ReumaBulletinen

TIDSKRIFT FÖR SVENSK REUMATOLOGISK FÖRENING · NUMMER 126 · 4/2018

Reumadagarna i Uppsala 2018
Program och abstracts

ReumaBulletinen

ReumaBulletinen är Svensk Reumatologisk Förenings tidskrift och utkommer med sju nummer per år

Ansvarig utgivare
Cecilia Carlens
Reumatologiska Kliniken
Karolinska Universitets-sjukhuset
171 76 Stockholm
Tel: 070-737 5390
cecilia.carlens@karolinska.se

Redaktör
Tomas Bremell
Reumatologi
Sahlgrenska Universitetssjh
Gröna Stråket 12
413 45 Göteborg
Tel 031-342 33 78
tomas.bremell@vgregion.se

Red.medlemmar
Bengt Lindell
bengt@lindell.cc
Milad Rizk
milad.rizk@ltv.se
Ioannis Parodis
ioannis.parodis@sll.se

Har du flyttat eller bytt mejladress?
Gör eventuella ändringar på: **www.svenskreumatologi.se** eller mejla till: **koordinator@svenskreumatologi.se**

Produktion
Mediahuset i Göteborg AB
Marieholmsgatan 10C
415 02 Göteborg
www.mediahuset.se
Tel 031-7071930

Annonser
Dan Johansson
dan@mediahuset.se
Olle Lundblad
olle@mediahuset.se

Layout
Eva-Lotta Emilsdotter
lotta@mediahuset.se

Tryck
Åkessons - GPC Tryck
Emmaboda - Växjö

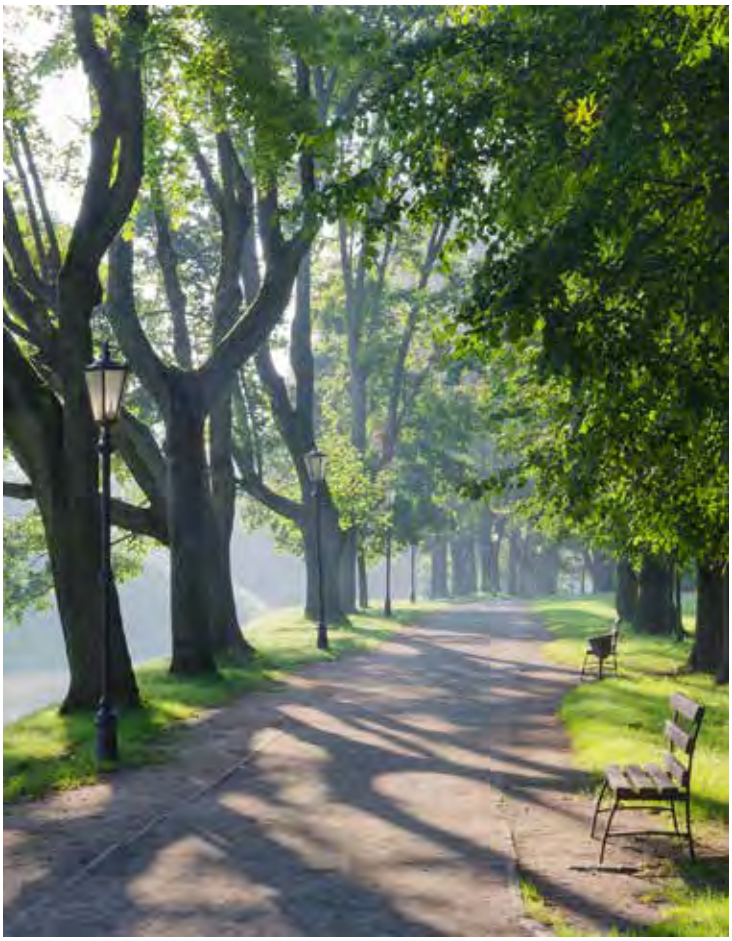
Distribution
Distribueras som posttidning
ISSN 2000-2246 (Print)
ISSN 2001-8061 (Online)

Utgivningsplan 2018

Nummer	Manusstopp	Utgivning
Nr 1 RB	1 februari	2 mars
Nr 2 RB Vetenskap	15 mars	18 april
Nr 3 RB	25 april	25 maj
Nr 4 RB	6 augusti	27 augusti
Nr 5 RB	22 september	25 oktober
Nr 6 RB Vetenskap	10 oktober	13 november
Nr 7 RB	10 november	14 december

Innehåll · 4/2018

3 Välkomna till Reumadagarna i Uppsala
4 Presentation av föreläsare
8 Årets värd - Akademiska Sjukhuset Uppsala, Reumatologsektionen
12 Uppsala akademiska reumatologiforsknings historia
15 Mötesprogram
18 Reumadagarna 2018 - Abstracts
58 Register - Abstracts
60 Reumakalender



Omslagsbild: Uppsala universitet

Välkomna till Reumadagarna i Uppsala

Vilken fantastisk försommar vi haft! Ofta är de vackra ljusa försommarkvällarna kyliga, men nu har vi fått njuta av ljusa och varma kvällar i över en månads tid. Jag läste nyligen i en av våra dagstidningar att sannolikheten för en så varm maj som vi haft i år är ca 2-3 på en miljon år i Sverige, så det gäller att glädjas i nuet.

I helgen ägnade jag ett antal timmar åt att läsa olika statliga utredningar och andra rapporter inför vårt och Reumatikerförbundets seminarium i Almedalen den 4 juli. Några av de utredningar och rapporter om vården som tagits fram senaste åren är Effektiv vård, En god och nära vård, En kunskapsbaserad och jämlik vård och Tillitsdelegationen. Utöver det finns tex SKLs rapport Intermountain Healthcare – styrning för kvalitet i ett högpresterande system och SKLs rapport Svensk sjukvård i internationell jämförelse 2018. Allt finns tillgängligt på internet. Det är intressant läsning som ger mycket att reflektera över. När ni läser detta har seminariet i Almedalen redan ägt rum, men läs gärna SRFs remissvar som löpande publiceras på hemsidan.

Den 19 till 21 september är det dags för årets Reumadagar i Uppsala. Som tidigare har SRFs vetenskaplige sekreterare, Per-Johan Jakobsson, hållit ihop planeringen av det vetenskapliga programmet tillsammans med professorskollegiet och kollegor från värdkliniken i Uppsala. Vice ordförande Lotta Ljung och förre vice ordförande Gerd-Marie Alenius har bidragit till att få ihop hela arrangemanget tillsammans med organisationskommittén från Uppsala, kongressbyrån MKON och de övriga arrangörerna. Programmet är imponerande.

”Värdkliniken bjuder på en spännande öppningsföreläsning”

Vi har tre temasymposier, den här gången med fokus på immunologi och genetik vid reumatisk sjukdom samt SLE. Bland annat kommer vi att få lära oss mer om hur behandling med check-point inhibitorer vid cancersjukdom kan leda till uppkomst av reumatisk sjukdom, ett område där vi inom reumatologin behöver vara med och förstå och lära hur vi bäst ska behandla dessa patienter. Föreläsarna är både inhemska och utländska experter inom sina respektive områden och vi är oerhörd glada att alla ställer upp och bidrar till att våra Reumadagar kan hålla en så hög vetenskaplig kvalitet.

På förmiddagen den 19 september är det tid för gruppmöten av olika slag och det officiella programmet börjar kl 11.30 med att Värdkliniken i Uppsala och Organisationskommittén hälsar oss välkomna. Efter lunch bjuder värdkliniken på en spännande öppningsföreläsning med titeln ”Hunden, hälsans bästa vän?”. Det ser jag särskilt mycket fram emot eftersom jag själv är rysligt allergisk mot hundar. För mig är hunden tyvärr inte min hälsas bäst vän, men det kanske den kan bli, eller är det för sent?

Liksom förra året har vi tre guldsponsorer. De står för var sitt symposium om RA, axial Spondylartrit respektive Psoriasisartrit. Jag kan glädjande konstatera att vi tillsammans med det tvärvetenskapliga programmet även i år täcker in stora delar av reumatologin under dessa tre intensiva och förhoppningsvis mycket lärande, inspirerande och nätverkande dagar. Vi ses i Uppsala! Varmt välkomna!

Cecilia Carlens
ordförande i Svensk Reumatologisk Förening
cecilia.carlens@karolinska.se

Antagna vid styrelsemötet 2018-05-23

Nya ordinarie medlemmar
Sofie Bergsten, Ljungsbro
Victoria de Porta, Östersund
AnnaCarin Horne, Sollentuna
Elisabeth Skoglund, Uppsala
Magnus Wieslander, Sundsvall

Nya associerade medlemmar
Vasiliki Boukovalas Jansson, Skövde
Linnea Lönn, Uppsala

Presentation av föreläsare

Så är det Uppsalas tur att vara värd för årets reumadagar som går av stapeln 19-21 september. Liksom förra året består SRF programmet av tre sessioner som avhandlar nyheter inom reumatologisk sjukdom och immunologi, reumatologisk sjukdom och genetik samt en session om SLE. Till detta hör guldsponsorernas lunch- och frukostsymposier som berättar om RA, axial SpA och PsA.

Låt oss dock börja med presentation av årets Nanna Svartzföreläsare, Professor Merete Lund Hetland.

Meretes föreläsning inleds med en översikt av DANBIO registret och dess användbarhet som studierapporteringsformulär (eCRF) vid prövarinitierade kliniska studier samt dess betydelse för registerforskning. Detta följs av en översikt av pågående forskning inom RA som inkluderar prediktion av dosreduktion av antireumatiska läkemedel, biosimilarer samt motivationshöjande verktyg för träning.

Merete Lund Hetland - biografi

Professor Merete Lund Hetland is a professor at University of Copenhagen, Denmark, and a consultant at the Department of Rheumatology, Rigshospitalet, Glostrup, Denmark. Merete Hetland obtained her MD from the University of Copenhagen in 1988, and became a specialist in rheumatology in 2000. She received her PhD on the bone metabolism in male and female runners in 1997, and her DMSc in modern treatment strategies in rheumatoid arthritis in 2011, both at the University of Copenhagen. Since 2000, she has been responsible for the Danish nationwide clinical register for patients with rheumatoid arthritis (DANBIO) and since 2015 for the nationwide Danish Rheumatologic Biobank. Merete Hetland's current research focus is on inflammatory joint diseases, treatment strategies, predictors, RCT and observational studies. Over the years, Merete Hetland has worked as a personal investigator in multiple clinical trials of rheumatoid arthritis. She has delivered a variety of publications, including 194 manuscripts, eight book chapters and >300 abstracts, as well as given more than >120 lectures at national and international congresses and meetings.

