus, cyclophosphamide, and leflunomide. Anti- TNF treatment has been effective in some patients, but preliminary experience from controlled trials is not encouraging, even with disease worsening observed in some patients. Several reports suggest beneficial effect of rituximab and a large controlled trial in 200 patients is ongoing. The International Myositis Assessment and Clinical Studies (IMACS) group has recently developed and partially validated the outcome measures for disease activity and damage in PM and DM that can be now used for assessment in clinical trials and this fact should improve the evaluation of the treatment benefit and comparison between different treatment modalities in the future.

O7

New possibilities in the treatment of vasculitis

Vladimir Tesar
Charles University, Prague, Czech Republic

Cyclophosphamide dramatically improved the outcome of patients with ANCA-associated vasculitis (AAV – Wegener granulomatosis and microscopic polyangiitis), but, unfortunately at the expenses of serious acute (leukopenia, infections) and chronic (myelodysplasia, secondary malignancies) toxicities. Although the cumulative dose of cyclophosphamide may be substantially reduced by limiting the length of induction treatment and by using cyclophosphamide pulses instead of oral continuous cyclophosphamide

the search for at least comparably effective and less toxic treatment is clearly warranted. Mycophenolate mofetil is currently compared with cyclophosphamide as an alternative induction treatment in early systemic AAV, but, rather surprisingly, mycophenolate was shown to be inferior to azathioprine as a maintenance treatment of AAV. Experience with biologic treatment in AAV has been until recently very limited, although e.g. alemtuzumab (anti-CD52) was demonstrated to induce remission even in patients refractory to conventional treatment. Rituximab was very recently shown to be as effective as cyclophosphamide in inducing remission of newly diagnosed AAV and in uncontrolled study repeated preemptive courses of cyclophosphamide were able to prevent relapses of AAV. The role of rituximab in the maintenance treatment of AAV is currently tested in the randomized controlled trial.

Due to the relative paucity of AAV, patients with suspected AAV should be referred to specialized centres with the immediate availability of ANCA titres, kidney biopsy evaluation, dialysis and plasma exchange, intensive care unit and access to and experience with the biologic treatment for refractory patients.

O8

New prospective biologicals in the treatment of rheumatoid arthritis

Ladislav Šenolt
Institute of Rheumatology, Prague, Czech Republic

The treatment of rheumatoid arthritis (RA) has undergone dramatic changes during recent years. New and effective cytokine and cell targeted therapies have become available in clinical practice. Blocking pro-inflammatory cytokines such as tumor necrosis factor (TNF)-alpha, interleukin (IL)-1 or IL-6 as well as B-cell depleting therapy and blocking activation of T-cells dramatically improved outcome of patients with RA. However, despite this progress, majority of patients with RA still do not reach complete remission. Advances in the current knowledge of pathogenic processes of RA and the progress in manufacturing biotechnologies are contributing to the development of novel therapies for immune mediated diseases being in different phases of clinical trials. Prospective biological agents for RA targeting different cytokines/immune mediators (e.g. GM-CSF, IL17 or IL-23), catalytic enzymes (e.g. cathepsins) and cell targeted therapies (e.g. newer inhibitors of B-cells) will be discussed. In addition, new disease modifying antirheumatic drugs known as small molecules that target cellular kinases (e.g. p38, JAK or Syk) as well as new local therapeutics for RA (e.g. anti-FAS) have promising results from early phase clinical trials. Hopefully, promising results of some clinical trials will determine new therapeutic targets and help to extend therapeutic armamentarium for patients with RA.

O9

Pathogenetic background of spondylarthritis

Joachim Sieper
Charité University Berlin, Germany

The exposure to bacteria, such as infections leading to reactive arthritis or gut bacteria in case of Crohn's disease, and the presence of HLA-B27 are important prerequisites for the development of spondyloarthritis (SpA). Furthermore, MRI- and histological studies clearly indicate that inflammation in the axial skeleton occur at the bone/cartilage interface suggesting that the cartilage might be the target of the immune response. How bacteria, HLA-B27 and the cartilage directed immune-response interact is a matter of debate. It is also not clear which part of the immune systems mediates this interaction: adaptive vs innate immune system, T-cells vs non T-cells? However, a further clarification of these mechanisms is crucial for the development of curative therapies in the future. Regarding the current status of targeted therapies, only the blockade of TNF-alpha has been proven to be highly effective but not any of the other immunological targets tested so far in therapeutical trials.

O10

New approaches in the diagnostics and monitoring of spondyloarthritis

Maxime Dougados
René Descartes University, Paris, France

Recently, the international scientific society dealing with outcome measures in spondyloarthritis (e.g. ASAS) has promoted an initiative aimed at proposing new criteria for the recognition of patients presenting with axial symptoms and suffering from spondyloarthritis.

These criteria are very important because of at least 2 reasons:

The first one is the official recognition of the concept of spondyloarthritis and thereafter, that the description of patients with regard to their clinical presentation (e.g. axial versus peripheral versus extra-articular clinical features) is more relevant than recognition of a sub-entity of spondyloarthritis (e.g. ankylosing spondylitis, psoriatic arthritis c).

The second one is the integration in the set of criteria of investigations currently performed in daily practice e.g. HLA b27 typing and MRI of the sacroiliac joints in case of normal pelvic X-rays.

While comparing these criteria with the previous modified Rome criteria, we could notice 3 main items of interest for our daily practice.

Besides the axial symptoms, these criteria are emphasizing the criteria of the recognition of the other clinical features of spondyloarthritis (e.g. peripheral arthritis, enthesiopathy, extra-articular features).

The evidence of structural damage of the sacroiliac joints is no more mandatory to be in a position to classify a patient. MRI finding of inflammatory signs of sacroiliitis (e.g. sub-chondral bone edema) is sufficient to recognize such sacroiliac joint involvement. Even in case of both normal plain pelvic X-ray and MRI of the sacroiliac joints, the patient can be recognized as suffering from spondyloarthritis as soon as he/she is B27 positive and presents at least 2 clinical features suggestive of spondyloarthritis.
Concerning the monitoring of the patients, it has to be emphasized that each clinical feature has to be assessed independently (e.g. axial manifestations, peripheral arthritis, enthesiopathy, extra-articular features). Besides the well known BASDAI, it has been proposed a new composite index integrating a biological marker (e.g. CRP): ASDAS. Finally, the objectives and tools permitting the measurement of mobility of the spine will be discussed.

O11

Long-term efficacy and safety of anti-TNF therapies in ankylosing spondylitis, experiences from nation-wide registry ATTRA

Karel Pavelka
Institute of Rheumatology, Prague, Czech Republic

Anti-TNF therapy of ankylosing spondylitis (AS) is very effective therapy influencing axial, peripheral and extraskeletal manifestations of AS. Most evidence comes from RCT, but additional valuable information comes from registries.
The patients with AS were included in Czech national registry ATTRA and Anti-TNF therapy was indicated according to guidelines of Czech Rheumatological Society. Authors reporting most important outcomes: BASDAI, CRP, HAQ, drug survival rates, predictors of drug discontinuation and serious adverse events.
879 patients with AS were followed up to 4 years. Drug survival rates were 87,1%, 77,5%, 73,2% and 67,4% which was longer than in RA (p<0,001). There was a trend for longer survival on etanercept than on infliximab (p=0,057). Significant risk factors for treatment discontinuation were female gender (RR 2,22; p=0,001) and CRP (RR 1,33; p=0,025). The initial BASDAI was 6,4 }1,7 and the final after 3 years was 3,1±2,6 (p<0,001). Initial CRP was 31,0 (26,5 mg/l which dropped to 5,2) 10,2 mg/l after 3 years. The number of patients working increased from 48% to 63% after 1 year. The tolerance was good and proportion of patients with serious adverse events and serious infections was lower in ankylosing spondylitis group then in RA group. Results from Czech registry ATTRA document long-term good efficacy and safety of Anti-TNF in AS in routine clinical practice.

O12

Vascular diseases in ankylosing spondylitis

Sándor Szántó, Nóra Bodnár, Rudolf Gesztelyi, Ádám Kemény-Beke, Zoltán Szekanecz
University of Debrecen, Hungary

Clinical observations proved that cardiovascular events are the most remarkable cause of morbidity and mortality in patients with ankylosing spondylitis (AS). Beyond the traditional risk factors of atherosclerosis, clear links have been established between the chronic inflammation and the cardiovascular diseases. Asymmetric dimethylarginine (ADMA), a major endogenous inhibitor of nitric oxide synthase, has been newly identified as risk factor for endothelial dysfunction in rheumatoid arthritis, such as the elevated serum level of anti-heat shock protein-65 (anti-hsp65) antibody for carotid intima-media thickness (ccIMT).
Forty-three AS patients and 40 age- and gender-matched controls, free of cardiovascular diseases or atherosclerotic risk factors were studied. Plasma level of ADMA and anti-hsp65 were determined by high pressure liquid chromatography and by ELISA technique, respectively. Endothelium-dependent flow-mediated vasodilation (FMD), ccIMT and pulse-wave velocity (PWV) were measured by B mode high-resolution ultrasonography. Correlations were determined between these parameters and disease duration, smoking history, body mass index, BASDAI, BASFI, metric parameters, acute phase reactants and HLA-B27 status.
The serum levels of anti-hsp65 were significantly higher in AS patient compared to healthy controls (110.9 U/ml vs 9.9 U/ml, p<0.001). Similarly, elevated ADMA levels could be detected in AS patients than in healthy controls (0.95 μmol/l vs 0.71 μmol/l, p<0.001), while the serum level of its inactive stereoisomere, the symmetric dimethylarginine (SDMA) was similar in AS patients and healthy controls. The lower FMD reflected the endothelial dysfunction, and the elevated ccIMT and PWV indicators of intima-media hyperplasia and arterial stiffness suggested micro- and macrovascular impairments in AS patients. ccIMT and PWV positively correlated with diseases duration and wall-occiput distance, moreover ccIMT with BASFI, and these vascular parameters negatively correlated with the lumbar spine mobility and chest expansion.
The identification of predisposing factors for atherosclerosis and the early detection of endothelial dysfunction or macrovascular discrepancies may be crucially important in the prevention of early mortality in AS.

O13

Do we need traditional DMARDs in the biologic era?

Witold Tlustochowicz
Military Institute of Medicine, Warsaw, Poland

The features that characterize a good medicine are safety and efficacy; the feature that is welcomed by the payer is a low price. The target which the treatment of rheumatoid arthritis aims at is to achieve remission, which is easier in the first months after the disease onset. Another welcomed feature of a medicine is its prompt action. In the recent decade, we have been observing an upswing in the development of biological therapies, which oust treating with traditional disease-modifying antirheumatic drugs. The medication safety assessment has shown that the total number of adverse events related with the use of either traditional or biological medicines is similar; the differences appear to be rather organ-specific. After applying methotrexate, transaminase activity is observed to increase in 17% of patients, 18–19% of patients are nauseous, and so is a similar percentage after sulphasalazine. Leflunomide causes diarrhea in 17%. Biological medications, on the other hand, result in skin reactions in from 10% (adalimumab) to 30% (etanercept) of patients. Infusion-related reactions are reported in from 11% (infliximab) to 9–25% (rituximab). Severe infections, often fatal, include tuberculosis and central nervous system infections and are more common in patients treated with biological medications. Methotrexate efficacy depends on its dose and low disease activity is attained in 37–50% of patients treated. In the case of leflunomide, such a result is reported in 20%, and with sulphasalazine or cyclosporine it is observed in 16% and 17% of patients, respectively. Combining traditional medications results in low disease activity in 70% of patients. Anticytokines, when used in monotherapy, enable low disease activity to be attained in 24–28% of patients. When combined with methotrexate, anticytokines result in low disease activity in 18–49%, also in cases where methotrexate was ineffective before. The advantage of treating with biological medications is the fact that they act fairly promptly, i.e. their beneficial effect is seen as soon as after 8–12 weeks. Only glucocorticosteroids are superior in this respect since they act after 1–2 weeks. Methotrexate is slightly slower in its action (after 12 weeks), other medications after 16 weeks. Hence, combining traditional drugs with glucocorticosteroids in the early phase is reasonable; no differences in radiological lesion progression are then observed in comparison to biological medications. The medications discussed here differ dramatically in terms of pricing – in Poland a one-year therapy with oral methotrexate costs around € 30, with sulphasalazine € 300, with subcutaneous methotrexate and leflunomide € 750, and with biological medications it costs € 10,000–14,000. The efficacy, safety and price prove that traditional medications are superior to biological ones; the latter should be used only when the former have proved ineffective. Thus, EULAR recommendations on treating RA are reasonable and should be applied in full.

O14

How to use different biologicals for optimal treatment of patients with rheumatoid arthritis?

Josef Smolen
Medical University, Vienna, Austria

O15

DMARD and biological treatment modalities in childhood

Emese Kiss
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory disease in childhood. It includes seven subgroups with different clinical phenotypes. The disease may lead to joint destruction, growth retardation and disability. Due to ongoing disease activity JIA often extends into adulthood. The importance of adequate therapy is underestimated. Objective: To review different therapeutic modalities in JIA based on literature data and personal/site experiences.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line treatments for JIA, but rarely may control adequately signs and symptoms mainly of the polyarticular disease. Corticosteroids can be used in systemic or intraarticular forms limited to the active phases of JIA and the dominant joint inflamed. Triamcinolone hexacetonide is superior of the derivatives for intraarticular use. Disease modifying antirheumatic drugs (DMARDs) belong to second-line treatment. Methotrexate (MTX) is the gold standard for management of polyarthritis providing significant clinical benefits. The main limitations of its use are toxicity and incomplete response. Other DMARDs – sulphalazine, cyclosporine, hydroxychloroquine, azathioprine – may be used for resistant disease in combination with MTX, but are not well-tolerated. Leflunomide is not approved in pediatric practice. Biological therapies revolutionized the treatment and the outcome of JIA. Biologics are monoclonal antibodies or fusions proteins which can block specifically pro-inflammatory cytokines (e.g. TNF-α, IL-1b, IL-1R or IL-6) participating in the pathogenesis of JIA. Etanercept (ETN) (a fully human soluble tumor necrosis factor alpha (TNF-α) receptor fusion protein) was approved at first for polyarticular-course JIA after failure or intolerance to MTX. Randomized, controlled studies confirmed the efficacy and safety of ETN in JIA with or without MTX. In an 8 years

long-term open label extension trial high proportion of patients reached ACR pedi 30, 50, 70, and 90 responses. The rate of serious advers events and medically important infections was low and did not increase with long-term exposure to ETN. Although there were no reported cases of malignancies, lymphomas, demyelinating disorders or lupus, as well as tuberculosis or opportunistic infections, JIA patients should be carefully monitored. There are data indicating the efficacy of infliximab (a chimeric monoclonal antibody to TNF-α), but a relatively high discontinuation rate was observed. Adalimumamb (a human anti-TNF monoclonal antibody) has been approved since 2008 for polyarticular JIA from the age of 13 in Europe, and seems to be an alternative for ETN regarding efficacy issues. Systemic-onset JIA (SO-JIA) is the most severe form, and does not always respond to available treatments. As IL-6 plays a key role in its pathogenesis, it is not surprising that randomized, controlled trials demonstrated sustained clinical improvement and an acceptable risk-benefit profile for tocilizumab (TCZ) (a humanized monoclonal antibody to IL-6 receptor) in SO-JIA. Future perspectives include modified TNF inhibitors, IL-1 blockade with anakinra, rilonacept and canacinumab or blockade of co-stimulatory molecules. Autologous haemopoietic stem cell transplantation is an option for those who fail to respond to any of above listed therapeutic modalities.
The treatment of JIA has become more judicious, but is still challenging. Although in the era of biologicals the outcome is much better, there are no convincing data about their influence on joint destruction, growth retardation, functional disability, and with an exception of etanercept about their long-term safety.

O16

Enthesitis: Evolving concepts and sonographic evaluation

Péter Bálint, Péter Mandl, Katalin Ács, Éva Ruzicska
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Enthesitis – inflammation of the origin and insertion of ligaments, tendons, aponeuroses, annulus fibrosis and joint capsules – is a widely accepted clinical, histopathological and imaging feature of spondylarthropathy (SpA). Inflammation may occur at any enthesis in SpA, though it is most frequent in the entheses of the lower limbs. Pathological examination of enthesitis in SpA demonstrates local inflammation, fibrosis, erosion, and ossification. Bursitis and synovitis may also occur adjacent to the entheses, and it has been recently postulated that the enthesis may be the initial site of joint inflammation in SpA.
The clinical assessment of enthesitis in SpA is predominantly performed by eliciting tenderness at the enthesis. Several studies have demonstrated that musculoskeletal ultrasound examination provides a more objective and reliable index of enthesitis as compared to clinical examination. Specifically gray-scale ultrasound can be used to assess the manifestations (tendon hypoechogenicity, bursitis, enthesophyte, erosion etc.) and dimensional (tendon thickness) aspects of enthesitis, while Power and Color Doppler are used to assess the vascularisation of the tendon and activity of related bursae. The OMERACT/EULAR US Group has previously developed an ultrasound definition of enthesopathy based on its sonographic characteristics that is widely used. In the past decades different clinical and ultrasound enthesitis scores have been developed, these will be discussed in detail. Finally, we would propose a definition of enthesitis based on the accepted US signs.

O17

Incidence of scleroderma spectrum disorders in Slovenia

Alenka Šipek Dolničar
University Medical Centre, Ljubljana, Slovenia

Objective was to investigate the incidence of scleroderma spectrum disorders (SDS) in the Ljubljana region of Slovenia with a population of 518,921 Caucasians older than 18 years.
From 01.01.2007 to 31.12.2009 authors prospectively examined all patients older than 18 years suspect of suffering from SSc who were admitted to their department or referred to outpatient clinic by GPs or rheumatologists. Authors department is the only rheumatology referral center in the Ljubljana region. Since some SSc patients seek help from dermatologists, pulmonologists, angiologists, and gastroenterologists, these sub-specialists were requested to refer these patients to authors. Clinical assessment, certain biochemical and immunoserological tests, and capillaroscopy were done in each patient. Skin thickness was assessed using the modified Rodnan total skin thickness score. Depending on presentation additional tests were ordered, e.g. chest X-ray, pulmonary function tests incl. DLCO, cardiac echosonography, hand and feet X-ray, esophageal X-ray. Using the modified working classification of SDS (scleroderma spectrum disorders) proposed by Maricq and Valter the patients were classified as having CREST syndrome, limited cutaneus SSc (lcSSc), diffuse cutaneus SSc (dcSSc), SSc sine scleroderma, and UCTD with SSc features. Patients with Raynaud's phenomenon, pathological capillaroscopy and ANA or other auto-antibodies suggestive of SSc were classified as having prescleroderma.
During the study period we examined a total of 100 patients. Fourty-one new cases of SDS were diagnosed (37 females, 4 males), aged 58,9 }15,1 years (24-86 years). The overall age-adjusted annual incidence of SSc in their population was 2,6 per 100,000 adults per year (95%CI=1,72-3,55). The overall annual incidence of SDS in Slovenia seems

to be higher compared to recent incidence reports form Spain and Greece. Use of different classification criteria, which in our case recognized earlier stages of the disease, might be the reason. Further investigations are needed to clarify the importance of early forms of the disease in diagnosis and treatment of systemic sclerosis.

O18

Clinical importance of nailfold capillaroscopy in the early diagnosis of systemic sclerosis

Maurizio Cutolo
University of Genoa, Italy

Nailfold videocapillaroscopy (NVC) represents the best and safest method to detect and to analyze morphological microvascular abnormalities, especially in presence of secondary Raynaud's phenomenon. In normal conditions or in primary Raynaud phenomenon (but not during the cold-exposure test), the nailfold capillaroscopic pattern shows regular disposition of capillary loops along the nailfold bed and no abnormal enlargements or capillary loss.
In patients with primary Raynaud phenomenon, however, one or more abnormal capillaroscopic findings, should alert the physician to the possibility of secondary Raynaud phenomenon, owing to the presence of a previously undetected connective autoimmune disease, for example systemic sclerosis (SSc).
Morphological markers of microvascular damage include giant capillaries, microhemorrhages, loss of capillaries, the presence of avascular areas and angiogenesis; these features characterize more than 95% of patients with overt SSc even if are not observed concomitantly.
These sequential and dynamic capillaroscopic changes are typical of the microvascular involvement in SSc, and can be described by the term "eSSc pattern".
Most importantly, imaging with NVC enables the early differentiation between primary and secondary Raynaud phenomenon by identifying morphological patterns specific to various stages of SSc (patterns "early", "active" and "late"); the inclusion of these NVC patterns could increase the sensitivity of classification criteria for SSc.
Reduced capillary density on NVC correlates with a high risk of developing digital skin ulcers and the presence of pulmonary arterial hypertension, and can therefore be used as a marker of SSc severity and progression.
Therapies targeting underlying vascular disease in SSc improve symptoms of Raynaud phenomenon and reduce ischemic injury to involved tussue/organs; however, targeted treatment of fibrosis remains a challenge.
Immunesuppressive therapies still of efficacy in the modulation of the immune response underlying SSc and generally characterizing all connective tissue diseases (i.e. Cyclophosphamide, Rituximab, Ciclosporin).
Therefore, NVC represents the safest method to analyze microvascular abnormalities in SSc, and enables the early differential diagnosis between primary and secondary Raynaud phenomenon.
In addition, abnormal findings on NVC at baseline together with the presence of SSc-specific autoantibodies indicate a very high probability (over 80%) of developing definite SSc, whereas their absence rules out this outcome.
Early diagnosis of SSc could enable the early start of treatment, which could slow disease progression and clinical complications.

O19

Lung involvement in systemic sclerosis

Nemanja Damjanov
Institute of Rheumatology, Belgrade, Serbia

Systemic sclerosis (SSc), or scleroderma, is a chronic systemic connective tissue disease characterized by small blood vessels alteration and destruction, immune system activation and diffuse fibrosis of the skin and internal organs. Gastrointestinal tract and lungs are most frequently affected.
Interstitial lung disease (ILD) and pulmonary hypertension (PH) are the most important findings of lungs and heart involvement in SSc. Approximately two thirds of SSc patients develop ILD. PH is present in about 20% of patients, usually associated with severe lung disease. The estimated incidence of PAH among 384 patients with SSc, followed for median od 41 month in France, was 0.61 cases per 100 patientyears. The high incidence of postcapillary PH highlights the value of RHC in investigating suspected PAH(2). Of the SSc-related deaths, about 35% are attributed to pulmonary fibrosis, and 26% to pulmonary arterial hypertension (PAH) (3). ILD is found in close to 70% of patients at autopsy, most commonly histologicaly presented as nonspecific interstitial pneumonia (NSIP). The earliest pathologic findings are small blood vessels endothelial lesions and signs of alveolitis, followed by signs of coagulation process activation, fibroblast proliferation and differentiation.
Symptoms of lung involvement in SSc are not specific and are seen late, in advanced stage of the disease. The most common symptom is breathlessness (dyspnea), initially on exertion and later at rest. The most common sign of ILD are bilateral basal inspiratory crackles. Later, in the advanced disease stage, symptoms and signs of right heart failure and right ventricular strain may appear (loud pulmonary component of the second heart sound on auscultation or a left parasternal heave).
High-resolution computed tomography(HRCT) is the diagnostic procedure of choice for early detection of ILD. Other methods used for the detection of

lungs and heart involvement in SSc are chest X-ray, bronchoalveolar lavage, lung function tests, Power Doppler ultrasonography (PDUS) of heart, and thoracoscopic lung biopsy. Useful methods to diagnose ILD in SSc could also be technetium-labeled diethylenetriamine pentaacetate (99mTC-DTPA) clearance time and induced sputum(4). Beside the early detection of lung involvement, imaging methods could help in differential diagnosis of other diseases causing ILD and PH, early differentiation between treatment responders and nonresponders, and assessment of treatment efficacy.

Early diagnosis of lung involvement in SSc is extremely important for the initiation of treatment with higher probability of slowing or stopping the disease progresssion. Still, we lack consensus about when to start aggresive antinflammatory and immunosuppressive treatment in patients with SSc and ILD. Cyclophosphamide seems to be effective treatment option in the early phase of ILD, but more randomized clinical trials are needed to clarify this and other treatment aproaches in SSc patient with ILD.

Possible future treatment options in SSc are strategies to abolish the pathological activation of TGF-beta signaling in SSc fibroblasts (the blockade of cell surface molecules capable of activating latent TGF-beta, blockade of ligand by the pan-isoform-specific antibody, soluble TGF-beta receptors and a recombinant latency associated peptide, as well as inhibitors for ALK5 and Smad3). Other therapeutic targets could be connective tissue growth factor (CTGF)/CCN2, platelet-derived growth factor (PDGF) and endothelin-1. Potential new therapies currently under assessment in clinical trials are imatinib mesylate, i.v. immunoglobulin infusion, stem cell transplantation and B-cell depletion(5).

Interstitial lung disease is the leading cause of death in patients with SSc. New insight in pathogenesis of lung damage in SSc and make will allow development of new therapeutic approaches toward the better treatment and outcome.

O20

Emergency states in systemic sclerosis

Luc Mouthon
Hopital Cochin, Rene Descartes University, Paris, France

O21

Composite measures

Piet van Riel
Radboud University Nijmegen Medical Centre, The Netherlands

In the past decade treatment strategies for patients with rheumatoid arthritis (RA) have changed dramatically. Patients are being treated earlier and more aggressively than in the past; in addition far more therapeutic options are available, which has increased the complexity of the management of patients with rheumatoid arthritis. These processes have had an influence on the outcome of patients with RA and on the way they are being evaluated. Patients with RA show a fluctuating disease course. These variations are partly due to the disease itself and partly due to the treatment.

To obtain a good picture of the course of the disease within a patient, frequent standardized assessments of several variables reflecting the disease process will be necessary. Apart from process variables that represent the present disease activity, outcome variables should be measured. Outcome variables are disease aspects or consequences that develop over the course of the RA. They are the sum of the past process. Examples are joint erosions and cartilage damage; disability/handicap; psychological, social and economical consequences; toxicity; co-morbidity; and ultimately death.

Ideally, it would be best to look not only at present and past disease activity but also at variables that predict future process and outcome. That way, treatment can be timeously adjusted to the expected disease course and an undesirable outcome can be prevented/delayed.

Evaluation can have different scopes. One may wish to evaluate an individual patient's disease course or the efficacy/toxicity of treatment in a single patient, or differences in disease course or treatment efficacy/toxicity in groups of patients. The instruments for the different scopes are not always the same. What will be a good measure for group results does not have to be the optimal choice for an individual patient. The choice of the instrument will also depend on the situation in which they are being used (daily clinical practice, long-term observational studies, randomized clinical trials). For all assessments, however, it is important to use a valid and standardized measure. The instrument should measure what it is supposed to measure, it should be reproducible and feasible (time, expense, personnel). For the sake of comparability with previous assessments or with other groups/patients, a standard instrument or technique should be used.

O22

Patient related outcomes in routine monitoring of rheumatoid arthritis patients

Burkhard F. Leeb
Center for Rheumatology, Stockerau, Austria

What is the primary task of any instrument for disease activity assessment? To provide the physician with sufficient information about the disease course and to sound the alarm in case of worsening. In addition, the tool should be time sparing and easy to apply. Any kind of therapy and its respective monitoring should not be based exclusively either upon serological parameters or the patient's pain assessment

or the physician's ideas, but should be guided by the actual activity and the course of the underlying disease. In general, it seems to be that rheumatologists are much more focused on joints (respectively on joint counts) than on pain or functional deficiencies. Ironically however, we are aware, that in more than half of the visits to rheumatologists no formal joint count is performed. Additionally, it is well known that the results of joint counts are highly assessor dependent, indicating sources of error by the individual physician's evaluation of swelling or tenderness in case of varying investigators in the same patient. This inter-individual variance may be improved by consensus meetings; however, is this feasible in daily routine? All composite indexes employ a certain number of joints to be investigated, the DAS28 e.g. 28 joints including 22 hand and finger joints. If the disease mainly affect the patient's feet, is it less active then? In clinical trials this factor plays a lesser role, though, in daily routine – treating individual patients – of course an important one. Another relevant problem is given by the equal weighting dedicated to each joint included into the different counting models applied. Yet, ask a patient about the significance of the fifth metacarpophalangeal joint or the knee with respect to her/his general well-being and functionality. If rheumatologists perform joint counts relatively seldom, and appreciate the problems of composite indexes, how can they claim that non-rheumatologists should apply those instruments appropriately. Moreover, it is well known that patient's self assessment, e.g. by a HAQ, gives as reliable information as a formal joint count by a physician with respect to prognosis and monitoring of RA. Why also shouldn't we consider alternative ways for disease activity assessment than counting joints? Some exclusively patient related outcomes (PROs) as the RADAI or the RADAI-5, the RADAR, or the HAQ family including the RAPID3 have been developed and validated. Time to score for most of those questionnaires can be estimated below 25 sec. Internal consistency of the RAPID3 and the RADAI-5 was found significantly higher than the one of the DAS28 or the CDAI. The PROs as well as the indexes proved to be in highly moderate agreement, while agreement between PROs and indexes appeared to be lower. Nevertheless, it has to be pointed out that neither the degree of agreement between the RADAI-5 and the RAPID3 nor between the DAS28-ESR and the CDAI does allow for direct interchange ability of the two respective scales. Up to now those questionnaires, however, did not achieve a standing comparable to the BASDAI in the monitoring of seronegative spondylarthropathies. It's somewhat sort of weird, that for another inflammatory joint disease a patient related measure has an outstanding position with respect to monitoring. Of course no tool is capable of replacing a thorough clinical patient examination. It is true for all instruments that only stable low values give notice of an uncomplicated disease course and that variations have to be interpreted according to the single component's changes. The easier such indexes are applicable, the more they will be used by practising physicians. A better and more uniform way of documenting the individual patient's disease can be anticipated to ultimately result in improved rheumatology patient care.

O23

Development of remission and minimal disease activity cut-points for the juvenile arthritis disease activity score (JADAS)

Angelo Ravelli, *Consolaro Alessandro*
University of Genoa, Italy

Recent advances in therapeutic options, namely the introduction of biologic agents, have markedly increased the potential for achieving a remission or minimal disease activity (MDA) state. Therefore, accurate criteria for defining remission and MDA are needed.

Disease activity status can be defined using a categorical model, which requires simultaneous fulfilment of multiple criteria, each of them with a threshold value, or using a dimensional model, which is based on pooling individual measures of disease activity into a composite disease activity score and enables definition of remission through the calculation of a numeric cut-point. The first approach has been followed in the development of the current JIA remission criteria (Wallace criteria), and in the preliminary definition of MDA.

The identification of the remission and MDA cut-points of the recently developed composite disease activity score for JIA, the JADAS.

For the purposes of this study, the JADAS-10 version was used. The JADAS-10 is computed as the simple sum of 4 variables, each with a 0–10 range: the physician's global assessment, the parent's global assessment, the normalized ESR and the reduced active joint count.

A total of 602 consecutive patients were included in the study. At each visit, all main physician- and parent-centered outcome measures were recorded. JADAS-10 could be calculated for 432 patients in 914 visits. At each visit, both physicians and parents were asked to rate independently the disease status as remission or active disease. Furthermore, authors assessed the presence of remission by Wallace criteria and, after grouping patients in oligoarthritis or polyarthritis, of MDA by the preliminary definition.

In the first step, we calculated the JADAS-10 values corresponding to the 75th percentile of score distribution among patients who were classified as having disease remission by physician's and parent 's subjective rating and Wallace criteria, or having MDA. In the second step, we calculated, by means of the receiver operating characteristic (ROC) curve analysis, the JADAS-10 values that showed the best

trade-off between sensitivity and specificity (i.e. the best accuracy) in discriminating between patients who had remission or active disease according to the physician, the parent, or the Wallace criteria, or who had MDA according to the preliminary definition.
The results in the 2-step analysis are shown in table. The numbers obtained for each definition using the 75th percentile or ROC curve method were then averaged. The values obtained for remission were further averaged achieving the value of 2.0, The values obtained for MDA are 2.3 for oligoarthritis and 2.9 for polyarthrtritis
The value of 2.0 is the remission cut-point for the JADAS-10 proposed for use in future clinical trials on JIA. The proposed cut-points for MDA in oligoarthrtitis and polyarthritis are 2.3 ad 2.9, respectively.

	Remission			MDA	
	Physician	Parent	Wallace crit.	Oligoarthr.	Polyarthr.
75th pct.	2.1	2.5	1.0	2.0	1.7
Best accuracy	2.9	2.8	1.0	2.6	4.2

O24

Outcome measures in the rehabilitation of musculoskeletal conditions

Ernst Wagner, Tamás Palotai
Special Hospital for Rheumatology of the Regional Health Insurance of Lower Austria, Baden, Austria

A wide array of scores is available to evaluate the outcomes of rehabilitation. However, there is debate whether disease-specific scores, generic scores, or combinations thereof are most likely to give a realistic picture of the actual health status of a patient. Disease-specific scores include the Hannover Functional Questionnaire for measuring back pain related disability (HFFbR), the Health Assessment Questionnaire (HAQ, rheumatoid arthritis), the Constant Score (shoulder), the Western Ontario McMaster (WOMAC) questionnaire (osteoarthritis of the knee and hip, joint arthroplasty, dimensions of pain, stiffness, and function), the Roland Morris Questionnaire (RMQ), and the Oswestry Questionnaire (for back pain). Generic scores include the Medical Outcomes Study short form 36-item questionnaire (MOS SF-36), MOS SF-12, the Pain Disability Index (PDI), the Sickness Impact Profile (SIP), the Nottingham Health Profile, EuroQol (EQ-5D) for assessing quality of life, and the Mainz Pain Staging System (MPSS) for assessing pain chronification. Evaluations of the psychometric properties of currently used scores have raised questions as to their ability to measure various quality-of-life dimensions, their sensitivity to change (e.g., when used in in-patient rehabilitation), and the influence of comorbidities (such as musculoskeletal conditions in sites other than the signal joint, pain chronification, medical comorbidities, depression, or cognitive impairment). Including more robust outcome measures of rehabilitation may provide additional meaningful information, especially in terms of cost and effect. Such measures could cover items such as the medical costs of illness, the costs of care following rehabilitation, and the influence of rehabilitation on sick leaves, early retirement, pain level, self efficacy (i.e., ability to cope with the disease), and quality of life. Our own investigations have confirmed the low sensitivity to change of the HAQ (in a 3-week in-patient rehabilitation program) and the usefulness of the MPSS, where improvement of pain and functional abilities in chronic non-specific low back pain during in-patient rehabilitation was strongly correlated with the stage of chronification.

O25

Neuroendrocrine-immune network in rheumatic diseases

Maurizio Cutolo
University of Genoa, Italy

Clinical observations indicate a strong influence of the neuroendocrine system on the immune function in chronic inflammatory diseases. It is obvious that these neuroendocrine pathways influence the development of the immune system by interfering with the thymus in that almost all hormones of the HPA and HPG axes support the gradual involution of the thymus.
Similarly, hormones of these two axes also hinder B-cell lymphopoiesis, which was particularly demonstrated for 17 Ŕ-estradiol. On the other hand, CRH, ACTH, and 17 Ŕ-estradiol exert some immunostimulatory effects whereas glucocorticoids and androgens generally suppress immune responses. The action of the different hormones is influenced by the immune stimulus (foreign antigens or autoantigens) and subsequent antigen-specific immune responses, the cell types involved during different phases of the disease, the target organ with its specific microenvironment, timing of hormone increase in relation to the disease course (and the reproductive status of a woman), the concentration of hormones, the variability in expression of hormone receptors depending on the microenvironment and the cell type, and intracellular and extracellular peripheral metabolism of hormones leading to important biologically active metabolites with quite different anti-inflammatory and proinflammatory function. Circadian rhythm of disease-related symptoms with a peak in the early morning hours confirms that the neuroendocrine system has a strong influence on these chronic immune/inflammatory diseases. The influence is transferred by the circadian undulation of the activity of hormonal and neuronal neuroendocrine pathways linking the brain to immune cell activation. Finally, circannual variations of the vitamin D endocrine system are now also recognized as an important immune modulatory factor involved at least in autoimmune rheumatic diseases. These immunomodulatory and anti-inflam-

matory activities might be particularly efficient in rheumatoid arthritis patients and support a therapeutic role of 1,25-dihydroxy vitamin D3 in such a disease. In addition, vitamin D may play an important role in the maintenance of B-cell homeostasisand the correction of vitamin D deficiency may be useful in the treatment of B-cell–mediated autoimmune rheumatic disorders such as systemic lupus erythematosus.
New therapeutic strategies are based on circadian/ circannual rhythms and generally on understanding the complex neuroendocrine/ immune system in more detail.