Vi är väldigt glada att Merete kommer till reumadagarna i Uppsala och presenterar sin aktuella forskning. Låt oss fortsätta med de tre tematiska sessionerna:

Merete Lund Hetland, årets Nanna Svartzföreläsare

Temasymposium 1 - Reumatisk sjukdom och immunologi

Denna föreläsning inleds med att Professor Anna Rudin ger en översikt av biologiska anticancerläkemedel som aktiverar immunsystemet följt av föreläsare Laura Cappelli och fallrapport från inskickade abstracts.

Lauras föreläsning kommer att avhandla följande: "There is growing recognition of new autoimmune syndromes due to cancer immunotherapy. Immune checkpoint inhibitors (ICIs) have improved the prognosis for a variety of advanced stage malignancies. ICIs block T cell co-stimulation to enhance anti-tumor immune responses. Due to non-specific activation of T cells and concomitant inflammatory responses, ICIs can cause off-target tissue damage, known as immune-related adverse events (IRAEs). IRAEs with rheumatic phenotypes are being increasingly recognized, including inflammatory arthritis, sicca syndrome, myositis, and vasculitis. This lecture will describe the mechanism of action of ICIs and how they may cause IRAEs. We will discuss clinical presentation, diagnosis and treatment of rheumatic IRAEs. Additionally, we will evaluate the use of ICIs in patients with preexisting autoimmune disease and cancer, focusing on initial evaluation and monitoring while on immune checkpoint inhibitor therapy. "

Laura Cappelli, inbjuden föreläsare

Laura Cappelli - biografi

Laura Cappelli is an Assistant Professor in the Department of Medicine, Division of Rheumatology at Johns Hopkins School of Medicine and a member of the Johns Hopkins Arthritis Center. She attended the University of Pennsylvania for her Bachelor's and Master's degrees. She earned her MD at the Johns Hopkins University School of Medicine and completed internal medicine residency at Johns Hopkins Hospital. She completed her Rheumatology fellowship at Johns Hopkins in 2016 and joined the faculty. While she was in fellowship, she obtained a MHS in Clinical Investigation from the Johns Hopkins Bloomberg School of Public Health. Her main research and clinical interest is rheumatic disease occurring after cancer immunotherapy. She also cares for patients with all types of inflammatory arthritis and performs clinical and translational research in rheumatoid arthritis. She has published 15 peer reviewed articles in the areas of cancer immunotherapy induced disease and rheumatoid arthritis. She chaired the first study group at the American College of Rheumatology meeting on immune related adverse events due to cancer immunotherapy and has given lectures nationally and internationally on this topic.

Temasymposium 2 - Reumatisk sjukdom och genetik

Denna föreläsning inleds av Professor Lars Rönnblom med en introduktion av reumatologisk genetik och DISSECT-projektet. Detta följs av inbjuden föreläsare Johanna Dahlqvist som presenterar aktuell forskning inom genetik och ANCA-associerad vaskulit, varefter Gunnel Normark presenterar genetik inom Sjögren följt av ett patientfall inom SLE.

Johannas föreläsning har titeln "Hur kan vi förbättra diagnostiken och behandlingen av patienter med ANCA-associerade småkärlsvaskuliter (AAV)" AAV är ovanliga men allvarliga autoimmuna sjukdomar där nuvarande behandlingsarsenal är begränsad och ospecifik. För att kunna förbättra behandlingen behöver vi öka kunskapen

Johanna Dahlqvist, inbjuden föreläsare

om de molekylära processer som initierar och underhåller AAV. Vi har startat ett nordiskt samarbete som i ett första steg syftar till att i detalj kartlägga genetiska faktorer som påverkar sjukdomsprocessen vid AAV. I nästa steg kommer effekten av de genetiska varianterna att studeras på molekylär och cellulär nivå, så att vi därigenom får en bild av vilka molekylära nätverk som är inblandade i patogenesen vid AAV och hur dessa kan manipuleras i behandlingssyfte. Tack vare vårt nordiska nätverk som består av 10 olika centra har fler än 1100 patienter inkluderats i projektet. Förutom DNA-prover har omfattande kliniska data insamlats för alla patienter, vilket ger oss den unika möjligheten att identifiera samband mellan sjukdomsmanifestationer hos den enskilda patienten, individens genetiska predisposition och de molekylära processer som pågår i immunförsvaret.

Johanna Dahlqvist - biografi

Johanna Dahlqvist genomgick läkarutbildningen vid Uppsala universitet (UU) och disputerade sedan där inom ämnet Klinisk genetik 2011. Sedan 2013 kombinerar hon en tjänst som ST-läkare vid Enheten för reumatologi på Akademiska sjukhuset med en tjänst som forskare vid Inst. för medicinsk biokemi och mikrobiologi vid UU där hon leder ett projekt rörande genetiken bakom ANCA-associerade vaskuliter. Sedan 2016 har Johanna Dahlqvist uppehåll från dessa tjänster för en post-doc-period vid Broad Institute of MIT and Harvard i Cambridge, USA. Hennes forskningsprojekt där fokuserar på reglering av gentranskript associerade med autoimmuna sjukdomar.

Temasymposium 3 - SLE

Denna föreläsning inleds av Professor Elisabet Svenungsson med föredraget ”APS, sjukdomsmekanismer och praktisk handläggning” följt av Dr Dag Leonard´s föreläsning om kardiovaskulär sjukdom vid SLE. Sessionen avlsutas med ”Nya behandlingar vid SLE” av Professor Anders Bengtsson.

Guldsponsorernas symposier

SRF är väldigt glada för det viktiga stöd vi får från våra guldsponsorer och inte minst de tre symposierna som anordnas av företagen och inskickade abstracts.

Lunchsymposium av BMS: RA

Ever more autoantibodies in RA – why you should care – By Dr Diane van der Woude

Synopsis

Rheumatoid factor, antibodies to citrullinated proteins, antibodies to carbamylated proteins, antibodies to acetylated proteins... what do they mean for your patient with rheumatoid arthritis? Is it useful to measure them? And might changes in levels predict treatment outcomes?

This presentation will share the latest insights on new autoantibodies in rheumatoid arthritis. In the past years, several new autoantibodies directed against post-translational modifications have been described in RA. Much progress has been made and basic, translational and clinical studies have shed more light on their role in RA. These autoantibodies are a potent prognostic marker when it comes to the risk of developing RA, and play a key role in current pathophysiological hypotheses. Especially the strong association between autoantibodies and genetic and environmental risk factors is intriguing and has fuelled new ideas of how RA might develop. The latest concepts of how these autoantibodies contribute to disease onset will be discussed, along with the implications for autoantibody testing in everyday clinical practice.

Kort presentation av Diane van der Woude

Diane van der Woude is rheumatologist at the Leiden University Medical Center and Head of outpatient department. Her research interests include Rheumatoid arthritis; Autoimmunity; Autoantibodies and Risk factors for autoimmune disease. She is the authors of 54 journal articles and holds several grants awards.

Dr Diane van der Woude

Frukostsymposium av NOVARTIS: axSpA

AxSpA - inside and out - a journey from inflammation to structural damage and clinical symptoms by Professor Rik Lories

Synopsis

New bone formation potentially leading towards ankylosis of the sacroiliac joints and the spine is the main type of structural damage to the skeleton that characterizes axial spondyloarthritis. New data from animal models, from imaging and patient cohort studies support the view that sustained suppression of inflammation by therapeutic interventions is able to slow down the ankylosis process, at least in a large proportion of the patients. Although specific growth factor molecular signaling pathways are key to drive the progenitor cell differentiation process that leads to ankylosis, inflammation plays an important role, most likely in combination with biomechanical factors, in both the onset and progression of disease. Therefore, early and effective treatment strategies and smoking cessation are important in daily patient management, in particular in those individuals at risk to develop progressive ankylosis. Whether different treatment strategies will have distinct effects on ankylosis, should be further explored.

Kort presentation av Rik Lories

Rik Lories directs the Laboratory for Tissue Homeostasis and Disease that is part of the Skeletal Biology and Engineering Research Center at KU Leuven. He is a consultant physician in the Division of Rheumatology at the University Hospitals Leuven. KU Leuven, the largest and oldest university in Belgium, ranks 40th in the Times Higher Education World 2017 Ranking and tops Reuter’s 2017 ranking of Europe’s most innovative universities.

His research focuses on endogenous tissue responses in the joint with specific attention towards translational questions in

Professor Rik Lories

chronic arthritis, in particular osteoarthritis, axial spondyloarthritis, and psoriatic arthritis. Currently full Professor ("gewoon hoogleraar") at KU Leuven, he obtained his medical degree summa cum laude in 1996. He subsequently started specialty training in internal medicine and rheumatology. In 2003, he was certified as rheumatologist. In 2003 he also obtained a PhD in biomedical sciences at KU Leuven. He received PhD (4 years) and Postdoctoral fellowships (6 years) from the Flanders Research Foundation.

He has (co-)authored over 140 publications, including original research reports or reviews in Nature Medicine, Nature Communications, Journal of Clinical Investigation, PNAS, Nature Reviews Rheumatology, Osteoarthritis and Cartilage, Annals of the Rheumatic Diseases and Arthritis and Rheumatology.

Frukostsymposium av Eli Lilly: PsA
IL17 inhibition in PsA; Taltz, a new treatment option by Associate Prof. Peter Franz Peichl

Synopsis
I will present the clinical study program for Taltz (ixekizumab), a new treatment for psoriatic arthritis. Taltz is a humanized immunoglobulin G4 (IgG4) monoclonal antibody that with high affinity and selectivity binds with interleukin 17A (IL-17A) cytokine. The efficacy and safety of Taltz was established in two phase 3, randomized, double-blind, placebo-controlled trials involving >670 adults with active PsA. SPIRIT-P1 evaluated the efficacy and safety of Taltz in patients with active PsA who had never been treated with a biologic DMARD. SPIRIT-P2 evaluated the efficacy and safety of Taltz in TNFi experienced patients with active PsA who had failed one or two TNF inhibitors.

Results from both studies demonstrated that patients treated with Taltz achieved significant improvement in joint and skin symptoms. In both studies, the primary efficacy endpoint was the proportion of biologic-naïve and TNFi-experienced patients at 24 weeks achieving ACR20 response. In SPIRIT-1 58 % of patients treated with Taltz vs. 30 % for placebo achieved ACR20. In SPIRIT-2 53 % of patients treated with Taltz vs. 20 % for placebo achieved ACR20. Treatment-emergent adverse events in both studies were more frequent with Taltz than placebo. The majority of TEAE were mild or moderate in severity; <5% were rated severe.