O26

Klinefelter's syndrome, Turner syndrome and rheumatic diseases

Jozef Rovenský, Richard Imrich, Elene Košková, I. Lazúrová, J. Payer
National Institute of Rheumatic Diseases, Pieštany, Slovakia

Klinefelter's syndrome is a gonosomal aberration occurring in males. The disorder is characterized by microorchidism. Another typical although not constant symptom of this disorder is gynecomastia, with almost normal male secondary sex characteristics. The etiology of this disease remains unknown. Previous studies have shown that this disorder is a genetic chromosomal abnormality associated with the presence of one additional chromosome due to abnormal division. Thus, the affected individual has 47 chromosomes with the resulting chromosomal configuration of XXY in a classical form, or 46,XY/47,XXX in a mosaic form. Large population studies have estimated the incidence of Klinefelter's syndrome at 1:1000 live-born male babies. The locomotor apparatus of persons affected by the syndrome is characterized by acromicria clinodactyly, concrescence of thoracic vertebral bodies, and spinal osteoporosis not only in older individuals but also in younger persons. The association of Klinefelter's syndrome with organ as well as non-organ specific autoimmunity is probable but poorly documented in the current literature. We present the association of Klinefelter's syndrome (KS) with inflammatory rheumatic diseases, i.e. rheumatoid arthritis (RA), juvenile idiopathic arthritis, psoriatic arthritis, polymyositis/dermatomyositis, systemic lupus erythematosus, systemic sclerosis, mixed connective tissue disease, the antiphospholipid syndrome, and ankylosing spondylitis. These include two case reports of patients with KS concurrently associated with RA or antisynthetase syndrome, respectively, previously reported by the author and his coworkers. Attention is paid to the pathogenesis and the course of the disease in patients with KS. In patients with Turner's syndrome monosomy, the X chromatin pattern is negative in about 60%; most of these patients have a 45,X sex chromosome constitution. In our case report we found 2 patients with Turner syndrome associated with rheumatoid arthritis and juvenile chronic arthritis. A 26 year old patient developed progressive course of the disease and therefore a combined therapy by antimalarial drugs and methotrexate had to be administered. RA was seronegative. Turner's syndrome was diagnosed at the age of 8. In another patient with Turner's syndrome diagnosed at the age of 13, polyarthritic syndrome and exsudative pleuropericarditis due to infection appeared at the age of 17. The latter indicated a development of juvenile idiopathic arthritis with systemic manifestations, the disease yielded to 1-year therapy. The presentation outlines the existing relations between Turner's syndrome and the development of juvenile idiopathic arthritis and/or arthritis of the RA type. The importance of early screening of autoimmune rheumatic disorders in patients with Klinefelter's and Turner syndromes, is emphasized.

O27

Hypothalamic-pituitary-adrenal function in rheumatoid arthritis

Richard Imrich
Center for Molecular Medicine, Bratislava, Slovakia

The hypothalamic-pituitary-adrenal (HPA) system is a powerful neuroendocrine control mechanism involved in many core body functions including metabolic and energy homeostasis. The HPA axis has been considered an important immune modulator primarily in view of potent anti-inflammatory effects of cortisol in high physiological and pharmacological doses. A significance of variations in cortisol concentrations at the lower (unstimulated) normal range for immune regulation is less understood. In the context of chronic inflammation, upregulated HPA function with higher production of cortisol would be anticipated in rheumatoid arthritis (RA) and other inflammatory diseases. On the other hand, the inappropriately low HPA function has been suspected to be a permissive mechanism for excessive immune response leading to autoimmunity development. The data accumulated so far support only subtle alterations in HPA axis function in RA, mainly at the adrenal level, particularly in a subset of premenopausal onset women. Such interpretation is supported by consistent findings of lower levels of adrenal androgens, particularly DHEAS, in premenopausal onset RA patients. Consequences of the subtle HPA alterations in RA for the disease development remain unclear. From a broader perspective, the lack of appropriate response from the HPA axis to chronic inflammation in RA can be simply seen as an ongoing adaptation to the diseased state with higher priority to the proper regulation of core body functions over the immune homeostasis.

O28

The presence and function of nicotinic acetylcholine receptors on osteoclasts, and their effect on osteoclastogenesis

Péter Mandl[1,2], Silvia Hayer[2], Despoina Sykoutri[2], Gyula Poór[1], Josef Smolen[2], Kurt Redlich[2]
[1]National Institute of Rheumatology, Budapest, Hungary, [2]University of Vienna, Austria

In the last few years, the discovery of various neurotransmitter receptors on osteoblasts, osteoclasts and osteocytes suggested that neurotransmitters, either released by neurons (sympathetic or sensory nervous system) or acting as local cellular signaling molecules (e.g. non-neuronal cholinergic system) may participate in the control of bone metabolism. Smoking has been traditionally associated with bone loss; contradictory effects of nicotine, a primary agonist of nicotinic acetylcholine receptors (nAChRs) have been described on osteoclasts. However the actual presence and function of these receptors on osteoclasts has previously not been characterized. Objective: To investigate the presence and function of nAChRs on osteoclasts. To investigate the potential effect of nAChRs on osteoclastogenesis.
Authors investigated the presence of nAChR subunits α1, α3, α4, and α7 in osteoclasts derived from mouse bone marrow and spleen, differentiated in the presence of RANKL and M-CSF. NAChR subunits were identified by PCR. The effect of nAChR agonists (nicotine, epibatidine) on osteoclastogenesis and bone resorption was evaluated in in vitro osteoaclastogenesis and dentin slice bone resorption essays as well as by flow cytometry. Results: Using PCR we were able to confirm the presence of nAChR subunits α1, α3, and α4 in mouse bone marrow and spleen derived osteoclasts differentiated in the presence of RANKL and M-CSF. Using the nAChR agonist nicotine to simulate cholinergic activation we showed that nicotine (2 μM–1 mM) dose-dependently reduced the number of TRAP (tartrate-resistant acid phosphatase) positive multinucleated cells (osteoclasts). Similar effects were observable with the potent nAChR agonist epibatidine (10 nM–1 μM). Osteoclast size and nuclei number as well as the size of resorption pits on dentin slices, reflecting the bone-resorbing capacity of osteoclasts, showed a parallel significant decrease upon the administration of nicotine. In qPCR examinations performed with the nAChR agonist nicotine, nicotine dose-dependently reduced the expression of osteoclast markers cathepsin-K and MMP-9. In addition we observed a significant decrease in the number of TRAP positive mononuclear cells (osteoclast precursors), paralleled with an increase in the number of TRAP negative mononuclear cells. NAChR agonists had no significant effect on the overall cell numbers within the essay. Using 7-AAD-Annexin staining in flow cytometry experiments, we could not detect a significant difference in the ratio of apoptotic cells between nicotine-treated and untreated cells, suggesting that the effect of nicotine is not realized through an apoptosis-inducing effect.
Authors shown that osteoclasts express nAChRs. The presence of these receptors and the effect of the nAChR agonists suggests that the cholinergic nervous system may play a regulatory role in osteoclastogenesis.

Oral presentations of satellite symposia (OS)

OS1

Rapid radiographic progression and therapy choice in rheumatoid arthritis

Peter C. Taylor
Imperial College London, United Kingdom

Inflammation is the major factor driving the progression of structural damage in rheumatoid arthritis (RA), which results in a decline in functional capacity and quality of life. The severity of inflammation and progression of joint damage varies from patient to patient. In patients where inflammation is more severe, extensive damage can occur within only a few years of disease onset. Identifying patients with RA at high risk of rapid radiographic progression enables immediate and intensive intervention and a greater opportunity to change the course of disease. According to the recent EULAR recommendations bad outcome independently could be predicted by a) the presence of autoantibodies, that is, rheumatoid factor and/or anticitrullinated peptide antibodies, particularly at high levels; b) high disease activity as measured by composite indices (DAS, DAS28, Simplified Disease Activity Index and Clinical Disease Activity Index), swollen joint counts or acute phase reactants (C reactive protein, erythrocyte sedimentation rate); c) early occurrence of erosions. These factors have recently also been amalgamated into a risk model, a convenient tool to predict the risk of rapid radiographic progression from routine laboratory parameters. Infliximab has been evaluated in both short- and long-term disease in rapidly progressing patients and has been shown to rapidly reduce/normalize CRP level, demonstrating suppression of inflammation and inhibition of radiological progression. Rapidly progressing patients may benefit from initial treatment with infliximab plus MTX combination therapy. Golimumab were also effective at reducing the signs and symptoms in patients with active RA, and has been shown to inhibit radiographic progression both in RA and in PsA.

OS2

Golimumab: An effective and convenient therapy to address the needs of patients with rheumatoid arthritis

Iain McInnes
University of Glasgow, Scotland

It is generally agreed that a TNF-inhibitor should be the first biologic addition after an incomplete response to MTX or combination of DMARDs in rheumatoid arthritis (RA). However, understanding the perceptions of patients who live with rheumatoid arthritis (RA) and their views on its treatment can provide a valuable perspective to the rheumatologist and may help to shape our management strategies. The RAISE (Rheumatoid Arthritis: Insights, Strategies & Expectations) Patient Device Handling Survey was executed to better understand the impact of these specific concerns among patients with rheumatoid arthritis. A structured, in-person, interviewer-assisted survey was utilized to gather data from patients with RA from Canada, France, Germany, and the United Kingdom. A combined total of 425 patients using one of 2 autoinjectors (adalimumab or etanercept) completed the survey. The issue most commonly reported by patients was pain/burning on injection by up to 36% of patients. The most commonly reported features that patients believed were important to have in an autoinjector were the location of the autoinjector button, a means for determining that the medication had been delivered correctly, as well as a device that is easy to use, comfortable/easy to hold, and simple to learn.
Golimumab, a recently approved TNF-inhibitor was tested in a highly comprehensive clinical trial program. Golimumab has been proven to be effective at reducing the signs and symptoms in patients with active RA, and has been shown to inhibit radiographic progression both in RA and in PsA. Clinically meaningful improvements were seen in HRQoL, HAQ-DI, fatigue and pain in RA. The safety profile of golimumab is similar to other anti-TNF agents, with overall low rates of discontinuation due to AEs and injection site reactions. Golimumab administered with the SmartJect autoinjector may ensure that the anti-TNF-α efficacy standards are simultaneously met with the needs identified in the RAISE survey – through innovation that involved both experts and RA patients.

OS3

Spondyloarthritis: Many manifestations of one disease – a multidisciplinary approach to management

Joachim Sieper
Charité University, Berlin, Germany

While ankylosing spondylitis (AS) is generally characterized by sacroiliitis, co-existing peripheral arthritis and extra-articular manifestations, such as gut and eye involvement, are commonly seen with the disease. In fact, as many as 50% of patients with AS also present with anterior uveitis, and a similar proportion may have subclinical inflammation of the gut. Psoriasis is also seen in approximately 20% of patients with AS. Rheumatologists frequently encounter patients with these manifestations and understand the importance of recognizing these symptoms. The new ASAS classification criteria for axial SpA also underlines the relevance of extra-

articular manifestations. While there appears to be no difference in efficacy for the currently available TNF-α inhibitors with regard to treatment of AS axial symptoms, there are differences regarding extra-articular symptoms. If treatment with a TNF-α inhibitor is warranted, the monoclonal antibodies would appear to be preferred for the management of AS with current or likely future extra-articular manifestations and comorbid conditions. Currently, infliximab is the best studied monoclonal antibody with a wide spectrum of proven efficacy. Clinical data with the recently introduced golimumab also show rapid, significant, and sustained improvement in the signs and symptoms of AS including ASAS responses, BASDAI, BASFI, health-related quality of life and sleep quality. Clinical improvements were maintained in the long term.
Psoriatic arthritis (PsA) is characterized by skin lesions, nail involvement, and joint inflammation. Through consensus, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recently published recommendations for the treatment of PsA based on the level of evidence of effect on each established clinical manifestations. For disease manifestations, including peripheral arthritis, spinal disease, skin disease, enthesitis, and dactylitis, infliximab received a Grade A recommendation, indicating that it has category 1 evidence of efficacy in treating these aspects of PsA. Although not available at the time the GRAPPA recommendations were developed, the monthly subcutaneous anti-TNF golimumab has also demonstrated significant improvements in signs and symptoms of active PsA and associated skin and nail psoriasis through week 24. Long-term data provide additional support in managing patients with golimumab.

OS4

The need for early intervention in spondyloarthritis

Maxime Dougados
René Descartes University Paris, France

Spondyloarthritis (SpA) was first recognised 30 years ago as a distinct entity among the inflammatory rheumatic disorders. Current diagnostic criteria (e.g. Amor's and Modified New York) are specific for established disease; however, their use in early disease is limited by their requirement for evidence of radiographic sacroiliitis, which only appears in later disease, and sometimes may not appear at all. Early diagnosis is also hindered by the non-specific nature of early presenting symptoms, such as lower back pain and stiffness.
Although non-specific, it has been shown that these early symptoms may still be substantial, affecting patient function, ability to work and quality of life even when overt signs of disease are absent upon physical examination or radiography. It is during the first 10 years of disease that the majority of structural damage occurs, and physical functional impairment and disability are related to the level of structural damage of the lumbar and cervical spine. Both structural damage and impaired physical function are related to work disability in SpA patients. Treating early, therefore, is essential for optimal patient and socioeconomic outcomes.
It has been shown that patients with SpA are most likely to respond to biologic therapy whilst in the early stages of disease. Significant beneficial effects on clinical, and quality-of-life measures can be achieved by treating early with biological therapies; however, these therapies are not currently routinely administered to these patients due to the requirement in treatment guidelines for radiographic sacroiliitis.
The development and usefulness of imaging techniques such as MRI and ultrasonography that allow early detection of inflammation have led to the development of new ASAS criteria for the diagnosis and assessment of SpA. Spinal inflammation can be detected years before sacroiliitis is visible on traditional X-rays, allowing for early diagnosis and referral, and thus early treatment. Consequently, the recent ASAS criteria and recommendations include these imaging techniques as key tools in disease management. Early diagnosis and classification of disease allows early appropriate treatment, which in turn, with regular monitoring, allows the patient to achieve the best clinical, and quality-of-life outcomes.

OS5

Efficacy of etanercept in the treatment of ankylosing spondylitis

Tamás Palotai
Special Hospital for Rheumatology of the Regional Health Insurance of Lower Austria, Baden, Austria

Major progress has been made in the field of spondyloarthritis (SpA) in the last decade, especially with regard to new therapies, imaging, early diagnosis and treatment and better defined outcome parameters and treatment goals. The emergence of biologic disease modifying drugs has arguably been the most significant advance, revolutionising the management of ankylosing spondylitis (AS). A growing body of evidence now supports the efficacy and safety of etanercept (ETN), the first biologic therapy approved for the treatment of AS, both in clinical trials and national patient registries.
ETN has been shown to be effective in improving the clinical symptoms of AS, including physical function and spinal mobility, in several studies. In the ASCEND trial, ETN-treated patients saw benefit as early as 2 weeks after starting therapy, and patient reported outcomes were also significantly better in the ETN group compared with the sulfasalazine (SSZ) group. Patients initially treated with SSZ and switched to ETN in the extension study, showed significant improvements in efficacy and quality-of-

life measures. Additionally, the results suggest that ETN treatment may be associated with a decrease in healthcare resource utilisation and improvement in the number of patients working full time.
AS is a chronic disease and as such requires a long-term management strategy. Several studies support the long-term efficacy of ETN in the treatment of AS, with sustained improvements in clinical symptoms being shown over 5 years. As well as improvements in clinical outcomes, ETN is well tolerated and demonstrates a durable safety profile. Adverse events often associated with anti-TNF treatment include infections (e.g. TB), IBD and uveitis. In a 5-year study of ETN for the treatment of AS, serious infections occurred at a rate of 0.03 events per subject year and IBD and uveitis occurred at 0.01 and 0.14, respectively. No cases of TB or opportunistic infections were reported.
In the ESTHER trial, the efficacy of ETN was investigated versus SSZ in early AS (disease duration <3 months). Acute inflammatory lesions were detected using whole-body MRI. Improvements in active inflammatory lesions (e.g. on the spine and sacroiliac joint) were significantly greater in the ETN group than the SSZ group, which correlated with the strong clinical response seen with ETN-treated patients.
Registries provide a valuable source of real-world data, especially long-term survival on therapy. From European registries, drug survival rates for anti-TNF therapies were better in AS than in rheumatoid arthritis (RA). Additionally, registry data has shown that quality-of-life measures were significantly better in AS patients treated with anti-TNF therapy than in RA.
Overall, these results support the use of ETN therapy for the long-term management of this chronic disease and suggest that earlier intervention with anti-TNF therapy may provide optimal patient outcomes.

OS6

Evaluation of radiological progression in the management of ankylosing spondylitis

Joachim Sieper
Charité University Berlin, Germany

Historically, classification criteria for ankylosing spondylitis (AS) – such as the Modified New York or Amor's criteria – have relied on radiographic features such as evidence of sacroiliitis on pelvic X-ray for a definitive diagnosis. However, these criteria have poor sensitivity in the early phase of disease as obvious structural abnormalities in the sacroiliac joints may take years to develop, and undifferentiated spondyloarthritis may never progress towards radiographic sacroiliitis. Over a 2-year follow-up period, only a small proportion of patients will show progressive radiological changes of the sacroiliac joint and the spine. Furthermore, radiological changes reflect consequences of inflammation, but not inflammation itself. Similarly, when assessing disease activity in patients on therapy, monitoring radiographic progression (e.g. bone formation) is an important outcome marker, but this has limited use in early disease.
For this reason, interest has focused on imaging techniques that show acute inflammation as a diagnostic criterion and as an indicator of disease progression. This is the case with MRI, which even in early disease offers good specificity for the detection of axial lesions such as sacroiliitis and spondylitis. Such is the potential for these new techniques, that ASAS undertook development of updated classification criteria for spondyloarthritis and AS. MRI and traditional X-rays all have their relative advantages and disadvantages, and the optimal use of each is still to be determined. Alongside these imaging techniques are new scoring methods for assessing spinal inflammation such as the SPARCC and Berlin Method, which have been developed as scoring tools for clinical trials but might be also some of value in daily clinical practice.
Recent interest has also focused on chronic changes in the bone as shown by the T1-sequence on MRI, because early chronic changes such as bone marrow replacement by fatty deposition probably precedes new bone formation seen on X-rays and is only detectable by MRI. A combined analysis of active and chronic bone changes on MRI and chronic changes (mostly new bone formation) as shown by X-rays will help to clarify the complex interaction between inflammation and new bone formation, which is typical for AS. Such clarification is crucial for the development of optimal treatment strategies for patients, with the aim of achieving clinical remission and a complete inhibition of any radiological progression.
Simply having these imaging tools included in diagnostic and monitoring criteria does not necessarily mean that they will be widely used; the ability to read and interpret MRI is not currently common amongst rheumatologists. More training in this area is needed as these skills could prove to be key competencies for rheumatologists in the future.

OS7

Towards optimal management of the rheumatoid arthritis patient

Paul Peter Tak
University of Amsterdam, The Netherlands

A wealth of advances has been made recently in the management of rheumatoid arthritis (RA) in terms of new therapies and treatment strategies. This has driven a need to develop clear recommendations for effective management of RA, and utilisation of these therapies and strategies. The ultimate goal of treatment for RA should be achieving the best care for each patient and this year EULAR published their evidence-based guidelines for the optimal management of RA.

The EULAR recommendations cover the immediate use of synthetic DMARDs first line, treatment targets (low disease activity/remission) and frequency of monitoring, switching therapy on treatment failure (both synthetic and biological DMARDs), and initiation of biological therapies (in combination with MTX wherever possible). As well as being clinically effective, these recommendations were all shown to be cost-effective from current data.

With the range of treatment options available, a personalised approach towards RA management is necessary, in which specific treatments are matched to individual patients. This strategy would minimise the number of patients experiencing an inadequate response to therapy, reduce the frequency of disease flare and also minimise the risk of exposure to the potential side effects of an ineffective treatment.

The identification of predictive markers of response to different biological agents is the first step in achieving personalised medicine for RA. Published data suggest that TNF inhibitors are most effective in patients with high baseline levels of TNF-alpha as well as the presence of lymphocyte aggregates in the synovium. However, the clinical response cannot be predicted sufficiently to be used in the context of individualised medicine, thus indicating the involvement of other, as yet unknown mechanisms. Experience with B-cell depletion therapy has consistently shown that RA patients seropositive for rheumatoid factor and/or anti-citrullinated protein antibodies achieved better clinical responses than seronegative patients. Recently, we have also found that the type I interferon signature negatively predicts the clinical response to rituximab treatment in RA.

Widespread adoption of the present evidence-based guidelines and growing understanding of predictive markers of response will ultimately lead to further improvement in quality of care for RA patients.

OS8

Clinical results with etanercept in early rheumatoid arthritis

Tom Huizinga
Leiden University Medical Center, The Netherlands

Over the past decade, significant advances have been made in the management of rheumatoid arthritis (RA) in terms of treatment strategies and therapeutic options. Several studies have clearly demonstrated the importance of early, aggressive intervention to minimise radiographic progression and subsequent disability. Evidence suggests that there is a window of opportunity in early RA during which intervention can have the greatest impact on the course of the disease and on patient outcomes. Early treatment has therefore been accepted by rheumatologists as the optimum strategy.

Several studies have shown that achieving remission and preventing joint damage are now realistic objectives in many RA patients. In the COMET study, patients with early RA were randomised to methotrexate (MTX) or MTX in combination with etanercept. At week 52, DAS28 remission was achieved in 50% of the patients receiving MTX plus etanercept, significantly more than the 28% of patients receiving only MTX. Radiographic progression and work disability at week 52 were also significantly lower in the group taking combination therapy.

Furthermore, a sub-analysis of COMET patients at 2 years found that very early intervention (disease duration<4 months) with etanercept in combination with MTX provided significantly better disease control with better remission and low disease activity scores than early intervention (disease duration 4 months to 2 years). Thus, maximal benefit from biologic therapy with etanercept may be achieved in the first 4 months after RA diagnosis. These findings clearly support intensive therapy with TNF inhibitors in early RA to achieve rapid remission and to preserve patient quality of life and the ability to work.

Etanercept has also been shown to reduce disease severity and improve HAQ and SF-36 scores in RA patients over 2 years of treatment. Quality of life scores are worse in established RA than early RA, and early therapeutic intervention may lead to greater improvement in the mental and emotional components of these diseases. This supports the need for prompt referral to a specialist, rapid diagnosis and timely therapy with these new agents.

As maximum benefit from therapy can be achieved during early or very early disease, monitoring disease activity and response to therapy is essential to ensure patients are treated with the most appropriate therapy. Recent advances in imaging tools such as MRI and ultrasound offer the ability to detect signs of inflammation and disease progression in early RA. In addition, disease assessment tools such as METEOR allow rheumatologists to quickly and uniformly monitor disease activity and tailor treatment accordingly.

OS9

Ten years of TNF-blockers for treating rheumatoid arthritis: What have the registries taught us?

Emilio Martin Mola
Hospital University La Paz, Madrid, Spain

National biologic registries play an important role in evaluating the safety and efficacy of biological therapies in a real-world setting. Since the first TNF-blocker was approved for the treatment of rheumatoid arthritis (RA) over 10 years ago, thousands of patient-years of data has been collected by these registries. A variety of national biologic registers are currently collecting data around the world. This wealth of data, which is augmented every year, provides crucial information for clinicians. In the absence of head-to-head trials, registry data offers opportuni-

ties to examine potential differences between specific anti-TNF agents used in RA in terms of safety, efficacy and, in some instances, cost-effectiveness.
Registries are not without their limitations. The observational nature of registries provides many challenges in the design and analysis of study questions regarding the benefits and risks of biologic agents. The absence of randomisation can lead to several biases, including channeling bias and time-related biases. Nevertheless, biologic registries provide valuable insights into the optimal treatment of various rheumatic conditions.
Registries provide a source of long-term drug survival data, which can be considered an indicator for real-life effectiveness; (e.g. DanBio, ATTRA, STURE, SCQM, BIOBADASER). Important data on the long-term safety of biologics in RA – specifically in terms of the relative risk of serious infections (e.g. tuberculosis), malignancy and cardiovascular disease – are also provided by registries (e.g. RATIO, BSRBR). In addition, registries have demonstrated that the use of biologics has a positive effect on mortality within the RA population.
As well as improving the quality of life of RA patients, there is an increasing volume of data (e.g. from the STURE registry) on the effect biologics have on the capability of RA patients to return to work. Clinicians can be reassured of the safety of these therapies, and these data also allows them to select the most appropriate agent for the management of each patient.
Results from registries, when considered alongside clinical trial data, can provide information on the optimal management of rheumatic conditions. Registry data also provide the opportunity to elucidate key differences between therapy options in terms of safety and efficacy and help inform clinical decisions.

OS10

Access to innovative rheumatoid arthritis treatments in EU

Gyula Poór
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

Over the past decade biological treatments have been shown to be extremely effective not only in reducing disease activity of rheumatoid arthritis but also in slowing the underlying joint destruction and functional disability.
The average prevalence of rheumatoid arthritis (RA) has been estimated at 0,49% in Europe and the total number of RA patients amounts to 1.9–2.0 million. The overall number of 180,000 treated RA patients with biologics (TNF inhibitors) means that about 9–10% of all the RA patients were on biological treatment in Europe in 2008 and there have been large differences in the usage of drugs among European countries. In the analysis the clear front-runner was Norway followed by Belgium, Iceland and Denmark while Germany, Italy, Austria and all the Central-Eastern European countries provided access to biologics to their patients below the EU average.
The most important determinant of access proved to be the economic conditions, including GDP, health expenditure/capita, reimbursement and special budget restrictions. Access to innovated therapy is also strongly influenced by medical conditions, like treatment guidelines, level and affordability of medical care and access to specialists (rheumatologists) and additional factors. In order to improve access to biologics relevant recommendations to rheumatologists are outlined in the presentation.

OS11

Classification and management of rheumatoid arthritis – the 2010 news

Josef Smolen
Medical University, Vienna, Austria

OS12

Treat to target – implement today for tomorrow

Karel Pavelka
Institute of Rheumatology, Prague, Czech Republic

International task force of academic rheumatologists published consensus document “Treat to target”. This concept reflects current advances in treatment of RA and it is based on several pillars:
a) early diagnosis of RA
b) establishing the remission as a main target of the therapy
c) introducing regular assessment of activity using validated numerical screening systems
d) adjustment of therapy in regular intervals, if target is not achieved.

The principals were formulated in following bullets:
The primary target for treatment of rheumatoid arthritis should be a state of clinical remission.
Clinical remission is defined as the absence of signs and symptoms of significant inflammatory disease activity.
While remission should be a clear target, based on available evidence low disease activity may be an acceptable alternative therapeutic goal, particularly in established, long-standing disease.
Until the desired treatment target is reached, drug therapy should be adjusted at least every 3 months.
Measures of disease activity must be obtained and documented regularly, as frequently as monthly for patients with high/moderate disease activity or less frequently (such as every 3 to 6 months) for patients in sustained low disease activity or remission.
The use of validated composite measures of disease activity, which include joint assessments, is needed in routine clinical practice to guide treatment decisions.
Structural changes and functional impairment should be considered when making clinical decisions, in

addition to assessing composite measures of disease activity.
The desired treatment target should be maintained throughout the remaining course of the disease.
The choice of the (composite) measure of disease activity and the level of the target value may be influenced by considerations of co-morbidities, patient factors and drug related risks.
The patient has to be appropriately informed about the treatment target and the strategy planned to reach this target under the supervision of the rheumatologist.

OS13

Importance of ultrasonography in early detection and monitoring of rheumatoid arthritis patients

Walter Grassi
University of Ancona, Italy

Ultrasonography (US) has opened new avenues of research to rheumatology in recent years, as demonstrated by an explosion in the number of publications. US has a number of properties which make it particularly attractive as an imaging tool in daily clinical practice. These include the lack of radiation exposure, the ability to assess the joints in a dynamic fashion and the power to measure tissue perfusion, and therefore inflammation. US may have a relevant impact on final diagnosis or therapeutic choices in patients with rheumatoid arthritis (RA). It is highly sensitive to the identification of fine, soft-tissue changes and it should be considered as an integral part of the clinical examination in most patients. US should be regarded as the first-line imaging modality in early detection and monitoring of patients with RA. It may provide an immediate cheap solution to the diagnostic dilemma of joint pain by providing imaging findings highly suggestive for diagnosis especially in the context of a confusing clinical and radiographic setting. Key diagnostic findings on US include fluid collection inside the joint cavity and/or synovial tendon sheath and/or synovial bursae, synovial proliferation, and increased blood perfusion. Bone erosions can be easily detected even when conventional X-ray is negative. Synovial perfusion can be evaluated by using a subjective semiquantitative scale of color signals, a quantitative measurement of color pixels or by analyzing the Doppler curves. An adequate consensus has not yet been reached on the best method to evaluate the Doppler signal. One of the most relevant potentialities of the power Doppler in RA is that of being able to discriminate between hypervascular and fibrous pannus. Although the impact of US on final diagnosis or therapy monitoring has not yet been defined, over the last few years an increasing number of rheumatologists have started to utilize US in their daily clinical practice and there is now considerable evidence that the role of US imaging in assessing both activity and severity of synovitis is growing year by year and that US routinely performed by rheumatologists should be encouraged.

OS14

The diverse role of the RANK/RANKL/OPG system

Gyula Poór
National Institute of Rheumatology and Physiotherapy, Semmelweis University, Budapest, Hungary

The discovery of RANKL/RANK/OPG system has revolutionized our understanding of bone remodeling by the late 90s. The receptor RANK on osteoclasts can be activated by RANKL produced by osteoblasts that can be inhibited by another osteoblast product, the decoy receptor osteoprotegerin.
In the last decade the diverse role of the system has been discovered. In postmenopausal osteoporosis the immunesuppresive effect of estrogen is suspended and via increased cytokine production of immune cells and via increased RANKL production of osteoblasts enhanced bone resorption will occur. In osteolytic bone metastasis tumor cells secrete factors (eg. PTHrP) that upregulate the expression of RANKL while in osteoblastic metastasis beside predominating bone forming process bone resorbing process with elevated RANKL production is also present. Paget's disease of bone and related syndromes proved to be suitable to study genetic background of the RANKL system and mutations in the system are frequently associated with these disorders. In rheumatoid arthritis cytokines, including RANKL produced by activated immune cells are responsible for the three types of bone loss: intraarticular erosion, periarticular osteopenia and generalized osteoporosis. RANKL itself has a proinflammatory effect as well based on the stimulation of cytokine producing osteoclast precursors and the prolonged survival of dendritic cells. The network has been implicated in the pathogenesis of atherosclerosis as well. According to our knowledge the high OPG levels are mainly associated with plaque calcification while RANK expression correlates with destabilization and rupture of calcified plaque.
The discovery of the significance of this ubiquitous network in other tissues will give us special possibilities in the close future.

OS15

Bone strength – role of trabecular and cortical bone

Péter Lakatos
Semmelweis University, Budapest, Hungary

For a long time, trabecular bone has been in the focus of interest as the major determinant of bone strength. The role of cortical bone in maintaining bone strength has been investigated in details during

the last decade. The cortical structure was thought to be responsible for stiffness of bone only. However, according to recent data, cortical appears to play a more essential role in defining the resistance of bone tissue to physical forces. Approximately, 40–75% of axial load in the spine is taken up by the cortical, while it is close to 90% in the inter-trochanteric area of the femur. Cortical porosity is an important factor in determining bone strength. This type of porosity is increasing with age, and it quickly deteriorates the load-bearing capacity of bone tissue resulting in increased fracture frequency. Improving cortical porosity could dramatically reduce fracture risk. Most of our anti-osteoporotic drugs are acting mostly on the trabecular. The human monoclonal anti-RANKL antibody, denosumab has been shown to be beneficial on cortical bone, as well. This fact may be an additional component in the outstanding anti-fracture efficacy of this drug. Also, the positive cortical effect may distinguish denosumab from other anti-resorptive medications.

OS16

Effect of denosumab treatment of bone turnover markers and BMD

Pavel Horak
Palacký University Olomouc, Czech Republic

Denosumab is a new drug with unique mechanisms of action, which has a potential to be used in several clinical conditions associated with increased bone turn-over. In the robust clinical program of the phase 3 trials multiple aspects of its efficacy were studied. Denosumab was also compared with established antiporotic therapy with alendronate.

The DECIDE study was designed to determine whether the mean percent change in total hip BMD in 1,189 postmenopausal women with low BMD receiving denosumab is not less than that observed in patients receiving alendronate sodium (noninferiority study).

Patients were randomized to receive SC denosumab injections (60 mg every 6 months plus oral placebo weekly or oral alendronate weekly (70 mg) plus SC placebo injections Q6M. At month 12, denosumab significantly increased BMD at all sites measured (total hip, trochanter, femoral neck, lumbar spine) compared with alendronate. Absolute difference in change in BMD between the 2 treatment groups was statistically different (P<0.0001). At the total hip (primary endpoint), statistically significant increases in BMD were observed for the denosumab group compared with those treated with alendronate (3.5% vs 2.6%; P<0.0001). Denosumab also significantly increased BMD from baseline compared with that of alendronate at the lumbar spine (5.3% vs 4.2%; P<0.0001), trochanter (4.5% vs 3.4%; P<0.0001), femoral neck (2.4% vs 1.8%; P=0.0001), and one-third radius (1.1% vs 0.6%; P=0.0001). SCTx-1 decreases from baseline were significantly greater in the denosumab treatment group than in the alendronate group at months 1, 3, 6, and 9 (P≤0.0001). At 12 months, sCTx-1 changes were similar in the denosumab and alendronate groups. Decreases in sP1NP levels were significantly greater in the denosumab group than in the alendronate group at months 1, 3, 6, 9, and 12 (P≤0.0001).

The STAND trial in 504 women previously treated with alendronate evaluated the effects of transitioning to denosumab on changes in BMD and biochemical markers of bone turnover, and on safety and tolerability compared with continuation of alendronate therapy. The primary endpoint was the percent change from baseline in total hip BMD at 12 months. BMD at the total hip increased by 1.90% from baseline at month 12 in subjects transitioning to denosumab compared with a 1.05% increase from baseline in subjects continuing on alendronate therapy (P<0.0001). Significantly greater gains in BMD were observed at month 12 at the lumbar spine, femoral neck, and one-third radius with denosumab therapy than with alendronate therapy. Significantly greater increases in BMD were observed as early as month 6 with denosumab therapy for all measured skeletal sites except the one-third radius (P<0.05 for other sites). Denosumab significantly reduced serum CTx-1 levels (P<0.0001) at all measured time points compared with alendronate. Reductions were rapid and sustained through month 3, with an attenuation of the reduction at the end of the dosing interval at month 6. In the continued alendronate group, median serum CTx-1 levels remained near baseline throughout the study, consistent with the expected pattern for ongoing alendronate therapy. P1NP reductions with denosumab were significantly greater than with alendronate beginning at month 1, with maximal steady-state reduction observed by month 3 and attenuation of reduction noted at the end of the dosing interval.

The incidence of adverse events and serious adverse events was balanced between groups in both trials. The FREEDOM trial was a 3-year, international, randomized, placebo-controlled study that enrolled 7,868 postmenopausal women, of which 7,808 were evaluated. The study was designed to show the anti-fracture efficacy of denosumab. The sub analysis of FREEDOM determined if BMD is a “good surrogate” for the effect of treatment to decrease fracture risk and whether changes in BMD observed with denosumab treatment account for the decrease in fracture risk and to estimate the proportion of change in fracture risk that is explained by change in BMD, or so called PTE (*p*roportion of *t*reatment effect *e*xplained) index. Using a time-dependent model, the predicted risk of new vertebral fracture was plotted against the change of total hip BMD from baseline to the time of fracture. An estimated PTE by BMD change was derived. PTE was estimated to be 51%. Using a fixed model

approach, the predicted risk of nonvertebral fracture was plotted against the change of total hip BMD from baseline to 36 months. An estimated PTE by BMD change was derived and was estimated to be 87%. Changes in total hip BMD may be a good surrogate marker for the effect of denosumab on fracture risk.

OS17

Clinical evidence for antifracture protection of denosumab

Socrates Papapoulos
Leiden University Medical Center, The Netherlands

Animal and, more recently, human genetics have revealed the critical role of RANKL in osteoclastogenesis and bone resorption leading to the development of a specific inhibitor for the management of skeletal disorders. Denosumab, a fully human antibody to RANKL, was shown in pharmacokinetic/dynamic studies to persist in the circulation following a single sc injection and to rapidly and efficiently decrease bone resorption. Subsequently, different dosing regimens were explored in the management of patients with osteoporosis, metastatic bone disease, cancer treatment-induced bone loss and rheumatoid arthritis in clinical trials involving nearly 20,000 patients.
In the pivotal study of denosumab in osteoporosis (FREEDOM) 7868 women aged 60-90 years were randomized to receive sc denosumab 60 mg or placebo every 6 months for 3 years together with calcium and vitamin D. Compared with placebo, denosumab decreased the risk of new vertebral fractures by 68%, the risk of hip fractures by 40%, the risk of nonvertebral fractures by 20% and the risk of major osteoporotic fractures by 35%. The frequency and severity of adverse events was similar between denosumab and placebo-treated patients. Preplanned and post-hoc analyses showed, in addition, consistent effects in women with increased fracture risk (e.g in women ≥75 yrs denosumab reduced the risk of hip fractures by 62%). Furthermore, compared to weekly alendronate in women who were either treatment-naïve or had been treated previously with alendronate, denosumab induced significantly higher increases in BMD at all skeletal sites and was preferred by nearly 80% of patients.
Commonly used treatments of patients with non-metastatic cancer of the prostate and the breast, androgen-deprivation therapy (ADT) and aromatase inhibitors, respectively, lead to bone loss and increase the risk of fractures. In a 3-year study of men with non-metastatic cancer on ADT, compared to placebo, denosumab reduced the incidence of new vertebral fractures by 62%, an effect consistent with that observed in postmenopausal women with osteoporosis.
These results, together with those obtained in patients with metastatic bone disease and rheumatoid arthritis make denosumab an extremely promising therapy of disorders affecting the skeleton characterized by absolute or relative increase in bone resorption.

OS18

Anabolic therapy in the severely osteoporotic patient

Astrid Fahrleitner-Pammer
Medical University of Graz, Austria

What can we do when antiresorptive agents are not enough? Osteoporosis is a cost intensive disease that affects more than one third of the female population and 20 percent of the males in European countries. Osteoporosis and the consequent fractures, especially clinical vertebral fractures and hip fractures, are not only associated with increased mortality, but also a reduced health-related quality of life. Treatment aims to reduce the risk, incidence and burden of osteoporosis-related fractures. Antiresorptive agents such as bishosphonates, SERMs, HRT or denosumab lead to a decreased bone resorption, however the target cells of these compounds are osteoclasts and the effect is limited to the small parts of bone surface where remodeling takes place. Teriparatide as bone anabolic agent targets the osteoblasts and osteocytes and the effect is expected in the whole skeleton. In the placebo-controlled Fracture Prevention Trial (FPT), daily teriparatide treatment for 19 months reduced the risk of vertebral and non-vertebral fractures in postmenopausal women with severe osteoporosis. Teriparatide (TPT) has a limited treatment duration and is typically used as a second-line treatment option in postmenopausal women with severe osteoporosis. Thus, many patients receiving teriparatide have previously been treated with antiresorptive therapy and require further osteoporosis medication after teriparatide is discontinued. This is an important issue, as nowadays we are frequently confronted with patients on long term bisphosphonate therapy, with suppressed bone turnover, low to normal bone density but incident fractures – it's good to know that we have sufficient data on the effect of TPT not only in treatment naive patients but also in pre-treated patients. Furthermore, we know that patients after TPT not only need to preserve the acquired bone but clearly further benefit from antiresorptive treatment. Beside data on bone density and fracture incidence TPT has also proven to improve quality of life and reduce pain.

OS19

Clinical presentation and treatment of glucocorticoid-induced osteoporosis

Willem F. Lems
Vrije Universty Medical Centre Amsterdam, The Netherlands

Glucocorticoids (GC) have strong anti-inflammatory effects, but their use may also lead to side effects:

osteoporosis and associated fractures. Osteoporotic fractures, particularly of the spine, hips and ribs, are among the most devastating. Glucocorticoid-induced osteoporosis (GIOP) is the most common cause of secondary osteoporosis.

GC predominantly have an inhibiting effect on the activity of osteoblasts and osteocytes, resulting in depressed bone formation. Thus, theoretically, anabolics should be, based on the pathogenesis of GIOP, the drugs of first choice in GC-treated patients. Nowadays, only PTH 1-34 (teriparatide) has been investigated in GC-treated patients; no data are available in GC-treated patients from PTH 1-84. It can be expected that in the near future new drugs, interfering with the Wnt signaling pathway, e.g. monoclonal antibodies against sclerostin, might also have strong bone formation stimulating effects.

For both alendronate and risedronate an increase in bone mineral density (BMD) and reduction of vertebral fractures have been observed in RCTs in patients treated with (high dose) GC.

In the one-year alendronate study (5), an RCT in 477 patients, the effects on BMD were better in the alendronate group than in the placebo-group, both at the lumbar spine and at the hips, but the reduction in new vertebral fractures was not statistically significant: 2,3% versus 3,7% (RR: 0,6; 95% c.i.: 0,1–4,4). In a follow-up study, the second year, the vertebral fracture risk was decreased: 0,7% versus 6,8% (p=0,026). However, the follow-up study was performed in (only) 208 out of 477 patients. No reduction in non-vertebral fractures was observed: 9,8% versus 5,4% (alendronate), not significant.

The GIOP-studies with risedronate are more robust: two one-year studies were performed, one in patients starting with a GC ("prevention"), and one in patients chronically treated with a GC ("treatment"). Taken together, 518 patients are enrolled: a statistically significant risk reduction for new vertebral fractures was found: 16% versus 6% (70% risk reduction, p=0,01). Nonvertebral fractures were found in 6% (placebo) versus 6,5% (risedronate).The number of patients in the GIOP-studies with risedronate were larger, which made it possible to perform a sub-analysis in 184 GC-treated men: a relative risk reduction was also found: RR 0.18, p=0,008.

Thus, in both the alendronate and the risedronate studies, there was no reduction in non-vertebral fractures, which might be a type II error.

What about the other anti-osteoporotic drugs? No data in GC-treated patients are available for strontium-ranelate, which is remarkable, since strontium ranelate induces an increase in bone formation and a reduction in bone resorption, thus counteracting the effect of GC on bone.

For ibandronate, a superior effect on BMD and vertebral fracture rate has been shown in patients after heart-transplantation.

A randomized controlled trial, comparing the effects of zoledronate with that of risedronate has recently been presented: the increase in BMD was larger in the zoledronate treated patients than in the risedronate treated patients. However, the clinical relevance of this difference can be questioned, since increases in BMD does not necessarily indicates increases in bone strength.

Since vitamine D increases intestinal calcium absorption and has a positive effect on bone strength, the Osteoporosis Working Group of the Dutch Rheumatologists investigated in an RCT the use of active vitamine D versus alendronate: the increase in BMD was larger in the alendronate group.

Recently, Saag et al published an 18 month RCT, comparing the anabolic agent teriparatide with alendronate in 428 women and men with osteoporosis, who received GC (>5mg per day) for at least three months. The bone mineral density in the lumbar spine increased more in the teriparatide group than in the alendronate group: 7,2% versus 3,4%. Remarkably, a difference in new vertebral fractures was observed: 0,6% in the teriparatide group versus 6,1% (alendronate) (p=0.004). As in other studies, no difference was found in non-vertebral fracture rate. Additionally, in the second period of 18 month of treatment, again a difference in vertebral fracture rate was observed.

In summary, patients treated with GC who are at high risk for fractures, should be treated with calcium, vitamin D and a bisphosphonate. For those who have a very high fracture risk, such as those patients with a new fracture during bisphosphonate use, treatment with an anabolic agent (teriparatide) could be attractive.

OS20

B-cell therapy: A "positive" direction to personalized healthcare in rheumatoid arthritis

Zoltán Szekanecz
University of Debrecen, Hungary

OS21

Tocilizumab efficacy: The science of IL-6R inhibition

László Czirják
University of Pécs, Hungary

OS22

Safety of tocilizumab in patients with rheumatoid arthritis: Analysis of long-term extension studies

Ronald van Vollenhoven
Karolinska University Stockholm, Sweden

P1

Major histocompatibility complex class I. chain-related gene A: Risk and protective alleles in systemic lupus erythematosus pathogenesis

Marketa Fojtíková[1], Peter Novota[1], Pavlina Cejkova[2], Dana Tegzova[1], Satu Pesickova[1], Karel Pavelka[1], Marie Cerna[2]
[1]Institute of Rheumatology, [2]Charles University, Prague, Czech Republic

The genetic components influence the development of systemic lupus erythematosus (SLE) and several GWA studies show the risk areas within major histocompatibility complex, 6p21.3. Because genetic-epigenetic and genetic – environmental interactions are required for the disease development and the genes of the major histocompatibility complex (HLA) genes and the major histocompatibility complex class I chain-related gene A (MICA) are involved in the antigen presentation to CD4+ and CD8+ a δγ respectively, and may vary among populations' authors performed and analysed of the HLA class II and MICA gene polymorphism in Czech, Slavic population. In MICA gene they defined alleles of the microsatellite polymorphism of the transmembrane (TM) region in exon 5 of with the (GCT)n repetitions and MICA-A5.1 allele with G insertion whose are in linkage disequlibrium with the extracellular parts of MICA protein.
All of 123 SLE patients fulfilled at least 4 of the ACR criteria, as control group they investigated 99 healthy Czech individuals. SSP PCR and PCR-fragment analysis were used for HLA class II and MICA TM polymorphism alleles detection.
Of all five alleles (MICA – A4, A5, A5.1, A6, A9) detected in Czech population the MICA-A5.1 was significantly more common in SLE than in controls (55.7% vs. 39.9%, Pcorrected 0.005, OR 1.88, CI95% 1.29-2.77) whereas the MICA-A6 were occurred only in 10.6% SLE unlike 19.7% in controls (Pcorrected 0.035, OR 0.48, CI95% 0.28-0.82). There were no statistical differences in genotype distribution among two groups.
The HLA – DRB1*03 allele was found in 22.8% SLE and 10.6% controls, Pcorrected 0.008, OR 2.5, CI95% 1.44-4.27 and similarly the HLA – DRB1*03-DQB1*0201 haplotype is significantly associated with risk to SLE: the frequency in SLE group was 44.7% in comparison to 15.2% in controls, pc<0.0001; OR 4.54 CI95% (2.36-9.09).
The MICA-A5.1 allele together with HLA – DRB1 *03 is strongly associated with SLE [pc<0.000001; OR 9.71 CI95% (3.4–27.7)]. Authors didn't find linkage disequilibrium between MICA and HLA class II (DRB and DQB) alleles. 4. They did not find any significant association between MICA or HLA class II alleles and clinical and serological manifestation of SLE.
The MICA-A5.1 allele increases the risk for SLE in HLA – DRB1 *03 susceptible individuals. They confirm the role of HLA – DRB1*03-DQB1*0201 haplotype in the development of SLE in the Slavic population.

P2

Rheumatoid arthritis and prolactin: Association with disease activity and joint damage

Marketa Fojtíková[1], Jana Tomasová Studýnková[1], Maria Filková[1], Zdeňka Lacinová[2], Jindřiška Gatterová[1], Karel Pavelka[1], Jiří Vencovský[1], Ladislav Šenolt[1]
[1]Institute of Rheumatology, [2]Charles University and General University Hospital in Prague, Czech Republic

Prolactin (PRL) is a pituitary hormone which acts as a cytokine with multiple roles in immune response and activation of synovial cells. Some autoimmune diseases are associated with increased serum PRL levels. The aim of this study was to evaluate the levels of PRL in serum and synovial fluid in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) and to examine whether PRL might be associated with laboratory and clinical disease activity of RA.
A total of 29 patients with RA and 26 patients with OA were included in the study. The concentration of PRL in the serum and synovial fluid was measured by immunoradiometric assays, and the levels of serum anti-citrullinated protein/peptide autoantibodies (ACPA) and IgM rheumatoid factor (IgM-RF) were analysed by ELISA. Disease activity score (DAS 28) and radiographic evaluation by Larsen score were assessed.
The levels of PRL in serum (299.55±27.28 vs. 230.59±16.61 mIU/l, p=0.041) as well as in synovial fluid (338.85±33.49 vs. 245.97±21.88 mIU/l, p=0.024) were significantly higher in patients with RA than in those with OA. A moderate correlation was found between disease activity of RA and levels of PRL in synovial fluid (r=0.485, p=0.010). Furthermore, serum PRL levels correlated significantly with the total Larsen score (r=0.4838, p=0.014).
Prolactin levels in serum and synovial fluid are increased in patients with RA compared to those with OA. These findings suggest that prolactin may play a

role in disease severity and the process of joint damage in RA.

P3

Lipid peroxidation and antioxidant enzyme activities in patients with systemic lupus erythematosus

Attila Kovács[1], Do Huy Quai[2], Aranka László[2], Ilona Varga[2]
[1]Hospital of Hungarian State Railways, Szolnok, [2]University of Szeged, Hungary

Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease where tissue damage is caused by depositions of pathogen autoantibodies and immune complexes. Mechanism of oxydative stress generated by free oxygen radicals can also play a role in the pathogenesis of SLE, while antioxidant enzymes take part in the defending mechanisms. Authors aim was to measure the oxidative and antioxidative status in long-term treated SLE patients in order to gain new data for the understanding of pathogenesis.
Products of lipid peroxidation and several antioxidant enzyme activities were determined by standard methods in the blood plasma and red blood cell (RBC) haemolysate of 46 Hungarian patients with SLE and of 37 blood donors as controls.
In patients with SLE, the activities of RBC catalase (0.697 vs 0.916 U/mg protein, $p<0.05$) and superoxide dismutase (2.536 vs 3.201 U/mg protein, $p<0.005$) reduced, while the activities of RBC reduced glutathione (GSH) (0.758 vs 0.530 U/mg protein, $p<0.005$) and lipid peroxidation (0.473 vs 0.356 nM MDA/mg protein, $p<0.001$) and glutathione peroxidase (GSH-Px) (0.829 vs 0.650 U/mg protein, $p<0.05$) increased significantly as compared to the controls. There was not found any significant difference in the values of plasma GSH and lipid peroxidation. Positive Pearson's correlations were detected between the RBC haemolysate lipid peroxidation and RBC GSH-Px ($r=0.66$, $p<0.05$), the RBC lipid peroxidation and GSH ($r=0.32$, $p<0.05$), the RBC GSH and GSH-Px ($r=0.43$, $p<0.05$), the plasma GSH and RBC GSH-Px ($r=0.39$, $p<0.05$) and the plasma GSH and lipid peroxidation ($r=0.92$, $p<0.01$).
The findings on the examined pro- and antioxidative status suggest a regulatory and compensatory mechanism in long-term treated SLE patients. Excessively generated free radicals may play part not only in the pathogenesis of SLE but in the maintenance of chronic inflammation.

P4

Lupus nephritis: The therapeutic aspects

Teuta Backa, Alma Idrizi, Myftar Barbullushi, Argjend Tafaj, Alketa Koroshi
UHC Mother Teresa, Tirana, Albania

Recently, are provided supportive evidence that intermittent pulse cyclophosphamide has more favourable therapeutic index in the treatment of lupus nephritis (LN). 40 patients (28 females and 12 males, with a mean age 33±4.3 years) with LN were studied prospectively during a period of 5–52 months. The patients were divided in three groups: the first group of 13 patients (mean age 31.4±4.9 years) was treated with cyclophosphamide, the second group of 14 patients (mean age 32±4.8 years) was treated with prednisolone, and third group of 13 patients (mean age 34.2±3.1 years) was treated with cyclophosphamide and prednisolone. Nephrotic range proteinuria was present in 19 patients, respectively according to the groups in 6, 7 and 6 patients. 10 patients (4, 3, 3) had impairment renal function (creatininemia ≥ 2 mg/dl). After 6 months of treatment proteinuria decreased in 12 patients (6, 3, 3 according to the groups). Difference was significant between first and second group, and first and third group ($p<0.038$, $p<0.05$). Renal function improved in 7 patients (according to the groups in 4, 2, 1 patients; $p<0.05$, $p<0.04$). 3 patients, one of each group, died due to the progression of the disease. Pulse cyclophosphamide treatment in their patients was more effective than that with prednisolone alone and both combined. The patients had less undesirable effects than therapy with other medicaments.

P5

Flaccide hypokalemic paralysis in a patient with primary Sjögren's syndrome

Teuta Backa, Alma Idrizi, Myftar Barbullushi, Kliti Hoti
UHC Mother Teresa, Tirana, Albania

Clinically significant renal disease is rare in Sjögren's syndrome (SS). Although hypokalemia in patients with SS is a frequent sequela of renal tubular acidosis (RTA), severe symptomatic decrease in serum potassium concentration has been described only in few cases. Authors describe a case with flaccide hypokalemic paralysis as the presenting finding of primary SS. A 38 year-old woman complained of nausea, weakness, fatigue, weight loss, recurrent attacks of conjunctivitis, increase of water intake, constipation, dry skin, eyes, and oral cavity, and she was diagnosed as having hypokalemic periodic paralysis. Decreased effective refractory period and ST-T changes and generation of U wave were present in electrocardiogram. Laboratory investigations confirmed the diagnosis of hyperchloremic metabolic acidosis with a normal serum anion gap. Antibodies to Ro (SS-A) and both Schirmer's and Rose-Bengal tests were positive, suggesting for primary SS. Intravenous potassium replacement and after the use of potassium citrat orally, as well as the treatment with prednisolon were successful.

P6

Vascular endothelial growth factor and basic fibroblast growth factor in systemic lupus erythematosus with Jaccoud´s arthropathy

Zbynek Hrncir, Marcela Drahosova, Ctirad Andrys, Petr Bradna, Tomas Soukup, Jan Toms
University Hospital, Hradec Králové, Czech Republic

Jaccoud´s arthropathy (JA) is a defined type of deforming involvement of small hand joints. JA is most commonly observed in systemic lupus erythematosus (SLE). The joint deformities in JA are usually related to tendosynovitis and less frequently to synovial hypertrophy, but may mimic rheumatoid arthritis (RA). Vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) are important angiogenic growth factors in rheumatoid proliferative synovitis.

To specify the position of JA in SLE (SLE-JA+) using VEGF and bFGF as indirect markers of synovial proliferation in relation to SLE without JA (SLE-JA–), RA and control group (CG) of healthy persons.

Total group of 83 SLE (classification ACR/1982, updated 1997) under study included 10 SLE-JA+ and 73 SLE-JA–. The group of RA (classification ACR/1987) included 50 patients, and the CG 40 blood donors matched according to age and sex. Joint deformities in SLE-JA+ fulfilled descriptive criteria for JA according to the method of van Vught (score of JA index>5/11). Serum levels of VEGF and bFGF were measured with specific ELISA kits according to the manufacture´s protocol (Quantikine Human VEGF Immunoassay and Quantikine HS Human FGF basic Immunoassay, RD Systems, Minneapolis). Data obtained were statistically processed using Medcalc-SigmaStat program. Results (pg/ml) were expressed as the median and 95% CI for the median.

VEGF serum levels were obtained as follows: SLE-JA+ 335 (95% CI: 182-863), SLE-JA– 207 (95% CI: 168-256), RA 404 (95% CI: 273-530), and CG 220 (95% CI: 214-258). Significant differences were found between SLE-JA+ and SLE-JA– ($p<0.005$), and between SLE-JA+ and CG ($p<0.006$), but not between SLE-JA+ and RA ($p>0.05$). Significant differences were found also between SLE-RA– and RA ($p<0.001$), and between RA and CG ($p<0.001$), but not between SLE-JA– and CG ($p>0.05$). bFGF serum levels were obtained as follows: SLE-JA+ 1.200 (95% CI: 0.470-7.328), SLE-JA– 8.260 (95% CI: 6.331-10.170), RA 11.720 (95% CI: 6.947-14.804), and CG 5.850 (95% CI: 4.500–8.559). Significant differences were found between SLE-JA+ and SLE-JA– ($p<0.006$), between SLE-JA– and RA ($p<0.002$), and also between SLE-JA– and CG ($p<0.003$). Significant differences were obtained also between SLE-JA– and RA ($p<0.01$) and between RA and CG ($p<0.002$), but not between SLE-JA– and CG ($p>0.05$).

The data obtained by means of investigation of serum levels of VEGF and bFGF significantly differ the subgroup of SLE with JA from the SLE subgroup without this disorder; in case of VEGF also suggest to overlapping similarity between SLE with JA and RA according to this angiogenic marker. Further studies are necessary.

P7

Vascular endothelial growth factor and epidermal growth factor in patients with systemic sclerosis and systemic lupus erythematosus

Radim Becvar[1], Ivana Putova[1], Michal Tomcik[1], Simona Skacelova[1], Dana Tegzova[1], Radka Svobodova[1], Jiri Stork[2], Petr Zatloukal[3], Alena Zatloukalova[3]
[1]Institute of Rheumatology, [2]General Teaching Hospital, [3]Clinic of Pneumology and Thoracic Surgery, Prague, Czech Republic

Systemic sclerosis (SSc) is a generalized connective tissue disease, which presents as thickening and fibrosis of the vessel walls, skin and involvement of visceral organs. Vascular involvement plays a crucial role in all phases of SSc course. Certain growth factors display various effects on the vessel wall and stimulate proliferation of fibroblasts and their biosynthetic activity. In systemic lupus erythematosus (SLE) vascular lesions, Raynaud's phenomenon, cutaneous vasculitis, and ulcers and gangrene of the fingers and toes, small cutaneous infarction, or lupus profundus are all well recognized. Certain vascular lesions are also suspected in cerebral SLE. The aim of this study was to determine in a group of patients with SSc serum concentrations of vascular endothelial growth factor (VEGF) a potent angiogenic molecule, and epidermal growth factor (EGF) and to correlate the obtained data with the disease subsets, selected clinical findings and laboratory data. Total 99 patients (10 males and 89 females) were examined – 23 with diffuse form, 47 with limited form, 6 with sclerodermа sine scleroderma, 1 with overlap syndrome, and 4 individuals with undifferentiated connective tissue disease. All individuals underwent routine laboratory tests and the examination of different visceral organs. Serum levels of VEGF and EGF were assayed using commercial ELISA kits. Mean serum VEGF concentration was in SSc 96.31 pg/ml and in SLE 108.36 pg/ml did not exceed the normal range, while mean EGF concentrations were 180.89 ng/ml in SSc and 276.43 ng/ml in SLE and were higher than normal range. In SSc there was no correlation of these factors with the presence of anti-topoisomerase I or anticentromere antibodies. When authors correlated the VEGF levels with occurrence of digital ulcers they found a significant association ($p=0.01$) only in diffuse subgroup. Similarly, in this subgroup EGF levels correlated with the occurrence of sclerodactyly but not with basal lung fibrosis. There were observed no association for the limited subgroup of patients. In their study VEGF seemed to be a potential marker of acral

ulcers and EGF for sclerodactyly only in the diffuse type of disease. The real significance of these factors should be further studied on larger cohorts of SSc patients.

P8

Prevalence, incidence and survival of diffuse systemic sclerosis in Dalmatia county, Croatia

Mislav Radić, Dušanka Martinović Kaliterna, Josipa Radić, Damir Fabijanić, Vedran Kovačić
University Hospital Split, Croatia

To estimate the prevalence, incidence and survival of diffuse systemic sclerosis (dSSc) in Dalmatia. Authors department of rheumatology and clinical immunology is the only tertiary referral centre for the Dalmatian County, which has a population of approximately 750 000 Caucasian people. A census of dSSc cases for the period 2005–2007 was conducted in Dalmatia County, using hospital record review for case identification. Diagnoses were verified by medical record review. The exact 95% confidence interval (CI) based on binomial distribution was created for the incidence and prevalence estimates. The exact 95% confidence interval (CI) based on binomial distribution was created for the incidence estimate. Cases of limited systemic sclerosis were excluded. All patients were evaluated by the American College of Rheumatology criteria for the classification of systemic sclerosis.
Based on 56 verified cases of dSSc, prevalence was initially estimated to be 7.4 cases per 100,000 adults (95% CI 3.1-15.2), with an annual incidence of 1.6 new cases per 100 000 adults per year (95% CI 0.5-4.1). Gender prevalence estimate were significantly higher for women than for men. Median survival was 11 years. Factors negatively affecting survival included male sex (hazard ratio 1.65, 95% CI 1.15-2.40) and older age at diagnosis (hazard ratio 1.03, 95% CI 1.01-1.04).
This study establishes baseline estimates of dSSc occurrence and characteristics in a large Croatian cohort consisting of Causation people. These data should facilitate research regarding the role of geographic, ethnic and environmental factors for this disease in comparison populations.

P9

Impact of metacarpophalangeal and proximal interphalangeal joints flexion contractures on disability and health-related quality of life in systemic sclerosis

Mislav Radić, Dušanka Martinović Kaliterna, Josipa Radić
University Hospital Split, Croatia

To assess the impact of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints flexion contractures on disability and health-related quality of life (HRQoL) in systemic sclerosis (SSc).
Authors evaluated 44 SSc patients during hospital stay. HRQoL was assessed by the SF-36, global disability by the health assessment questionnaire (HAQ), hand disability by the Cochin Hand Function Scale (CHFS) and global hand and wrist mobility by the Kapandji index.
Twenty-eight (63.6%) patients had MCP or PIP joints flexion contractures at the time of evaluation. Patients with MCP or PIP joints flexion contractures showed significantly more pitting scars ($p<0.001$) than others. Patients with MCP or PIP joints flexion contractures had significantly greater HAQ (1.31±0.58 vs. 0.80±0.42, $p<0,05$), CHFS (25.20±19.80 vs. 15.90±13.88, $p<0.001$) scores than others. Hand and wrist mobility were significantly diminished in patients with DU (Kapandji score 73.5±25.9 vs 82.8±19.8, $p<0.001$). The presence of the MCP or PIP joints flexion contractures did not alter significantly the physical component, but influenced the mental component (43.38±12.53 vs 39.58±9.54, $p<0.05$) of the SF36.
SSc patients with MCP or PIP joints flexion contractures have reduced wrist and hand mobility, increased global and hand disabilities and decreased mental component of HRQoL.

P10

Peripheral neuropathy in systemic sclerosis patients

Diana Vučina, Dušanka Martinović Kaliterna, Mislav Radić
University Hospital Split, Croatia

The etiology of neuropathy in systemic sclerosis is unknown. An autopsy of a patient with systemic sclerosis and neuropathy showed severe sclerosis of the spinal peripheral nerves with extensive degeneration of nerve fibers.
Because systemic sclerosis patients report neuropathic symptoms including numbness, paresthesias, and dysesthesias, authors assessed peripheral nerve function in such patients and compared them with rheumatoid arthritis patients.
The neurologic assessment included a neurologic history, neurologic examination, nerve conduction studies (NCS), electromyography (EMG), and quantitative sensory testing (QST).
Eleven systemic sclerosis patients underwent complete neurologic examination, nerve conduction studies (NCS) and quantitative sensory testing (QST). Neurologic examination revealed reduced vibration (4) or pinprick (3) sensation in the upper or lower extremities, focal atrophy or proximal weakness (2), and decreased deep tendon reflexes (2). NCS showed reduced sensory nerve action potentials (1) and carpal tunnel syndrome (1). QST of the upper and lower extremity revealed increased cold or vibration detection thresholds in 6 of 11 patients. Fourteen rheumatoid arthritis patient s without rheumatoid vasculitis underwent complete neurologic examination, nerve con-

duction studies (NCS) and quantitative sensory testing (QST). Mild distal symmetric sensory neuropathy (2) was confirmed.
Authors findings suggest that peripheral neuropathy occurs in systemic sclerosis patients at a higher frequency than in rheumatoid arthritis patients. Larger, prospective studies using the more sensitive QST as well as pathologic studies of nerve, including cutaneous innervation, are needed to further assess the characteristics and etiology of the neuropathy in systemic sclerosis and rheumatoid arthritis.

P11

Systemic sclerosis – clinical and immunological features of 211 patients of Slovak population

Jozef Lukáč, Oľga Lukáčová, Jozef Rovenský, František Máliš, Peter Poprac, Alena Tuchyňová, Roman Stančík, Darina Kozáková, Karol Bitter
National Institute of Rheumatic Diseases, Piešťany, Slovakia

The project was focused on clinical symptoms and organ involvement influencing the course and prognosis of patients with systemic sclerosis (SSc). Clinical symptoms, laboratory parameters, autoantibodies will be evaluated in correlation to skin score, organ involvement, and disease duration.
In the years 2006–2008 – 211 patients with definite diagnosis of SSc were enrolled. There were 173 female and 36 male patients at the age 53.4 years average (range from 17 to 78 years). 19 of them had diffuse SSc and 168 limited SSc. 21 patients fulfilled criteria of CREST syndrome, 2 had polymyositis/systemic sclerosis, one – dermatomyositis/systemic sclerosis. In all patients, assessment of lung (high resolution computer tomography, diffuse capacity of CO), heart (electrocardiography, echocardiography), oesophagus motility, thermography of the hands, disability, capillaroscopy will be done. They did HAQ-DI, modified Rodnan score and laboratory examination, including autoantibodies.
Average Rodnan´s score of skin involvement was 12 (range from 2 to 36), 22,7% of patients have skin score more that 14. Hypomotility of oesophagus grade I was found in 88 and grade II. in 84 patients, another patients had normal finding. Diffusing capacity of CO was reduced in majority of patients: average DLCO was 45,8% of normal values (range from 19 to 86%). Antinuclear antibodies (Hep2) were positive in 183 patients (86,7%). Autoantibodies to anti-DNA topoisomerase I have proved in 62 patients (33,8%) and anti-centromere autoantibodies in 17 patients (9,2%). Quality of life was estimated by health assessment questionnaire (HAQ). Average HAQ value was 0.78 (0,75–2,7).
The monitoring of these parameters could help to early distinguishing severe forms of SSc and early introducing of effective treatment in patients with unfavourable prognosis of SSc.

P12

Altered cellular immunity in diffuse cutaneous systemic sclerosis

Gábor Papp[1], Ildikó Fanny Horváth[1], Sándor Baráth[1], Edit Gyimesi[1], Péter Szodoray[2], Margit Zeher[1]
[1]University of Debrecen, Hungary, [2]Rikshospitalet University of Oslo, Norway

Although the exact mechanisms behind fibrotic disorders of systemic sclerosis (SSc) are not fully understood, recent studies highlighted the key roles of the innate and adaptive immune system in the pathogenesis of the disease. The objective of this study was to evaluate a wide spectrum of peripheral immune-competent cell types with regulatory and effector properties, reflecting overall disturbances in immune homeostasis, characteristic to SSc. Authors also assessed visceral organ involvements, and evaluated the relation between the cell proportions and the clinical symptoms of the disease.
They enrolled eighteen patients suffering from diffuse cutaneous SSc and fifteen healthy individuals in the study. Peripheral blood lymphocyte subgroups were quantified by flow cytometry, soluble cytokines were assessed by ELISA, serum complement levels were determined by nephelometry and autoantibodies were determined by indirect immunoflourescence technique. Functional tests of CD4+CD25+ Treg cells were carried out to compare the suppressor properties of these cells between controls and patients.
Patients with SSc had higher percentages of activated CD3+/HLA-DR+ T cells than controls. When comparing naive vs. memory subsets of CD4+ and CD8+ T cells, a shift toward central memory phenotype was observed for both. Natural killer (NK) and Th17 cell percentages were increased, while Th1, T regulatory type 1 (Tr1), CD4+CD25+ T regulatory (Treg) and NK T percentages were decreased in patients, compared to controls. The in vitro functional assay demonstrated lower suppressor activity of CD4+CD25+ Treg cells in SSc. They found negative correlations between modified Rodnan skin score values and Tr1 cell percentages and between complement levels and CD4+CD25+ Treg cells as well. Additionally, they found decreased interleukin (IL)-10 levels in SSc. Their data suggest that the increased Th17/CD4+CD25+ Treg ratio and the altered regulator function of CD4+CD25+ Treg cells play important role in the development of the disease by tipping the fine balance towards enhanced immune reactivity. Moreover, their study reveals the potential role of the decreased profile of IL-10-producing Tr1 cells in the progression of the disproportional immune responses in SSc.

P13

Evaluation of the cardiopulmonary status in systemic sclerosis patients with ergospirometry and stress echocardiography

Daniella Hulló[1], Gergely Ágoston[1], János Varga[1], Imre Lajkó[1], Ágnes Milassin[1], Attila Somfay[1], Albert Varga[1], Attila Pálinkás[2], László Kovács[1]
[1]University of Szeged, [2]Erzsébet Hospital, Hódmezővásárhely, Hungary

The early detection of pulmonary arterial hypertension and interstitial lung disease can determine the treatment and the prognosis of systemic sclerosis (SSc). In the early stage, non-invasive stress tests may be more sensitive, than resting functions.
Sixteen (13 female, 3 male) patients with systemic sclerosis, (7 diffuse, 9 limited cutaneous form) were studied. The mean age of the patients was 49 (26-60) years, the average disease duration was 11 (1-35) years. 6 patients were positive for anti-Scl-70, and 7 for anti-centromere antibody. In 7 patients pulmonary fibrosis was confirmed by high resolution computed tomography (HRCT). In addition to body pletysmography+diffusion capacity measurement, a detailed cardio-pulmonary exercise test (ergospirometry) was performed. All patients underwent a complete resting echocardiography. Stress echocardiography was performed during bicycle exercise with the patient being in semi-supine position.
Resting lung function tests revealed severe restrictive ventilatory dysfunction as defined by a reduced total lung capacity and forced vital capacity in 5 patients. Carbon monoxide diffusion capacity (DLCO) was abnormally low in 15 of the 16 patients (mean: 57±19% predicted). Cardiopulmonary exercise test indicated reduced exercise capacity (WR: 62±28% predicted), impaired aerobic capacity (VO2/kg: 56±17% predicted) and decreased aerobic threshold (41±17 VO2%). 8 patients demonstrated oxygen desaturation (Sat: 94±6% vs. 88±4%) during exercise. Resting echocardiography revealed pulmonary hypertension in 12/15 patients. In all patients, pulmonary arterial pressure increased abnormally during exercise with an average change of 29,1±12 Hgmm from baseline.
Impaired alveolo-capillary gas exchange can be detected in the majority of SSc patients, even in those who do not have manifest interstitial lung disease or structural heart disease. Cardiopulmonary exercise test adds more information in terms of exercise tolerance, aerobic capacity, metabolic profile and gas-exchange related ventilatory equivalent during exercise. Stress echocardiography is more sensitive than routine resting ultrasound in the detection of pulmonary hypertension. Cardiopulmonary and echocardiographic exercise testing may be indicated in SSc patients with apparently normal or only slightly abnormal resting function in order to detect early pulmonary vascular or interstitial involvement. The prognostic value of these examinations as indicators of the progression of microvascular damage will be prospectively assessed.

P14

Selected risk factors for coronary heart disease in patients with psoriatic arthritis, who were treated in the rheumatology clinic in Wroclaw between 2008–2009

Renata Sokolik, Dominik Samotij, Agata Sebastian, Arkadiusz Chlebicki, Piotr Wiland
Rheumatology Clinic, Wroclaw, Poland

Psoriatic arthritis (PsA) is a chronic disease, which is characterized by inflammatory arthritis associated with psoriasis. Patients with psoriasis are at significantly higher risk for cardiovascular death.
The aim of this research work was to analyze the selected risk factors for coronary heart disease such as increased total cholesterol level, total low-density lipoprotein level and decreased high-density lipoprotein cholesterol level, elevated levels of uric acid in the blood, C-reactive protein (CRP) and fixed factors such as age and gender in patients with PsA.
The study group consisted of 37 patients with PsA who were treated in the Rheumatology Clinic in Wroclaw between 2008-2009. The mean age of the study group was 42. The mean values of erythrocyte sedimentation rate (ESR), CRP, total cholesterol level, HDL, LDL, TGL, uric acid, glicemy and presence of cardiovascular disease were analyzed.
The mean disease activity score (DAS 28) was 4,43, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 6,4. The mean values of ESR were 22,00 mm/hr, CRP 13,24 mg/l, total cholesterol level 216,24 mg/dl, HDL 57,73 mg/dl, LDL 134,70 mg/dl, TAG 118,80 mg/dl, uric acid 4,98 mg/dl, glicemy 87,73 mg/dl. 42,8% of patients had hypertension and 17,85% diabetes mellitus. Authors found a positive correlation between ESR and CRP ($r=0,65$, $p<0,05$), age and total cholesterol ($r=0,4$, $p<0,05$), age and LDL ($r=0,3$, $p<0,05$), DAS 28 and BASDAI ($r=0,8$, $p<0,05$) and a negative correlation between ESR and total cholesterol ($r=–0,5$, $p<0,05$), CRP and HDL ($r=–0,45$, $p<0,05$).
It's important for patients with PsA to regularly measure cholesterol levels and to assess cardiovascular risk because of the negative correlation between CRP and HDL, a rapid reduction of inflammatory parameters should be established.