Associate Prof. Peter Franz Peichl

Kort presentation av Peter Franz Peichl

- Associate Prof. Peter Franz Peichl, MD, MSc
- Medical degree University of Vienna for Internal Medicine and rheumatology/osteology
- MSc for Medical Oeconomics Danube University Krems 2005
- Associate Professor for clinical Immunology 2006
- From 1886 to 1992 LabHead and Senior Scientist Novartis Research Institute Vienna
- At this time (2018) 85 reviewed publication
- Since 2006 Chairman Dept of Internal Medicine & Competence Center for bone and joint disease Evangelisches Krankenhaus Vienna Austria and since 2018 Medical Director of Evangelisches Krankenhaus Vienna Austria
- Member of the German S3 guidelines for osteoporosis treatment
- Major research interest and achievements: clinical immunology and osteology.

Med dessa föreläsningar får vi en en spännande översikt över det reumatiska forskningsspektrat och till detta kommer såklart alla våra nationella abstracts som presenteras under postersessionen. Under året har vi räknat ihop tjugo nationella avhandlingar som försvarats och godkänts. Sessionen "Axplock avhandlingar" ger oss inblick i reumaforskarsverige. Till detta delas det ut stipendier och priser där mottagarna får möjlighet att kort berätta om sina projekt.

I det tvärvetenskapliga programmet kommer vi att lära oss mer om hur man kan arbeta vid övergången från barn till vuxen för personer med juvenila reumatiska sjukdomar. Teamet på Astrid Lindgrens barnsjukhus på Karolinska berättar om rekommendationerna från EULAR och PReS och hur de praktiskt arbetar med detta. Sessionen om systemsjukdomar kommer ge en allmän överblick från teamet om de många olika aspekter som vården behöver ta hänsyn till vid systemsjukdomar. Vad gäller familjeplanering/-bildning visar studier att personer med reumatiska sjukdomar upplever att de får olika och ibland motstridiga råd från reumatikervården. Sessionen med

Cecilia Fridén

inbjuden föreläsare Cecilia Fridén syftar till att öka kunskap om hur personer med reumatiska sjukdomar bör handläggas i vården före och under graviditet samt vid amning.

Kort presentation av Cecilia Fridén

Cecilia Fridén, leg fysioterapeut, lärare i idrott och svenska, docent vid Sektionen för fysioterapi, Karolinska Institutet. Anställd som FoU-chef på professions- och fackförbundet Fysioterapeuterna. Disputerade 2004 inom idrottsmedicin med avhandlingen "Neuromuscular performance and balance during the menstrual cycle and the influence of premenstrual symptoms". Har efter disputation och en post doc period i Boston forskat och undervisat inom fysisk aktivitet och träning vid olika diagnoser och tillstånd, bl a vid reumatisk sjukdom. Har även fortsatt att studera hur kvinnliga könshormoner och p-piller kan påverka fysisk prestation och risk för idrottsskada. Driver även en del pedagogisk forskning med inriktning mot interprofessionellt lärande. Är en av författarna till boken Graviditet, hälsa och träning. Kommer att föreläsa om graviditetens fysiologi kopplat till fysisk aktivitet och träning.

Per-Johan Jakobsson
Vetenskaplig sekreterare
per-johan.jakobsson@ki.se

Uppsala slott

SRF´s STYRELSE 2018

Cecilia Carlens
Ordförande
Reumatologiska Kliniken
Karolinska Universitetssjukhuset
171 76 Stockholm
Tel: 070-737 5390
cecilia.carlens@sll.se

Lotta Ljung
Vice ordförande
Reumatologkliniken
Västerbotten
Norrlands Universitetssjukhus, 901 85 Umeå
Tel: 090-7851374
lotta.ljung@vll.se

John Svensson
Facklig sekreterare
Reumatologenheten
Sundsvall
851 86 Sundsvall
tel vx 060-18 10 00
john.svensson@lvn.se

Elisabet Lindqvist
Kassör
Sektion reumatologi
Skånes Universitetssjukhus
221 85 Lund
Tel: 046-17 16 19
elisabet.lindqvist@skane.se

Per-Johan Jakobsson
Vetenskaplig sekreterare
Reumatologiska Kliniken
Karolinska Universitetssjukhuset
171 76 Stockholm
Tel: 08-517 700 00
per-johan.jakobsson@ki.se

Katarina Almehed
Utbildningsansvarig
Reumatologi/Sahlgrenska Universitetssjukhuset
413 45 Göteborg
Tel: 031-342 10 00 vx
katarina.almehed@vgregion.se

Ylva Borgas
Ledamot, yngreläkarrepresentant
Reumatologkliniken
Sektionen Reumatologi
Skånes Universitetssjukhus
205 02 Malmö
Tel: 040-332489
ylva.borgas@skane.se

Årets värd för reumadagarna

Det är snart dags för Reumadagarna i Uppsala. Intresset för konferensen är stort och väntas locka över 500 deltagare. Vid öppningsföreläsningen är hunden i fokus. En ny svensk studie vid Uppsala universitet som visar att hundägare har en lägre risk för hjärt-kärlsjukdomar kommer att presenteras. På värdsymposiet kommer D-vitamin att diskuteras: hur hälsosamt är det egentligen med tillskott av ”solvitaminet”?

Några av Reumatologsektionens medarbetare: ST-läkare Elisabeth Skoglund, sektionschef Johan Back, överläkare Gunnel Nordmark, överläkare Ann Knight och ST-läkare Ioanna Giannakou.

Det är en hektisk dag vid Reumatologsektionen på Akademiska sjukhuset. Flera medarbetare är lediga för att delta på EULAR-kongressen (European League Against Rheumatism) i Amsterdam. Mellan patientmöten och andra åtaganden hinner några av klinikens medarbetare ändå samlas en kort stund i lunchmatsalen för att berätta om värdskapet inför årets Reumadagar.

– Precis som tidigare år har programmet en bred ansats. Samtidigt har vi försökt att lyfta fram profilområden som är typiska för Uppsala och den forskning vi bedriver här, säger Ann Knight, överläkare och docent vid Reumatologsektionen.

Hon ingår i den lokala programkommittén tillsammans med Johan Back, överläkare och sektionschef, Gunnel Nordmark, reumatolog, överläkare och docent, Eva Baecklund, överläkare och lektor samt Lars Rönnblom, överläkare och professor.

Hundägare friskare?

Onsdagens öppningsföreläsning ”Hunden, hälsans bästa vän” hålls av Tove Fall, veterinär och docent i epidemiologi vid institutionen för medicinska vetenskaper vid Uppsala universitet. Hon kommer att presentera en ny studie som tittat på sambandet mellan hundägande och hjärt-kärlhälsa hos över 3, 4 miljoner svenskar mellan 40- och 80 år. Resultaten visar bland annat att hundägare har en lägre risk att dö (oavsett orsak), men också att drabbas eller dö av hjärtkärl-sjukdom. Resultaten är särskilt intressanta då det sedan tidigare är känt att personer med RA (reumatoid artrit) har en ökad risk att utveckla eller dö i hjärtkärl-sjukdom.

Vid värdsymposiet på onsdag eftermiddag kommer professor Håkan Melhus att diskutera D-vitaminets betydelse och hur hälsosamt det är med tillskott av ”solskensvitaminet”. Livsmedelsverket har beslutat att fler livsmedel ska berikas och nivåerna i mjölk och matfett fördubblas.

– Men beslutet är kontroversiellt och forskare och läkare är inte överens, säger Ann Knight som ska moderera symposiet.

På torsdagen hålls två temasymposier. Ett handlar om ”Immune checkpoints and rheumatic disease”. Checkpointhämmare är cancerläkemedel som har en avgörande betydelse vid framförallt cancerformen malignt melanom och lungcancer. Läkemedlen stimulerar immunförsvaret och ser till att tumörer kan bekämpas mer effektivt. Bland biverkningar av dessa läkemedel har noterats autoimmuna symptom, inklusive reumatiska sjukdomar, säger Ann Knight.

– Vi reumatologer kommer att möta patienter som drabbats av reumatiska symtom efter behandling med dessa nya läkemedel

DISSECT-projektet

Vid det andra temasymposiet som handlar om reumatisk sjukdom och genetik kommer professor Lars Rönnblom att berätta om DISSECT-projektet (Dissecting disease mechanism in three systemic inflammatory autoimmun diseases with an interferon signature). Projektet, som är ett internationellt samarbete kring sjukdomarna SLE, Sjögrens syndrom och myosit, syftar till att försöka förstå orsaker och sjukdomsprocesser samt likheter vid dessa tre sjukdomar.

Gunnel Nordmark kommer att berätta mer om sin forskning ”Två varianter av Sjögren baserat på genetik och klinik”.

– Jag ska presentera forskningsresultat som visar att de ärftliga variationer vi har hittat delar in Sjögrens syndrom i två skilda grupper med olika sjukdomsbild och risk för utveckling av hjärtkärlsjukdom.

Utmsyckning i sjukhusets korridor

Det tredje temasymposiet behandlar SLE och antifosfolipidantikroppssyndrom (APS) (), en sjukdom som ofta är kopplad till SLE. APS leder till blodproppar i vener eller artärer och kan även ge upphov till upprepade missfall. Symposiet tar även upp kardiovaskulär sjukdom samt nya behandlingar vid SLE.

– Programmet erbjuder också två intres-

santa frukostsymposier som handlar om Axial Spondyloarthritis (axSpA) samt om nya behandlingsmöjligheter vid psoriasisartrit, säger Ann Knight.

På det sociala programmet är kongressmiddagen planerad till Rikssalen på Uppsala slott. Slottet började att byggas 1549 och ingick i den serie av borgar som Gustav Vasa och hans söner lät uppföra. På slottet har inte bara festligheter ägt rum, här begicks Sturemorden och flera för Sverige avgörande beslut har fattas här, bland annat att Sverige skulle delta i 30-åriga kriget, och drottning Kristina beslutade 1654 att abdikera från sin tron.

– Årets SRF-middag kommer att hållas på torsdag i orangeriet i Botaniska trädgården, säger Gunnel Nordmark.

Huset som orangeriet ligger i kallas Linneanum och invigdes 1807, till hundraårsminnet av Carl von Linnés födelse. Kvar från Linnés tid är bland annat Linnélagrarna, fyra av Carl von Linnés lagerträd som odlats i jättebaljor i 250 år.

På fredag vid lunchtid avslutas årets Reumadagar med en högtidsföreläsning av professor Merete Hetland till minne av Nanna Svartz.