P15

^{166}Holmium-phytate-radiosynoviorthesis in rheumatoid arthritis. Five years clinical results. Phase III. prospective study

Margit Szentesi, Pál Géher
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

166-Holmium-phytate produced by authors: radiation type beta energy maximum: 1,84 MeV; radiation type gamma energy maximum: 0,66 MeV; soft tissue penetration: maximum 8,4 mm; average: 3,3 mm; half-life: 26,9 hours; particle size: 0,6-2 μm Study objectives: Examination of anti-inflammatory effect of 166-Holmium-phytate injection.
Phase III, prospective study. 30 patients suffering from chronic synovitis, rheumatoid arthritis were examined. The protocol commenced with screening. The patients were selected according to inclusion and exclusion criteria. Holmium phytate injectable suspension marked by 600 MBq 166-Holmium phytate injectable suspension, and 40 mg of 1 ml triamcinolone acetonide and 1 ml of lidocaine 1%. There were 60 month follow-up period after the administration of the isotope. Inflammatory activity of the affected knee-joint was tested prior to treatment, and the 3rd and 3, 6, 9, 12, 24, 36, 48 and 60 months after the treatment. Evaulation was based on the criteria as described by Müller, Rau and Scütte the score system was developed by the authors.
During the study period, inflammation decreased. In the first five years excellent and good results were recorded in 93.3%. Five years after radiosynoviorthesis 93.3% of patients did not need another punction. Administration of Holmium-166 phytate is a safe procedure. Authors did not detect any symptoms of radiation sickness. They found no deviations in either haematological or chemical parameters during the study period.
Holmium-166 phytate isotope is an effective radiopharmacy treating synovitis. Due to its physical parameters it is optimal to treat large joints (knee) and medium size joints (hips, shoulder, elbow, wrist, ankle). Effective dosage is 555-925 MBq.

P16

Regulation of CD3 expression on human T-lymphocytes

György Nagy, Barbara Érsek, Zoltán Wiener, Melinda Rácz, Edit Buzás, Viktor Molnár, Pál Géher, András Falus
Semmelweis University, Budapest, Hungary

Rheumatoid arthritis (RA) is characterized by increase production of proinflammatory cytokines, cartilage destruction and bone erosions. T-lymphocyte involvement in the pathology of RA is well widely accepted and points to a local dysregulation of T cell function in the inflamed joint. Synovial T-lymphocytes of patients with RA display hyporesponsiveness upon antigenic stimulation, the expression of T cell receptor zeta chain is downregulated in these cells. The precise molecular mechanism of T cell dysfunction in RA is not understood. Nitric oxide (NO) that regulates physiological T cell activation, is overproduced in RA according to authors previous data. Several lines of evidence suggest that both tumor necrosis factor (TNF) and NO may contribute to T cell dysfunction. Their previous data indicate that TNF treatment selectively downregulates CD3ζ chain in a dose dependent manner on human T-lymphocytes. Here they investigated the potential mechanism of the TNF induced ζ chain downregulation. CD3 zeta and epsilon chain expression were determined by Western blot and by flow cytometry. NF-kB reporter plasmid containing Jurkat cells were used to study the role of NO on NF-kB activation. mRNA expressions were studied by microarray and quantitative real-time RT-PCR. Selective inhibition of NF-kB or blocking of the lysosomal compartment fails to restore the TNF induced CD3 zeta chain downregulation. TNF induced micoRNA mir-155 upregulation is inhibited by NO pretreatment. TNF treatment does not regulate CD3 epsilon chain expression. Pretreatment with NO donor (180 uM) prevents TNF induced zeta chain downregulation. According to their present data, NO treatment does not regulate TNFR1 and TNFR2 expression. These data suggest that NO influences TNF induced T cell activation and TNF induced CD3 zeta downregulation, which may contribute to T cell dysfunction in RA.

P17

The impact of the anti-cyclic-citrullinated peptide antibody status in the management of patients with early rheumatoid arthritis in Hungary: Results from an interim analysis

Péter Juhász[1], Katalin Dankó[2], Katalin Fazekas[3], Ramóna Gaál[1], Judit Korda[1], Hajnalka Laczkó[4], Nóra Nusser[5], Katalin Seregély[6], János Szász[7], Eszter Tóvári[8], Edit Vereckei[1], Orsolya Nagy[9], Gyula Poór[1]
[1]National Institute of Rheumatology and Physiotherapy, Budapest, [2]University of Debrecen, [3]Szent Ferenc Hospital, Miskolc, [4]Vaszary Kolos Hospital, Esztergom, [5]Zsigmondy Vilmos Hospital, Harkány, [6]Bács-Kiskun County Hospital, Kecskemét, [7]I. Rheumatology Clinic, Székesfehérvár, [8]Integrated Health Care Institution of Pécs, [9]Abbott Laboraties (Hungary) Ltd., Budapest, Hungary

Data indicate that anti-cyclic citrullinated peptide (anti-CCP) antibodies are highly predictive for erosive disease in populations with early RA. The objective of this prospective, 12-month observational trial was to assess the impact of anti-CCP status on clinical decision-making and the management of patients with early RA. Here authors report interim results from the subset of Hungarian patients.

Socio-demographic data and medical history of the involved patients were collected. TJC, SJC, DAS28, HAQ-DI were assessed quarterly. Concomitant anti-rheumatic medication, CRP, ESR, anti-CCP and/or RF data were collected. Radiographic assessment of the affected joints (baseline and 12-month) was also performed. At each visit, investigators were asked to evaluate the impact of patient's serology and different outcome measures on treatment decisions.

A total of 605 early RA patients (diagnosed within 6 months) were enrolled in Hungary. 12-month follow-up data were available from 276 patients: mean age at baseline was 56.26 (±13.78) years and 71.38% of the patients were anti-CCP positive. Baseline disease activity showed a mean TJC 15.88 (±6.66), a mean SJC of 10.1 (±6.8), a mean DAS28 score of 6.43 (±0.93), and the mean HAQ-DI score was 1.51 (±0.78). At baseline, 34% of the patients had cardiovascular disorders. At baseline, a majority of patients were treated with DMARD monotherapy (mainly methotrexate) combined with corticosteroids. At 12 months, the mean DAS28 score had decreased to 3.52 (±1.44), mean ESR changed from 42.82 (±23.1) to 21.78 (±15.67) mmh/1hr and mean CRP value decreased from 24.75 (±26.61) to 8.53 (±10.68) mg/l. The HAQ-DI score also decreased to 0.81±0.62 at 12 months, but remained above a value representative for the general population. Biologic response modifiers were used in 5.79% of patients at baseline and in 19.92% at the end of the study. Anti-CCP status was "a very" or "the most important" factor for treatment decisions in 53.63% and 49.64% of the cases at baseline and 12 months, respectively. Anti-CCP status was also an important predictor for initiation of therapy with biologic response modifiers. At 12 months, CRP chosen in 55.07% of cases was a more important factor than anti-CCP for therapy decision-making.

Authors preliminary data suggest that approximately half of the investigators considered anti-CCP status as an important factor in treatment decision, but traditional inflammatory measures remain more influential factors for treatment decisions. DMARD therapy was effective in the treatment of early RA symptoms, but despite decreases in clinical and laboratory markers of disease activity, the group of patients analyzed here did not achieve low disease activity or remission levels, and was left with functional disability, indicating that therapy with traditional DMARDs was suboptimal. It will be interesting to see whether these trends can be confirmed in the analysis of the full data set.

P18

Correlation between clinical manifestation and immune-genetic determinants at patients with psoriatic arthritis in Republic of Moldova

Liliana Groppa, Liudmila Gonta, Eugeniu Russu
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

Psoriatic arthritis is an inflammatory joint disease associated or no with psoriasis and presents a heterogeneous clinical pattern, expressed by different manifestations such as poli-oligoarthritis from mild to very severe forms, erosive and destructive mutilate arthritis, DIP arthritis and very particular psoriatic axial diseases. The aetiology is unknown but genetic factors are believed to be of importance. The pattern of inheritance is proposed to be polygenic. The aim of this study was to analyze:

– the prevalence of inflammatory manifestations, such as polyarthritis, oligoarthritis, axial disease, DIP arthritis and mutilate arthritis in patients with psoriatic arthritis in Republic of Moldova;
– the clinical manifestations of psoriatic arthritis and associations with immunological disorders by appreciation of lymphocytes cell determinants (CD) with identifying markers for aggressive joint disease
– the clinical manifestations of psoriatic arthritis and associations with human leukocyte antigens (HLA-antigens) and identifying markers for aggressive joint disease.

Ninety-nine patients with psoriatic arthritis with defined joint disease were examined clinically, radiological, and with laboratory-based analyses. Disease classification and diagnosis have been based on CASPAR criteria. All patients who were included into the study selected from the Depts. of Rheumatology from the 3rd Municipal Clinical Hospital and from the Dept of Dermatology which were invited to a prevalence study. Every patient was included in separate group from those five groups by Moll and Wright (polyarthritis, oligoarthritis, axial disease, DIP arthritis and mutilate arthritis) and statistical analyses have been done between these groups. The correlation of clinical manifestations and potential markers of aggressive joint disease with HLA associations and lymphocytes clone determinants (CD) were analyzed in all patients with psoriatic arthritis which were included into the study.

They have found a high prevalence of HLA-B7, B17, B27, B37 and HLA-A2, A3, A7 and A29 which were increased in comparison with controls (p=0.012, pc=0.024, RRf=3.1), but the strongest predictive factors among patients with polyarthritis and axial disease of psoriatic arthritis for an aggressive disease, in a multiple logistic analysis and polifactorial correlation, were HLA-B27, B11, B37, B69. A significant linkage (p=0.0001, RRf=2.9) was found. Ninety-four controls with the same ethnic background as the pa-

tients were randomly selected from the population of Republic of Moldova. An association was found between CD determinants of lymphocytes (CD2, CD3, CD4, CD8, CD19, CD20, CD22) and psoriatic arthritis, but most important were: for DPI arthritis and oligoarthritis CD3, CD8 in comparison with controls (p=0.001, pc=0.014, RRf=3.1); for polyarthritis form CD2, CD4, CD8 in comparison with controls (p=0.003, pc=0.009, RRf=2.6); for axial disease CD4, CD8 and CD22 in comparison with controls (p=0.001, pc=0.021, RRf=3.5), and for mutilate arthritis CD2, CD4, CD19, CD20, CD22 in comparison with controls (p=0.001, pc=0.029, RRf=2.8) with significant linkage for all groups (p=0.001, RRf=2.4-3.3).
The prevalence of inflammatory joint manifestations, such as polyarthritis, axial disease and mutilate arthritis was high among patients with psoriatic arthritis in Republic of Moldova. There were several strong association between HLA-antigens (B7, B17, B27, B37, A2, A3, A7, A29), lymphocytes CD2, CD3, CD4, CD8, CD19, CD20, CD22 and psoriatic arthritis. The strongest predictive factors among patients with polyarthritis and axial disease of psoriatic arthritis for an aggressive disease were HLA-B27, B11, B37, B69 with a significant linkage (p=0.0001, RRf=2.9).

P19

Assessment of clinical efficiency of tocilizumab in disease evolution of patients from Moldova with rheumatoid arthritis

Liliana Groppa, Daniela Cepoi-Bulgac, Eugeniu Russu, Laura Vremis, Hellis Osama
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

Assess the impact of biological basic drug tocilizumab in the clinical course of rheumatoid arthritis; Identify changes in laboratory parameters of rheumatoid arthritis; Determine the safety of tocilizumab in patients with rheumatoid arthritis.
Inclusion criteria: a reliable diagnosis of rheumatoid arthritis established on the basis of diagnostic criteria of the ACR, 1987; age 20–60 years; lack of clinical efficacy of ongoing basic treatment. Exclusion criteria: patients with definite diagnosis of rheumatoid arthritis, but with concomitant chronic diseases: pathology of the liver, heart, lungs, infections (HIV, tuberculosis), oncopathology, patients with rheumatoid arthritis over 60 years. All patients were divided randomly into 2 groups. Group A (25 patients) received treatment methotrexate 10 mg/week and folic acid 5 mg/week in combination with tocilizumab 8 mg/kg. Group B (25 patients) received treatment methotrexate 10 mg/week and folic acid 5 mg/week in combination with placebo. Complete clinical examination consisted of monitoring joint indicators: number of swollen and painful joints (the joints of the index 28), Ritchie index and Lee, a general analysis of blood and urine markers of inflammation (CRP, fibrinogen), a detailed biochemical analysis of blood, immune markers and X-ray.
The number of swollen joints in group A significantly (p<0,01) decreased by 6 months of treatment (from 9,58 to 1,9, Rf=0,02) compared with group B (from 7,13 to 6,4, Rf=0,3). Also reduce the number of painful joints and index DAS28 statistically more pronounced (p<0,001) in group A (from 19.08 to 5,7, Rf=0,0001 and DAS28 from 6,36 to 4,1, Rf=0,01) compared with group B (from 16,2 to 13,2, Rf=0,1 and DAS28 from 6,5 to 6,1, Rf=0,4). There was a significant (p<0,001) decline in the inflammatory process in patients of group A (DRR from 7,5 to 1,0, Rf=0,003 and ESR from 41 to 17, Rf=0,02) compared with group B (SRB from 6,4 to 5,1, Rf=0,2 and ESR from 38 to 28, Rf=0,1). According to the criteria of remission ACR20/50/70 – they are the patients of group A for 6 months of treatment amounted to 73,78%/52,08% and 34,72% respectively, which substantially exceeded (p<0,001, Kendall=2,6) rates of group B, which accounted for 29,97%/13,32%/3,33%.
Conclusions to 24 weeks of treatment tocilizumab:
– Improved clinical indices of rheumatoid arthritis (morning stiffness, the indices of articular syndrome, functional joint status);
– Detect a decline of inflammation (ESR, CRP, DAS28);
– Efficiency tocilizumab seen after the first injection and significantly reduces disease activity at an early stage of treatment;
– The frequency of adverse events in group A did not differ from that in group B; – Patients taking tocilizumab a marked improvement in quality of life.

P20

Influence of glucose level control in blood on evolution of inflammatory joint syndrome at patients with a diabetes mellitus type 2.

Liliana Groppa, Lia Chislari, Eugeniu Russu, Zinaida Anestiadi
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

The lead researches in the field of defeat of joints at patients with a diabetes mellitus type 2 have revealed the certain quantity of inflammatory parameters associated with a painful syndrome and joints symptoms. These parameters include: quantity of the painful and swollen joints, C-reactive protein, ESR, fibrinogen and their correlation with a level of glycosidation haemoglobin (HbA1c). Therefore, the task is put, what factors define presence and deterioration of joint syndrome and occurrence of progressing functional insufficiency. The interrelation between an inflammatory joint syndrome and a diabetes mellitus assumes amplified glycosidation of connecting tissue and especially collagen that supports high activity of inflammation. According to the literature at patients who received intensive treatment concerning a dia-

betes mellitus, lower have been determined levels of articulate inflammation, probably, in consequence low glycosidation of collagen integuments and articulate sinovium. The purpose of research has consisted in studying parameters of joint inflammatory syndrome at patients with diabetes mellitus type 2.
Research last 12 months in which 72 patients by a diabetes mellitus of the second type, with a different degree of an inflammatory joint syndrome and the control of glucose in blood have been included. Patients involved in research have been comparable on age and sex. The quantity of the painful and swollen joints, a level of C-reactive protein, fibrinogen, HbA1c and ESR have been investigated. Correlation of level HbA1c with quantity of the painful and swollen joints, a level of C-reactive protein, fibrinogen and ESR by indexes Pearson and simple-T-test has been lead.
Research of inflammatory joint syndrome has revealed a high level of activity which was shown: a plenty of the painful (9,5±1,2) and swollen (11,4±1,4) joints, a high level of C-reactive protein (48,7±1,1 UN/ml), fibrinogen (3,8±0,23mmol/l) and ESR (31±1,21mm/oră). Evolution of a parameter with glucose control (HbA1c) has been submitted by various gradation: from 6,1% up to 12,5%, on the average 9,4±0,3%. Presence of significant correlations between high parameter HbA1c and growth of parameters of active inflammatory joint process has been revealed: with C-reactive protein (r=0,89, p<0,01), fibrinogen (r=0,91, p<0,001) and ESR (r=0,79, p<0,01). Also have been determined correlative parameters of the average importance (r=59-65) for quantity of the painful and swollen joints.
Expressed painful joint syndrome has been revealed at patients with a diabetes mellitus type 2 which was shown by high parameters of amount of the painful and swollen joints, the increased level of C-reactive protein, fibrinogen and ESR. The lead research has revealed value of glucose control over evolution of joint syndrome: the insufficient control of a level of glucose in blood conducts to aggravation of joint syndrome that has been proved to revealing of significant correlations with level HbA1c.

P21

Research of a bone metabolism at patients with diabetes mellitus type 2.

Liliana Groppa, Lia Chislari, Eugeniu Russu, Zinaida Anestiadi
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

Rheumatologists long time admitted that fact, that the diabetes mellitus contributes to occurrence of septic arthritis, and also, is the often reason of neuropathic joint. It is not a discovery that fact, that skeletal connecting tissue, joints and perijoint structures are amazed, therefore atherosclerotic diabetic plate and growth basal membrane of capillaries matrices' disorganization of connecting tissue which are consequence of diabetes mellitus grow out. These infringements can be divided into two groups: the first is characterized by reduction of mineral density of bone and early osteoporosis which appears not owing to infringement of bone formation and increase bone resorption. The second group includes infringement of connecting fabric formation, but it does not play a significant role. The purpose of research. On the basis of the aforesaid authors aimed to study parameters of a bone metabolism, and also to investigate parameters remodelled and the general bone metabolism at patients with a diabetes mellitus type 2.
Research proceeded 12 months and have been involved 41 patient with a diabetes mellitus type 2 at which various degrees of degenerate defeat of joints have been revealed. As control group – 35 person comparable on age and sex. Levels acid and alkaline phosphatase, parathormone, concentration of calcium (the general and ionized), a level of index – T determined have been investigated by USG-osteodesitometric.
The results: a degree of osteoarthritis. At the majority of patients with diabetes mellitus type 2, involved in research, the diagnosis of osteoarthritis stage 3 degrees has been put. Thus, at 9,7% (n=4) of patients in1 stage of disease has been diagnosed, for 26,8% (n=11) – 2 stage, at 46% (n=19) – 3 stage and only 17% (n=7) of patients – a terminal stage of defeat joints. In control group at 85% of patients 2 stage of osteoarthritis has been revealed. Evolution of biochemical parameters. In both groups of patients increase of concentration acid (gr. I=7,1; gr.II=6,61 UN/l) and alkaline phosphatase (gr. I=125,5; gr.II=129,4 UN/l) was revealed, concentration only acid tartrat-resistant phosphatase at patients with a diabetes mellitus type 2 however statistically significantly (p<–2,5, that correlated with osteoporosis.
Value of infringement of a bone metabolism expressed by amplification of processes bone resorption and deterioration of current degenerative joint pathology in a combination with osteoporosis were typically for patients with the second type of a diabetes mellitus. It is known, that osteoporosis constantly promotes degenerate osteo-articulate defeats at patients with a diabetes mellitus type 2 that conducts to a progression of functional joint insufficiency that burdens disease, and detection of factors which increase risk of osteoporosis gives an opportunity of definition patients for which additional researches are necessary and dictates necessity of assignment anti-osteoporosis treatments. In research by statistical analysis there were appreciate correlation of various bone metabolism parameters and presence osteoporosis at degenerate diseases of joints at patients with the second type of a diabetes mellitus.

P22

The role of Th17 cells in spondylitis ankylopoetica

Attila Balog[1], Balázs Szalay[2], László Kovács[1], Daniella Hulló[1], Barna Vásárhelyi[2]
[1]University of Szeged, [2]Semmelweis University, Budapest, Hungary

Different subtypes of CD4+ lymphocytes including Th1, Th2, regulatory and Th17 subsets have a major role in the determination of intensity and nature of immune responses. The aim was to investigate baseline prevalence of these cell types in spondylitis ankylopoetica (SpA) and its alteration upon infliximab therapy. 9 patients with SpA were enrolled this prospective study and took peripheral blood from them at the completion of NSAID-therapy, then on the 2nd and 6th week following infliximab treatment. Cell prevalence was compared to that obtained in 8 age-matched controls. The results indicated higher than normal Th17 cell prevalence in SpA that was not affected by infliximab therapy. The percentage of Th17 cells in controls was 0,71 [0,65-0,82]. The percentage of Th17 cells in SpA group was on the baseline visit 1,32 [0,54-2,6]*, 1,51 [0,69-1,65]* on the 2nd week and 1,37 [0,8-1,57]* on the 6th week. The occurrence of other cell types was comparable to that in controls. This finding supports the contribution of Th17 cells to SpA. All patients had a good clinical answer according to the BASDAI score. The benefits of infliximab therapy, however, are independent on Th17.

P23

Frequency of myostitis-specific and myositis-associated autoantibodies in the serum of patients with idiopathic inflammatory myopathies

Katalin Dankó[1], Melinda Vincze[1], Judit Tumpek[1], Lászlóné Szőllősi[1], Peter J. Charles[2]
[1]University of Debrecen, Hungary, [2]Kennedy Institute, Imperial College London, United Kingdom

As in other connective tissue diseases (CTDs), idiopathic inflammatory myopathies (IIMs) are characterized by the production of a series of autoantibodies (Abs) to various cellular constituents. Some of these Abs are found specifically in patients with polymyositis/dermatomyositis, known as myositis-specific autoantibodies – MSAs. Others can be found in several type of connective tissue diseases. These are known as myositis-associated autoantibodies – MAAs. Myositis-specific or myositis-associated autoantibodies are present in about 40% of patients with myositis. These antibodies define distinct clinical subsets, suggesting that they may play an active role in the immunopathogenesis of myositis. The most common MSAs are anti-aminoacyl-tRNA synthetases in polymyositis and anti-Mi-2 antibodies in dermatomyositis. Finally more then 10 myositis specific autoantibodies (SRP, PL-7, PL-12, etc.) are known. With a few exceptions, each patient has only one of these autoantibodies. Among MAAs, the most frequent are anti-SSA and anti-SSB autoantibodies. According to recent studies more than 20 MAA are recognised in CTD patients. The objective of authors study was to determine the frequency of MSAs and MAAs in the serum of their patients. Sera and clinical data were collected from 363 patients with IIM followed longitudinally. The proportion of females and males was 2,9:1 as usually in IIMs. 65% (n=236) of the patients suffered from polymyositis (PM), 29% (n=104) had dermatomyositis (DM), 5% (n=19) had juvenile dermatomyositis (JDM) and 1% (n=4) had amyopathic dermatomyositis (ADM). Sera were screened by enzyme-linked immunosorbent assay and line-immunoassay technology. Diagnoses were determined using the Bohan and Peter classification as well as recently proposed classifications. 27,27% (n=99) of the patients showed MSA and 47,93% (n=174) MAA positivity. The most frequent MSA among MSA positive patients was anti-Jo1 Abs 48,5% (n=4). The anti-PL-12 Abs had been associated with DM, the other MSAs had been found mostly in PM patients. The most common MAA among MAA positive patients was anti-SSA Abs 46,6% (n=81). Authors studied the association of MSAs and MAAs too. According to their results MAAs are commonly associated to anti-Jo1 Abs 17,24% (n=30). They found double MSA positivity in 3 patients. In conclusion they can declare that the frequency of MSAs and MAAs in the serum of Hungarian patients with idiopathic inflammatory myopathies corresponds with former international studies. Their further purposes are to define the clinical and genetical properties of their MSA and MAA positive patients.

P24

Anti-Pm-Scl autoantibody positivity in patients with idiopathic inflammatory myopathy

Andrea Váncsa[1], Peter J. Charles[2], Júlia Németh[3], Andrea Ponyi[4], Judit Tumpek[1], Melinda Vincze[1], Katalin Dankó[1]
[1]University of Debrecen, Hungary, [2]Kennedy Institute, Imperial College London, United Kingdom, [3]National Institute of Health, Budapest, [4]Semmelweis University, Budapest, Hungary

The current study was performed to determine the prevalence of anti-Pm-scl autoantibody, as well as its association with other autoantibodies, clinical characteristics, disease course and response to therapy in 374 patients with idiopathic inflammatory myopathy (IIM).
All patients fulfilled the Bohan and Peter classification criteria. ANA and anti-centromer antibodies were detected by immunfluorescence on Hep-2 cells. Anti-topoisomerase-I (Scl-70) antibody and the myositis associated autoantibodies (SS-A, -SS-B) were test-

ed by ELISA. The cut-off value was 10 U/ml for the anti-SS-A, -SS-B, -Scl-70 autoantibodies. Anti-SRP, -Pm-Scl 75 and 100 autoantibody were detected by immunoblot method.
The prevalence of scleromyositis among patients with IIM was 3.47%. Anti-Pm-scl antibody was present in 11 (2.9%) IIM patients (female:male:7:4; 1 juvenile dermatomyositis, 1 juvenile polymyositis, 1 dermatomyositis, 4 polymyositis, 3 scleromyositis, 1 Sjögren overlap myositis) and 23.1% of scleromyositis patients. At the time of diagnosis mean age was 47.2 (6.3–71) years. Mean follow-up time from diagnosis was 9.09 (3–19) years. Regarding additional antibodies in these patients, the following was found. Speckled and nucleolar ANA positivity was found in four patients. Autoantibodies against both to the Pm-scl 75 and 100 autoantigen could be detected in one patient with scleromyositis and only against the Pm-scl 100 autoantigen in one patient with polymyositis. Anti-scl-70 and -Pm-scl antibody coexpression was found in one juvenile polymyositis patient. No anti-centromer antibody was found in any of the patients. Co-expression of anti-SRP, -Mi-2 and -Pm-scl autoantibody was found in one polymyositis patient. Regarding the myositis associated antibodies, anti-SS-A positivity was found in 27.3% of Pm-scl positive IIM patients. Most commonly occuring skin sings were facial erythema, V-sign, poikiloderma, heliotrop rash, Gottron papula in scleromyositis. Presence of anti Pm-scl autoantibody was associated with clinical signs similar to the characteristics of antisynthetase syndrome. Interstitial lung disease was in 36.4%, Raynaud phenomen in 72.7%, arthritis and mechanic hand in 27.3% in IIM patients and calcinosis could not be found in any of the patients. Disease course was found to be monocyclic in 45.4% of patients and responsive to corticosteroids and the other patients responded well to second line treatment.
The results are consistent with those from other published series. Anti-Pm-scl autoantibody positive IIM is a rare entity associated with monocyclic disease course and good response to therapy.

P25

Association of idiopathic inflammatory myositis and myasthenia gravis

Anna Bazsó[1], Anna Polgár[1], Edit Vereckei[1], Mária Judit Molnár[2], Gyula Poór[1], Emese Kiss[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Semmelweis University, Budapest, Hungary

Idiopathic inflammatory myositis (IIM) is defined as idiopathic inflammatory disease of the muscles. However the course of this disease is heterogenous, and the pathogenesis remains unclear. The four major criteria to diagnose polymyositis: 1. symmetrical weakness of the proximal muscles and anterior neck flexors, 2. elevation of serum skeletal-muscle enzymes (i.e. creatinine phosphokinase and lactate dehydrogenase or aldolase), 3. electromyographic abnormalities, and 4. muscle biopsy histopathology abnormalities. The measurement of myositis-specific autoantibodies may be useful for predicting the clinical course, treatment, and outcome. Myasthenia gravis (MG) is characterized by fluctuating muscle weakness. Results from an edrophonium (Tensilon) test, electromyography and a serum antiacetylcholine receptor antibody (anti-AchR Ab) assay are diagnostic. According to previous publications the frequency of this association is rare.
Hereby, authors report 3 associating cases with IIM and MG. Out of the 45 patients with IIM as a total of 3 have been identified with coexisting MG. Two patients were presented with dermatomyositis and one with polymyositis. In both cases the IIM started earlier with 2-10 years before. Both patients had elevated CPK and LDH levels, had EMG findings characteristic for IIM, biopsy was performed in all cases confirming perivascular mononuclear cell infiltrate in DM and perimysial inflammation is PM. One patient presented myositis specific autoantibody; namely anti-JO1. Myositis associated autoantibody was not presented in any of the cases. Result of AchR Ab was available for 2 of the 3 patients and was typically positive. Thymectomy was indicated in one case of the patients. Therapy were pyridostigmine and ISU(azathioprin, cyclophosphamide). The appearance of an other disease was suspected by the non-specific signs of the control EMG and more severe symptoms of the skeletal muscle system. Two of them have extramuscular symptoms as idiopathic lung disease (ILD), and paraneoplasy was excluded.
Idiopathic inflammatory myositis and myasthenia gravis are autoimmune diseases affecting skeletal muscles. Although the pathogenesis and clinical profiles are different, they have some common features therefore the association of polymyositis and MG may cause differential diagnostic difficulties. Immune suppressive therapy may control both diseases, however the therapeutic response may be different. Careful examination is necessary to exclude the presence of malignancy, as both diseases may occur as paraneoplastic syndrome. Systematic review is required to determine the exact frequency of IIM and MG. Further research may reveal probable common pathogenic pathways.

P26

Anti muscarinic receptor-3 autoantibodies in secondary Sjögren's syndrome

Magdolna Deák, Nóra Árgyelán, Attila Balog, Daniella Hulló, Gyula Pokorny, Mária Kiss, Gábor Tóth, László Kovács
University of Szeged, Hungary

The authors previously demonstrated the presence of anti-muscarinic receptor-3 (m3AchR) antibodies in primary Sjögren's syndrome (pSS). However, the clinical presentation of Sjögren's syndrome overlap-

ping various systemic autoimmune diseases, and the prevalence and epitope-specificity of anti-m3AChR in these entities is not clear.
Data on 56 patients with rheumatoid arthritis (RA) and 84 with systemic lupus erythematosus (SLE) were compared with those on 47 pSS patients. Subjective and objective sicca symptoms were evaluated by means of a questionnaire, and of sialometry and Schirmer's test, respectively. Patients with both subjective and objective glandular dysfunction were considered as subjects with sicca complex, and further immunoserological and histological examinations were initiated to assess whether the condition can be classified as secondary Sjögren's syndrome. Three immunodominant epitopes of the m3AChR were synthesised with solid-phase peptide-synthesis, and used as antigen in ELISA. Fatigue and quality of life was assessed with validated questionnaires. Correlations were searched for between the glandular function and various clinical features, anti-m3AChR autoantibody-positivities and –specificities and the health status parameters.
Eleven RA patients and 21 SLE patients proved to have sicca complex. In both patient groups, higher age correlated with the presence of sicca symptoms. The peptide of the second extracellular loop of m3AChR reacted with the sera of 38% of the pSS, 41.5% of SLE, and 21.6% of RA patients. The peptide of the third extracellular loop bound 38% of pSS, 41.5% of SLE and 23.3% of RA patients, while the epitope located in the intracellular portion of the m3AChR reacted with 17.6% of pSS, 23% of SLE and 13.3% of RA patients. The autoantibody levels to the two extracellular epitopes were significantly higher in all the three disease groups than in the healthy controls, but were not statistically different among the patient groups or subgroups of SLE or RA patients with or without sicca complex.
Sicca complex and secondary Sjögren's syndrome occur in a significant proportion of SLE and RA patients. The second and third extracellular loop of the m3AChR may be antigenic in pSS and also in SLE and RA. Further studies are expected to reveal a more detailed characterisation of the background of exocrine insufficiency in systemic autoimmune diseases.

P27

The immune-modulating role of vitamin A, D and E in the pathogenesis of primary Sjögren's syndrome

Ildikó Fanny Horváth, Gábor Papp, Sándor Baráth, Péter Szodoray, Margit Zeher
University of Debrecen, Hungary

Earlier findings underlined the important immune-regulatory functions of the fat-soluble vitamin A, D and E. The aim of the present study was to investigate the immune-modulating role of fat-soluble vitamins in 25 patients with primary Sjögren's syndrome (pSS) and 15 healthy individuals to search for correlations between vitamin levels and various clinical and immunological parameters.
Plasma vitamin A, D, and E levels were determined by high performance liquid chromatography. Peripheral natural killer cells, natural killer T cells, T-cell subsets, B-cells, IL-10 producing regulative Tr1 cells, CD4+CD25+ Treg cells and T-helper (Th)17 were determined by flow-cytometry. Various Th1- and Th2-related soluble cytokines were assessed by ELISA, while intracytoplasmic cytokines (IFN-gamma, IL-4, IL-10 and IL-17) were measured by flow-cytometry. Correlation was assessed between vitamin levels and immunological, also clinical parameters.
Vitamin A levels did not differ between patients and controls, yet in patients with extraglandular manifestations (EGMs) a significant decrease in vitamin A levels was apparent compared with pSS patients without EGMs (P=0.005). Vitamin E levels were increased in patients compared with controls (P=0.004), whereas Vitamin-D levels were similar in pSS and control subjects. In patients, vitamin A showed a positive correlation with both NK cell (P=0.038) and Th17 cell (P=0.025), and a negative correlation with Schirmer's test values (P=0.035). Positive correlation was found between vitamin E and NK cells (P=0.043), Th1 cells (P=0.049) and the Th1/Th2 ratio (P=0.043). In the control group, authors found correlation between vitamin E and serum IL-10 levels (P=0.003).
Their data suggest that fat-soluble vitamins may be important in immune-regulatory responses in patients with pSS and might control the initiation and perpetuation of autoimmune processes in the disease.

P28

Thalidomide in the treatment of Behcet´s syndrome in a 16 year old girl

Elena Koskova[1], Daniela Salatová[2], Stanislava Blažičková[1], Vladimír Bošák[1], Jozef Rovenský[1]
[1]National Institute of Rheumatic Diseases, Piešťany, [2]Pediatric Rheumatology Outpatient´s Department, Žilina, Slovakia

The article presents the case study of a 16 year old girl with Behcet's disease (BS), condition which is observed in Slovakia very rarely. The patient suffered from a severe form of BS manifested by panuveitis, vascular retinitis of the right eye, aphthae and aphthous ulcers of oral mucosa, skin vasculitis with multiple maculopustular lesions, nodular lesions similar to erythema nodosum, as well as arthritis. Ocular manifestations were treated successfully with systemic and local corticosteroids and with cyclosporin A, however, conventional treatment of the mucocutaneous lesions with colchicin failed to be effective. Due to the relapse of the disease and severity of its manifestations, the therapy with thalidomid was started. Special attention was given to the specific indicators of the cell mediated immunity. Therapy with thalidomide lasted

23 months. Six months after it was started clinical remission, decrease of inflammatory activity and increase of HLA – DR on monocytes occurred.
Thalidomide therapy resulted in the recovery of diminished levels of HLA – DR expressions on monocytes. Authors recommend to use the therapy with thalidomide cautiously because of the teratogenic effects of this agent and potential occurrence of polyneuropathy which was the reason why the therapy with thalidomide had to be stopped in their patient.

P29

Investigation of connective tissue diseases depending on serologic markers in young women who have somatisation disorders order and carried out systemic interrogation in details

Ozgur Tanriverdi
Safak Health Group Goztepe Hospital, Istanbul, Turkey

Connective tissue diseases (CTD) are insidious disease groups which progress with systemic complaints. Except for active periods, diagnosis of diseases depends on suspicion and detailed interrogation. Investigation of serologic markers such as antinuclear antibodies (ANA), anti- SM, C-reactive protein (CRP), rheumatoid factor (RF), complement-3 (C3), anticardiolipin antibodies (ACL), on patients who complain about somatisation disorder have been aimed.
Totally 42 women patients who supply to policilinic were studied. There were any different age features of there patients who have some symptoms in terms of somatisation disorders. In system interrogation alopecia, arhtralgies, photosensitivity, oral ulcers, genitally ulcers, myalgies, menstruations disorders, and other systemic sypmtoms were carefully examined. Serologic markers of patients were evaluated. All patients who have everyone systemic disorders such as known rheumatological diseases, diabetes mellitus, malignancies were excluded.
Mean age was 21.6±7.2 years. Abortus and stillbirth history were available in 7 of patients. According to desired laboratory analysis, positive CRP in 11 patients, positive RF in 3, positive ACL IgG in 7, positive ACL IgM in 6 and mightly degree diffuse homogenous positive ANA in 5 were found. Positive ACL was found in 5 of 42 policlinic patients who define Raynaud phenomenon (RP), and diagnosed according clinical observations. 6 case which define suspicious RP were available. Sjögren's syndrome was diagnosed for a patient. Systemic lupus erythematosus was diagnosed in 2 patients.
It is probable that findings which feature with detailed interrogation of non-specific complaints without have certain a system may be caught in young women who have somatisation disorders. In there patients, desiring of serologic markers and following of theirs in terms of serologic and clinic even if there are negative are required for a long time.

P30

The effect of the different doses of alfacalcidol on regulatory T-cells in patients with undifferentiated connective tissue disease

Éva Zöld, Sándor Baráth, János Kappelmayer, László Csáthy, Edit Gyimesi, Ágota Hajas, Margit Zeher, Gyula Szegedi, Edit Bodolay
University of Debrecen, Hungary

The Vitamin-D hypovitaminosis increase the risk of the development of several autoimmune diseases. The supplementation of Vitamin-D may be effective to improvement of immunoregulatory error of patient with UCTD, but since no data are available about optimal dosing. The aim of this study was to perform a quantitative and functional analysis of CD4+CD25+highFoxP3+T cells (nTreg) and CD4+IL-17+T cells, and to evaluate the plasma levels of proinflammatory cytokines in patients with UCTD before and after five weeks different dose (0,5–1–1,5 ug/day) alphacalcidol supplementation.
Authors studied sera from 15 UCTD patients with Vitamin-D insufficiency. Plasma levels of 25(OH)D were measured by HPLC method. Flow cytometry was utilized to determine the quantification of nTreg and IL-17 expressing TH17 cells, the plasma concentrations of cytokines, interleukin (IL-6), IFN-γ, IL-17, IL-10, TNF-α was confirmed by ELISA. Results The plasma 25(OH)D levels were risen after different doses alphacalcidol administration compared to the baseline levels, but the elevation was not significant after 5 weeks treatment. At the same time the 5 weeks alphacalcidol treatment decreased the number of the IL-17 expressing TH17 cells and improvement the number of nTreg cells, proportionately with the elevation of Vitamin-D. The higher elevation of the plasma levels of Vitamin-D was connection with the decreasing of the levels of TNF-α, IL-6, IL-17. Whereas the serum levels of previous Th1 and TH17 related cytokines were lower, the soluble IL-10 levels increased following the alphacalcidol treatment. The Vitamin-D analogue could increase the capacity of nTreg cells to suppress the proliferation of autologous CD4+CD25- T cells, which was related with higher dose of alphacalcidol treatment.
The alphacalcidol improved the TH17/Treg functional imbalance, reduced both Th1 and TH17 related cytokines, promoted the T regulatory profiles, enhanced the number and function of nTregs, correlating with the increasing of Vitamin-D levels. Their findings support the idea that the clinical application of Vitamin-D in patient with UCTD may influence and restore TH17/nTreg imbalance, therefore could be beneficial in the management of the disease.

P31

What is the minimum duration of symptoms to suspect undifferentiated arthritis?

Burkhard F. Leeb[1], Pia M. Haindl[1], Klaus P. Machold[2], Bernhard Rintelen[1], Manfred Herold[3]
[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Universitätsklinik III AKH Wien, [3]Universitätsklinik Innsbruck, Austria

Undifferentiated arthritis is a condition which is not well defined yet. A multinational project dealing with diagnosis and management of undifferentiated peripheral inflammatory arthritis (UPIA) defined the condition by at least one clinically swollen joint irrespective of disease. Other definite rheumatologic disorders like rheumatoid or psoriatic arthritis, crystal arthropathies and connective tissue diseases needed to be excluded. The aim of this study was to evaluate the time factor from symptom onset until diagnosis of UPIA.
A systematic literature review was performed using search terms for UPIA, early arthritis cohorts, registries or clinics and data on symptom duration (from symptom onset until inclusion in the studies or arthritis cohorts). Synovitis was defined by swelling of the joint, tenderness or impaired range of motion. No further diagnostic criteria was necessary. Cohorts focusing on early rheumatoid arthritis were excluded. Databases screened included Medline (1970 until April 2009), Cochrane Clinical Trials, EULAR and ACR abstracts 2007–2008. Additionally the literature results of the multi national UPIA project were screened. The focus was set on finding all published cohorts to evaluate their symptom duration at inclusion. Cohorts which were subgroups of another cohort were summarised within that population. Based on the literature results an expert panel consisting of 17 Austrian rheumatologists discussed the results and participated in a Delphi process to decide on a consensus for national recommendations.
Overall 32 different cohorts of patients with early inflammatory arthritis were found. Two groups can be described: cohorts with pure undifferentiated arthritis, excluding early rheumatoid arthritis (ERA) and other rheumatologic disorders and secondly cohorts with mixed population (including ERA). In the undifferentiated arthritis group (n=8) the minimum duration of symptoms at time of inclusion was 4 weeks. The maximum duration ranged from 8 weeks to two years. Evaluating mixed cohorts (n=19), minimum duration of symptoms was 2 to 12 weeks, though the majority having 4 weeks as inclusion criteria. The maximum duration of synovitis until inclusion was 3 months to 2 year, with the majority of cohorts setting the limit at 12 months. 4 recent congress abstracts on undifferentiated arthritis showed a tighter time limit. Depending on the study the duration of symptoms must not have exceeded 4 to 16 weeks. In a second step 17 Austrian rheumatologists elaborated a consensus which recommends at least 4 weeks of clinical synovitis in at least one joint until the diagnosis of UPIA is made. 2 weeks seemed too stringent whereas more than 4 weeks may delay referral and assessment by a specialist. Based on Oxford level of evidence (published march 2009) this recommendation is level 5, which is expert opinion.
A clear definition of UPIA including not only clinical parameters but also a time factor is warranted to allow further diagnostic, therapeutic and prognostic studies within this population. Worldwide the inclusion criteria in early inflammatory arthritis cohorts differed widely. Cohorts of undifferentiated arthritis or mixed populations included patients with duration of synovitis of 2-4 weeks minimum and 3 years maximum. The minimal duration of symptoms to suspect UPIA is expert's opinion. Austrian rheumatologists recommend 4 weeks before diagnosis of UPIA is made. The study was performed as part of 3e Initiative "How to investigate and follow up undifferentiated peripheral inflammatory arthritis?"

P32

Initial therapy in patients with undifferentiated peripheral inflammatory arthritis: A systematic literature review

Burkhard F. Leeb[1], Pia M. Haindl[1], Hans Peter Brezinschek[2], Bernhard Rintelen[1], Gabriele Eberl[3]
[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Universitätsklinik Graz, [3]Rheumaklinikum Malcherhof, Baden, Austria

Disease modifying antirheumatic drugs (DMARD) including biologics are widely used for treatment of early rheumatoid arthritis (RA) where treatment is started as soon as the diagnosis is made to enhance good clinical as well as functional and radiological outcome. In contrast, undifferentiated arthritis is a condition which is not well defined and standardised treatment protocols are not yet available. The multi national 3e project defines an undifferentiated peripheral inflammatory arthritis (UPIA) as a condition with at least one clinical swollen joint and where other definite rheumatic diseases have been excluded. This study was performed to evaluate evidence on the efficacy of initial therapy in patients with UPIA.
Authors performed a systematic literature research on the prognostic and diagnostic value of therapy in UPIA. Various key terms for UPIA and treatment were used. Databases screened until April 2009 included Medline, Cochrane Clinical Trials, EULAR and ACR abstracts 2007–2008. According to predefined inclusion and exclusion criteria, two investigators selected manuscripts for final analysis. Types of studies included were randomised controlled trials and observational cohort studies.
13 studies fulfilled the criteria. Presumably non steroidal antiinflammatory drugs (NSAID) would be the first line therapy. No study was found evaluating

outcome of different NSAID treatments or NSAID versus placebo in patients with undifferentiated arthritis. No synovectomy study was included as they were second line treatment studies. 2 studies on antibiotics showed no difference in clinical outcome or remission rate. Intramuscular or intraarticular glucocorticoid (GC) was investigated in 5 studies (2 including DMARDs). It did not have any effect on RA prevention, but it was clearly shown that GC improves signs and symptoms of synovitis at least for a brief period of time (significant results at week 4). Treatment studies with DMARDs (n=5) showed improvement of clinical parameters, but the rate of remission was not influenced. A comparison of methotrexate (MTX) with salazopyrine (Hider et al, n=359) showed that significantly more patients stayed on MTX therapy over 5 years [OR 2.2 (1.1 to 4.5)]. A randomised placebo controlled trial over 30 months (van Dongen et al, n=110) showed that MTX prolongs the period of persistence in an undifferentiated state, but does not prevent RA. In a subgroup analysis patients with positive ACPA [HR 4.9 (1.88–12.79)] had a higher risk of RA diagnosis over time. In both studies MTX delayed radiographic progression. Oxford level of evidence was 2b. Furthermore, 3 studies on biological therapy were found. Abatacept was investigated in patients with polyserositis and ACPA positivity. Infliximab and Etanercept improved clinical parameters and CRP levels, but the results were not significant.

Conclusion:

– As initial therapy glucocorticoids ameliorate signs and symptoms of synovitis, but do not prevent persistence of disease.
– Methotrexate may postpone but not prevent the development of RA.
– MTX delays radiographic progression.
– Further studies are needed focusing on remission of synovitis rather than diagnosis of RA. The study was performed as part of 3e Initiative “How to investigate and follow up undifferentiated peripheral inflammatory arthritis?”.

P33

Optimal time to start disease modifying therapy in patients with undifferentiated peripheral arthritis: A systematic literature review and expert consensus

Burkhard F. Leeb[1], Pia M. Haindl[1], Gabriele Eberl[2], Manfred Herold[3], Bernhard Rintelen[1]

[1]Lower Austrian State Hospital Weinviertel Stockerau, [2]Rheumaklinikum Malcherhof, Baden, [3]Universitätsklinik Innsbruck, Austria

Undifferentiated arthritis is a condition which is not well defined and a standardised management protocol is not yet available. In a multi-national project undifferentiated peripheral inflammatory arthritis (UPIA) was defined as at least one clinically swollen joint irrespective of disease duration and after exclusion of other definite rheumatologic disorders. As synovitis may be of limited duration starting disease modifying antirheumatic drugs (DMARD) too early may be seen as over treatment. On the other hand the chance of preventing radiological damage shall not be missed. Evaluation of optimal time to start treatment with DMARD in UPIA.

Authors performed a systematic literature research using different key terms for UPIA, DMARD and therapy. Databases searched included Medline (from 1970 until April 2009), Cochrane Clinical Trials, EULAR and ACR abstracts 2007–2008. According to predefined inclusion and exclusion criteria, two investigators selected manuscripts for final analysis. Based on the literature results experts decided in a Delphi process on a consensus for national recommendations.

Overall only 2 studies fulfilled the inclusion and exclusion criteria. There was no study focusing on different time points from symptom onset until therapy and evaluating disease outcome. One study by Wiles et al investigated function after five years of DMARD therapy. 384 patients with inflammatory polyarthritis with at least 2 swollen joints of 4 weeks duration were included. The results showed that patients receiving DMARD therapy (including SSZ, MTX, HCQ and steroids) within 6 months of disease onset had a significantly lower HAQ score at 5 years than patients with later therapy (OR 0.88 [0.44;1.77] versus 2.26 [1.23;4.13] adjusted for a propensity score). The second study by Quinn et al evaluated a management protocol in patients with undifferentiated arthritis of the hands. A logistic regression analysis showed that synovitis at 12 weeks is significantly correlated with DMARD therapy at 12 months ($p<0.001$, PPV 0.97 and NPV 0.82). In a second step 17 Austrian rheumatologists discussed the different perspectives based on literature and experience. Finally they decided on the recommendation for treatment start. They recommend ‘If limited disease is unlikely DMARD therapy should be started immediately with tight control’. This national recommendation is categorised as expert opinion (Strength of Recommendation D, Oxford Level of Evidence Grade V).

Conclusion:

– No prognostic studies are available investigating different time points of DMARD therapy start in patients with undifferentiated peripheral inflammatory arthritis.
– Austrian experts recommend starting DMARD therapy as soon as possible in patients with UPIA when limited disease is unlikely.
– For future high quality treatment studies a homogenous study population and a clear definition of undifferentiated arthritis will be needed. The study was performed as part of 3e Initiative “How to investigate and follow up undifferentiated peripheral inflammatory arthritis?”.

P34

A comparison of patient questionnaires and composite indexes in routine care of rheumatoid arthritis patients

Burkhard F. Leeb, Judith Sautner, Harsono T. Mai, Pia M. Haindl, Bernhard Rintelen
Lower Austrian State Hospital Weinviertel Stockerau, Austria

The objective was to evaluate the agreement between the Routine Assessment of Patient Index Data 3 (RAPID-3) and a modified version of the Rheumatoid Arthritis Disease Activity Index (RADAI-5), as well as the Disease Activity Score including a 28 joint count (DAS28-ESR) and the Clinical Disease Activity Index (CDAI) in daily routine.
One hundred and twenty-eight rheumatoid arthritis (RA) out-patients completed the RADAI-5 and the RAPID-3. Simultaneously, the DAS28-ESR and the CDAI were applied. Cronbach's Alpha as a measure for reliability was calculated and factorial analysis was performed. For agreement analysis, Kendall's Tau was calculated.
Time to score the questionnaires was 25 seconds. The median RADAI-5 was 2.8 (0-9.2), the median RAPID-3 3.3 (0-8.6), the median DAS28-ESR 2.95 (0.43-6.24), and the median CDAI 5.6 (0-37.5). Cronbach's Alpha for the RADAI-5 was 0.906 and 0.871 for the RAPID-3, however, only 0.165 for the DAS28-ESR and 0.210 for the CDAI, respectively. Factorial analysis revealed that both questionnaires and the DAS28-ESR, but not the CDAI, constitute monodimensional instruments. Tau for the agreement between the RADAI-5 and the RAPID-3 appeared to be 0.587 ($p<0.001$), and to be 0.582 ($p<0.001$) between the DAS28-ESR and the CDAI, while it was lower for the relationship between the questionnaires and the composite indexes.
Reliability of the RAPID-3 and RADAI-5 was significantly higher than of the indexes. The questionnaires as well as the indexes proved to be in highly moderate agreement, while agreement between the questionnaires and the indexes appeared to be lower.

P35

Usefulness of procalcitonin measurement in differentiating between activity of systemic autoimmune disease and bacterial infection

Olga Sleglova[1], Helena Dejmková[1], Jana Uhrova[2], Jaromir Belacek[3]
[1]Institute of Rheumatology, [2]Institute of Clinical Biochemistry, [3]Charles University, Prague, Czech Republic

To evaluate the usefulness of testing for serum procalcitonin (PCT) in the differential diagnosis of infectious complications and acute disease exacerbation in patients with systemic autoimmune diseases.
125 patients with systemic autoimmune diseases who were admitted to the inpatient department for suspected acute infection or acute exacerbation of their disease were prospectively tested for PCT concentrations. Concurrently, the levels of C-reactive protein (CRP), white blood cell counts (WBC), C3 and C4 complement components were established. The group of patients with infection comprised of two subgroups: with systemic and localised infection. Control group included 87 ambulatory patients with autoimmune diseases without any signs of deterioration.
The serum PCT levels were significantly higher in patients with infections than in patients with an active systemic disease (PCT mean±SEM 4.560±1,513 vs. 0,254±0,029, $p<0,001$). The levels of CRP and white blood cell counts were also higher in patients with infections; the differences between C3 and C4 complement component values were not statistically significant. PCT serum concentrations were not elevated in any of the patients included in control group, and they were not affected by the current corticosteroids or immunosuppressive treatment. The sensitivity of the PCT test for an infectious complication (cut-off value=0.5 ng/ml) was 52.4%, specificity 94.0% and diagnostic accuracy 80.2%. The area under ROC curve for PCT was 73.21%.
The increased serum PCT levels demonstrate good specificity for the evidence of infection in patients with systemic diseases. The sensitivity of PCT serum values is lower and it is therefore suitable to complement the assessment with another high-sensitivity indicator, such as CRP.

P36

Measurement of interleukin-1-receptor antagonist in patients with systemic lupus erythematosus could predict renal manifestation of the disease

Boglárka Brúgós[1], Emese Kiss[2], Gyula Szegedi[1], Sándor Sipka[1], Margit Zeher[1]
[1]University of Debrecen, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Interleukin receptor-1 antagonist (IL-1Ra) is a good indicator of disease activity in patients with systemic lupus erythematosus (SLE). Glucocorticoids are the most frequently used drugs in SLE.
Authors goal was to compare the IL-1Ra activity of SLE patients with and without renal involvement and find out the effect of different dosage of glucocorticoids administered in 17 patients with active SLE without renal involvement; 7 patients with inactive- and 8 patients with active lupus nephritis (LN) and 10 healthy controls.
IL-1Ra levels were measured in the serum of SLE patients with Human Luminex analyzer.
In both patients with active SLE without nephritis and with lupus nephritis serum levels of IL-1Ra ($p<0.001$) was significantly higher compared to the controls.

IL-1Ra was significantly higher in patients with active lupus nephritis than in patients with inactive LN (p=0.028). The dose of methylprednisolon was significantly higher in active lupus nephritis group as compared to the inactive LN group (p=0.013).
SLE patients with higher IL-1Ra are at lower risk of developing nephritis. The higher doses of methylprednisolon needed in active lupus nephritis could be due to steroid resistance and IL-1Ra polymorphism. Measurement of IL-1Ra level in SLE patients could help to predict future renal involvement.

P37

Involvement of specific types of laminin in glomerulal basement membrane of patients with lupus nephritis and monitoring of serum levels of laminin as possible marker of organ damage

Hana Ciferska[1], Pavel Horak[1], Josef Zadrazil[1], Zuzana Hermanova[2], Yrjo Konttinen[3], Martin Tichy[1]
[1]University of Olomouc, [2]Faculty Hospital, Olomouc, Czech Republic, [3]University of Helsinki, Finland

Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disorder characterized by a wide array of clinical manifestations, one of them is lupus nephritis (LN). The production of antibodies against the extra cellular matrix/ basement membrane (BM) could cause alternates in structure of BM namely in lamin and integrin components of BM.
The aim of authors study was to asses the changes in the BM of the pilot group of 4 patients with lupus nephritis (2 type III. and 2 type IV) by labeling isoforms of laminin (lm-α1,- α2,- α4,- α5,- β1,- β2) and integrin (int-α1,- α2,- α3,- α6,-β1,- β4) by using immunohistochemistry with chain specific monoclonal antibodies for human specimen. There were 6 healthy controls. The serum levels of lamin were assed by commercial ELISA Takara Mirus Bio, Otsu, Japan) in 34 patients with SLE (3 men a 31 women, with LN 20 patients, without LN 14) and in 20 healthy controls. The mean serum levels of laminin in group of patients with SLE were 640,23±199,54 ng/mg, in the group with LN 604,25±228,97 ng/mg, and without LN 691,64±131,55 ng/mg and in the control group 522,7±144,61ng/ml.
There was not observed higher expression of laminin chains α1 a β1, which was found in murine models of lupus nephritis [16]. There was observed lower expression of integrin α3 in patients with LN. Patients with SLE had higher serum levels of laminin and the difference between the healthy controls was statistically significant. However the larger number of patients must be assessed as well as with different type of organ manifestation to explore the potentional benefit of the serum lamin levels measurement.

P38

Challenges and experiences of teaching courses of the modified Rodnan skin score assessment in systemic sclerosis

Tünde Minier[1], Ruxandra Ionescu[2], Simona Rednic[3], Nemanja Damjanov[4], Cecília Varjú[1], Zoltán Nagy[5], László Czirják[1]
[1]University of Pécs, Hungary, [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, [3]University of Medicine and Pharmacy Iuliu Hatieganu, Cluj-Napoca, Romania, [4]Institute of Rheumatology Belgrade, Serbia, [5]Szatmár-Bereg Hospital and Medical Bath, Fehérgyarmat, Hungary

Authors previously demonstrated that in case of unsatisfactory results of a first teaching course it is possible to reach good results after an early repeated course based on two teaching courses of modified Rodnan skin score (MRSS) assessment in Hungary. The question under study is whether a repeated teaching course is required to maintain good results after a first, successful teaching process.
Two consecutive teaching courses were organized by two Romanian EUSTAR centres for the same rheumatologists, to evaluate and compare the inter-observer variability. Coefficients of variation, the intra-class correlation coefficients (ICC) and the within patient standard deviations (within patient SD) are reported.
The ICC showed good agreement between 12 participants of both the first teaching course (0.639) and of the course seven months later (0.684). The analysis of the SSc subsets showed similar coefficients of variation in dcSSc patients and the whole patient group at both MRSS teaching courses (25.9% and 30.6% vs. 32.5% and 35.1% in the whole patient groups). The coefficients of variation in lcSSc subgroups were higher in both teaching courses (42.1% and 45.9%) compared to the dcSSc subset. The within patient SD was higher in dcSSc compared to the lcSSc subset in both courses (3.6 and 6.3 in dcSSc subset, vs. 3.4 and 3.8 in lcSSc subset). Almost half of the examiners of these two courses were involved in daily clinical practice of general rheumatology, and there were no significant differences in the within patient SD values and coefficients of variance between this particular group compared to the other half of rheumatologists working in tertiary care centres.
For rheumatologists, a good ICC that is close to 0.7 can be achieved by an intensive practical demonstration of the MRSS assessment. These results remain stable without the need for another, repeated teaching cycle. When the first course has not lead to satisfactory results, good results can be obtained during a repeated course. One of the main tasks of the MRSS teaching course is to emphasize the difference between the skin thickening (sign of and active process) and skin tethering (most commonly seen after long disease duration, when the skin is already thinned be-

cause of atrophy).The high inter-rater variations seen in the assessment of some patients demand that, in clinical studies, the same investigator should assess the same patient at each visit.

P39

Construct validity evaluation of the European Scleroderma Study Group activity index, and investigation of possible new disease activity markers in systemic sclerosis

Tünde Minier[1], Zoltán Nagy[2], Zsófia Bálint[1], Helka Farkas[1], Gábor Kumánovics[1], Diána Simon[1], Cecília Varjú[1], Péter Németh[1], László Czirják[1]
[1]University of Pécs, [2]Szatmár-Bereg Hospital and Medical Bath, Fehérgyarmat, Hungary

To evaluate the construct validity of the European Scleroderma Study Group (EScSG) activity index, and to propose modifications if necessary. To test the value of different markers of endothelial cell activation, angiogenesis, fibrosis, alveolar type II epithelial cell lesion, B-cell and T-cell activation in the assessment of disease activity in systemic sclerosis.
131 consecutive patients were investigated and re-evaluated 1 year and 3 years later. Modified Rodnan skin score (MRSS), skin ulcers and joint contracture numbers, hand anatomic index (HAI), body mass index, spirometry, carbon monoxide diffusing capacity (DLCO), left ventricular ejection fraction, pulmonary arterial hypertension, HAQ-DI, patient skin self assessment questionnaire, and biomarkers of endothelial cell activation (von Willebrand factor antigen [vWFAg], soluble E-selectin [sE-selectin], soluble P-selectin glycoprotein ligand-1 [sPSGL-1]), angiogenesis (vascular endothelial growth factor [VEGF]), fibrosis (procollagen type I N-terminal propeptide [PINP], procollagen type III N-terminal propeptide [PIIINP], collagen type I carboxiterminal telopeptide [CTX-1]), alveolar type II epithelial cell lesion (Kerbs von Lungren 6 antigen [KL-6], surfactant protein-D [SP-D]), B-cell (B-cell activation factor [BAFF], A proliferation-inducing ligand [APRIL]) and T-cell activation (soluble CD40 ligand [sCD40L]) and anti-DNA topoisomerase-I titers were recorded, in addition to the data required for the EScSG activity index. Statistical analysis was performed by categorical principal component analysis (CATPCA).
The EScSG activity index appeared in the same dimension as the HAQ-DI, ulcer score and joint contractures, MRSS, patient reported skin score and HAI by CATPCA. Parameters of lung involvement appeared in another dimension. Authors constructed a 12 point activity index, which was equally associated with both dimensions, by adding the FVC/DLCO, change in DLCO, change in the ulcer scores, HAQ-DI and patient reported skin score. Biomarkers including VEGF, sPSGL-1, CRP and albumin were related to both the EScSG and the 12 point index, though they did not improve the total variance of the model.
The construct validity of the EScSG activity index is good, though the lung-related disease activity may not be sufficiently represented. Further validation steps may be required for both the EScSG and their 12 point index.

P40

Patient and physicians global assessment on disease activity of rheumatoid arthritis

Bernadette Rojkovich[1], András Inotai[2], Ágnes Mészáros[2], Emese Jászay[1], Katalin Imre[1], Györgyi Mészáros[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]Semmelweis University, Budapest, Hungary

The treatment of rheumatoid arthritis (RA) must be based on decision between patient and rheumatologist. Treatment targets ('T2T') have been defined to improve outcomes of RA by decreasing disease activity. The patients global assessment (PGA) on disease activity is incorporated into a disease activity score (DAS). Patients and physicians very often focus on an entirely different aspect of disease activity. The aim of this pilot study was to investigate the relationship between patient and physicians global assessment on disease activity and evaluate what disease activity matter for the patients.
This cross-sectional, non interventional study involved 253 rheumatoid arthritis patients. Two cohorts of consecutive patients were recruited from the outpatient clinic, one subgroup of patients received traditional DMARDs (n=168), the other, the severe destructive subgroup of RA patients were at least for 6 month on biological therapy (n=85). The measures included demographic variables, disease activity parameters, and health related quality of life assessment. Comparison of the parameters between the two independent subgroup was performed using two sample t-test. Paired-samples t-test was used to evaluate the relationship between physician's and patient's VAS. In recorded and systemically analyzed interviews with 20 RA patients, authors asked about what disease activity parameters matter to the patients and what are the most important, intrusive and overwhelming symptoms of disease activity.
Statistically significant differences ($p<0.0001$) could be observed within the total study population between patient's (mean: 39,6) and physician's (25,2) global assessment on disease activity, measured on 100 mm VAS. The mean DAS-28 score was 3.8 in the biological treatment subgroup, indicating an average decrease of 2.1 DAS-28 score if comparing it to the baseline (average initial DAS-28 was 5.9 when starting biological treatments). There were statistically significant differences among patients with non biological treatment versus biological treatment in demographic and base characteristics concerning age (57,8/52,9; $p=0.003$), patient's opinion on disease activity (50,0/34,7; $p<0.0001$), patient's pain (49,1/34,8; $p<0.0001$) and disease activity score

(4,5/3,8; p<0.001). However, RAQoL (12,1/12,9), physician global assessment on disease activity (26,1/24,0) showed no significant difference. Joint swelling (19/20), pain (18/20), fatigue (18/20), malaise (18/20) morning stiffness (17/20) were important symptoms of disease activity for the patients.
These data suggest that patients in the biological subgroup represent a more severe initial health status than patients treated with DMARDs only. Biologics have improved the prognosis for rheumatoid arthritis. Treating according to target can assure optimal outcomes of RA and rheumatologist have to inform the patients about it. However equally important would be the prioritization of the patient's perspective. This pilot study demonstrates that pain, swollen joints and fatigue, malaise are most important symptoms of disease activity for patients and however they are less easily measured by the traditional outcomes markers. Physicians consistently rate patient disease activity lower than the patients do.

P41

The rheumatoid arthritis EULAR response criteria compared to the RADAI-5 response in daily routine

Bernhard Rintelen, Pia M. Haindl, Judith Sautner, Barbara A. Leeb, Christiane Kaspar, Burkhard F. Leeb
Lower Austrian State Hospital Weinviertel Stockerau, Austria

Authors presented the RADAI-5 [1] as a shortened and simplified version of the RADAI [2] and defined its disease activity categories with up to 1.4 as a remission like state, 1.6 up to 3.0 as mild-, 3.2 up to 5.4 as moderate- and from 5.6 up to 10.0 as high disease activity (DA) [3]. They also have calculated threshold for improvement (> 1.7) and deterioration (> 1.5) [poster submitted EULAR 2009]. This investigation was done to compare response according to the EULAR response criteria and response as expressed by the RADAI-5 in a rheumatologic outpatient department and a private office.
364 RA patients (81% f, 55% RF pos, mean age 60±12.6, mean disease duration 100 months±103.4) were assessed according the RADAI-5 and DAS28 longitudinally. 1208 assessments (mean 3.33±1.80/pat.) could be evaluated. They calculated RADAI-5 -improvement and worsening in the consecutive assessments, and the EULAR response (improvement ≥ 0.6 or ≥ 1.2 according to the DAS28). Gamma was calculated to show the relationship in improvement with respect to the two instruments, kappa for the respective agreement of the two tools to define disease activity.
Mean DA according to the RADAI-5 was 3.19 (±2.10), and 3.33 (±1.18) according to the DAS28, indicating mild DA according to the RADAI-5 and moderate DA according to the DAS28 respectively. 290 assessments indicated a remission like state, 358 mild-, 375 moderate- and 189 high DA according to the RADAI-5 whereas 344, 241, 547 and 80 according to the corresponding DAS28 criteria respectively. According to the RADAI-5, 134 assessments had an improvement whereas 166 according to the EULAR criteria (among them 71.6% moderate and 28.4% good responses). According to the RADAI-5 in 569 assessments a stable disease and in 139 a deteriorating disease could be identified, whereas in 605 assessments no response according to the EULAR criteria had to be noticed. Gamma to elucidate the relationship between the EULAR response and the RADAI-5 response was 0.749 (p<0.0001), however, the agreement between the disease activity categories was only fair (κ=0.340, p<0.0001).
The RADAI-5 seems to be more stringent to define RA remission like state as well as indicating improvement than the DAS28. Nevertheless RADAI-5 responses show significant correlation to the EULAR response criteria in daily routine.

P42

Proposals for thresholds to express improvement and deterioration in rheumatoid arthritis patients according to the RADAI-5

Bernhard Rintelen, Judith Sautner, Christiane Kaspar, Pia M. Haindl, Barbara A. Leeb, Burkhard F. Leeb
Lower Austrian State Hospital Weinviertel Stockerau, Austria

Authors introduced a fully patient administered tool for disease activity assessment measurement in rheumatoid arthritis (RA) patients, the RADAI-5 [1]. Subsequently authors defined disease activity categories namely a remission-like state, as well as categories for mild, moderate or high disease activity [2]. RADAI-5 changes expressing improvement and deterioration of the disease failed to be established.
368 RA patients (81% f, 55% RF pos, mean age 60±12.7, mean disease duration 101.5 months±104.1) were assessed according to the RADAI-5 and the DAS28 longitudinally. Additionally patient`s satisfaction with the disease status (PATSAT) according to the Austrian school marking system (1=excellent to 5=unsatisfactory) was evaluated. Patients with a PATSAT improvement of at least 1 in two or more consecutive evaluations were taken as the reference to elaborate the minimal patient relevant RADAI-5 change for improvement calculating the mean of the corresponding RADAI-5 values. The same procedure was applied to define the respective RADAI-5 changes for worsening. Spearman´s rho was calculated to show correlation according to DAS28- and RADAI-5 changes. Thereafter the corresponding DAS28-changes in patients showing improvement, stable disease or worsening according to the RADAI-5 were calculated.
1225 assessments (mean 3.33±1.80/pat.) could be evaluated. Since the RADAI-5 is expressed by a num-

ber with an even first decimal, authors decided, that change in disease activity should be expressed by a number with an odd decimal to avoid misinterpretation of the result. In 161 patients (403 assessments, mean 2.07±0.27/pat.) an improvement of at least 1 PATSAT level could be noticed in two consecutive assessments. The mean change of the RADAI-5 in these patients was -1.67 (±1.69) and subsequently a RADAI-5 change of<-1.7 is proposed as the minimal patient relevant reduction expressing improvement. In 160 patients (374 assessments, mean 2.36±0.85/pat.) a worsening of at least 1 point in PATSAT in two consecutive assessments could be found. The mean RADAI-5 change in this group was + 1.47 (±1.78). They therefore propose a RADAI-5 increase of>1.5 as the threshold for worsening. DAS28- and RADAI-5 changes in the improvement-group were significantly correlated (Spearman´s rho=0.479; p<0.01). The mean DAS28 reduction in improving patients according to the RADAI-5 was –1.04±1.13. The DAS28 change in stable patients amounted to –0.09±0.78, and in worsening patients to +0.66±0.88.
Patient relevant thresholds for improvement and worsening according to the RADAI-5 could be elaborated (improvement>1.7, worsening>1.5). DAS28- and RADAI-5 improvement proved to be significantly correlated.

P43

Summary findings of a systematic review of global ultrasound scores for the assessment of synovitis in rheumatoid arthritis

Péter Mandl[1], Péter V. Bálint[1], Esperanza Naredo[2], Richard J. Wakefield[3], Maria-Antonietta D'Agostino[5], on behalf of the OMERACT-EULAR Ultrasound Group
[1]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary, [2]Hospital Severo Ochoa, Madrid, Spain, [3]University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom, [4]Paris-Ouest-Versailles Saint Quentin en Yvelines University, Paris, France

This report presents the results of a recent systematic review performed by the OMERACT-EULAR Ultrasound Group on the metric properties of global ultrasound scores used for the detection of synovitis in rheumatoid arthritis. The review highlights current gaps in the literature, including a lack of clear definitions as well as varying reliability and validity data with respect to various scores composed of a wide range and number of joints.
Authors performed a literature search of PUBMED and EMBASE (from 1984 to March 2010). Original research reports and reviews written in English involving rheumatoid arthritis (RA), musculoskeletal and Doppler ultrasound and scoring systems were included. The design, subjects, methods, imaging protocols, and performance characteristics studied in the research papers were reported.
Of 3004 identified reports, 14 articles were selected to be included in the review. The search was limited to English language articles and included both original and review articles. The overwhelming majority of articles in the review featured a blinded design, sample size ranged between 24–278 patients. Only 28% of the included studies included control patients. The number of joints assessed by ultrasound varied between 5–60 joints. All studies included clinical examination as a comparator for assessing construct validity, with all except one study including laboratory values as well. Imaging modalities (x-ray, US and MRI) were used in 43% of the studies as a comparator. Construct validity varied according to the number and size of examined joints; responsiveness changed according to the component tested and the size of the joint. With regard to feasibility, time of evaluation was variable (15-60 min) and increased with the number of joints involved in the examination. The majority of articles evaluated both gray-scale (GS) and Power Doppler (PD), with GS either evaluated globally or in separate components (synovial hypertrophy and synovial fluid) in addition to PD activity, which was evaluated separately. No study assessed a composite synovitis scoring system consisting of a combination of GS and PD.
In order to be able to make assumptions on global disease activity it is necessary to move from the single joint to patient level. Based on the systematic review of the literature it is presently difficult to suggest a minimal number of joints to be included in a global US score for synovitis and which scoring system to use at joint level. A reliable standardised, semi-quantitative scoring system combining GS and PD (Global Ultrasound Scoring System, GLOSS) is currently developed by the OMERACT-EULAR Ultrasound Workgroup for synovitis in RA that is applicable to all joints and is consistent between machines.

P44

Ultrasound for detecting abnormal effusion and synovial proliferation in the knee – which knee position is the best?

Péter Mandl[1], Lene Terslev[2], Wolfgang A. Schmidt[3], Myriam Brossard[4], Péter V. Bálint[1], Esperanza Naredo[5], Richard J. Wakefield[6], Maria-Antonietta D'Agostino[7] on behalf of the OMERACT-EULAR Ultrasound Group
[1]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary, [2]University of Copenhagen Hospitals at Hvidovre and Glostrup, Denmark, [3]Medical Centre for Rheumatology Berlin-Buch, Immanuel Krankenhaus, Berlin, Germany, [4]Versailles-Saint Quentin en Yvelines University; APHP, Ambroise-Paré Hospital, Boulogne-Billancourt, France, [5]Hospital Severo Ochoa, Madrid, Spain, [6]University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom, [7]Paris-Ouest-Versailles Saint Quentin en Yvelines University, Paris, France

It has previously been shown that ultrasound (US) is more sensitive than clinical examination for detecting knee joint effusion. However, no agreement exists for the best positioning of the knee to obtain optimal information on effusion and synovitis.
Investigate which of 3 different knee positions (neutral position with/without quadriceps contraction, 30° flexion without quadriceps contraction) provides the best information about synovial fluid (SF) and synovial hypertrophy (SH) in rheumatic disorders. Investigate which of these positions better predicts abnormality. Evaluate the magnitude of difference for measuring SF in three major recesses (suprapatellar, medial- and lateral parapatellar recess) of the knee according to various degrees of flexion.
In two subsequent studies 407 knee joints of 206 (129 and 77) consecutive patients with rheumatological disease involving the knee joint were examined by US in 17 centers. 20 control patients without knee pathology or symptoms were included in the first study. To evaluate SF and SH, the suprapatellar recess of the knee was examined in 3 scans: longitudinal midline, 30° lateral and 30° medial from midline, in neutral position (0° flexion) with and without quadriceps muscle contraction, and in 30° flexion of the knee without quadriceps muscle contraction. In the second study the largest sagittal diameter of SF in suprapatellar longitudinal midline, transverse medial and lateral midpatellar transverse scans at different (0, 15, 30, 45, 60 and 90°) degrees of flexion of the knee was measured. Cluster analysis and mixed model analysis were used for analysing data in the first study. ROC curve and AUC were used for determining the best position for measuring SF in both studies.
Cluster analysis revealed that the midline position 0° flexion, with contraction correlated best with the presence of SH. Medial position 0° flexion, with contraction was the variable most correlated with SF in mms and presence of SF. Results were also confirmed by the three-level mixed model analysis. In the second study ROC curve analysis revealed that the suprapatellar scan and 30° position are the best associations for predicting effusion. Logistic regression demonstrated that SF height in the suprapatellar and lateral parapatellar recess was highest at 30° of flexion, while that in the medial parapatellar recess was highest at 15° of flexion.
Midline and lateral scans in neutral position with quadriceps contraction are the most sensitive position for detecting synovitis and the best predictor of abnormality (effusion yes/no) and 30° flexion is the best position to predict fluid in knee joints. Fluid height in all three recesses increases with the knee in the flexed position as compared to the neutral position. Every knee and scan position has distinct cut-off values to detect abnormal effusion and to aid in globally evaluating effusion and synovial proliferation.