Reumatologsektionen

När Akademiska sjukhuset i Uppsala invigdes 1876, var det ett av de modernaste i Norden. Mycket har hänt och det har åter blivit dags att modernisera sjukhuset. Sedan 2014 pågår ett omfattande nybyggnations- och utbyggnadsprojekt som förväntas vara klart 2023.

Sedan mars i år har sjukhuset även en ny sjukhusdirektör, Eric Wahlberg, specialist i kärlkirurgi och adjungerad professor. Han har bland annat varit centrumchef vid Universitetssjukhuset i Linköping och affärsområdeschef inom Praktikertjänst.

”Vi försöker verkligen arbeta i team och ingen fråga är för dum för att ställas”

– Sjukhuset har också varit med om en omfattande omorganisation och för två år sedan gick vi från att vara ett eget verksamhetsområde till att ingå i en större sektion tillsammans med hud, venerologi, endokrinologi, gastroenterologi och njurmedicin, säger Johan Back, reumatolog, överläkare och sektionschef för reumatologsektionen.

Precis som många andra reumatologkliniker i landet kämpar även teamet i Uppsala med bemanningsfrågan; i samband med omorganisationen har ett par specialister slutat och det har varit en utmaning att rekrytera nya erfarna specialister.

– På ST-sidan har vi det betydligt lättare. Vi har fem ST-läkare och i oktober börjar ytterligare en ST. Det är förstås väldigt roligt att så många blivande specialister vill göra sin utbildning här, men samtidigt, kan arbetsbelastningen bli ganska tung då vi haft få specialister som också måste hinna med handledning och undervisning vid sidan av mottagningsverksamheten, säger Johan Back.

Även om det periodvis har varit tufft att helt klara målet för vårdgarantin, ser Johan Back nu en ljusning. Två nya specialister har rekryterats och förutsättningarna att klara det höga inflödet av remisser har förbättrats.

Akademiska sjukhuset är ett regionsjukhus och upptagningsområdet innefattar Dalarnas län, Gävleborgs län samt Södermanlands och Västmanlands län.

– Vi får in cirka 45 remisser per vecka och nu har vi endast några ströpatienter som vi inte klara inom vårdgarantins 90 dagar.

Reumatologsektionen är en förhållandevis liten klinik och det finns en stark sammanhållning med högt i tak, menar Johan Back.

– Vi försöker verkligen arbeta tillsammans i team och ingen fråga är för dum att ställas. Vi vänder och vrider på frågeställningar och ventilerar eventuella patientärenden på så kallade knäckronder som vi har tillsammans varje torsdag.

Nivåstrukturering

Bristen på vårdplatser är en annan utmaning. Reumatologsektionen har sju vårdplatser.

– Vi skulle behöva 10 platser, men vi saknar sjuksköterskor. Vi har inte heller våra egna vårdplatser, uppstår en tom plats kan den tas i anspråk av akutmottagningen. Så vi har både planerad och akut inläggning, vilket ibland kan ställa till det.

Innan vi skiljs åt hinner vi diskutera den pågående debatten kring nivåstrukturering och den högspecialiserade vården. Reumatologsektionen har föreslagit att Akademiska sjukhuset i Uppsala ska få bli en högspecialiserad enhet för ANCA-associerade vaskuliter samt för stamcellstransplantationer vid systemisk skleros.

Gunnel Nordmark menar att dessa diagnoser helst bör skötas på ett regionsjukhus.

– Jag tror att det är bra att samla patienterna till ett eller flera regionsjukhus där det finns en lång klinisk erfarenhet och kompetens att hantera dessa diagnoser som inte är så vanliga. Sedan vore det olyckligt om man koncentrerar dessa patienter till ett enda universitetssjukhus i landet. Då förlorar regionsjukhusen i kompetens. Dessutom skulle det också bli opraktiskt för patienterna. Vi väntar nu med spänning på den fortsatta utredningen.

Eva Nordin


Drottning Kristina.

POST CONGRESS

Ett sammanfattande möte från kongressen.
Kostnadsfritt för läkare, sköterskor och övrig vårdpersonal.

Post EULAR
10 sept 2018

Stockholm
Lokal:Scandic Continental

Inbjudan

Göteborg aug 2018

Regionalt möte
- En samling med kollegor och en sammanfattning från EULAR 2018, i Amsterdam.

Vi hälsar er hjärtligt välkomna till Post Congress EULAR i Stockholm den 10 sept 2018.

Datum: 10 sept, 2018
Tid: 17.30-20.00, följt av mingel och lättare förtäring
Plats: Scandic Continental Hotel, Vasagatn 22, Stockholm

Föreläsare:
Carl Turesson och Aikaterini Chatzidionysiou

Program

17.30-18.00	Samling, kaffe och smörgås
18.00-18.55	Föreläsningsdel 1: Highlights från EULAR
18.55-19.15	Kaffepaus
19.15-20.00	Föreläsningsdel 2: Highlights från EULAR
Ca 20.00	Avslutande mingelbuffé

Med förhoppning om en trevlig kväll!

Anmälan på www.mediahuset.se/calendar eller direkt via länken: www.mediahuset.link/EULAR-Sthlm
Du kan även scanna QR-koden med din mobil och komma direkt till anmälningssidan.
Ev frågor till kontakta Helen Semmelhofer, E-mail: helen@mediahuset.se, Telefon: 031-707 19 30, 0730-755 744

Mediahuset i Göteborg AB

Vi tackar våra utställare:

Pfizer abbvie AMGEN Bristol-Myers Squibb Celgene Lilly NOVARTIS Pfizer SANDOZ A Novartis Division SANOFI

Mötet arrangeras i enlighet med LERs regelverk avseende:
Programinnehåll, Inga sociala aktiviteter, Kostnad för måltider, Föreläsararvoden, Utställare kan ej påverka det vetenskapliga programmet.

Reumatologi i Uppsala och vid Akademiska Sjukhuset

Starten till den reumatologiska verksamheten i Uppsala kanske kan dateras till år 1700 då Samuel Skragge, Provincialmedicus i Västmanland, kom till källan vid Sätra och fann att vattnet var av sådan kvalitet att han beslöt att anlägga en hälsobrunn.

Den medicinska grunden för verksamheten var humoralpatologin, och patienterna uppmanades att dricka brunn för att komma i sunda vätskor. Sätra Brunn donerades 1747 till Uppsala universitet som successivt utvecklade verksamheten (fig. 1). En viktig anledning till att den medicinska vården utvecklades var att från 1753 enbart läkare från medicinska fakulteten vid Uppsala universitet var intendenter på Sätra brunn. Den siste läkaren vid brunnen från medicinska fakulteten i Uppsala var reumatolog och docent Ulla Lindqvist, men 1998 lämnade Uppsala Universitet helt verksamheten. Landstingen hade då successivt minskat remisserna till Sätra brunn och verksamheten passade heller inte heller in i universitetets övriga verksamhet. Under 1900-talet hade dock omfattande rehabiliteringsprogram utvecklats för bla reumatoid artrit och spondylartrit och många reumatiker har genom åren haft stor glädje av behandlingarna vid Sätra brunn.

Vid Akademiska sjukhuset bedrevs reumatologin länge inom ramen för medicinklinikens verksamhet och först på 1980-talet fick reumatologin en egen vårdavdelning och mottagning. Redan långt tidigare bedrev dock många kollegor i Uppsala forskning inom områdena inflammation och autoimmunitet och på ett förtjänstfullt sätt medverkat till reumatologins utveckling. Mest känd är kanske Robin Fåhræus (fig. 2) som beskrev blodsänkan i sin doktorsavhandling 1921. Robin Fåhræus gjorde en mängd upptäcker inom reologin och han kallades till en professur i patologisk anatomi vid Uppsala universitet 1928. För sina upptäckter var han nominerad till Nobelpriset i medicin ett flertal gånger, men erhöll aldrig priset. Han är dock för alltid förknippad med sänkningsreaktionen och SR är än idag ett av de vanligaste laboratorieproven som ordineras inom sjukvården. Alla reumatologer och deras patienter är intresserade av ”sänkan” och SR utgör som bekant en viktig komponent i DAS 28.

Fig 1a, b Sätra Brunn i slutet av 1800-talet.

Immunologin utvecklas

Under 1970 och 1980- talet utvecklades immunologin i Uppsala och flera forskare kom att arbeta med mekanismerna bakom autoimmunitet. Hans Wigzell ledde institutionen för immunologi vid biomedicinskt centrum (BMC) och flera av dagens professorer inom reumatologin fick sin forskarutbildning eller fördjupade sina immunologiska kunskaper i den stimulerande miljö som fanns vid institutionen. Lars Klareskog kom tidigt till ”immunologen” efter ett framgångsrikt avhandlingsarbete om HLA systemets uppbyggnad. Han påbörjade då de experimentella studier av mekanismerna bakom reumatoid artrit som senare utvecklades inom kliniken. Rikard Holmdahl var hans doktorand som sedan disputationen fortsatt med en djurexperimentell forskningslinje med fokus på mekanismerna bakom kronisk artrit. Lars Rönnblom var också doktorand vid institutionen och hade Gunnar Alm som handledare. I denna lilla forskargrupp var fokus interferonsystemets funktion, vilket vid denna tidpunkt uppfattades som udda bland de klassiska immunologerna. Intressant i sammanhanget är att Gunnar Alm bedrev storskalig produktion av interferon vilket gavs till patienter med maligna sjukdomar såsom neuroendokrina tumörer, myelom och leukemier vid Akademiska sjukhuset. Flera av de interferonbehandlade patienterna utvecklade autoimmun sjukdom och denna oväntade biverkan gav uppslaget till Uppsala klinikens framstående forskning kring SLE och interferonsystemet.