P45

Tumor necrosis factor alpha and soluble tumor necrosis factor receptor type 1 levels comparison in blood serum in rheumatoid arthritis and ankylosing spondylitis patients

Inita Bulina[1], Daina Andersone[1], Vladimirs Lavrentjevs[2], Janis Arajs[2], Ineta Astica[2], Julija Zepa[2], Evita Sikora[2], Sarmite Abelite[2], Inta Jaunalksne[2]
[1]Latvian University, [2]Pauls Stradins Clinical University Hospital, Riga, Latvia

Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are chronic autoimmune diseases with unknown reason which affect people in age of ability to work. Proinflammatory cytokine TNF-alpha and soluble tumour necrosis factor receptors TNF-alpha type 1 and type 2 plays important role in pathogenesis of rheumatoid arthritis (RA) [1,2] and ankylosing spondylitis (AS). Biological treatment blocks pathological pathways in this proinflammatory cytokine actions.
Detection of TNF-α, TNF-R1 (p55 sTNF-R) usefulness in blood serum and before anti-TNF-α treatment could help to choose more suitable patient's group for anti-TNF-α treatment and to show the data about TNF-alpha level role in cases of autoimmune arthritis. RA and AS patient blood samples had been collected for detection TNF-alpha and TNF-R1 in Pauls Stradins Clinical University Hospital. 31 RA patients and 22 AS patients participated in the study. All 31 RA patients had high disease activity (DAS >5,1) and all 22 AS patients had high disease activity according BASDAI>4. TNF-alpha and TNF-R1 had been detected in blood serum with ELISA method for all patients. None of the patients from RA and AS group receive biological treatment during authors study. Statistical analyses had done by Student's t test.
The average of the age of RA patients group was 47,08 (distribution from 23 till 72 years old) and AS patients group was 40,9 (distribution from 29 till 59 years old). There was 25 women and 6 men in RA group and 7 women and 15 men in AS group. Distribution of TNF-alpha in RA group was 8 pg/ml till 120 pg/ml (average =33,15 pg/ml) and in AS group was 7 pg/ml till 135 pg/ml (average=25,79 pg/ml). Distribution of TNF-R1 in RA group was 1,9 mkg/ml till 5,7 mkg/ml (average=2,94 mkg/ml) and in AS group was 1,2 mkg/ml till 3,6 mkg/ml (average=2,11 mkg/ml). There was no difference in TNF-alpha levels in RA and AS group (p=0,189), but there was difference in TNF-R1 level in RA and AS group p=0,0003.
The further studies are necessary for detection cytokines and there soluble receptors in blood serum to analyze their role in autoimmune arthritis processes.

P46

Radiological particularities of joint involves in women with ankylosing spondylitis in correlation with HLA-B27 antigen

Oxana Sirbu, Liliana Groppa, Eugeniu Russu
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

The present report is an analysis of the 30 female patients who have attended the clinic in the past 6 years in whom ankylosing spondylitis has been diagnosed. Several of them have been observed over several years; a full clinical examination has always included a note on the spondylometer reading, and on the chest expansion, as this is reduced at an early stage in the disease with analysis of antigens HLA-B27. Radiographs of the sacroiliac joints were taken in all cases, and other parts of the skeleton were X-rayed and CT when there were clinical indications.
As the condition progressed other sites were frequently involved, and the cervical spine in particular was often affected; 9 patients complained of pain here and 4 showed radiological changes with high correlation of HLA-B27 ($p<0,01$, RR=0,99). This was not, however, noted as an initial symptom, although authors found it to be the presenting feature in 5% of their cases. Pains around the shoulder were also common, being reported by 7 patients, but not so high correlative index (RR=0,75) and only two had persistent stiffness here, and one had radiological abnormality. In one patient persistent pain with localized tenderness of the left iliac crest was a troublesome symptom. Changes in these joints show a very variable rate of progress; complete fusion took place in one patient after only 5 years of symptoms and all of them had HLA-B27 positive, whereas in 2 other patients only minimal abnormalities were present after 20 years. In one of these last 2 patients there was extensive paravertebral calcification in the lumbar spine associated with slight sacroiliac changes. Where fusion is complete the outline of the joint can still be seen as a "ghost" joint, at the upper end of which there is often a denser point of calcification, the "star" sign. Sacroiliac involvement was present in every case although occasionally the most advanced radiological changes were observed elsewhere, while there were still only early sacroiliac changes but there were not so high correlation with HLA-B27 ($p<0,05$, RR=0,6). One such case with minimal sacroiliac abnormality and extensive lumbar paravertebral calcification has already been mentioned. In another patient the hips were mainly affected. The impression was gained that radiological changes outside the sacroiliac joints were less frequent than in men. Paravertebral calcification had statistically important correlation with HLA-B27 (RR=0,95), but also appeared to be less common in this small series, but it could develop within 5 years of the onset of symptoms. In 3 patients it was extensive and affected the whole spine. When the costovertebral joint was grossly involved, it gave the appearance of a flared rib. The development of a massive "bridge" of calcification with no history of trauma was watched in one case by serial films, as it arose between the bodies of L3 and L4 over the course of 2 years with presents of antigen HLA-B27. There did not appear to be in this series an unduly frequent involvement of the cervical spine, but lesions of the symphysis pubis were common. These consisted of erosions, widening, and sclerosis, and were accompanied in two patients by local tenderness. Painful lesions with radiological changes were also observed at sites away from articular structures at HLA-B27 positive patients.
Some clinical and radiological features of thirty female patients with ankylosing spondylitis are described with correlative analysis with antigen HLA-B27. This disease appears to run a milder course in women than in men, but a very variable rate of development is noted and present more highly correlation with antigen HLA-B27 (RR=0,95-0,99) then in men. Radiological abnormalities in the symphysis pubis were frequently seen ($p<0,01$). Bilateral lesions of the hip joints developed rapidly in two patients HLA-B27 positive, and were the cause of severe disability.

P47

Experience with the use of Quantiferon test, a novel method to detect tuberculosis, in two arthritis centers in Budapest, Hungary

István Á. Juhász[1], Judit Korda[2], Bernadette Rojkovich[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Because the immunosuppressive effect of biological treatments is well known the early recognition of infection is of utmost importance for arthritis centers administering biological therapies. TB occupies a prominent place among the adverse effects of TNF-alpha inhibitors and several diagnostic procedures exist for its detection. Although culture is the most definitive test, it takes too much time. Intracutan tuberculin test with purified protein derivate (PPD) requires less time, however it is not specific for human pathogen Mycobacteria and it gives positive reaction in patients immunized with Bacillus Calmette-Guérin (BCG). Discrimination between BCG vaccination and tuberculosis infection is possible using the gamma-interferon (Quantiferon) test that is less time consuming but more expensive than PPD. The experience gained during the use of Quantiferon test in the setting of biological therapy in two arthritis centers in Budapest is presented. The authors analyze the collected results of this recently introduced test on a limited number of patients, taking into account the immunosuppressive effects of co-medication, and give their opinion

during a case presentation of a 50-year-old man with SPA treated with infliximab who developed TB and was diagnosed with the use of Quantiferon test.

P48

Experiences with tumour necrosis factor alpha inhibitors in patients with juvenile idiopathic arthritis: Hungarian data from the National Institute of Rheumatology and Physiotherapy registry

Krisztina Sevcic[1], Ilonka Orbán[1], Valentin Brodszky[2], Anna Bazsó[1], Zsolt Balogh[1], Emese Kiss[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Corvinus University, Budapest, Hungary

Objective of the study to report the efficacy and safety of tumour necrosis factor alpha (TNF-alpha) inhibitors (etanercept and adalimumab) in a cohort of patients with juvenile idiopathic arthritis (JIA) treated in a single paediatric rheumatologic centre.
Patients with JIA under the age of 18, treated with TNF-alpha blockers at the Paediatric Rheumatologic Centre of the National Institute of Rheumatology and Physiotherapy (Budapest, Hungary) from 2002, were enrolled in an open, observational study. At baseline patient and disease characteristics were registered. Disease activity was evaluated (before start of the treatment and after every three months) according to the JIA core set of the American College of Rheumatology Paediatric definition of improvement (ACR Pedi). Adverse events (AEs) were documented.
In all, 72 patients were evaluated. Mean (SD) age at onset was 5.5 (3.8) years, mean disease duration was 7.4 (3.9) years. All disease activity parameters improved significantly in the first three month of treatment. After 3 and 12 months of treatment 88% and 76% of patients achieved the criteria of the ACR Pedi 30. Adverse events were uncommon. After 12 month more than 85% of patients continued the therapy.
Anti-TNFα agents (etanercept and adalimumab) are effective, safe and well tolerated in JIA patients. Extension of this study for a longer follow-up period and to the patients with JIA after the age of 18 (with validated and comparable disease activity parameters) is needed to evaluate the long-term effectiveness and safety of the TNFα inhibitors.

P49

Treatment of adult juvenile idiopathic arthritis patients with TNF-blockers and effect of switching to a second anti-TNF agent. Data from the Czech National Registry

Katerina Jarosova[1], Karel Chroust[2], Lucie Burešová[2], Jiří Vencovský[1]
[1]Charles University Prague, [2]Institute of Biostatistics and Analyses, Brno, Czech Republic

The objective was to analyze the efficacy and safety of TNF-α blocking therapy in adult patients with juvenile idiopathic arthritis (JIA) who have switched among tumour necrosis factor (TNF) antagonists. ATTRA is a Czech national registry of patients with different forms of chronic arthritis who are treated with biologics. Using this registry, authors analysed adult JIA patients, who switched from one TNF antagonists to another anti-TNF treatment. Patients were treated in recommended doses for RA and the first drug was either infliximab (65%), or etanercept (23%), or adalimumab (14%). Those patients, who failed to improve in DAS28 by at least 1.2 after 3 months at 2 consecutive visits, who lost the response during the treatment, or who had to be discontinued due to adverse event, were switched to alternative anti-TNF. Survival on therapy for individual TNF-blockers after 1 and 2 years was calculated. Clinical efficacy was assessed with DAS28. Safety assessments were done for all patients during the whole follow-up period. No guidelines have been issued for preference of the 1st or 2nd anti-TNF drug type and this was left purely to treating physician decision and was based on the assessment of overall clinical situation.
One hundred and five adult JIA patients were treated with anti-TNF agents. Mean age of patients was 25.2 years, duration of disease was 15.4 years and 62.9% were women. Twenty five (23.8%) patients received more than one TNF antagonist. DAS28 showed excellent and persistent improvement for those patients, who remained on the first drug. DAS28 at week 0 was 6.38±0.71 and decreased significantly to 2.87±1.46 at week 54 and 2.55±1.31 at week 108. Response to second anti-TNF was also significant, although with smaller differences to baseline DAS28; weeks 0, 54 and 108 were 5.97±0.9, 3.18±1.97, and 3.94±0.61, respectively. Survival on the treatment was not statistically different in the first users in comparison with switched patients (p=0.501); somewhat lower adherence to therapy was seen with the second agent (in first users and in switched patients, respectively: 1st year – 0.91 (95% CI: 0.85-0.97) and 0.80 (95% CI: 0.64-0.96); second year – 0.74 (95% CI: 0.64-0.83) and 0.61 (95% CI: 0.37-0.84)). Adverse events that lead to treatment discontinuation were observed during 1st and 2nd year of treatment with the first anti-TNF in 6% and 10% and in 4% and 12% with the second agent. Treatment discontinuation due to inefficacy was observed with the 1st anti-TNF in 1% and 4%, and in 5% and 0% with the 2nd anti-TNF% during treatment years 1 and 2.
Anti-TNF treatment in adult patients with juvenile idiopathic is effective and safe. Similarly to patients with RA, it is possible to regain efficacy after switching to second anti-TNF-blocker in a majority of patients, although with somewhat lower difference between entry and 2 years DA28 evaluation. Good adherence to therapy was observed for both first and second TNF antagonists.

P50

Biological therapy in patients with rheumatoid arthritis (observation for longer time)

Oľga Lukáčová, Jozef Lukáč, Jozef Rovenský
National Institute of Rheumatic Diseases, Piešťany, Slovakia

Rheumatoid arthritis (RA) is a chronic disease, with evaluation of deformity, disability. Aim of therapy is clinical remission, prevention of structural changes and disability, improve quality of life. In therapy of RA authors used biological drugs too.
Authors observe patients with biological therapy (etanercept, infliximab, adalimumab, rituximab, abatacept). They observe the number of tender and swollen joints, DAS 28, HAQ. Infliximab: 42 patients (33 women, 9 men), at the age 49 years average (range from 33 to 69 years). Duration of RA is 13 years (2–23 years). AE: infections, severe course of salmonelosis, alergy, hearth insufficiency. DAS 28 decrease from 6.78 to 3.75, HAQ decrease from 1.78 to 1,3. Adalimumab: 49 patients (45 women, 4 men), at the age 50.6 years average (range from 33 to 66 years). Duration of RA is 14 years (3–33 years). AE: infections, melanoma, pneumonia, non specific infection, allergy. DAS 28 decrease from 6.8 to 2.5, HAQ decrease from 1.7 to 1,6. Etanercept: 25 patients (22 women, 3 men), at the age 46.5 years average (range from 33 to 62 years). Duration of RA is 14,68 years (5–27 years). AE: vasculitis, uveitis, severe leucopenia, lung fibrosis, severe pneumonia, allergy. DAS 28 decrease from 6.8 to 4.4, HAQ decrease from 1.6 to 1,4. Rituximab: 21 patients (17 women, 4 men), at the age 52.2 years average (range from 33 to 73 years). Duration of RA is 12.4 years (3–24 years). AE: headache, severe leucopenia, allergy. DAS 28 decrease from 6.4 to 3.7, HAQ decrease from 1.7 to 1,5. Abatacept: 7 patients (4 women, 3 men), at the age 48.4 years average (range from 36 to 64 years). Duration of RA is 10.8 years (4–23 years). DAS 28 decrease from 6.4 to 3.7, HAQ decrease from 1.7 to 1,5.
All monitoring drugs are similar in effect. In their group of patients they observe decrease of clinical activity, number of tender and swollen joints, decrease CRP, DAS 28, HAQ.

P51

A long-term follow up in the Czech National Registry ATTRA: Efficacy of anti-TNF-alpha inhibitors on the quality of life in rheumatoid arthritis and ankylosing spondylitis patients

Katarína Hviščová[1], Liliana Šedová[1], Karel Chroust[2], Lucie Burešová[2], Karel Pavelka[1]
[1]Institute of Rheumatology Prague, [2]Masaryk University, Brno, Czech Republic

The anti-TNF-alpha therapy has dramatically changed the treatment of the immune-mediated inflammatory diseases such as rheumatoid arthritis (RA) and ankylosing spondylitis (AS). The main therapeutic goals are the induction and maintenance of remission, the control of radiographic progression and the prevention of irreversible disability. In the Czech national register of biological treatment in rheumatology (ATTRA) there is a possibility to evaluate the quality of life and to compare the outcomes in both diseases.
1053 RA and 315 AS patients, treated with infliximab, adalimumab and etanercept, were included in the Czech national register of biological treatment in rheumatology. Authors examined the HAQ and EuroQol values and compared during the treatment for up to 4 years. The results were compared among the 3 drugs – between diagnosis and during the observation time. 139 patients with RA and 25 with AS have reached the 4 years follow up.
The improvement of the HAQ score and EuroQol was significant between week 0 and week 54 ($p<0.001$) and remained significant over the long-term follow up in all evaluated biologicals as well as in both diagnosis. There were no significant changes between RA and AS in HAQ score ($p=0.558$) and in EuroQol ($p=0.111$) during the treatment.
The disability of RA patients evaluated by HAQ score was significantly worse at the beginning of the therapy than in the AS group ($p<0.001$); however the improvement between baseline and week 54 was comparable for both diagnoses. The HAQ score had significantly improved during the first year of treatment and the improvement remained stable without any significant changes in the next three years of follow up. There were no significant differences between RA and AS patients in disability evaluated by EuroQol at the beginning of the therapy.

P52

Assessment of fatigue in patients with ankylosing spondylitis receiving biological TNF antagonist therapy

Secil Demirdal, Fatıma Yaman, Hasan Toktas, Vural Kavuncu
Afyon Kocatepe University, School of Medicine, Afyonkarahisar, Turkey

Ankylosing spondylitis (AS) is a chronic, inflammatory arthritis that predominantly affects the axial skeleton, causing patients to experience severe pain and stiffness. Additionally, fatigue is reported to be a common complaint among patients with AS and it was reported that fatigue is associated with pain, stiffness, global well-being, mental health, and functioning. In this study, authors aimed to evaluate the fatigue in patients with AS receiving different biological TNF antagonist therapies.
Fourty-three patients with diagnosis of AS according to the modified New York criteria and receiving biolog-

ical TNF antagonist therapy over a period of one year were included in the study. The patients were divided into three groups according to the medication: group 1 (n=17, infliximab), group 2 (n=16, adalimumab), and group 3 (n=10, etanercept). The patients completed questionnaires assessing disease activity (The Bath AS Disease Activity Index-BASDAI), functional capacity (The Bath AS Functional Index-BASFI), global well-being (the Bath AS Patient Global Score-BAS-G), depression (Beck Depression Inventory-BDI), and quality of life (The AS Quality of life -ASQOL). Fatigue was assessed with the BASDAI fatigue item, Fatigue Severity Scale (FSS), and Multidimensional Assessment of Fatigue (MAF).

The mean age of patients was 37.2±12.1 years. The mean scores of BASFI, BASDAI, BAS-G, BASDAI fatigue item, FSS, MAF, BDI and ASQOL were 4.4±.2.9, 2.6±1.8, 4.8±2.5, 4.2±2.7, 3.8±1.7, 21.06±9.95, 10.1±9.4 and 6.9±5.9, respectively. Patients had low scores and there was no statistically difference among the groups in the way of the questionnaires (p>0.05).

All patients had low scores of self-reported fatigue measurements. This study has permitted authors to see that the severity of fatigue did not have a statistically significant difference among the patients receiving biological therapies including infliximab, adalimumab, and etanercept.

P53

Methotrexate-naive psoriatic arthritis patients respond rapidly to infliximab plus methotrexate therapy – results from the RESPOND trial

Helena Raffayova[1], N. Kungurov[2], A. Kubanova[3], A. Baranaskaite[4], A. Venalis[5], L. Helmle[6], E. Nasonov[7]

[1]National Institute of Rheumatic Diseases, Piešťany, Slovakia, [2]Ural Dermatovenerology Institute, Jekaterinburg, Russia, [3]Centra DermatoVenerology Institute, Moscow, Russia, [4]Kaunas MedicalUniversity Hospital, Lithuania, [5]Vilnius University Hospital, Lithuania, [6]Schering-Plough Corp., Budapest, Hungary, [7]Central Rheumatology Institute, Moscow, Russia

To compare the onset of efficacy of infliximab (IFX) + methotrexate (MTX) vs. MTX alone in MTX naive psoriatic arthritis (PsA) patients with active disease.

Patients ≥18 years of age with active PsA (≥5 swollen and tender joints + one of the following; ESR≥28 mm/hr, CRP≥15 mg/L, morning stiffness ≥ 45 min.) were included in this randomized, prospective, open-label, multi-center, multi-national study. Patients were naive to MTX, anti-TNF agents, and could not be on DMARDS. Patients were randomized (1:1) to either IFX (5 mg/kg) intravenous at week 0, 2, 6, and 14 + MTX (15 mg/week) or MTX (15 mg/week) alone. Study visits were at week 0, 2, 6, 14, and 16. The primary assessment was the proportion of ACR20 response at week 16 – secondary assessments included; change in DAS28, EULAR response at each visit, the change in PASI and CRP and were assessed at each time point. The study complied with Good Clinical Practices.

57 patients enrolled in the IFX + MTX group (mean age 40.1±12.3 years, 48.2% male)‡ and 58 in the MTX group (mean age 42.3 years±10.5 years, 61.1% male)‡. Overall by the week 2 visit, 85.7% of patients in the IFX + MTX vs. 35.2% in the MTX alone group achieved a Good (23.2% vs. 0.0%) or Moderate (62.5% vs. 35.2%) EULAR response (all p<0.0001). Compared to MTX alone, a greater number of IFX + MTX patients achieved ACR50 (46.2% vs. 6.1%, p<0.0001) and ACR70 responses (15.4% vs. 0.0%, p=0.0042) by week 6. For patients with a baseline PASI score ≥2.5, a ≥75% improvement from baseline was achieved by 54.3% of patients receiving IFX + MTX compared to 20% receiving MTX alone at week 6 (p=0.003). Similarly, at 6 weeks, significantly more IFX + MTX patients achieved a ≥90% improvement in PASI from baseline than MTX alone (25.7% vs. 2.9%, p=0.0063). At weeks 14 and 16, 91.2% and 97.1% of patients in the IFX + MTX treatment group had a ≥75% improvement in PASI Score compared to 37.5% and 54.3% in the MTX alone group at the same time points (both p<0.0001). There was a rapid reduction in plasma CRP in the IFX + MTX group compared to the MTX alone group at week 2 (median change in CRP, -12.0 mg/L vs. –3.4 mg/L, p<0.0001).

A significantly greater proportion of MTX naive PsA patients – when treated with IFX + MTX – attain an early response to treatment in terms of arthritic and psoriatic signs and symptoms compared to MTX alone. † (Remicade Study in Psoriatic arthritis patients of methotrexate-Naive Disease) ‡ ITT analysis set.

P54

Biologic therapy and pregnancy

Ilona Ujfalussy[1], Bernadette Rojkovich[2], Éva Koó[2], László Czirják[3], Cecília Varjú[3], Zoltán Szekanecz[4], Katalin Nagy[5], Ilonka Orbán[6]

[1]Ministry of Defence, State Medical Centre, Budapest, [2] Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, [3]University of Pécs, [4]University of Debrecen, [5]Markhot Ferenc Hospital, Eger, [6]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Most of the autoimmun rheumatic diseases are more common in young women. Because of this, childbearing potential, reproductive issues related to the disease and its management are essentials. Authors objectives were to search data among Hungarian rheumatic patients on fetal and/or pregnancy outcomes following exposure to anti-TNF-α agents. They perfomed a telephone or e-mail questionnaire among the physicians of the biologic centres.

At this point among the Hungarian rheumatic patients, treated with anti-TNF-α therapy, 7 pregnancy

occurred. All women stopped antirheumatic treatment after conception. 4 women has given life 5 healthy children. There was one elective abortion for the asking of the mother. One of the pregnancies is underway. At this baby mild form of cervical hygroma was diagnosed, but there is no evidence of any serious malformation. In two cases infliximab treatment was discontinued during pregnancy. During lactation, due to active disease, the new exposure to the drug caused severe allergic reaction. 4 male rheumatic patients' wife became pregnant during treatment. All of this pregnancies ended in live birth.
The FDA classified these biologics as pregnancy risk category B, which means that no adverse pregnancy effects have been observed in animal studies, but there have been insufficient controlled human studies. Their report describes 10 pregnancies related to anti-TNF-α therapy, without any congenital malformation. Data are limited, but the currently available data do not seem to support a large access risk of adverse pregnancy or fetal outcomes in women exposed to this new form antirheumatic drugs.

P55

TNF-alpha antagonist treatment of renal amyloidosis complicating rheumatoid arthritis. A five-year follow-up of two patients

Györgyi Mészáros[1], Kálmán Polner[2], Bernadette Rojkovich[1], István Á. Juhász[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]St. Margit Hospital, Budapest, Hungary

Amyloid A (AA) amyloidosis is a rare but serious complication of diseases that stimulate a sustained and substantial acute-phase response, such as RA. The major factor responsible for the development of AA amyloidosis – besides genetic predisposition – is the increased synthesis and subsequent degeneration of serum amyolid A (SAA) – an acut-phase reactant – under chronic inflammatory conditions. Therapy in systemic amyloidosis is aimed at reducing or eliminating the precursor protein – in this case SAA – production, thereby prohibiting further deposition of amyloid fibrils in organs. Blocking proinflammatory cytokines (IL-6, TNF-alpha, IL-1) that regulate SAA synthesis by biologics is a promising therapeutic option for amyloidosis A in inflammatory rheumatic diseases. Given the hypothesis that amyloidosis is a dynamic process of deposition and removal, resolution of amyloid deposits may be expected. Among the organs involved renal manifestation is the most frequent in AA amyloidosis (90%). Two cases of severe, long-standing RA are presented, where amyloidosis was proved by renal biopsy in the background of the nephrotic syndrome (proteinuria, oedema) and renal insufficiency. The first patient began etanercept in 2005, 4 months after amyloidosis was diagnosed. After a few months authors changed to adalimumab, which is still continued. Proteinuria disappeared, carbamide nitrogen and creatinine values are in the normal range since then. In the second case, etanercept therapy was induced 3 years after the histological diagnosis of renal amyloidosis A. (Till then, cyclosporin was given). Inflammatory activity of RA was depressed dramatically, but renal insufficiency showed slow progression so 5 and a half year after the diagnosis of amyloidosis hemodialysis had to be introduced. Despite of the unsuccessful attempt to stop the renal process, the anti-TNF therapy certainly slowed down the development of renal insufficiency by reducing disease-activity of the RA. Moreover, the patient did not need any other drug for her joint disease that could worsen her renal status. Their cases support the results of other studies that biologics can improve amyloidosis complicated inflammatory rheumatoid diseases. According to the literature, etanercept is safe and effective in RA patients with AA amyloidosis even in those undergoing hemodialysis.

P56

HLA-DRB1*15 is associated with very high levels of anti-cyclic citrullinated peptide antibodies and non response to infliximab in rheumatoid arthritis

Judit Laki[1,2], Emeli Lundström[2], Omri Snir[2], Johan Rönnelid[3], Sædis Sævarsdottír[2], Marius Wick[2], Lars Alfredsson[3], Lars Klareskog[2], Leonid Padyukov[2]
[1]Ministry of Defence, State Medical Centre, Budapest, Hungary, [2]Karolinska Institutet, Stockholm, [3]Uppsala University, Sweden

P57

On the occurrence of compelling reasons for the interruption of treatment with TNF-alpha inhibitors

Éva Lányi, Pál Géher
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

In the treatment of rheumatic diseases the application of biological therapy with TNF-alfa inhibitors has gained on importance and popularity. Authors aim was to investigate the occurrence – if any – of serious side effects on TNF-alfa-inhibitors leading to interruption of the first TNF-alfa-inhibitor treatment. Starting in 2005, up till now 328 patients were treated In their department with TNF-alfa inhibitors. Among them 157 patients suffered from rheumatoid arthritis (RA), 152 from ankylosing spondylitis (AS) and 19 from psoriatic arthritis (PA). 141 patients were treated with infliximab (RA: 66, AS: 71, PA: 4), 95 patients with adalimumab (RA: 49, AS: 39, PA: 7) and 92 patients with etanercept (RA: 42, AS: 42, PA: 8). For infliximab the administrated dosis (applied in the 0., 2nd, 6th week, and later every 8th week) was 3 mg/bodyweigh kg for RA patients and 5 mg/bodyweigh kg for AS and PA patients. The dosis for adalimumab was 40 mg/every second weeks and for etanerceps 50 mg/weeks.

It was found that from the 328 treated patients 30 patiens had serious advers effects leading to the interruption of the therapy with TNF-alfa-inhibitors. 9 patients had allergy, 16 patients had serious infections, 1 patient had symptoms of demyelnisation, 1 patients suffered from acut psychosis, 3 patients had very bad compliance. Allergy: 9 patients had allergy against TNF-alfa–inhibitors: 7 received infliximab, 1 adalimumab, 1 etanercept. All signs of allergy were acut, occurring within 24 h of the application of the infusion: erythema, dyspnoe, change in the blood pressure, the shivers, indisposition, etc. At the second time after the premedication the signs were present again. In case of subcutan injection the erythema was present after the second time, too. Infections: 16 patients suffered from severe infections – 7 had pneumonia, 4 upper respiratory tract infection, 1 had peritonitis, 1 had herpes genitale and 3 had tuberculosis. This result underlines the importance of special care fornavoiding contact with virus carriers.
It is very important to carry out regular and often repeated controls. If the time between two controlls is not too long, there is a better chance to notice the adverse effects and timely intervention can be performed. As part of the adverse effect is not very serious the first time, with appropriate intervention one may eventually save the successfully treatment with TNF-alfa-inhibitors. The majority of infections occurred in RA patients which could be connected with the fact that those patients receive also other immunsuppressive medication decreasing further their resistance against infections.

P58

Difficulties in the management of patients with biological therapy

Katalin Nagy, Judit Jász, Mária Pelsőczy, Eszter Deák
Markhot Ferenc Hospital, Eger, Hungary

The introduction of biological therapy in inflammatory rheumatic diseases has great potentials. However the adverse events test authors knowledge many times during the management of patients. They treated 60 patients in their arthritis centre in Eger, since March 2008. Currently 44 are under treatment, 28 with rheumatoid arthritis (RA), 11 with ankylosing spondylitis (AS) and 5 with psoriatic arthritis (PsA). 31 patients – without any problems – are in remission with the first chosen biological agent. Onto the request of 1 patient with AS the treatment was discontinued after one year, because the patient was well. They were forced to switch therapy in 14 patients, in 10 cases due to ineffectivity or loss of effectiveness, and in 8 cases due to side effects. 17 events leading to the discontinuation or switch of therapy were observed: 8 allergic reactions, 1 psoriasiform skin lesion, 1 cardiac decompensation, 1 significant elevation of hepatic enzymes, 1 recurring herpes simplex, 3 repetitive respiratory infections (patients with AS who requested the end of therapy), 1 sepsis (result of acute exacerbation of COPD), 1 pregnancy (RA patient with combination of MTX and biological therapy, both were ended at the signs of pregnancy. At pregnancy week 16 no fetal abnormality was diagnosed). Their main goal is successfully treat patients who were affected by sides effects.

P59

Tocilizumab induced Tako-Tsubo cardiomyopathy in a patient with rheumatoid arthritis

Angéla Tóth[1], Ilona Márkus[1], Klára Barabás[2], László Krivanek[2], Gyula Poór[1]
[1]National Institute of Rheumatology and Physiotherapy, [2]Health Service of First District of Budapest, Hungary

Tako-Tsubo syndrome (TTS), is an enigmatic cardiomyopathy characterized by apical asynergy & left ventricular dysfunction in the absence of significant coronary disease. 70–80% of new TTS cases appear in postmenopausal women. These patients present with mild to moderate chest pain, have ST elevation in lead V3 through V6, and have a modest increase in cardiac laboratory markers. Although exact etiology of TTS is unknown, microcircular dysfunction, transient vasospasm or regional myocarditis may lead to the temporary left ventricle dysfunction. TTS cardiomyopathia is a type of nonischaemic cardiomyopathy in which sudden temporary weakening of the myocardium is present. The condition is also known as the "broken heart syndrome" because this weakening can be triggered by emotional stress. Stress induced cardiomyopathy is a well-recognized cause of acute heart failure, lethal ventricular arrhytmias. Rheumatoid arthritis (RA) started in 1996 with high activity (DAS 28:6,97) in their 60 years old female patient. She was first treated with steroids, and methotrexate, and later with leflunomide. Because of the inefficiency of them tocilizumab was started (iv. infusion 8 mg/body weight kg). On the fourth day before the 4th infusion typical angina pectoris appeared, ECG examinations showed extensive anterior ischemia, Troponin T test was repeatedly negative. Echocardiography showed dilated left ventricle with akinetic apex. Acute coronarography showed winding blood vessels, later the heart MRI proved hypertrophy cardiomyopathy on the septal and apical segments of the left ventricular wall. The mentioned MRI diagnosis did not correspond with the clinical and ECG signs. The introduced biological therapy significantly decreased the clinical activity (DAS 28:2,59) of RA, but due to the developed cardial event it has been stopped. The patient now continues the former disease modifying treatment.
Stress induced cardiomyopathia in a patient with rheumatoid arthritis who has been given biological therapy is very rear in the scientific literature. The mechanism is still unknown. Vasospasm? Adrenalin effect? The mortality is very high.

This case raises 4 questions: 1. Has biological therapy any toxic effect on the myocardium? 2. May biological therapy be continued in this form of Tako-Tsubo syndrome? 3. Are there any other etiological factors of this syndrome? 4. Is this form of TTS is reversible or not? Adequate following may answer the questions.

P60

Comparison of occurrence of adverse events in patients with rheumatoid arthritis and ankylosing spondylitis treated with biologic therapy in Czech National Registry ATTRA

Šárka Forejtová[1], Hermann Mann[1], Karel Chroust[2], Lucie Burešová[2], Karel Pavelka[1]
[1]Institute of Rheumatology, Prague, [2]Institute of Biostatistics and Analyses, Brno, Czech Republic

To compare the occurrence of adverse events (AE) between rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients treated with biologics.
Data were collected in a observational, longitudinal cohort study of patients included in the National Registry ATTRA in the Czech Republic. Main outcome measure was the occurrence of any serious AE, non-serious AE, serious infection, non-serious infection and tuberculosis in patients with different diagnose. Differences between the numbers of patients with special AE were compared between the RA and AS cohort. Relative risks of development of AE adjusted to the number of patient-years of treatment with biologics were calculated.
1759 patients in the RA cohort and 932 patients in the AS cohort were included. There was significantly more serious AEs among patients with RA (10.3%) compared to patients with AS (4.4%), p<0.001. Patients with RA had also significantly more non-serious AEs (28.0% vs 20.2%, p<0.001), serious infections (2.5% vs 1.2%, p=0.016) and non-serious infections (18.4% vs 11.2%, p<0.001). There was no significant difference in the occurrence of tuberculosis (0.6% vs 0.2%, p=0.164). Converted to the number of patient-years on therapy, there was significantly higher occurrence of any serious AEs in patients with RA compared with AS: RR=1.76 (1.26–2.47). Patients with RA also had increased relative risks of any non-serious AEs: RR=1.04 (0.86–1.25), any serious infections: RR=1.58 (0.76–3.27), any non-serious infections: RR=1.23 (0.99–1.53) and risk of tuberculosis: 1.98 (0.20–20.04), but these differences were not statistically significant.
In authors cohort patients with rheumatoid arthritis treated with biologic therapy had 1.76 times increased risk of development of serious advers event compared with patients with ankylosing spondylitis.

P61

Acquired inhibitor to factor VIII in patient with rheumatoid arthritis previously on biologics

Katalin Imre[1], László Nemes[2], Bernadette Rojkovich[1]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]Ministry of Defence, State Medical Centre, Budapest, Hungary

Acquired inhibitors against coagulation factor VIII (FVIII), also termed acquired haemophilia A, neutralize its procoagulant function and result in severe or often life-threatening bleeding. The polyclonal autoantibodies against coagulation factor VIII spontaneously can arise in individuals with no prior history of clinical bleeding. Acquired haemophilia occurs rarely with the incidence of approximately 1 to 4 per million/year, with high mortality between 8–22%. About 50% of diagnosed patients were previously healthy, while the remaining cases may be associated with postpartum period, autoimmune diseases, malignancy, infections, or medications. Authors reports a 63-year-old caucasian female with acquired haemophilia caused by factor VIII inhibitor. Her underlying disease was a severe rheumatoid arthritis previously treated with anti-tumor necrosis factor alpha agents. Due to infections and surgical procedure (traumatic operation) last biological therapy was interrupted for five months. Two weeks after beginning again, severe haemorrhagic syndrome spontaneous hematomas, cutaneous hemorrhages and gastric bleeding developed. Coagulation tests showed a prolongation of activated partial thromboplastin time associated with a marked reduction of factor VIII activity, and increased factor VIII. Inhibitor quantitation was measured with Bethesda test. After treatment with Budapest protocol (cyclical administration of steroids, cyclophosphamide, and FVIII) and FEIBA a good clinical response was obtained. Early recognition, rapid diagnosis and prompt referral to a specialist centre are important to facilitate the optimum treatment of bleeds and improve outcomes. The treatment of acute bleeding episodes and the long-term eradication of the autoantibodies in acquired haemophilia are the main therapeutic strategy.