Första professuren i reumatologi och reumatologkliniken bildas

Uppsala kom att få en professor i reumatologi först 1991 då Roger Hällgren förord-

nades som professor i ämnet. Han hade ett brett intresse inom reumatologin och hans doktorander kom att studera olika aspekter av reumatoid artrit, spondylartrit, systemisk scleros och primärt Sjögrens syndrom. Sambandet mellan funktionen hos tarmens immunsystem och olika reumatiska sjukdomar intresserade särskilt Roger Hällgren och han utvecklade metoder att undersöka tarmens immunreaktivitet. Dagens högaktuella studier av sambandet mellan tarmfloran och de reumatiska sjukdomarna är på ett sätt en naturlig fortsättning av Rogers tidigare studier. Den kliniska verksamheten under 90-talet utvecklades parallellt med forskningen mot de reumatologiska systemsjukdomarna samtidigt som regionvården ökade. Reumatologkliniken blev 1997 en egen klinik med klinikchef som verksamhetsansvarig. Detta innebar att fler läkare kunde rekryteras och forskningen breddades. Den kliniska verksamheten utvecklades i takt med reumatologins framsteg, slutenvården krymptes till förmån för en expanderande öppenvårdsverksamhet och med större möjlighet att bedriva läkemedelsstudier och anställa forskningssköterskor. Efter flera omstruktureringar inom sjukhuset och med sammanslagningar av olika verksamheter ingår reumatologin sedan maj 2015 som en sektion i verksamhetsområdet Specialmedicin. Verksamheten leds nu av verksamhetschef Maria Lidén och sektionschef Johan Back. Fastän reumatologin relativt nyligen flyttat pågår nya diskussioner om ännu en flytt till sjukhusets pågående nybyggnadsprojekt. Trots flera omstruktureringar, orsakade av centrala beslut, har reumatologins kunna bibehålla en samlad väl fungerande verksamhet både inom slutenvård, dagsjukvård och mottagning, mycket tack vare en stabil och lojal medarbetarstab på alla nivåer. Vid enheten finns ca 60 medarbetare anställda och till kliniken är också rehab personal och medicinska sekreterare knutna. Av läkarstaben på 18 kolleger är 5 ST läkare och vi har just anställt ytterligare 2 ST. Som ST läkare hos oss finns goda möjligheter att tidigt involveras i olika forskningsprojekt men framför allt innebär vår väl sammanhållna, strukturerade verksamhet stora möjligheter att på kort tid se hela reumatologins bredd, att arbeta självständigt men med lätt tillgänglig handledning, både personlig och vid våra ”knäckronder”, veckans höjdpunkt för alla kolleger!

”Målsättningen är att identifiera nya terapeutiska målmolekyler för effektivare terapier”

Dagens forskning (fig 3, 4)
Forskningen vid reumatologkliniken i Uppsala har genom åren varit fokuserad på kliniska problem av stor betydelse för både patienter och sjukvård. Dit hör frågor om varför man drabbas av inflammatorisk reumatisk sjukdom och konsekvenserna av de olika sjukdomarna. Vår forskning är translationell där en långsiktig målsättning är att identifiera nya terapeutiska målmolekyler så att effektivare terapier kan utvecklas. Det faktum att flera av de kliniskt verksamma kollegorna i perioder arbetar vid vårt forskningslaboratorium har varit en viktig framgångsfaktor och gjort att både våra frågeställningar och forskningsmetoder varit relevanta. Den dramatiska utvecklingen av ny teknik och kunskap inom genetik och molekylärbiologi har vi utnyttjat, vilket gjort att vi inom några forskningsområden ligger i den internationella frontlinjen med många internationella samarbeten. I forskargruppen finns läkare, biologer, apotekare och civilingenjörer, där inte minst kompetens inom bio-informatik är ytterst viktig i dagens forskningsvärld med stora datamängder att hantera.

Ytterligare forskning med internationellt genomslag har varit Eva Baecklunds banbrytande studier av sambandet mellan inflammation och malignitet. I dessa omfattande epidemiologiska studier har hon elegant påvisat sambandet mellan höggradig långvarig inflammation och risken för lymfom hos patienter med reumatoid artrit. Dessa studier har haft stor betydelse för hur vi ser på läkemedelsbehandlingen vid RA och för användandet av och uppföljningen av biologiska läkemedel. De har också utgjort basen för ytterligare ett antal studier kring malignitet och andra reumatiska sjukdomar, bl a vid vår enhet.

Vi koordinerar flera forskningsnätverk inom landet och flera av dessa har en stark internationell förankring De viktigaste nätverken är det Svenska SLE-nätverket (koordineras av Lars Rönnblom), det Skandinaviska Sjögrennätverket (koordineras av Gunnel Nordmark), Skandinaviska nät-

Fig 2 Robin Fåhraeus (1888-1968) beskrev blodsänkan i sin avhandling 1921. En epokgörande upptäckt som gjorde att han nominerades till Nobelpriset i medicin.

Fig 3 Professor Lars Rönnblom, universitetslektor Eva Baecklund och professor Sule Yavuz på Rudbecklaboratoriet där forskargruppen i reumatologi har sitt laboratorium. Professor Yavuz från Istanbul är gästforskare i gruppen under ett år.

verket för genetiska studier av ANCA-associerade vaskuliter (koordineras av Ann Knight) samt Auto-Lymfom projektet (Koordineras av Eva Baecklund). För närvarande leder vi ett stort samarbetsprojekt mellan alla universitetskliniker i Sverige (Dissecting disease mechanisms in three systemic inflammatory autoimmune diseases with an interferon signature, DISSECT) som syftar till att klarlägga de biologiska sambanden vid SLE, primärt Sjögrens syndrom och myosit. I detta projekt ingår mer än 4000 patienter och kontrollpersoner. Allt detta arbete gör att vi har en bred kontaktyta inom reumatologin. Samtidigt tillhör forskargruppen i reumatologi en av de forskargrupper vid institutionen för medicinska vetenskaper som lyckats attrahera stora externa forskningsanslag.

Forskningsområden

SLE

Klinikens SLE-forskning leds av professor Lars Rönnblom som också är prefekt för Institutionen för medicinska vetenskaper. Forskningen berör mekanismerna för hur autoimmunitet uppstår och då särskilt interferonsystemets betydelse i både initiering av sjukdomen och dess progress. Dessutom studerar gruppen den genetiska bakgrunden till SLE och vi har bidragit till att mer än 35 av de idag identifierade riskgenerna för SLE har upptäckts i Uppsala. Vidare har kopplingen mellan riskvarianter av generna och olika kliniska manifestationer kartlagts där med dr Dag Leonard särskilt har fokuserat på de kardiovaskulära komplikationerna vid SLE.

Primärt Sjögrens syndrom

Docent Gunnel Nordmark koordinerar det Skandinaviska Sjögrennätverket med forskare från ett flertal centra i Sverige och Norge. Sjögrennätverket deltar även i det internationella samarbetet ”The Sjögren’s Genetics Network” – SGENE, där vi från Skandinavien har bidragit med den största patientkohorten. Från Uppsala leds studier av genetiska och epigenetiska förändringar med betydelse för sjukdomsutvecklingen och olika kliniska manifestationer. I samarbete med docent Eva Baecklund riktas ett särskilt intresse mot den genetiska bakgrunden till och mekanismerna för utvecklingen av lymfom hos dessa patienter.

Hematologiska maligniteter vid reumatisk sjukdom

Flera studier kring den ökade risken för lymfom och leukemi hos våra patienter med reumatisk sjukdom pågår. Docent Eva Baecklund är bland annat ansvarig för AUTO-LYMFOM studien där patienter med reumatisk sjukdom som sjuknar i lymfom inkluderas och blod och lymfomvävnad tillvaratas för vidare genetiska och molekylärbiologiska studier. Studien sker i samarbete med reumatologer och onkologer nationellt. Andra studier för att följa risk för lymfomutveckling efter behandling med biologiska läkemedel görs i samarbete med kollegor på Karolinska sjukhuset.

Systemiska vaskuliter

Docent Ann Knight koordinerar det nationella vaskulitnätverket. Projektet syftar främst till att utveckla bättre och mera kausal evaluering, prognostisering och behandling av vaskuliter. Detta ska åstadkommas genom att använda genetiska och kliniska data som markörer för svår sjukdom och recidivrisk hos patienter. Projekten är främst inriktade på de sk ANCA-associerade vaskuliterna: Granulomatös polyangiit, mikroskopisk polyangiit och Churg-Strauss syndrom (EGPA). Johanna Dahlqvist leder och koordinerar det skandinaviska samarbetsprojektet för djupgående genetiska analyser av ANCA-associerade vaskuliter.

Framtiden

Vid vår klinik finns ett stort forskningsintresse och en lång tradition av studier som klarlagt grundläggande sjukdomsmekanismer vid reumatisk sjukdom. Detta är en tradition vi gärna fortsätter. Dock är det så att dagens forskning kräver stora resurser, inte minst mot bakgrund av att den experimentella verksamheten fordrar många olika kompetenser och är dyr att bedriva. Dessutom krävs i nästan alla projekt stora och väl karakteriserade patientmaterial. Vi tror därför på ett fortsatt och utökat samarbete mellan de olika reumaenheterna i landet men också på ett fördjupat samarbete med de laboratorier som besitter särskild spetskompetens inom viktiga områden. Ett utökat samarbete mellan landets olika enheter i form av ”utbytestjänstgöring” vid våra olika forskningslaboratorier står högt på önskelistan så att vi alla breddar vårt kunnande. Dessutom gör det vårt arbete mycket roligare då just forskningssamarbeten svetsar oss samman omkring spännande upptäckter men också skapar personlig vänskap.

Lars Rönnblom
professor

Ann Knight
överläkare

Maria Lidén
verksamhetschef

Fig 4 En del av Uppsala teamet 2018. Bakre raden från vänster: Pascal Pucholt, Karin Hjorton, Lars Rönnblom, Sarah Reid, Alina Johansson, Niklas Hagberg. Främre raden från vänster: Maija Eloranta, Cane Yaka, Juliana Imgenberg-Kreuz, Gunnel Nordmark, Johanna Sandling, Anna-Maja Molin, Matteo Bianchi.