P62

Effectiveness of leflunomide in psoriatic joint and skin disease: Results from a multinational non-interventional study of psoriatic arthritis treated with leflunomide

F. Behrens[1,2], K. Pavelka[3], J. Štolfa[3], A. Sipek-Dolnicar[4], H. Burkhardt[1,2], On behalf of the OSPAL-Study Group
[1]Johann Wolfgang Goethe University, Frankfurt am Main, Germany, [2]Rheumazentrum Rhein-Main, Germany, [3]Institute of Rheumatology, Prague, Czech Republic, [4]University Medical Center Ljubljana, Slovenia

Psoriatic arthritis (PsA) is a chronic inflammatory joint disease that affects 5% to more than 30% of patients with psoriasis. Leflunomide has demonstrated significant effects on peripheral arthritis but there is a further need to study the effectiveness and tolerance in daily practice under routine care conditions. Objective was the evaluation of the effectiveness and tolerance of leflunomide in the treatment of active PsA in daily clinical practice.
Authors conducted a prospective 24-week observational study (OSPAL). 514 adult patients in Germany, Czech Republic and Slovenia with active PsA were treated with leflunomide (100 mg/d loading dose for 3 days followed by 20 mg/d). The primary endpoint was the proportion of patients classified as responder by Psoriatic Arthritis Response Criteria (PsARC). Results Out of 440 patients included in the analysis of PsARC, 380 met PsARC response criteria (86.4%; 95% CI: 82.8 – 89.4). Improvements between pre- and post-treatment examination were also found for pain (82.8% of patients), dactylitis (51.2%), fatigue (66.8%) and skin disease (64.6%). Ninety-eight adverse drug reactions (ADR) occurred in 62 patients (12.1%). The most commonly documented ADRs were diarrhoea (16.3% of all ADRs), alopecia (9.2%) and hypertension (8.2%), which are known side-effects of leflunomide. Three serious ADRs (SGPT increased, hypertensive crisis, increased transaminases) occurred in 2 patients (0.4%).
In daily clinical practice, leflunomide has been shown as an effective and well tolerated treatment for PsA, with beneficial effects not only on peripheral arthritis but also on pain, dactylitis, fatigue and skin disease.

P63

Association of methotrexate treatment and serum levels of Dickkopf-1 and cartilage oligomeric matrix protein in rheumatoid arthritis patients

Jerzy Swierkot, Katarzyna Gruszecka Marczynska, Agnieszka Matuszewska, Piotr Wiland
Wroclaw Medical University, Poland

In rheumatoid arthritis (RA) synovial inflammation results in focal erosion of articular bone and cartilage destruction. Dickkopf-1 (Dkk-1) regulates bone remodelling in animal models of inflammatory arthritis, but its role in patients with rheumatoid arthritis (RA) remains unclear. Measurements of the concentration of serum cartilage oligomeric matrix protein (COMP) is expected to be a novel biomarker indicative of cartilage destruction. There are contradictory reports on the impact of therapy on COMP and Dkk-1 titers and the correlation with treatment response. The aim of this study was to analyze the effect of methotrexate (MTX) treatment on bone and cartilage metabolism in patients with RA. Authors analyzed also whether treatment response was associated with characteristic changes of Dkk-1 and COMP.
37 patients with RA included in a study were examined. All patients were using weekly MTX (up to 25 mg per week) with adjuvant dose of 5 mg of folic acid two days after MTX. Disease activity and treatment response was determined by DAS 28 index. Dkk-1 and COMP were measured in serum samples in methotrexate naive patients and after six months of treatment.
The mean serum COMP level of the population did not change after treatment. However, patients with low serum COMP at baseline showed a significant ($p<0.05$) higher EULAR good response within 6 months, than patients with higher COMP values. The level of serum Dkk-1 decreased from 76,2 pmol/l to 67,1 pmol/l in 22 patients with good response and increased from 46,3pmol/l to 67,7 pmol/l in 9 patients with bed response after six months of treatment The changes were not significant perhaps due to small number of patients. Significant correlation was shown between serum Dkk-1 levels and C-reactive protein during the follow-up.
Their data indicate that low serum COMP before starting MTX alpha treatment predicts a higher EULAR good response.

P64

Life-threatening leucopenia during methotrexate therapy of rheumatoid arthritis

Petr Bradna, Jaroslav Maly, Tomas Soukup, Alzbeta Zavrelova, Jan Toms, Oldrich Siroky, Miroslav Pecka, Dalibor Milka
Charles University Faculty of Medicine and University Hospital, Hradec Kralove, Czech Republic

Methotrexate currently represents basic medication of rheumatoid arthritis. Serious leucopenia during methotrexate therapy isn't frequent, but it can be potentially life-threatening complication. Authors compared the patients with complicated leucopenia from district of about 1 million inhabitants in eastern Bohemia with group of patients, treated by University Hospital Rheumatological department, in which leucopenia was recorded without serious consequences. The aim of study was to find predisposing factors of serious course of the disease.
They found out rheumatoid arthritis patients, who were admitted to Department of Clinical Hematology from 2007 for serious leucopenia during methotrexate therapy,. These patients they compared with group of patients, treated for rheumatic diseases in University Hospital rheumatological clinic, who had proved leucopenia during the same time. They used the Statistica v.8 software for statistical evaluation.
Bone marrow depression with septic complications represents the reason of admission in 8 rheumatoid arthritis patients. There were two males and 6 females; average age was 72, 2 (58–78) years. Three of the patients were suffering with serious comorbidities, 2 had elevated serum creatinine. In two cases it

probably came to methotrexate overdose as a result of bad understanding of dosage. One half of all cases were fatal. They documented leucopenia in 48 cases of 2871 rheumatologic outpatient charts of University Hospital Rheumatological department. Only 4 cases of leucopenia were documented in rheumatoid arthritis patients (8, 3%). The vast majority of leucopenic patients were formed by systemic lupus patients with antiphospholipid syndrome of Sjögren's syndrome patients. Septic patients were significantly older, had more serious comorbidities, or reduce renal functions.
Leucopenia represents infrequent, but life-threatening complication in rheumatoid arthritis therapy by methotrexate. Features of bad prognosis were higher age, reduced renal functions and serious comorbidities and also drug overdose.

P65

Retrospective study of polymyalgia rheumatica treated with glucocorticoids plus methotrexate

Zsuzsa Schmidt, György Hittner, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Some patients of polymyalgia rheumatica (PMR) have a chronic-relapsing form and require glucocorticoids (GCs) for several years. GC-related side effects occur in the majority of cases, but no "steroid-sparing" agent proved to be efficacious so far.
Disease course and treatment were –retrospectively- studied in Hungarian PMR patients, efficacy of methotrexate (MTX) was analysed.
Ninety-seven PMR patients were studied. Patients were divided according to disease outcome and treatment mode. MTX was given randomly to patients not recovering with GCs, in a weekly dose of 10 mgs. PMR was diagnosed according to Healey's criteria. Recovery and remission of the disease were defined according to parameters of the PMR activity score. For statistical analysis the EpiCalc 2000 computer program was used.
60% of the patients recovered, 40% had a chronic-relapsing disease. Eigthy-one percent were treated with GC, whereas 19% were given GCs plus MTX. Sixty-three percent of the patients with GC therapy alone, whereas 44% of the MTX treated patients had complete recovery. Twenty-six percent of the chronic-relapsing group and 14% of the recovered patients were treated with MTX combination therapy. The initial daily dose of GCs (mg) was similar in patients with different outcomes (complete recovery 14.6±5.6 mg/die vs chronic/relapsing disease 15.7±5.9 mg/die, p=0.82). When comparing GC data in the different treatment groups (GC and GC+MTX), in patients with complete recovery no difference was observed in the duration (month) and cumulative dose (g) of GC therapy (14.1±7.3 vs 13.6±7.9, p=0.88: 2.8±0.1 vs 2.7±0.06, p=0.12), whereas in patients with chronic disease the addition of MTX reduced the daily dose (mg) as well as the cumulative dose (g) of GCs (3.2±1.8 vs 2.3±1.2, p=0.08; 5.3±1.1 vs 4.6±0.8, p=0.07), but the difference did not reach significance. GC treatment was required for a similar length of time (month) (50.5±25.7 vs 43.3±25.8, p=0.26).
One–third of the Hungarian PMR patients need GC treatment for several years. With MTX, in the long term either, no better recovery and no significant reduction of the GC dose could be achieved. Although authors results are in accordance with those of the PMR literature, compared to the widely accepted rules in RA with applying higher doses and a proper therapeutic schedule, the "insufficiency" of MTX in the treatment of PMR should be re-analysed.

P66

Sympathoneural and adrenomedullary responses to orthostasis in female patients with rheumatoid arthritis

Jozef Rovenský, Miroslav Vlcek, Adela Penesova, Martin Zlnay, Anna Scipova, Zofia Radikova, Richard Imrich
Institute of Experimental Endocrinology, Bratislava, Slovakia

The sympathetic nervous system (SNS) may affect immune regulation and thus facilitate the onset or exacerbation of rheumatoid arthritis. Surprisingly, a decreased sympathetic and adrenomedullar response to hypoglycemia was found in female patients with rheumatoid arthritis (RA) and systemic sclerosis suggesting altered SNS function in these patients. It is however unclear whether the SNS alterations are present in response to a moderate physiological stimulus.
The aim of the study was to assess SNS activity in responses to orthostatic challenge, a stimulus that activates the SNS during daily-life activities, in premenopausal RA patients and matched controls.
The testing was performed in 22 female RA patients (30±2 years, BMI 21.0±0.7 kg/m2) with low to moderate disease activity, and in 15 matched healthy females. The orthostatic test consisted of a stabilization period (30 min), legs-up position (15 min), upright position (10 min) and supine position (15 min). Blood samples for catecholamines and neuropetide Y (NPY) were taken at the end of each body position and at the 3rd min of upright position. Blood pressure and ECG for the analysis of heart rate variability (HRV) were recorded during the test.
At the baseline and during the orthostatic test, RA patients had higher norepinephrine (p=0.042) compared to healthy controls, however, a magnitude of norepinephrine response to upright position were comparable between the groups. Plasma concentrations of epinephrine and NPY did not differ between patients and controls during the test. Diastolic blood pressure tended to be higher at the baseline in RA subjects compared to healthy controls with the similar trend

during the orthostatic test. There was no difference in HRV parameters between groups.
The present results indicate only a modest increase in sympathoneural activity in RA, which may reflect the presence of chronic inflammatory status. Long-term consequences of the SNS overactivity to daily-life stimuli can have negative effects for cardiovascular risk in RA and disease activity itself.

P67

Age peculiarities of bone loss in women with rheumatoid arthritis

Vladyslav Povoroznyuk, Tetyana Karasevska
Institute of Gerontology AMS, Kiev, Ukraine

The course of rheumatoid arthritis is aggravated by decrease of mineral bone density parameters connected with bone remodeling disorders because of chronic inflammatory process and receiving glucocorticoids. The research is aimed at studying structural-functional bone tissue state in women with rheumatoid arthritis and determining age peculiarities of bone loss in the course of this disease.
82 women aged 30-69 years with rheumatoid arthritis were examined. BMD was measured by means of X-ray absorptiometry (lumbar spine, femoral neck, forearm and total body).
BMD parameters in connection with age are given in the Table. Parameters 30-39 years 40-49 years 50-59 years 60-69 years n 13 25 18 25 Age 31,6±1,4 45,2±2,7 55,1±2,1 67,5±3,2 Weight, kg 67,1±10,8 72,3±15,2 68,8±16,3 67,9±11,1 BMD Total body 1,12±0,01 1,11±0,02 1,04±0,03 0,98±0,02 BMD Radius UD 0,35±0,02 0,37±0,02 0,30±0,03 0,29±0,01 BMD Radius 33% 0,70±0,01 0,69±0,02 0,56±0,04 0,53±0,02 BMD Radius total 0,53±0,02 0,53±0,01 0,43±0,03 0,41±0,02 BMD Hip 1,01±0,03 0,97±0,03 0,87±0,04 0,78±0,04 BMD Spine 1,17±0,03 1,05±0,04 0,99±0,005 0,92±0,03
Age of women with rheumatoid arthritis influences bone loss of lumbar spine, hip bone and total skeleton. BMD decrease of radius must be mainly associated with peculiarities of the disease's course.

P68

Osteoporosis in patients of different age with ankylosing spondylitis

Vladyslav Povoroznyuk
Institute of Gerontology AMS, Kiev, Ukraine

To study the structural-functional state of bone tissue of patients of different age with ankylosing spondylitis (AS), 71 patients aged 19–49 years (mean age 29,3±1,1) with AS and 63 representatives of control group (CG) aged 20-48 years (mean age 31,7±1,2) are examined. Duration of diseases in group patients with AS is 9,5±0,6. Besides, patients of group with AS were divided in three sub-groups on age: 20–29 years – 30 persons, 30–39 years – 18 persons, 40–49 years – 15 persons; patients of CG were divided in three sub-groups on age: 20–29 years – 20 persons, 30–39 years – 20 persons, 40–49 years – 20 persons.
Structural-functional state of bone was evaluated by means of an ultrasound bone densitometer ("Achilles+", Lunar Corp., Madison, WI)). The speed of sound (SOS, m/s), broadband ultrasound attenuation (BUA, dB/MHz) and a calculated "Stiffness" index (SI,%), T and Z-range were measured.
Patients with AS have revealed a reduction of SI of bone tissue by 11,1% in comparison with CG; osteoporosis – in 17.5% of all group patients with AS; subgroup 20-29 years – 15,8%; 30-39 years – 14,3% and 40-49 years – 18,2% in accordance criteria WHO.
Considerable structural-functional disorders of bone tissue in patients with AS require densitometral monitoring and respective means of prophylaxys and treatment for this part population.

P69

Vitamin-D deficiency and insufficiency in Ukrainian population

Vladyslav Povoroznyuk, Nataliya I. Balatska, Victor Y. Muts, Tetiana Y. Solonenko, Volodymyr Vayda
Institute of Gerontology AMS, Kiev, Ukraine

Vitamin-D levels in peripheral blood have been assessed at Ukrainian Scientifical and Medical Center of Osteoporosis.
129 patients, aged 20–79 years (median 55.8±1.3) underwent peripheral blood sampling with subsequent assessment of 25(OH)vit D values by EIA test. Patients have been split into 5 groups according to their age: 20–39, 40–49, 50–59, 60–69 and 70–79 years old. 95 of them were females and 34 males.
Vitamin-D levels were assessed with the 25-OH Vitamin-D EIA Kit by means of the Immundiagnostic Enzyme-Immuno-Assay (EIA) for quantitave determination of 25-OH Vitamin-D in human serum and plasma. Results in groups: 25-OH Vitamin-D level in group 20-39yrs was 60.7±9.5 nmol/l; in 40–49yrs – 53.4±5.7 nmol/l; in 50-59yrs – 58.5±6.9 nmol/l; in 60-69yrs – 58.0±7.3nmol/l; in 70–79 years – 68.0±9.7 nmol/l. Average value throughout the assessed population was 58.4±3.5 nmol/l. Deficiency has been found in 11.7%, 14.3%, 17.1%, 17.2%, 11.1% of cases ("younger" to "older" group, respectively). Insufficiency: 47.1%, 57.1%, 57.2%, 62.1%, 48.2% of cases. Normal values of 25(OH) Vitamin-D have been determined in 41.2%, 28.6%, 25.7%, 20.7%, 40.7% (same group breakdown). In total the diagnosis of Vitamin-D deficiency was established in 14.7% of the subjects, insufficiency – in 55.0%; normal values in 30.3% of the population in question.
Patients in the following age groups: 40–49, 50–59, 60–69 years are most susceptible to deficiency and insufficiency of Vitamin-D. The occurrence of higher 25(OH)Vitamin-D levels in patient population between

70–79 years old might be explained by prophylactic intake of calcium and Vitamin-D preparations among this population.

P70

Effect of zolendronic acid in treatment of post-menopausal women with osteoporosis

Vladyslav V. Povoroznyuk, Nataliia Grygorieva, Volodymyr Vayda, Nataliia Dzerovych, Nataliya I. Balatska
Institute of Gerontology AMS, Kiev, Ukraine

Zolendronic acid is a new bisphosphonate used for treatment of postmenopausal osteoporosis. Authors based their findings on results of intravenous infusions of zoledronic acid in 162 cases, 25 of which – secondary.

To determine the efficacy and safety of intravenous infusions of zoledronic acid, and effects on vertebral pain, bone mineral density (BMD) in postmenopausal women with osteoporosis.

41 postmenopausal women with osteoporosis aged 49-83 years were examined: average age – 65.90±0.76 years, average height – 159.23±0.67cm, mean body mass – 67.84±1.25 kg.

Evaluation of pain syndrome and life quality was made with questionnaires. BMD was determined with Dual-energy X-ray absorptiometer "Prodigy" (GE Medical systems). 5 mg of zoledronic acid was administrated by intravenous injection. During the complex treatment patients received 1 tablet of calcium combined medicine (Calcium – 500 mg, Vit. D – 400 IU) 2 times a day during 12 months. Examination was performed before and after three, six, nine and twelve months of treatment course.

A reliable decrease of vertebral pain syndrome by visual analogue scale was observed up to nine months. The pain syndrome increased up to twelve months. However, the given index was lower than before treatment (insignificant changes). According to EuroQol 5D scale, life quality significantly improved. BMD of spine significantly increased in comparison with indexes before treatment after three ($t=5.68$; $p<0.00$), six ($t=4.88$; $p<0,00$), nine ($t=7.59$; $p<0,00$) and twelve ($t=5.55$; $p<0,00$) months. The BMD of femur (total) increased significantly after three ($t=4.76$; $p<0.00$), six ($t=8.06$; $p<0.00$), nine ($t=2.36$; $p=0.03$) and twelve ($t=2.60$; $p=0.02$) months. Dynamics of BMD were 6.48%, 8.57% on lumbar spine and 2.75%, 3.15% on femur (total) at six and twelve months, accordingly. The BMD of forearm increased considerably after three ($t=4.70$; $p<0.00$) and twelve ($t=2.30$; $p=0.004$) months. BMD of total body significantly increased after three ($t=2.65$; $p=0.01$), six ($t=3.31$; $p=0,003$), nine ($t=5.53$; $p<0,00$) and twelve ($t=2.83$; $p=0.01$) months.

Intravenous infusions of zoledronic acid (5 mg) were shown to be effectively increasing BMD, decreasing pronounced vertebral pain syndrome and improving life quality in postmenopausal women with osteoporosis.

P71

Prevention of osteoporosis in Northern youth

Milana Petrova N.
North-Eastern Federal University, Yakutsk, Russia

Examination of the population of Republic Sakha (Yakutia) for the purpose of early diagnosis of osteoporosis was carried out in Yakutsk city for the first time. Mineral density of bones was evaluated using the Osteometer DTX–200 (Nycomed, USA). A total of 3784 patients were surveyed. Women in age group of 50–59 years (N=694) were most common. Particular interest focused on individuals aged 11–30 years, as at this age there is an accumulation of calcium in bone tissue that ultimately determines bone density at older ages. The method of casual sample allocates a group of 51 persons aged 11–29 years: 19 boys and 32 girls. Average Z–score in girls 11–20 years of age was –0,7±1; in girls 20–29 years old –0,5±0,2; in boys 11–20 years, –1,2±0,8; in young men 20–29 years old, –0,8±1,3. The minimum, maximum values in these groups were –2, 3; –2, 2; –2, 1; –2, 9, respectively. For optimum density of bones the weight or body mass index (BMI) has great value. Average (±SD) BMI for girls 11–20 years=21,33±2,7 (18–27); girls 20–29 years=22,06±3,4 (16,2–28); boys 11–20 years=22,32±4,6 (16,5–32); young men 20–29 years=24,5±7,4 (17–40). In all age groups there were patients with BMI lower than 20 kg/m^2. In terms of physical activity, boys and girls 11–20 years are more active: only 2 walking daily less than 1 hour versus 8 at age 20–29 years – 8. Only: two boys (18 and 20 years old) fail to consume at least 3 portions of dairy products daily accept. Girls consume dairy products more often. Carbonated beverage and coffee to some extent were consumed in large amounts 18 girls and 13 young men. Unfortunately, several of the youths studied already had an accompanying pathology: diseases of kidneys – 5 girls and 1 boy; liver – 3 girls and 1 young man; endocrinological systems – 13 girls and 1 boy; nervous system –1 girl and 1 boy; gastroenteric pathology – 5 girls and 3 boys; bronchial asthma – 1 girl. Injuries were seen in 10 girls and 8 boys (most commonly a sports trauma). Girls take calcium preparations more commonly: girls till 20 years old (7), girls 20–29 years old – 8; boys till 20 – 5; young men 20–29 years old – only 2. Thus, their youth in Yakutsk city generally consume at least 3 servings of dairy products, consume drinks which might adversely affect bone density, have chronic diseases which can lead to decrease in mineral density of bones, and do not universally take calcium preparations. Health education in the schools and with parents, along with promotion of bone-healthy food appears to be necessary.

P72

The role of Vitamin-D and calcium in prevention of postmenopausal osteoporosis

Nikolov Tatjana[1], Vladimir Bobic[2], Branislav Bobic[1]
[1]Institute for Rheumatology Novi Sad, [2]Pfizer H.C.P, Corporation Beograd, Serbia

Osteoporosis is a systemic metabolic skeletal disease and has been the focus of interest of many different medical specialists over last few decades, mainly because of the increasing life expectancy in some parts of the world. The basic characteristics are low bone mineral density and reduced bone quality, which increase the risk of bone fractures. Consequences of osteoporosis significantly increase invalidity/disability, morbidity and mortality of the general population, making prevention of osteoporosis a topic of increasing importance.
To establish general and specific criteria in the prevention of postmenopausal osteoporosis in women with diagnosed osteopenia.
This prospective study examined 50 women (n=50), aged 50-60 years, within 5 years post menopause, with a DEXA scan results indicating osteopenia (T score from –1.0 SD to –2.5 SD). Authors measured bone mineral density with a DEXA osteodensitometric method on the lumbosacral spine and neck of femur twice during the study: at the beginning of the study and one year later after commencing the treatment with Vitamin-D and calcium. Women with a DEXA scan result corresponding to osteopenia were taking 800 IU of Vitamin-D and 1000 mg of calcium daily. They were also encouraged to maintain adequate physical activity and to follow recommended life-style and dietary advice.
After measuring bone mineral density on L1–L4 vertebras, results indicate significant statistical difference before and after the treatment ($t=4.169$, $p<0.01$). After measuring bone mineral density on neck of femur before and after the treatment, results show significant statistical difference ($t=3.367$, $p<0.01$).
With a continuous daily intake of 800 IU of Vitamin-D and 1000 mg of calcium during one year, there is an increase in mineral bone density but the post-treatment T score remains within a zone of osteopenia. In addition, there is no decrease in bone mineral density, therefore reducing the risk of osteoporotic fractures. Continuous recommended treatment with Vitamin-D and calcium proves beneficial in patients with osteopenia.

P73

A ten year study of clinical fractures, changes in density, risk factors and FRAX in normal and osteopenic postmenopausal women

Csaba Kiss, Éva Ruzicska, Gyula Poór
National Institute of Rheumatology and Phisiotherapy, Budapest, Hungary

It is well known that not only osteoporotic patients suffer fragility fracture but also normal and osteopenic. During a ten year follow-up period the density, risk of fracture, and FRAX could change significantly. Authors aim was to evaluate incident fractures, change in density, fracture risk, and FRAX in normal and osteopenic postmenopausal women during a ten year observation period At the outpatient clinic of National Institute of Rheumatology and Physiotherapy 151 normal and osteopenic postmenopausal women without medical therapy were followed for ten years. Mean age: 65.6±7.4 years, period of time: 9.3±2.1 years. The patients were measured by DEXA at lumbar spine and femoral neck. In order to evaluate change in density the measurement was repeated after ten years with the same equipment. In order to evaluate incident fractures change in risk factors and FRAX the patients filled out a life style questionnaire at the time of second DEXA (retrospective) measurement. The number of incident fractures were 7 (normal T-score: 0, osteopenic T-score: 7). Region of fractures: (2 Colles' fracture, 1 vertebra, 4 rib) mean age of patients suffering fracture: 69.2±9.2. Lumbar and femoral density were significantly lower in the whole population during the ten years observation period. Risk factors and FRAX didn't change significantly in the whole population. Incident fractures were found only in the osteopenic group In the whole population the density was lower and FRAX was higher. In the whole population the lower density and higher FRAX were frequent but fracture and change in risk fractures were rare. Osteopenic didn't differ from normal regarding the number of lower density and higher FRAX.

P74

Evaluation of Achilles tendon and plantar fascia in diffuse idiopathic skeletal hyperostosis by ultrasound and X-ray

Csaba Kiss, Ádám Mester, Péter Mandl, Éva Ruzicska, Péter Bálint, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

The objectives were to assess involvement of the Achilles tendon and plantar fascia in diffuse idiopathic skeletal hyperostosis (DISH) and degenerative spine disease (DSD) by both gray-scale (US) and power doppler ultrasound (PDUS). To correlate data with clinical symptoms and radiographic findings.
Bilateral calcaneus of 17 patients (mean age: 66+8.8, BMI: 30.5+3.9) with DISH were evaluated by US, PDUS and radiography. A control group of 20 patients (mean age: 62.1+11.9, BMI: 29.3+5.0) with DSD were also evaluated according to the same protocol. All subjects also underwent clinical examination. The patients were matched by age, gender and BMI for the case-control study.
US revealed significant differences in the frequency of unilateral (both left and right) and bilateral Achilles os-

sification (p=0.02 for each comparison) between the DISH group and the control group in favour of the former group. US showed no significant difference in the frequency of involvement of plantar fascia ossification between the two groups. PDUS revealed at both region (Achilles tendon p=0.07, plantar fascia p=0.01) ossification with significantly higher frequency in DISH compared to DSD. X-ray examination showed no significant difference in the frequency of ossification between the DISH and the control groups. The length (p=0.07) and width (p=0.04) of the ossification by X-ray was significantly greater at the right Achilles tendon in the DISH group.
Pain in the past affecting the Achilles tendon was more frequent in DISH (p=0.07). Pain at present as well as bilateral pain were more frequent in both regions in DISH (p=0.05).
The frequency of Achilles tendon ossification according to US and PDUS examination is different in DISH and DSD. The X-ray examination did not find significant differences in the frequency of ossification between the groups, however the dimensions (length and width) of the ossifications were found to be significantly different between the two groups. The clinical investigation revealed that both unilateral and bilateral Achilles tendon pain was more frequent in DISH.
According to authors clinical, radiological, and ultrasound examination there is a significant difference between DISH and DSD regarding the entheses around the calcaneus.

P75

Quantifying of serum concentration of beta crosslaps as a factor of estimate in efficacy bisphosphonate therapy in postmenopausal women with osteoporosis

Aleksandar Jovanovski[1], Olgica Rankovic[1], Jadranka Bozovic-Jelic[1], Zoran Grujic[2]
[1]Regional Hospital Sabac, [2]Special Hospital for rheumatology Banja Koviljaca, Serbia

Osteoporosis is a disease in which the density of bone are reduced, with an increased bone fracture risk. There are many biochemical metods of estimate in efficacy of therapy and among them quantifying of serum concentration of beta crosslaps as factor of bone degradation. The aim of the study: serum concentration of beta crosslaps it may be beneficial method of estimate in efficacy bisphosphonate therapy in postmenopausal women with osteoporosis.
Methodology: one year prospective study. Women with postmenopausal osteoporosis diagnosed by DEXA,treated by bisphosphonates (Alendronat 70 mg per week in one go and Ibandronate 150 mg monthly).BMD and T score was observed before and at the end of treatment and beta crosslaps before and after III, VI and XII month of beginning treatment.
98 women with osteoporosis with average age 60,28±5,14 years were treated in 3 hospitals in Serbia in the course of 2009. Before of treatment T score (LS spine) was from –2,6 to –3,7 SD, and BMD from 0,678 to 0,865 gr/cm^2;T score (hip) was from –2,4 to –3,5 SD, and BMD was from 0,481 to 0,605 gr/cm^2. After one year T score (LS spine) was from –2,0 to –3,1 SD, and BMD was from 0,775 to 0,988 gr/cm^2;T score (hip) was from –1,9 to –2,9 SD, and BMD was from 0,566 to 0,728 gr/cm^2. Serum concentration of beta crosslaps before treatment was 815,56 mcg/ml,after 3 month 241,67 mcg/ml,after 6 month 185,00 mcg/ml, at least after year 136,28 mcg/ml. Considerable difference ($p<0.05$ Student t test) in increase T score and BMD and highly significant ($p<0,01$, Student t test) in decrease of concentration of beta crosslaps in the tested group of patients after treatment was statistically found. Positive coherency in increase T score and BMD and decrease of concentration of beta crosslaps was statistically found.
Serum concentration of beta crosslaps can be used as efficient factor of estimate in efficacy bisphophonate therapy in postmenopausal women with osteoporosis.

P76

Proposition for a national training program in musculoskeletal ultrasound in Hungary, based on available programs in Europe and in the United States

Katalin Áts, Péter Mandl, Éva Ruzicska, György Hittner, László Hodinka, Péter Bálint, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Musculoskeletal ultrasound has a history spanning several decades in most countries in Europe and also in the United States. Initially developed by radiologists, it soon was adopted by other specialties in musculoskeletal medicine, primarily by rheumatologists, but also to a lesser extent by orthopaedic surgeons, sports medicine and physical medicine specialists. According to a recent survey, musculoskeletal ultrasound is widely used by rheumatologists in Europe, however there were significant differences in the availability and specifications of training, either as part of the rheumatology fellowship curriculum, or as part of discrete official training programs.
To compare the major characteristics of existing musculoskeletal ultrasound training programs in various countries of Europe and the United States. Develop guidelines for a national training program in musculoskeletal ultrasound for Hungary.
The reported structure, length, setup, as well as competency requirements of available musculoskeletal ultrasound training programs of various European countries as well as of the United States were compared and evaluated.
Based on the qualitative evaluation of available data regarding the programs, authors analysis revealed considerable differences in both the metric properties

	Official Training Program	Training period	Competency assessment Theoretical exam	Competency assessment Practical exam	Minimum No of scanning before exam	National Register
EUROPE	Common across Europe	3–36 months	Yes	Yes	200-500	Rare* Only in Germany, Finland, Romania, Slovakia, Switzerland
US	Yes	8 months	Yes	Yes	Not compulsory	No
HUNGARY (proposed)	Yes	12 months	Yes	Yes	Not yet decided	Yes

Table 1

(length, number of participants/tutors, etc.) and the competency requirements (written/oral tests, number of required exams, etc.) of the individual programs (*Table 1*). There was also considerable variety with regard to the format of the program, with ultrasound training being a part of the rheumatology curriculum in several countries, and the existence of, in many cases several discrete official training programs in other countries.

Based on the analysis of available training programs, the authors propose guidelines for a Hungarian National Musculoskeletal Ultrasound Program.

P77

Psychosomatic status in patients with gout

Larisa Rotaru, Liliana Groppa, Elena Deseatnicova, Mircea Revenco

State Medical and Pharmaceutical University, Kishinau, Moldova

Objectives of authors to study psychosomatic changes in patients with gout both intermittent and chronic evolution; and to elaborate methods of correction of psychosomatic changes.

Eighty-six patients with the diagnosis of gout (according to American College of Rheumatology [Wallace, 1977]) were examined. 29 of them had intermittent evolution (2 patients with primary attack and 27 patients with repeated attack) and 57 of them had chronic evolution. Age varied from 24 to 67 years old. Monoarticular onset had – 62 (72,1%) of patients, oligoarticular onset had – 21 (24,4%) and poliarticular onset – 3 (3,5%). The duration of the disease varied from 1 to 27 years. Number of tender joints at the examination (NTJ) and number of inflamed joints (NIJ) were determined. Pain level was appreciated by VAS. All the patients were tested by Hamilton scale and according to the method of psychological diagnostics of patient's attitude to the disease. On the background of basic therapy with allopurinol and diclofenac all the patients were randomized, divided into 2 groups. Group I received paroxetine, and Group II received placebo.

From 86 tested patients at 52 (60,5%) depression was found (light degree – at 14 (26,9%), medial degree gravity – at 27 (52%), heavy degree gravity – at 11 (21,1%)) – was revealed. In one month of paroxetine therapy the depression was spotted at 38 (44,1%) patients (light degree – at 23 (60,5%), medial degree gravity – at 10 (26,3%), heavy degree gravity – at 5 (13,1%)). Through 2 months – depressions was spotted at 32 (37,2%) patients (light degree – at 19 (59,4%), medial degree gravity – at 9 (28,1%), heavy degree gravity – at 4 (12,5%)), and in 5 months the depression was spotted – at 29 (33,7%) patients (light degree – at 18 (62,1%), medial degree gravity – at 7 (24,1%), heavy degree gravity – at 4 (13,8%)). There was found a medium correlation ($R=0,45$, $p<0,05$) between the NTJ and the presence of depression. Medium pain level constituted by VAS 56,2±7,1 mm. A correlation between the intensity of pain by VAS and the degree of depression was determined: for light degree depression ($R=0,33$, $p<0,05$); for medium degree depression ($R=0,45$, $p<0,05$); for heavy degree depression ($R=0,53$, $p<0,01$).

Application of different methods of psychological testing, that help to determine psychical changes, including type and form detection, is very important in diagnostics of psychosomatic disorders in the patients with gout. Received results show the presence of psychosomatic disorders in patients with gout and their positive dynamic including psychological status improvement and pain level reduction on the background of complex therapy with paroxetine.

P78

Cognitive dysfunction in the Czech population of patients with systemic lupus erythematosus

Radka Svobodova[1], Marie Posmurova[1], Vera Peterova[2], Petr Kozelek[2], Ivana Putova[1], Marketa Fojtíková[1], Ctibor Dostal[1], Marta Olejarova[1]

[1]Institute of Rheumatology, [2]Faculty Hospital of Charles University, Prague, Czech Republic

Involvement of the nervous system occurs in as much as 80% of patients with systemic lupus erythematosus (SLE). Diagnosis of neuropsychiatric involvement (NPSLE) is very difficult due to a variability of clinical presentation. Cognitive dysfunction (CD) is one of the most common manifestations of NPSLE. Its cause has not yet been entirely elucidated.

The aim of this study was to assess the prevalence of NPSLE in patients with SLE, and the prevalence of CD in the Czech population of patients with SLE, and to determine an association of CD with other types of NPSLE, brain MRI findings of blood-brain barrier

disorders, positivity for certain autoantibodies, and disease activity.
A group of 100 patients diagnosed with SLE according to ACR criteria was examined. Disease activity was evaluated using the SLEDAI index. All patients underwent a clinical neurological, psychiatric, and psychological examination, and based on the results of all three examinations, diagnosis and the type of NPSLE was established according to the ACR criteria. Autoantibody activity was examined in all patients.
Based on a neurological examination alone, diagnosis of NPSLE was established in 31% of patients. Following completion of a psychiatric and psychological examination, the occurrence of NPSLE increased to 73%. A various degrees of cognitive deficit were found in most of their patients (91%). A mild degree of cognitive deficit was found in 35% of patients, and cognitive dysfunction (i.e. a moderate to severe degree of cognitive deficit) was diagnosed in 57% of patients. In the group of patients with CD, occurrence of involvement of the nervous system was four times higher than in the group without cognitive dysfunction; furthermore, occurrence of cardiac involvement (22.8% vs. 14.0%; $p<0.05$) and antiphospholipid syndrome (28.1% vs. 20.9%; $p<0.05$) was also higher in patients with CD. In the group of patients with CD, occurrence of positivity for antiphospholipid autoantibodies was two times higher than in the group without dysfunction.
Cognitive dysfunction is a very frequent clinical manifestation of SLE; most of the patients (57% in authors group) suffer from a moderate to severe degree of cognitive deficit. Cognitive dysfunction can evade diagnosis, when only routine, standard neurological and psychiatric examinations are performed. A targeted psychological examination can increase the chance of diagnosis of CD up to 10 times. Since cognitive dysfunction can significantly decrease mental performance of a patient with SLE, his or her role in the society and at work, they recommend performing psychological evaluations in all patients with SLE on regular basis.