Mötesprogram

Onsdag 19 September

	Stora salen, plan 6	Sal B, plan 3
08.30-11.30	Tid för grupper	Fysioterapeuternas Precourse
11.30-11.45	Mötets öppnande. Kliniken och organisationskommittén hälsa oss välkomna till Reumadagarna!	
12.00-13.00		Lunchsymposium av BMS: RA
13.15-14.00	Öppningsföreläsning Moderator: Lars Rönnblom Hunden, hälsans bästa vän? - Tove Fall	
14.00-14.45	Värdsymposium Moderator: Ann Knight Vitamin D - ett helt solskensvitamin! - Håkan Melhus	
14.45-15.15	Eftermiddagsfika i utställningen	
15.15-16.30	**Stipendieutdelning** Celgene och SRF Eli Lilly och SRF Nanna Svartz - Reumatikerförbundet och Pfizer Tarkowskistipendium Presentation av guldsponsorer	
16.30-18	Tipsrunda och mingel med snacks i utställningslokalen	
19.00 --	Kongressmiddag på Uppsala Slott, Rikssalen	

Torsdag 20 September

	Stora salen, plan 6	Sal B, plan 3
07.45-08.45		Frukostsymposium av NOVARTIS: SpA
09.00-10.30	Temasymposium 1 - Reumatisk sjukdom och immunologi. Introduction to immune checkpoints - Anna Rudin Immuno-theraphy induced Rheumatic Disease- Laura Cappelli. Case: Immunerelated adverse event - a case from the clinic - Erik HellBacher	Familjeplanering Barnmorska Joanna Tingström Fysioterapeut Cecilia Friden Heka resan - Unga reumatiker Madeleine Beerman
10.30-11.00	Förmiddagsfika i utställningen, plan 2	
11.00-12.30	Temasymposium 2- Reumatisk sjukdom och genetik Introduktion reumatologi genetik och DISSECT-projektet- Lars Rönnblom Genetik och ANCA-Associaerad vasku-lit-Johanna Dahlqvist Två varianter av Sjögren baserat på genetik och klinik- Gunnel Nordmark	Systemsjukdomar Fysioterapi vid systemsjukdomar - Helene Alexanderson Omvårdnad vid systemsjukdom - Susanne Pettersson
12.30-13.15	Lunch, plan 2	
13.15-13.45	SRQ Vetenskap	
13.45-15.30	Postersession - Eftermiddagsfika i utställningen 6 bästa posters utses Foajén på plan 6	
15.30-17.00	Axplock avhandlingar Bästa abstracts	Avhandlingar Workshop Rehabmodulen
17.00-18.00	SRF:s Årsmöte Utdelning av årets ledstjärna och årets hedersmedlem	SveReFo Årsmöte
19.00	SRF-middag Botaniska Trädgården, Orangeriet	

Fredag 21 September

	Stora salen, plan 6	Sal B, plan 3
07.45-08.45		Frukostsymposium av Eli Lilly: PsA
09.00-10.30	Temasymposium 3 - SLE APS - Elisabet Svenungsson Kardiovaskulär sjukdom - Dag Leonard Nya behandlingar - Anders Bengtsson	Från barn till vuxna
10.30-11.00	Förmiddagsfika i utställningen, plan 2	
11.00-12.10	Nanna Svartz - föreläsning Merete Hetland Tack och välkommen 2019 till Falun	
12.10-12.30	Lunch Grab'n go	
12.10-15.30	Tid för grupper	

Reumadagarna 2018 - Abstracts

Välkommen till Reumadagarna i Uppsala. Reumaveckan/Reumadagarna arrangeras nu för femte gången - tidigare möten har hållits i Örebro, Halmstad/Tylösand, Umeå och Västerås.

Per-Johan Jakobsson
Vetenskaplig sekreterare, SRF

Artritsjukdomar

ABSTRACTNUMMER: 1463-A-1818 — 1

VITAMIN D IN INDIVIDUALS BEFORE ONSET OF RHEUMATOID ARTHRITIS - RELATION TO VITAMIN D BINDING PROTEIN AND ITS ASSOCIATED GENETIC VARIANTS

Mikael Brink[1], Linda Johansson[1], Evelina Nygren[1], Lisbeth Ärlestig[1], Johan Hultdin[2], Solbritt Rantapää-Dahlqvist[1]

[1]Folkhälsa och Klinisk Medicin/Reumatologi
[2]Medicinsk Biovetenskap/ Klinisk Kemi

Background
Vitamin D has been implicated as being involved in the aetio-pathogenesis of several autoimmune diseases including rheumatoid arthritis (RA). Previous studies present contradictory results. Vitamin D binding protein (DBP), the major transport protein, is also involved in various inflammatory processes. The aim of this study was to investigate the relationship between circulating levels of 25-hydroxyvitamin D [25(OH) D], DBP and polymorphisms in group-specific component (GC) in pre-symptomatic individuals and matched controls within prospective cohorts of the Northern Sweden.

Methods
Blood samples donated to the Medical Biobank prior to the onset of symptoms of RA (n = 515, mean [SD] time before the onset of symptoms 6.2 [9.3] years) and from matched (2:1) population-based controls (n = 267) were used. Plasma 25(OH) vitamin D levels were analyzed using liquid chromatography tandem-mass spectrometry and DBP levels were analyzed using enzyme-linked immunosorbent assay. GC polymorphisms (rs4588 and rs7041) were analyzed with TaqMan assays (Applied Biosystems).

Results
Levels of 25(OH) D or DBP were not statistically different between pre-symptomatic individuals and controls in a crude, or a multiple-adjusted logistic regression model. However, an increased risk for future RA was found in females of DBP (OR 1.0001 [95%CI 1.000-1.0003]), adjusted for carriage of the minor allele of rs4588, in a multiple-adjusted model ($p<0.05$).

Conclusions
This study indicated that vitamin D is not associated with the future risk of RA although increasing levels of DBP were however, associated with an increased risk of disease in females carrying the minor allele of a DBP encoding SNP.

ABSTRACTNUMMER: 1503-A-1818 — 2

EFFICACY AND SAFETY OF IXEKIZUMAB AT WEEK 52 IN BIOLOGIC NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS (SPIRIT-P1)

Vibeke Porsdal[3], Eric Lespessailles[6], Bruce Kirkham[4], Antonio Fernández Nebro[7], Ricardo Blanco[8], Christoph Strehblow[5], Jose Inciarte-Mundo[5], Vibeke Porsdal[5], Miriam García[5], Monika Kurzawa[5], Christophe Sapin[5], Piet Geussens[9], Philippe Goupille[2], Hasan Tahir[1]

[1] Barts Health NHS Trust, London, United Kingdom
[2] CHRU Tours, Tours, France
[3] Eli Lilly
[4] Guy's & St Thomas' NHS Foundation Trust and King's College, London, United Kingdom
[5] Eli Lilly and Company, Indianapolis, USA
[6] Hospital La Source, University of Orleans, Orleans, France
[7] Hospital Regional Universitario de Málaga, Málaga, Spain
[8] University Hospital Valdecilla, Santander, Spain
[9] University of Hasselt, Diepenbeek, Belgium

Background
Ixekizumab is a humanized monoclonal antibody, selectively targeting interleukin-17A with high affinity.At 24 weeks, ixekizumab was superior to placebo in achieving American College of Rheuma-

Table: Tabular results

	24 weeks (Double blind treatment period)				52 weeks (Extension period population)							
	Placebo (N=106)	ADA (N=101)	IXEQ4W (N=107)	IXEQ2W (N=103)	PBO/IXEQ4W (N=45)	ADA/IXEQ4W (N=49)	IXEQ4W/IXEQ4W (N=97)	Total IXEQ4W (N=191)	PBO/IXEQ2W (N=46)	ADA/IXEQ2W (N=48)	IXEQ2W/IXEQ2W (N=96)	Total IXE Q2W (N=190)
ACR20, %	30.2	57.4**	57.9**	62.1**	57.8	69.4	69.1	66.5	71.7	58.3	68.8	66.8
ACR50, %	15.1	38.6**	40.2**	46.6**	42.2	59.2	54.6	52.9	45.7	43.8	53.1	48.9
ACR70, %	5.7	25.7**	23.4**	34.0**	20.0	34.7	39.2	33.5	30.4	29.2	39.6	34.7
mTSS, LS mean CFB	0.49 (0.09)	0.10 (0.09)**	0.17 (0.08)†	0.08 (0.08)**	0.27 (0.8)	0.32 (1.0)	0.54 (2.1)	N/A	0.41 (0.8)	-0.03 (0.4)	0.09 (1.0)	N/A
DAS28-CRP, LS mean CFB	-0.8	-1.7**	-2.0	-2.0**	-1.9	-2.2	-2.3	-2.2	-2.1	-2.1	-2.4	-2.2
LEI (0), %[a]	19.3	33.3	42.6†	38.6‡	40.9	50.0	55.4	51.3	42.3	26.1	50.0	42.6
LDI-B (0), %[b]	25.0	77.8**	79.5**	76.9**	70.0	75.0	85.7	81.1	57.1	70.0	87.5	75.0
PASI75, %[c]	10.4	54.4**	71.2**	79.7**	61.3	64.7	78.8	71.0	65.5	66.7	81.8	73.5
PASI90, %[c]	6.0	36.8**	56.2**	67.8**	51.6	50.0	66.7	58.8	62.1	51.5	78.2	66.7
PASI100, %[c]	3.0	23.5†	42.5**	52.5**	48.4	35.3	56.1	48.9	44.8	45.5	67.3	55.6
SF-36 Physical component, LS mean CFB	2.9 (1.0)	6.8 (0.9)**	7.5 (0.9)**	8.2 (0.9)**	7.3 (9.6)	7.3 (7.7)	9.5 (9.5)	8.4 (9.1)	8.0 (8.5)	9.0 (8.8)	9.2 (9.4)	8.8 (9.0)
HAQ-DI MCID, %[d]	26.1	49.4**	49.0**	57.8**	43.2	60.5	57.1	55.0	40.0	47.6	57.1	50.6
%BSA, LS mean CFB[c]	-2.7 (1.4)	-9.5 (1.4)**	-12.0 (1.3) **	-10.6 (1.4)**								
Safety												

Original Ixek-00087335

TEAE, n (%)	50 (47.2)	65 (64.4) ‡	71 (66.4) †	67 (65.7) †	28 (62.2)	20 (40.8)	54 (55.7)	102 (53.4)	27 (58.7)	21 (43.8)	54 (56.3)	102 (53.7)
SAE, n (%)	2 (1.9)	5 (5.0)	6 (5.6)	3 (2.9)	1 (2.2)	5 (10.2)	4 (4.1)	10 (5.2)	1 (2.2)	1 (2.1)	0	2 (1.1)
Discontinued due to AE, n (%)	2 (1.9)	2 (2.0)	2 (1.9)	4 (3.9)	1 (2.2)	0	1 (1.0)	2 (1.0)	1 (2.2)	0	0	1 (0.5)

[a]Only patients with enthesitis and LEI >0 at baseline were included in the analysis.
[b]Post hoc analysis. Data are reported for patients with dactylitis, as qualitatively assessed by the investigator, at baseline and baseline LDI-B score >0.
[c]Data are reported for patients with baseline psoriatic lesion(s) involving ≥3% BSA.
[d]MCDI ≥0.35 improvement from baseline; only patients with a baseline HAQ-DI score ≥0.35 were included in the analysis.
†p≤.01 vs placebo; ‡p≤.025 vs placebo; §p≤.05 vs placebo; **p≤.001 vs placebo; ACR20=Americal College of Rheumatology 20% response; LEI=Leeds Enthesitis Index; LDI-B=Leeds Dactylitis Index-Basic; LS mean CFB=least-square mean change from baseline; mTSS=modified Total Sharp Score; SAE=serious adverse event; TEAE=treatment-emergent adverse event; ADA=adalimumab 40 mg; IXE=ixekizumab 80 mg.

tology (ACR) 20/50/70 response, resolution of enthesitis, dactylitis and inhibiting the progression of structural joint damage in biologic DMARD-naïve patients with active psoriatic arthritis. This analysis investigates the efficacy and safety of ixekizumab after 52 weeks of treatment.

Methods

In a phase 3, multicenter, double-blind randomized trial (SPIRIT-P1; NCT01695239), 417 patients were randomized to receive up to 24 weeks of treatment with placebo (N=106), adalimumab 40mg once every two weeks (Q2W; N=101), or ixekizumab 80mg every two weeks (Q2W; N=103) or every four weeks (Q4W; N=107) following an 160mg initial dose at baseline. Patients who completed the 24w visit enrolled in the open-label extension period (EP), and received ixekizumab Q4W or Q2W up to one year. Efficacy and safety were analysed using the EP population, i.e. all patients who received at least 1 dose of study drug. Missing values were imputed by non-response-imputation for categorical variables and modified baseline-observation-carried-forward approach for continuous variables.

Results

A total of 304 patients completed the EP. At Week 52 for the Q4W/Q4W and Q2W/Q2W groups, the response rates for ACR 20/50/70 were 69.1/54.6/39.2% and 68.8/53.1/39.6%, respectively. Throughout 52w, minimal changes in modified Total Sharp Score and improvement for enthesitis and dactylitis were observed. The improvement persisted through the EP in the Q4W/Q4W and Q2W/Q2W groups for Psoriasis Area and Severity Index 75/90/100 (78.8/66.7/56.1% and 81.8/78.2/67.3%), the changes from baseline to 52w for percent Body Surface Area involvement of psoriasis were -13.5% and -9.3%, respectively and for Nail Psoriasis Severity Index -16.5 and -21.6, respectively. The number of treatment-emergent adverse events in the EP was comparable to that observed in the first 24-week period; and the majority were mild or moderate in severity, see table for full results.

Conclusion

Over a 52-week period, ixekizumab demonstrated sustained efficacy improving articular signs and symptoms of PsA, as well as plaque-psoriasis and patient reported outcomes with safety comparable to those reported at week 24.

This study was sponsored by Eli Lilly and Company.

ABSTRACTNUMMER: 1504-A-1818 3

PERFORMANCE OF THE ERS-RA CARDIOVASCULAR RISK PREDICTION TOOL: EXTERNAL VALIDATION IN A LARGE SWEDISH COHORT WITH RA

Lotta Ljung[3,6], Peter Ueda[3], Katherine P. Liao[2], Jeffrey D. Greenberg[1,4], Carol J. Etzel[1], Daniel H. Solomon[2], Johan Askling[3]

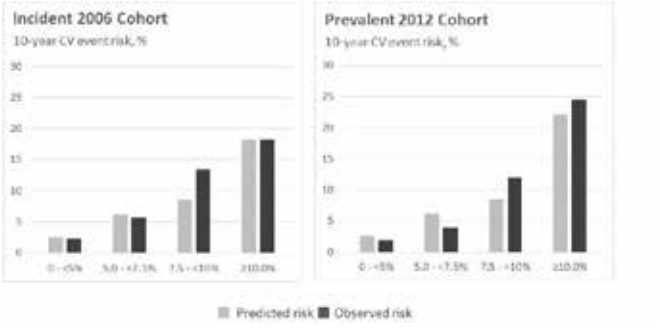
[1] Corrona LLC, Waltham, Massachusetts, USA
[2] Brigham and Women's Hospital, Boston, Massachusetts, USA
[3] Karolinska Institutet
[4] New York University School of Medicine, New York, USA
[5] Norrlands Universitetssjukhus
[6] Umeå Universitet

Background

Risk prediction tools developed for the general population tend to underestimate the risk of cardiovascular (CV) disease in patients with RA (1). An accurate and RA-specific CV risk prediction tool would ideally be integrated as a routine part of clinical practice in rheumatology, to identify patients with increased CV risks. For

Table and figure. Comparisons of the mean estimated and the observed 10-year CV risks within groups of estimated risk levels.

	Groups of estimated 10-year risk	N patients (%)	Mean estimated 10-year risk (%)	Observed 10-year rate (%)	Difference Observed rate – Mean estimated risk
Incident 2006 Cohort	<5%	884 (48)	2.5	2.3	-0.2
	5.0 to <7.5%	282 (15)	6.2	5.7	-0.5
	7.5 to <10%	43 (2)	8.6	13.4	4.8
	≥10.0%	638 (35)	18.3	18.3	0
Prevalent 2012 Cohort	<5%	4691 (32)	2.7	1.9	-0.8
	5.0 to <7.5%	1604 (11)	6.2	4.0	-2.2
	7.5 to <10%	1485 (10)	8.6	12.0	3.4
	≥10.0%	6705 (46)	22.2	24.5	2.3



example, 10-year CV risks above 7.5%, or 10%, could warrant specific preventive measures (2,3). The ERS-RA was derived and internally validated in the US Corrona RA registry (4). ERS-RA estimates the 10-year CV risk using dichotomous clinical variables, and includes variables on RA disease severity and activity.

Objectives
To assess the external validity of the ERS-RA in Swedish cohorts of patients with RA, with focus on the risk intervals of main clinical interest.

Methods
We identified two cohorts of patients with RA: (i) an "incident 2006 cohort" with RA patients in the Swedish Rheumatology Register from Jan 1, 2006 – Dec 31, 2011 who were also in the EIRA case-control study (n=2047, mean age 55±13 years, 72% women), and (ii) a "prevalent 2012 cohort" that included all RA patients in the Swedish Rheumatology Register between Jan 1, 2012 – Dec 31, 2015 (n=14485, mean age 61±14 years, 74% women). The 10-year CV risk was estimated using ERS-RA. Patients with a history of myocardial infarction or stroke were excluded. All patients were followed for the first of any of the following: a CV event (myocardial infarction, stroke, cardiovascular death), death, 10 years of follow-up, or Dec 31, 2015. Ten-year CV rates were expressed using the Kaplan-Meier method. In the prevalent 2012 cohort, the 10-year event rates were extrapolated from the observed (maximally four-year) rates (5). The C-statistic was estimated to assess discrimination. A measure of model calibration, the observed event rates were compared with the mean predicted 10-year risks.

Results
The C-statistic was 0.75 for both cohorts. Most patients had an estimated CV risk <5% or of >10% (See table). An accurate risk prediction was observed for estimated risks in the intervals <5%, and 5.0 to <7.5%. ERS-RA underestimated risk in the interval 7.5 to <10% (see Table and Figure).

Conclusion
In a Swedish population with RA, ERS-RA performed well in identifying patients with a very low and very high CV 10-year CV risk. In clinical routine practice, ERS-RA could be used to identify low and high risk individuals, who might be considered for additional CV risk factor evaluation and subsequent intervention.

References
1. Crowson CS, et al. Ann Rheum Dis. 2018. 2. Stone NJ, et al. Circulation. 2014. 3. https://www.nice.org.uk 4. Solomon DH, et al. Arthritis Rheum. 2015. 5. Cook NR, Ridker PM. JAMA Intern Med. 2014.

Variables	Male, n=508	Female, n=532
Age, years, mean, (SD)	57.7(4.4)	57.5(4.3)
BMI, mean, (SD)	27.7(4.1)	26.8(4.9)
hsCRP, (mean, SD)	2.2 (3.4)	2.4 (3.8)
CAC positive, (%)	293(58%)	137(26%)
CIMT positive, (%)	106(21%)	117(22%)
eGFR >90 ml/min	180(35%)	467(88%)
eGFR 60-90 ml/min	316(62%)	60(11%)
eGFR <60 ml/min	12(2%)	5(1%)
Smoking status, never	215(42%)	237(45%)
Smoking status, previous	206(41%)	191(36%)
Smoking status, active	86(17%)	102(19%)
Hypertension (%)	160(32%)	178(33%)
Diabetetes mellitus (%)	39(8%)	21(4%)
Dyslipidemia (%)	144(28%)	121(23%)

Table 1a Baseline characteristics of the study population by sex

	Male			Female	
	Odds ratio, multivariate*, (CI)	p-value		Odds ratio, multivariate*, (CI)	p-value
sUa, µmol/L,			sUa, µmol/L,		
31-305, Ref			143-229,Ref		
306-350	2.1 (1.2-3.7)	0.01	230-262	0.9 (0.5-1.7)	0.7
351-404	1.8 (1-3.3)	0.04	263-305	1 (0.5-2)	0.9
405-665	2 (1-3.8)	0.04	306-702	1.2 (0.6-2.3)	0.6

Table 2 Quartiles of sUa and age as predictors for presence of CAC (>0 CACs score) in male and female in multivariate logistic regression analyses adjusted for age, smoking, BMI, DM, DL, HT, hsCRP, EDU and PA.

ABSTRACTNUMMER: 1508-A-1818 4

URATE CORRELATES TO CORONARY ARTERY CALCIFICATION BUT NOT TO INTIMA MEDIA THICKNESS

Mats Dehlin[3], Panagiota Drivelegka[3], Valgerdur Sigurdardottir[3], Oskar Angerås[1], Lennart Jacobsson[3], Helena Forsblad d'Elia[2]

[1] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[2] Department of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden
[3] Dept of rheumatology and inflammation research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden
[4] Göteborgs Universitet

Background
Hyperuricemia is closely associated to cardiovascular disease (CVD) although it has not been defintively established whether it is a marker or a causative agent. Serum urate (SU) is strongly linked to the metabolic syndrome, hypertension, hyperlipidemia, kidney failure and higher BMI and higher levels are seen in men compared to women. Coronary artery calcification (CAC) is associated with future risk of atherosclerotic CV events in addition to the traditional cardiovascular risk factors (CVRF). CACs are present in atherosclerotic arteries and can be quantified and scored non-invasively by computed tomography. Carotid intima media thickness (CIMT) is a method of estimating atherosclerosis by assessing the level of arterial thickening present. CIMT can be used as a noninvasive marker of atherosclerotic disease with increasing CIMT linked to an increased risk of subsequent CV events. In the present study we have examined the relation between CACs, CIMT and SU in 1040 male and female with no history of myocardial infarction or stroke. ➤

Objectives
To examine the association bewteen SU and CAC and CIMT respectively in men and women seperately.