P79

Rehabilitation in rheumatology in the era of biological therapy

Márta Király, Judit Ortutay
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Chronic inflammatory rheumatic diseases have a long-term influence on health-related quality of life. They do not only need treatment for the medical consequences, but also for the psychological, social and economical consequences. The main role of rehabilitation is the improvement of quality of life in a multidisciplinary, client-centred, goal-directed and coping-oriented way. Rehabilitation techniques in rheumatology above medication are joint protection, physiotherapy, occupational therapy and psychological therapy. Measurement of health-related quality of life can be performed by different generic and specific questionnaires. With the spread of biologicals in the treatment of chronic inflammatory diseases, activity limitation can be improved earlier. Beside controlling disease activity, prevention of limitation of motion and deformity as well as maintenance of participation remains authors main therapeutic goal. Aim of their study was to investigate the changes in the need for rehabilitation among patients with chronic inflammatory rheumatic diseases receiving biologicals.
Three patients with psoriatic arthritis (APS), six patients with rheumatoid arthritis (RA) and four patients with ankylosing spondylitis (AS) filled out the Medical Outcome Study Short Form (SF-36) and either the Health Assessment Questionnaire (HAQ) or the Bath Ankylosing Spondylitis Functional Index (BASFI) at the beginning and three, and six months after the beginning of anti-citokin therapy. Among the investigated 13 patients, 1 APS patient received physiotherapy and 1 AS patient was treated with analgesic infusion in their Department.
All scores measuring disease activity decreased significantly among the patients in the third and sixth month. Within SF-36 domains, physical function and body pain improved in the course of the therapy, while general health, social function, mental health and vitality remained slightly impaired.
However biologicals have recently substantially improved the outcome of chronic inflammatory rheumatic diseases, their positive influence on disease activity and joint function still requires physiotherapeutic strategies and rehabilitation in order to prevent restriction in participation and to achieve a better quality of life.

P80

Inpatient rehabilitation of musculoskeletal diseases in centres of the Austrian Pension Insurance Institution – data of outcome measurement

Werner Kullich[1], Rudolf Müller[2]
[1]LBG, Institute for Rehabilitation, Cluster Rheumatology, Balneology, Rehabilitation, Saalfelden, [2]PVA – Pension Insurance Institution, Vienna, Austria

Inpatient rehabilitation in patients with disorders of the musculoskeletal system includes multifactorial, multidisciplinary interventions. In the sector of medical rehabilitation, approaches to quality assurance can be done by evaluating the outcome of the specific rehabilitation programmes in special inpatient rehabilitation centres of the social securities. Outcome measurements are helpful for quality improvement in rehabilitation. The measurements of quality of life, disability, and pain are very important items for outcome presentation. With the aid of a special data entry system, data of 8 rehabilitation

centres of the Austrian Pension Insurance Institution PVA (Bad Aussee, Gröbming, Bad Hofgastein, Bad Ischl, Laab im Walde, Saalfelden, Bad Schallerbach, Weyer) were computerised online to a central server and, thereafter, evaluated by the Ludwig Boltzmann Institute for Rehabilitation (Saalfelden) by use of an appropriate statistic software. The recorded data of 404 patients at the beginning and after a three-week inpatient rehabilitation stay were evaluated. The focus was on the following parameters: a) Changes of pain intensity were measured using the visual analogue scale; b) The state of health was recorded by the SF-36 Health Survey Questionnaire; c) The Western Ontario and McMaster Universities Osteoarthritis Indeces (WOMAC) of all patients after knee or hip replacement (TEP) were evaluated; d) As well, the Health Assessment Questionnaires (HAQ) of patients with rheumatoid arthritis were analysed. The outcome measurement demonstrates that patients complete inpatient rehabilitation with a lowered pain level (reduction of VAS: 4.6 to 3.2 on average). It is of particular importance that osteoarthritis patients benefit from significant improvements of the WOMAC stiffness and physical function subscales during inpatient rehabilitation after knee or hip replacement (TEP). The SF-36 Health Survey shows great improvements in the physical sum scale as well as in the general state of health.

P81

Clinical characteristics of 97 patients with inflammatory myopathy

Cecília Varjú, Tünde Minier, Mónika Péter, Krisztina Parti, Gábor Kumánovics, Dániel Kehl, Tímea Berki, Diána Simon, László Czirják
University of Pécs, Hungary

Idiopathic inflammatory myopathies (IIMs) are systemic autoimmune diseases affecting skeletal muscles and are characterized by production of autoantibodies directed against various cell structures. Objective: to study clinical characteristics of IIMs comparing the Bohan and Peter classification with the latest clinicoserological classification of 97 Hungarian patients by determining the prevalence of myositis specific autoantibodies (MSA) and myositis associated autoantibodies (MAA).
Patients were evaluated from 1996 until 2009 using a standard protocol at study entry. Based on the presence of proximal muscle weakness, skin symptoms abnormal electromyography, muscle biopsy, and creatinine kinase elevation, the patients were divided in three groups (64 definite, 21 probable, and 12 possible IIM). The female/male ratio was 71/26. The mean (SD) age of the patients was 55.3 (13.5) years. The median duration (quartiles) of disease was 7 (4-11.5) years with a follow-up of 6 (3-9.5) years.
Out of the 97 patients 46 had interstitial lung disease (ILD) and 44 had arthritis. 11 patients developed myocarditis/pericarditis, 47 Raynaud's phenomenon. The CRP level was elevated in 18 cases. MSA and/or MAA autoantibodies were present in 66 patients (68%). Regarding MSA, anti-Jo1 (14%), anti-Mi-2 (12%), and anti-SRP (11%) antibodies were most frequently found. 13 out of the 18 patients with anti-synthetase (anti-Jo1 and anti-tRNAHis) antibodies had ILD. The 12 cases with anti-Mi-2 antibody formation were associated with dermatomyositis (DM) and with a monocyclic disease course. The 11 patients with anti-SRP antibodies did not show any definite disease pattern. In MAA cases anti-Ro (23%), anti-U1RNP (12%), anti-Scl70 (9%), anti-La (8%), anti-Ku (5%), anti-Pm-Scl (4%), anti-centromere (2%), and the anti-RIB-P (1%) were detected. The anti-Ro positive patients characteristically had keratoconjunctivitis sicca, dry mouth and high ESR levels. According to the Bohan and Peter classification 25 patients had DM, 34 polymyositis (PM). The number of connective tissue disease associated overlap cases was 32 (18 systemic sclerosis, 5 systemic lupus erythematosus, 6 rheumatoid arthritis, 3 mixed connective tissue disease), and 6 patients had tumour-associated myositis (CAM). Using the clinicoserological classification 7 patients had "pure" DM, only 6 had "pure" PM, 78 had overlap myositis and 6 patients had CAM. Using Kaplan-Meier's method patients with "pure" DM or PM had a significantly better survival compared to cases with overlap myositis or CAM.
In the clinicoserological classification "pure" DM and PM cases showed a much better outcome than patients with overlap myositis or CAM. The clinicoserological classification together with the detection of autoantibodies are useful tools to define prognostic subsets and may help to choose adequate immunsuppressive treatment.

P82

Clinical characteristics of patients with immunodeficiency syndromes

Dóra Niedermayer, Gábor Kumánovics, László Czirják, Tímea Berki, Gábor Sütő
University of Pécs, Pécs, Hungary

Immunodeficiency disease is a heterogeneous group of disorders with recurrent respiratory tract infections and fever as the most common presenting finding frequently associated with defective immunoglobulin production. The disease starts between the 2nd and 3rd decade of life but symptoms occur many years prior to diagnosis. It may also present with autoimmune manifestations such as immune cytopenias or even systemic autoimmune diseases.
The objectives were to analyse the clinical characteristics of patients with adult immunodeficiency syndrome followed up at Rheumatology and Immunology Department, University of Pécs.
Ten patient's clinical and laboratory data were collected and analysed according to the following aspects:

clinical features, immunoserological changes, flow cytometry results, immunoglobulin levels.
7 out of ten patients were having recurrent severe sinopulmonary infections. 2 patients had underlying systemic autoimmune disease (SLE, Crohn's disease) and 1 patient had organ specific autoimmune disease (pernicious anaemia, autoimmune thyroid disease). B cell deficiency was found in seven patients, natural killer cell deficiency in six patients and decreased T cell count (CD3+, CD4+, CD8+) in four patients. Decreased immunoglobulin levels of all three subsets (IgA, IgG, IgM) were found in five patients, combined IgM and IgA deficiency in three patients and isolated IgA deficiency in two patients.
Patient with recurrent infections, fever and low immunoglobulin levels may need to be screened for an underlying immunodeficiency and immunologic abnormalities.

P83

Distinct phenotypes in mixed connective tissue disease: Subgroups and survival

Ágota Hajas[1], Péter Szodoray[2], Éva Zöld[1], István Csípő[1], Margit Zeher[1], Gyula Szegedi[1], Edit Bodolay[1]
[1]University of Debrecen, Hungary, [2]University of Oslo, Norway

Objective was to examine the autoantibody and dominant clinical symptoms cluster which characteristic the different phenotypes of MCTD.
The study contained 201 patients with MCTD. Five clinical parameters such as Raynaud's phenomenon, presence of absence of PAH, myositis, interstitial lung disease (ILD), erosive arthritis and two antibodies beside the anti-U1RNP, antiendothelial cell antibodies (AECA) and anti-CCP were selected for cluster analysis using K means cluster analysis methods.
The mean age of MCTD patients at the time of the investigation was 52.9±12.4 years and the mean follow-up of the disease was 12.5±7.2 years. MCTD patients were classified into 3 cluster groups. 'Cluster 1' included 77 patients, 'cluster 2' 79 patients, while 'cluster 3' 45 patients with MCTD. In 'Cluster 1' the prevalence of PAH (55.8%; $p<0.001$), Raynaud's phenomenon (92.2%; $p<0.001$), and livedo reticularis (24.6%, $p<0.001$) was significant higher than in cluster 2 and 3. In cluster 2, the incidence of ILD (98.7%; $p<0.001$), myositis (77.2%; $p<0.001$) was significant greater than that in cluster 1 and 3. In cluster 3 forty-two (93.3%) patients had erosive arthritis. Anti-CCP antibodies were present in 37 of 42 MCTD patients (88.0%) with erosions. PAH, angina, venous thrombosis was observed in 'cluster 1', and pulmonary fibrosis in 'cluster 2', musculoskeletal damage and osteoporotic fractures were most frequent in 'cluster 3'.
Cluster analysis is valuable to differentiate between various subsets of MCTD and is useful prognostic factors and disease course.

P84

About Wegener's granulomatosis: Results from a single centre

Anna Polgár, Gyula Poór, Emese Kiss
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Wegener's granulomatosis is a rare, ANCA positive vasculitis, involving upper and lower respiratory tract and kidneys. Based on its estimated 1/100 000 prevalence it may affect approximately 100 patients in Hungary.
Authors publish data of patients being under regular medical follow-up at their centre. Beside of 9 patients with definite Wegener's another 4 newly observed patients are under investigation at the time of abstract submission.
9 patients with established Wegener's showed diverse manifestations including paranasal involvement, more frequently mentioned in the literature, was found 5/9 cases. 5 patients' primary symptom was pulmonary involvement with coughing, only one of them had simultaneously upper and lower respiratory tract involvement. Pulmonary or paranasal sinus biopsy was done in 8/9 cases. One patient's main symptom was tracheal involvement, which leaded to subglottic stenosis, requiring therapeutic X-ray irradiation. She regularly needs endoscopic dilation therapy. Two patients had typical renal involvement (microhaematuria); in 2 others only light transient proteinuria was present. One patient suffered form iritis, one other from cutaneous ulceration and polyneuropathy. High titre c-ANCA was present in sera of 4 patients, p-ANCA in one. The diagnosis of 4 ANCA negative cases was confirmed by repeated biopsies. One patient developed psoriatic arthritis beside Wegener's. All of 9 patients were treated with cyclophosphamide (CYC), 5 according to Fauci schema, and 4 by Austin schema. 4 intravenous induction therapy and 2 oral CYC treatments are in process at the abstract submission date, showing good therapeutic response. One patient has long-time therapy-free remission after 6 years of CYC therapy. Two patients' CYC therapy was switched into azathioprine due to potential CYC-induced ovarian failure. One of them is in remission, but acquired severe respiratory tract infection (aspergillosis). The other has persistent disease activity, requiring rituximab, the off label authorization is in process.
Authors would like to draw attention to not always typical disease onset (some patients didn't have paranasal sinus involvement), some rare manifestations (subglottic stenosis). CYC treatment proposed effective, if not contraindicated. Accentuated attention has to be paid on infections, which might be severe, most often seen in respiratory tract.

P85

Formal pathogenesis of AA amyloidosis in rheumatoid arthritis

Miklós Bély[1], Ágnes Apáthy[2]
[1]Polyclinic of the Hospitaller Brothers of St. John of God, [2]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

AA amyloidosis (AAa) is one of the most insidious complications of rheumatoid arthritis (RA) and may furtively lead to death. The aim was to define the characteristics of AAa deposition in RA based on previous studies.
At the National Institute of Rheumatology 8083 patients died between 1970 and 1989, and among them 161 with rheumatoid arthritis (RA). AAa complicated RA in 34 (21.1%) of 161 patients. The existence and extent of amyloid A deposits in various organs, their incidence and severity in blood vessels of different size and tissue structures, furthermore the qualitative differences of amyloid A deposits were determined histologically, histochemically and by electron microscopic methods.
The rules of amyloid A deposition in RA: 1. Amyloidosis is a progressive, cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease. 2. Amyloid A deposition starts at the most common sites (the most frequently involved tissue structures) in the most frequently involved organ. 3. Frequency and severity of amyloid A deposition are different aspects of the same phenomenon usually running parallel to each other in different organs, in different blood vessels and in various tissue structures. 4. The rate (frequency, prevalence) and amount (quantity) of amyloid deposition are characterized (accompanied) by qualitative differences of deposited amyloid as well. 5. The early stage of amyloid deposition is characterized by minimal, loose, more soluble amyloid deposits. The later stages of amyloid deposition are characterized by massive, dense, less soluble amyloid deposits.
Only AAa is a direct complication of RA, but any type of amyloid deposits may also be present. All forms of amyloidosis connected to the circulation are systemic, and all forms of amyloidosis not connected to the circulation are isolated (localized). The rate and amount of amyloid deposits in various organs may be linked to the differences in blood supply per unit volume and influenced by the possible incidental elimination of deposited amyloid. The rate and amount of localized amyloid deposition is basically determined by the local production of amyloid precursors, by the length of time and by the possible elimination of deposited amyloid.

P86

High prevalence of amyloidosis AA in patients with adult onset Still's disease

Arkadiusz Chlebicki[1], Bożena Kowalewska[1], Eliza Roszkowska[1], Renata Wojtala[2], Piotr Wiland[1]
[1]Academic Clinical Hospital Wrocław, [2]Medical University, Wrocław, Poland

Adult onset Still's disease is systemic inflammatory disease characterised by fever higher than 39 °C, rash, arthritis, and multiorgan involvement like splenomegaly, hepatomegaly and lymphadenopathy. Amyloidosis AA is a progressive and fatal complication of chronic inflammatory diseases. The aim of this study was to assess the presence of amyloid fat deposits (AFD) in abdominal fat aspiration (AFA) in patients with adult onset Still's disease.
11 patients (4 males, 7 females) with adult onset Still's disease referred to the Department of Rheumatology in Wroclaw were studied regardless of duration of disease or laboratory abnormalities. Abdominal subcutaneous biopsy was performed and samples of fat tissue was stained with alkaline Congo red and examined by polarized light microscopy. Confirmation of AA-type was achieved in all patients immunohistochemically, using specific antibodies to AA protein. Laboratory findings such as ESR, CRP, serum creatinine level were compared using U-Mann-Whitney test in group with AFD and group without AFD.
Amyloid fat deposits were found in 7 (63,6%) patients (2 males, 5 females). Authors did not find any significant differences in laboratory findings such as ESR (44,71±38.16 mm/hour vs 13.0±6.98 mm/hour), creatinine serum level (0.89±0.1 mg/dl vs 0.88±0.15 mg/dl), between patients with and without AFD. The level of serum CRP was significantly higher in the group with AFD (66.06±59.61 mg/dl) than the group without AFD (16.86±27.44 mg/dl) (p=0.09, Z=1.70).
They found a very high prevalence (63,6%) of adult-onset Still's disease patients with amyloid fat deposits. The obtained results showed that high serum CRP level predisposed to progress of amyloidosis AA.

P87

Pregnancy in patients with systemic connective tissue diseases. Results of two-years study

Dana Tegzova[1], Katerina Andelova[2], Ivana Kucerova[2]
[1]Charles University, [2]Institute for the Care of Mother and Child, Prague, Czech Republic

The goal of the current project was to investigate the course of pregnancy in 93 patients with systemic connective tissue diseases in years 2007–2008, to describe them by type and severity and to explore their relationship with specific characteristic.
Pregnant women with systemic connective tissue diseases were evaluated every 3 months by a rheumatologist and gynaecologist. During clinical evalua-

tion, the basic demographic data were reviewed as well as the duration and type of immunosuppressive agent, corticosteroid dose, presence of autoantibodies, presence of organ involvement and its activity, the number and type of disease flares, thrombosis, the number of abortions and premature labours, newborn weight and presence of complications as gestational diabetes, hypertension and preeclampsia.
The followed group of 93 patients consisted from 36 patients with systemic lupus erytematodes (SLE), 18 with rheumatoid arthritis (RA), 6 with primary Sjögren's syndrome (SS), 3 with scleroderma,1 with dermatomyositis, 1 with Wegener's granulomatosis, 2 with spondyloarthritis ankylosans, 9 with primary antiphospholipid syndrome, 17 with undifferentiated connective tissue disease (UCTD).65 patients were treated with oral corticosteroids, 4 with cyclosporin A and 2 with azathioprin, 18 with low molecular weight heparin and/or salicylates. During the years 2007–2008 62 patients delivered, 12 of them delivered before 37th week of pregnancy. AV heart block was in 2 newborns. No congenital malformations were observed in this group. Authors found the higher number of gestational diabetes (GDM)-28 pregnancies were complicated by GDM (all GDM in corticosteroid treated group). Hypertension and preeclamsia complicated 22 pregnancies (l4 of them were SLE pregnancies with history of renal complication of SLE). 5 pregnancies were terminated in the first trimester for missed abortion. They found 4 abortions in second trimester (all 4 cases in patients with SLE with secondary APS). 15 patients were followed preconceptionaly.
In spite of the fact that systemic autoimmune diseases are connected to the risk for the course of pregnancy, the two years following showed the good pregnancy outcome in group of patients with several subtypes of systemic connective tissue diseases.

P88

Primary Sjögren's syndrome associated liver involvement

Gábor Sütő, Tímea Berki, László Pálinkás, Péter Németh, László Czirják
University of Pécs, Hungary

Liver involvement of primary Sjögren's syndrome is a common extraglandular manifestation. Some of these patients may have overlapping primary biliary cirrhosis (PBC) or autoimmune hepatitis (AIH). Citrate synthase is an ancient mitochondrial enzyme. Antibodies against citrate synthase may take part in the development of liver involvement of systemic autoimmune diseases.
Liver involvement was evaluated in 84 pSS patients (82 female, 2 male): the values of transaminase (AST, ALT) gamma-GT or ALP enzymes were rewieved. The sera of the patients were evaluated for antimitochondrial (AMA), anti-smooth muscle (SMA), anti-liver-pancreas (LP) and anti-citrate synthase autoantibodies. 24 patients had elevated enzyme activity associated with liver involvement. 2 had AMA and 4 had SMA antibodies. Anti-citrate antibodies did not associate with autoimmune liver diseases. The prevalence of PBC is 2.4%, AIH is 4.5% among pSS patients. Autoantibodies against citrate synthase do not seem to participate in liver damage associated with pSS.

P89

Muckle Wells syndrome in a Hungarian girl

Ilonka Orbán, Krisztina Sevcic, Emese Kiss
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Autoinflammatory diseases are a group of diseases caused by primary dysfunction of the innate immune system, characterized by recurrent attacks of fever, inflammation of serosal membranes, muscular, articular and cutaneous manifestations, high level of acute phase proteins, with absence of both autoantibody elevation and antigen-specific T-cells activation. CINCA/NOMID (Chronic Infantile Neurological Cutaneous and Arthropathy also called NOMID [Neonatal Onset Multisystem Inflammatory Disease], MWS (Muckle Wells), FCAS (Familial Cold Autoinflammatory Syndrome) are the Cryopyrin-Associated Periodic Syndromes (CAPS). They are a result of an autosomal dominant or de novo mutation of the cold-induced autoinflammatory 1 (CIAS-1) nod-like receptor 3(NLRP3) gene, on chromosome 1. These mutations result in inflammation driven by excessive production of the proinflammatory cytokine interleukin (IL)-1 beta. Biologic therapies that target interleukin (IL)-1 improve dramatically the symptoms. Objectives: The authors present the first confirmed MWS (T348) patient in the Hungarian population treated with canakinumab a fully humanised monoclonal antibody against IL-1 beta, a newly developed biologic therapy that has been approved for the treatment of CAPS in adults as well as children aged 4 years and older.
The 14 years old Caucasian female child had had recurrent migratory erythematous macules from the first day of her life. From seven months of age she had had relapsing episodes of high fever, weakness, abdominal pain, myalgia, arthralgias, arthritis of the hands, conjunctivitis, peri-orbital oedema, pharyngitis, headache, from two years sensorineural hearing loss. The attacks had come at irregular intervals and were accompanied by increased acute phase reactants. Additional chemistry, coagulation, complement,autoantibody investigations were negative. All bacterial and viral serologies were negative. PPD was non-reactive. There were not findings for malignant disorders. The family history was negative. At the patient with periodic fever that persisted with predictable course, molecular analysis of the CIAS1 gene demonstrated the T348 mutation. During childhood the girl had received long term NSAIDs, steroids, antibiotic treatments, but the periodic fever

syndrome persisted. After one dose 2 mg/kg of canakinumab administered as subcutaneous injection every 8 weeks had a complete response.
Although the patient showed characteristic clinical features of MWS, it was very difficult to find the right diagnosis. Sometimes still for the experts only the long term clinical observation help to differentiate it from systemic onset Juvenile idiopathic arthritis. The mutations determination of the cold-induced autoinflammatory (CIAS-1) gen confirmed MWS (T348) mutation. Canakinumab showed a rapid efficacy, the safety data are limited.

P90

Subcutan calcinosis: Case history

Angéla Fülöp, Bernadette Rojkovich
Polyclinic of the Hospitaller Brothers of St. John of God, Budapest, Hungary

Subcutan calcinosis significantly reduces the quality of life of patients, not only by producing cosmetic problems, local pain, movement restriction, but also by functional impairment which may be rather severe in certain cases. The treatment of subcutan calcinosis is a therapeutic challenge. The seronegativ polyarthritis of the 57 years old women began in 1999. A progressive, subcutan calcinosis proven by histology was recognized in 2003. On the basis of clinical symptoms (calcinosis, Raynaud's syndrome, sclerodactility, teleangiectasy), imunserology (negative anticentromer antibody) and radiological findings (calcinosis in hand and foot on X-Ray), authors diagnostised limited cutan systemic sclerosis (CREST syndrome). They did not find esophagus dysmotility, nor systemic signs. She was treated because of osteoporosis, too. For the 42 years old man, the progressive subcutan calcinosis began in 1995. CREST syndrome diagnosis was established in 1996 on the basis of clinical symptoms (calcinosis, Raynaud syndrome, oesophagus dysmotility, sclerodactility, teleangiectasy, polyarthritis) and laboratory signs (ESR: 70 mm/h, ANA 1:100: ++ speckled, RF negativity, anticentromer antibody positivity). He died because of hypostatical pneumonia secondary to immobilization due to an osteoporotic vertebral compression. Both patients were affected with osteoporosis, in spite of their younger age. Due to the small number of cases, to suggest the potential association between osteoporosis and subcutan calcinosis is not possible, however this question was raised and may be the object of further investigations. Surgical treatment of subcutan calcinosis executed in some cases was often followed by recidivism. Among calcium channel blockers, Diltiazem was found effective, sporadic case histories mention the use of colchicin and bisphosphonat. The therapy of subcutan calcinosis is not solved yet. Effective therapy for subcutan calcinosis needs further research.

P91

Diagnostic difficulties and therapeutic success in a case with primary central nervous system vasculitis

Edit Vereckei, Anna Bazsó, Gyula Poór, Emese Kiss
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Aim of the study to reveal the differential diagnostic difficulties of the rare isolated central nervous system vasculitis.
In the case history of the 35 years old male patient there were hypertension, hyperlipidemia and minor stroke with hemiparesis and dysarthria in 2001. In October of 2009 mental confusion, memory loss, and psychomotor slowing were detected. The computer tomography (CT) and magnetic resonance imaging (MRI) showed lesions mainly on the right side bifrontal and in the brain stem nuclei. Carotid stenosis there was not detected. The analysis of the cerebrospinal fluid showed intrathecal synthesis of IgG (index 1.06). With the exception of ANA, infect and immune serology were negative. Because of the suspicion of lymphoma the patient received treatment with high-dose intravenous methylprednisolone. Measured with Western blot immunoassay, the result of the 14-3-3 protein in the cerebrospinal fluid was not acceptable due to high level of proteins and red blood cells. The EEG pattern was normal, so the diagnosis of Creutzfeld-Jacobs disease could not either be confirmed or excluded. Despite of i.v. administered methylprednisolone, mannitol, pyracetam and s.c. LMWH therapy, the clinical improvement was slow and the MRI showed progression. A stereotactic brain biopsy was performed in the National Institute of Neurosurgery from the right frontal cerebral lobe. The histology revealed vasculitis in the cerebral parenchyma. The diagnosis was primary central nervous system vasculitis. No signs of vasculitis were detected in any other organs. Secondary forms – those are associated with infections or malignancy – could be excluded. Although, the corticosteroid treatment resulted in moderate clinical improvement, it was not sufficient enough, so cyclophosphamide therapy was applied monthly in 1000 mg per infusion tree times until now. The control brain CT showed remission.
The diagnosis of primary central nervous system vasculitis is still challenging. Clinical signs and symptoms are heterogeneous and not specific, therefore the diagnosis often delays. In this context, imagings, cerebrospinal fluid analysis, EEG, immune- and infect serology plays an important role in advancing the diagnosis. The most important diagnostic procedure is the brain biopsy.

P92

Scintigraphic, biochemical and clinical response to zoledronic acid treatment in patients with Paget's disease of bone

Judith Donáth, Gyula Poór
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Paget's disease of bone (PDB) is a focal disorder of bone remodelling characterized by increased osteoclast-mediated bone resorption. Zoledronic acid, a new generation of bisphosphonates was shown to inhibit bone resorption after a single 5 mg intravenous infusion. The aim of this study was to evaluate the early (up to 3 months) and late (at 24 months) scintigraphic, biochemical and clinical response to a single 5 mg infusion of zoledronic acid in patients with PDB. Blood tests were performed to measure levels of SAP in 43 patients (25 males, 18 females) with PDB (28 monostotic and 15 polyostotic), aged 42-89 years. Quantitative bone scintigraphy (QBS) was performed before and at 3 and 24 months after zoledronic acid infusion and the results were expressed as a ratio, obtained by comparing isotope uptake at an affected and an unaffected control site. Visual analog scale (VAS) were performed before, 3, 6, 12, 18 and 24 months after infusion. At 3 months after zoledronic acid infusion SAP levels were normalized in 38 cases out of 43 (88%). The SAP levels generally remained unchanged over the subsequent 21 months period. The infusion resulted in improvements measured on VAS scale in 39 cases out of 43 patients (90%). There were no significant correlation between the duration of the disease and the changes of SAP levels and the duration of the disease and the changes of VAS. QBS ratio changed significantly after zoledronic acid infusion ($p<0,001$). No significant changes from baseline were noted in either serum calcium or creatinine at 3 months. The most frequent side effect was flu-like syndrome, observed in 13 cases. In conclusion, single 5 mg infusion of zoledronic acid leads to a favourable clinical, biochemical and scintigraphic response in patients with Paget's disease of bone and there will be longer remission than that with other bisphosphonates.

P93

Undenaturated collagen type I. in the treatment of painful osteoarthritis of the knee

Roman Stančík[1], Jozef Rovenský[1], Jozef Zvarka[1], Maria Stancikova[1], Marian Hlavac[2], Vladimir Kubinec[2]
[1]National Institute of Rheumatic Diseases, Piešťany, [2]FDR Hospital, Banska Bystrica, Slovakia

Authors previous open clinical study in patients with osteoarthritis (OA) has shown that native, undenaturated type I collagen (COL-I) (dietary supplement Colafit made by Dacom Pharma, Czech Republic) is effective in the treatment of OA. The present randomized double-blind, placebo-controlled clinical trial evaluated the safety and efficacy of COL-I in the treatment of OA of the knee. The study conducted at 2 sites in Slovakia and enrolled 58 patients with painful knee OA (29 patients treated with COL-I and 29 patients with placebo) who satisfied radiographic criteria for knee osteoarthritis grade 2-3. Patients received either COL-I or placebo for 3 months, followed by an follow-up period of 1 month to determine the carry-over effects of the drug. The visual analogue scale (VAS), and WOMAC Index were evaluated at the beginning of the study and after 3 month's treatment and other 1 month follow-up.
The results indicate that COL-I treatment was effective resulting in significant reduction in the WOMAC score and VAS score from the baseline after 3 months treatment and after 1 months follow-up. Treatment with COL-I reduced the total WOMAC score by 38% as compared to 10% in placebo treated group and 37% vs 8% after 1 month follow up. COL-I treatment decreased VAS score by 41% after 3 month treatment vs 13% placebo and after 1 month follow-up 37% vs 11%. The incidence of adverse events was very low, similar in both COL-I and placebo groups.
Authors study showed that undenaturated collagen is effective in the treatment of painful OA of the knee.

P94

Effect of virgin olive oil phonophoresis on exercise-induced chondromalacia

Babak Nakhostin-Roohi[1], S. Bohlooli[2], F. Khoshkhahesh[3]
[1]Islamic Azad University-Ardabil Branch, [2]Ardabil University of Medical Sciences, [3]The University of Mohaghegh-Ardabili, Iran

The main purpose of this study was to evaluate effect of olive oil phonophoresis on female athletes' chondromalacia. Twenty-four female athletes suffered from chondromalacia participated in this study voluntarily. Patients were randomly assigned into olive oil (n=11) and piroxicam (n=13) groups. After filling WOMAC questionnaire, subjects were treated 12 sessions by olive oil or piroxicam phonophoresis. After 6 and 12 session physiotherapy, subjects filled questionnaire again.
There was significant reduction in symptoms of chondromalacia at the end of the therapy in both groups ($P<0.05$). In olive oil group, there was significant improvement in symptoms even after 6 sessions ($P<0.05$). There was no significant differences between groups in time series ($P>0.05$). May be owing to complex of anti-inflammatory and antioxidant agents, the effect of olive oil phonophoresis was faster than piroxicam.

P95

Significance of some oxidant and antioxidant enzymes in fibromyalgia

Daniela Cepoi-Bulgac
State Medical and Pharmaceutical University "Nicolae Testemitanu", Kishinau, Moldova

Despite the fact that significant research has been done in the field of fibromyalgia, many questions remain open.
Goals to study the relevance of some indices of oxidant and antioxidant systems in fibromyalgia and assess possible correlations between the tested indices and Tender Point Index.
30 patients with an established diagnose of fibromyalgia, based on ACR criteria were assessed according to a comprehensive plan, including some indices of the oxidant and antioxidant systems' activity, particularly: early, intermediate and late lipid peroxides (u/l), serum malondyaldehide (mkmol/l), serum total antioxidant activity (mmol/l), serum prooxidant activity (mkmol/l), superoxide dismutase (u/l), serum catalase (mkmol/l) and serum nitric oxide (mkmol/l). In an attempt to objectify the complaints of fibromyalgia patients, the Tender Point Index was used. To assess the relevance of these assays in fibromyalgia patients, a correlation analysis of performed.
Although most patients displayed some sort of abnormalities of the oxidant and antioxidant systems, not much of a correlation could be observed for most indices, except for nitric oxide, which proved to change most constantly with the higher values of Tender Point Index. However, the established correlation was of a second degree (0.47, $p<0.05$), and therefore is rather non-specific.
Although the results displayed a correlation of nitric oxide and higher values of Tender Point Index, the established correlation is quite unspecific and further analysis should be performed. Possibly, other fibromyalgia diagnostic tools should be used to assess the relevance of pro- and antioxidant systems' abnormalities in fibromyalgia patients.

P96

Direct costs of chronic low back pain in Austria

Ernst Wagner
RSKA der NOEGKK, Baden, Austria

Non-specific low back pain ranks on top of epidemiology statistics, with 1-year prevalences in industrialized countries ranging from 27–65%. Low back pain seriously impairs the quality of life of affected individuals and incurs substantial costs for society. The objective of this pilot study was to evaluate the direct costs of chronic non-specific low back pain in Austria.
Patients currently undergoing in-patient rehabilitation or out-patient treatment (physical therapy, balneotherapy) for chronic non-specific low back pain completed a specifically designed questionnaire on direct costs due to their condition in the past 12 months. 48 patients participated in the study.
Average direct costs per patient year as paid by the sick funds consisted of (1) medical costs (excl. in-patient rehabilitation): € 869 (highest cost factors: out-patient physical therapy: € 306; in-patient treatment: € 157); (2) in-patient rehabilitation: € 574; (3) non-medical costs, i.e., mainly household assistance and home adaptations: € 389; and (4) deductables and non-reimbursable medical costs: € 329. On average, patients had 2.7 co-morbidities (men: 2.2, women: 3).
This investigation confirms the high economic impact of chronic non-specific low back pain. Medical costs including in-patient rehabilitation amounted to € 1443, exceeding the costs of late-stage osteoarthritis (€ 1148per patient year). Considering its high prevalence (10% of adults), low back pain causes considerable costs for society. In-patient rehabilitation was the single most expensive direct cost factor. Future research will have to evaluate whether the results of this pilot study are representative of the entire population and to assess the long-term benefits of rehabilitative interventions. A remarkable finding was the high number of co-morbidities, which may explain the high utilization of health-care resources.

P97

National Health Service, insurance companies – from medical expert point of view

Krisztina Baraczka
Semmelweis University Budapest, Hungary

The aim of the present study was to investigate the proportion of rheumatologic diseases in Labour Court processes and proceedings for damages. According the new conception of National Health Service since 2008, beyond health deterioration, functional and working capacities are of great importance in Labour Court processes. Parallel with growing number of health and accident insurances, the number of proceedings for damages increase. Based on analysis of cases at law in years 2008–2009 established, those more than in 90% of Labour Court processes locomotor diseases are present. The mean age of the investigated persons varied between 40–50 years. Approximately in 15% of cases patients were underwent operation because of disc herniation. Neurological deficit was present only in 10%. Rehabilitation was performed nearly in all cases. It seems, that the basic problems are the insufficient number of proper working places, the over estimation of the role of operation and the real establishing of neurological deficits. Professional protocols concerning the treatment and rehabilitation and teaching process of National Health Service participants are demanded. In cases of health and accident insurance the main problem was the presence several rheumatologic diseases before the

entering into contract. Approximately in 80% of cases presence of disease was established retrospectively. The protocol of required investigations is insufficient concerning the locomotor diseases. Labour Court and civil low processes shatter the physical and psychical conditions of patients and clients. Professional protocols, clear cut medical investigations and documentation is demanded.

P98

Self help groups for patients with arthritis/rheumatism in Hungary

Judit Ortutay
National Institute of Rheumatology and Physiotherapy, Budapest, Hungary

Self help groups are member-run support groups, where people facing the same situation come together regularly to help one another. In a wider aspect they have training, community building, lobbying activities, and they have bridge-building activities between patients and health care. The first group was Alcoholics Anonymous in Chicago in 1935, followed by European groups only after the second world war: Arthritis Care was the first group established for patients with rheumatic diseases in 1947. Recently the EULAR-PARE board coordinates the work of the national leagues. In their country the Association of Hungarian Rheumatologists founded its Social League in 1986, followed by the national umbrella organisation, the Hungarian League of Patients with Rheumatic Diseases in 1999, which is represented in the EULAR-PARE too. The most important activities are: patient education, by organising conferences, editing teaching booklets and a quarterly newsletter, supporting new self help groups, co-operation between support groups of other patients, e.g. the Hungarian League Against Cancer, lobbying, share information of national and international level. The main programs of the past ten years are reviewed, the Hungarian program of the first World Bechterew Day is presented. The greatest problem is to recruit volunteers for permanent work. A new homepage is under construction now, however the use of the web is not common among elderly people. Future plans and activities are listed, for reaching the main goal of the league: active work for minimizing the impairment, improving functioning and participation caused by arthritis/rheumatism.