Methods
We identified 1106 (552 males) individuals who were screened for traditional CVRFs, such as hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), socioeconomic status (SES), BMI, high sensitive CRP (hsCRP), kidney function by eGFR (eGFR). CACs, reflecting calcification of coronary arteries, was determined according to Agatston1. CIMT was calculated as the mean of CIMT of the left and right coronary artery. We measured SU and related quartiles of it to CACs and CIMT with multiple logistic regression analyses adjusting for traditional CVRFs. CAC was defined positive if ≥1. CIMT was defined positive for ≥75 percentile. All study participants with a history of CVD (n=68, 44 male) were excluded.

Results
Of the 1106 participants, 68 were excluded due to history of CVD rendering a study population of 1040 individuals (508 males) with a mean age of 57.7 and 57.5 for male and female respectively. Age, BMI, EDU, SES, smoking status, PA, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (Table 1) and 65% of men displayed an eGFR below 90 mL/min compared to 12% of women. The three upper quartiles of SU (>306 μmol/L) all significantly ($p < 0.05$) predicted presence of CACs in male when adjusting for HT, DL, DM, smoking, PA, EDU, SES, BMI, hsCRP, eGFR and age in multivariate logistic regression, but not in women. CIMT showed no correlation to SU in men nor women.

Conclusions
Higher levels of SU is associated with presence of CACs in men but not with CIMT. This could suggest that SU is an innocent bystander that covariates with many, but not all, CVRFs. However, it could also imply biological differences in the effect of SU on calcification of coronary arteries compared to carotid intima thickening. Furthermore, SU may exert different effects depending upon biological age and degree of CVD development.

ABSTRACTNUMMER: 1509-A-1818 5

LIFE STYLE FACTORS AND COMORBIDITIES IN GOUT PATIENTS COMPARED TO THE GENERAL POPULATION

Lieke Scheepers[1], Anton Landgren[1], Lennart TH Jacobsson[1], Ulf Lindström[1], Eva Klingberg[1], Ulrika Bergsten[3], Mats Dehlin[1]

[1] Dept of Rheumatology and Inflammation Research, Institue of Medicine, Sahlgrenska Academy, University of Gothenburg
[2] Göteborgs Universitet
[3] R&D Department at Region Halland, Halmstad, Sweden

Background
Gout is the most common inflammatory arthritis and relatively much is known regarding its pathogenesis. It is clear that life style factors play a significant role in developing and maintaining disease.

Purpose
This study aimed to analyze lifestyle factors in prevalent gout patients by sex compared to age matched controls from the general population.

Methods
All patients above 18 years of age with an ICD 10-diagnosis of gout from Jan 2015 through Feb 2017 listed at any of twelve randomly selected primary health care centers or the rheumatology department at Sahlgrenska University hospital in the Western Sweden Health Care Region (WSHCR) were identified. They were sent a questionnaire, regarding demographics, life style factors such as smoking status, alcohol consumption, physical activity, body mass index (BMI; categorized into 4 levels in the analyses) and comorbidities such as diabetes and hypertension. All responders aged 18 – 84 years were matched to five control individuals, without gout, by sex and age. Control individuals were selected from a random sample of 52,348 individuals aged 16 – 84 years who participated in the National Public Health survey in Sweden year 2015. This survey is a national study on health, lifestyle and living conditions. Alcohol consumption was categorized as none and any with/without binge drinking behavior. Binge drinking was (liberally) defined as consuming more than four (women) or five glasses (men) on any occasion. Conditional logistic regression models were used to compare cases and controls with regard to lifestyle factors and comorbidities. Multivariate analyses were also performed, including BMI, smoking status, alcohol consumption, and physical activity.

Results
Of the 1,589 invited gout patients, 868 responded and 79.7% were male. Non-responders were more often young men. Mean age was 69.3 (std:10.5) years for men and 71.8 (std: 9.9) years for women with gout. Male gout patients were in multivariate analyses more likely to be overweight (OR 1.67 (95% CI: 1.31 – 2.14)), obese (OR 2.20 (95% CI: 1.64 – 2.94)), have binge drink behavior (OR 3.32 (95% CI: 2.39 – 4.62)), and had lower levels of physical activity compared to controls. Current smoking habits did not differ between male gout patients and controls. Female gout patients were in multivariate analyses more likely to be overweight (OR 1.87 (95% CI: 1.05 – 3.33)), obese (OR 3.62 (95% CI: 1.96 – 6.72)), and have binge drink behavior (OR 4.28 (95% CI: 1.92 – 9.53), but not did not differ with regard to current smoking habits or physical activity compared to controls. In bivariate analyses, comorbidities such as diabetes and hypertension, were significantly more common in gout patients among both sexes.

Conclusion
Compared to the general population, patients with gout were more often obese (in particular women) and had higher occurrence of binge drinking behavior (in particular men). The lower level of physical activity (men) and normal frequency of smoking among gout patients may be a consequence of the high comorbidity rates.

ABSTRACTNUMMER: 1512-A-1818 6

MARGINAL JAWBONE LOSS IS ASSOCIATED WITH ONSET OF RHEUMATOID ARTHRITIS AND IS RELATED TO PLASMA LEVEL OF RECEPTOR ACTIVATOR OF NUCLEAR FACTOR KAPPA-B LIGAND (RANKL)

Johansson L[2], Kindstedt E[1], Palmqvist P[1], Koskinen Holm C[1], Kokkonen H[2], Johansson I[3], Lundberg P[1] ,Rantapää Dahlqvist S[2]

[1] Department of Odontology/Molecular Periodontology, Umeå University.
[2] Department of Clinical Medicine and Public Health/Rheumatology, Umeå University, Umeå, Sweden.
[3] Department of Odontology/Cardiology, Umeå University

Background
The association between the two chronic inflammatory diseases, ➤

periodontal disease (PD) and rheumatoid arthritis (RA) has been addressed in recent years. Both the diseases share several risk factors (e.g., smoking and shared epitope) and features besides inflammation e.g. presences of bone destruction, and the link between rheumatic and dental pathology via citrullination.

Objectives
To investigate if periodontitis, presented as marginal jawbone loss, preceded onset of symptoms of RA. Furthermore, the plasma levels of receptor activator of nuclear factor kappa-B (RANKL), a cytokine crucial for bone resorption and anti-citrullinated peptide antibodies (ACPA) were analyzed in relation to RA development and jawbone loss.

Methods
Dental radiographs from the premolar/molar region of the jaws of 176 individuals of whom 93 had subsequently developed RA and 83 controls were used for measuring the levels of marginal jawbone loss. Of these 93 individuals who developed RA, 46 had radiographs on average 4 years before symptom onset of RA. 45 of these pre-symptomatic individuals were matched with one control based on sex, age when dental X-ray were taken and smoking status. Plasma RANKL concentration and ACPA (as anti-CCP2 antibodies) were analyzed using ELISA (BioVendor, Czech Republic & EuroDiagnostica, Sweden, respectively).

Results
Jawbone loss was significantly higher in never-smoking, pre-symptomatic individuals compare with controls and increasing levels of bone loss was associated with higher risk to develop RA later in life (hazard ratio=1.06, 95%CI 1.01, 1.11). The jawbone loss increased significantly during the predating time. Among smokers, no association was found. RANKL-positive pre-symptomatic individuals had a significantly higher levels of jawbone loss particularly in individuals positive for both RANKL and ACPA compared with those being positive for one factor or double negative.

Conclusions
Higher levels of marginal jawbone loss were found to precede the onset of symptoms of RA in non-smokers. Pre-symptomatic individuals whom were RANKL positive, and particularly ACPA-positive individuals had a significantly increased levels of jawbone loss.

ABSTRACTNUMMER: 1514-A-1818 7

PREDICTORS FOR CLINICALLY DIAGNOSED GOUT – 30 YEARS FOLLOW-UP IN THE MALMÖ PREVENTIVE PROJECT COHORT, SWEDEN

Meliha Kapetanovic[1], Peter Nilsson[2], Carl Turesson[1], Martin Englund[3], Nicola Dalbeth[4], Lennart Jacobsson[5]

[1] Department of Clinical Sciences Lund, Section of Rheumatology, Lund University and Skåne University Hospital, Lund, Sweden
[2]Department of Clinical Sciences, Lund University, Malmö, Sweden; Center of Emergency Medicine, Skåne University Hospital, Malmö, Sweden
[3] Clinical Epidemiology Unit, Orthopaedics, Department of Clinical Sciences, Lund University, Lund, Sweden
[4] Department of Medicine, University of Auckland, Auckland, New Zealand
[5]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden

Background
Gout is the most common form of inflammatory arthritis worldwide. Hyperuricemia is a crucial risk factor. The relative importance of other risk factors, some of which are associated with serum urate (s-UA) levels, is slightly more controversial. Our aim was to identify predictors for clinical gout cohort from a population survey, the Malmö Preventive Project (MPP) - a large-scale screening and case finding program in Malmö, Sweden.

Methods
A total of 33346 individuals (67% men, mean age 46 years at inclusion, mean follow-up 28 years) were screened between 1974 and 1992. The survey included: 1. A Questionnaire with 260 questions (socioeconomic factors, alcohol consumption, smoking, physical activity, dietary habits, history of gout, other co-morbidities) 2. A Physical examination (including body mass index (BMI) and blood pressure) and 3. Laboratory tests (i.e. s-UA, fasting glucose, s-creatinine). The Malmö modification of the Michigan alcoholism screenings test (Mm-MAST) was used to identify the alcohol risk consumption (Mm-MAST score ≥2). Subjects were followed to the date of first gout diagnosis, death, migration from the area, or December 31st 2014. In order to identify all gout diagnoses (using ICD-codes) given at visits to physicians in primary care, in specialized in-patient (from 1974) or out-patient specialized care (from 2001) MPP cohort was linked to the regional Skåne Healthcare Register and to the National Patient Register, respectively. Individuals with a history of gout before the inclusion in MPP (n=11) were excluded. Possible risk factors/markers at baseline associated with incident gout were analysed using Cox-regression models.

Results
Of 33346 individuals participating in MPM project, 1275 individuals (3.8%); 1014 men (4.5%) and 261 (2.4%) women were clinically diagnosed with gout over the nearly 30 years of follow-up. In both men and women s-UA >405 at baseline (age-adjusted) was the strongest factor associated with incident gout. In addition, higher age, higher baseline BMI, higher s-triglycerides, hypertension and current smoking were associated with incident gout in both sexes. A Mm-MAST score of ≥2 was associated with incident gout only in men while higher ESR was associated with incident gout only in women (Table).

Table. Baseline predictors of development of gout over 30 years of follow-up

	Baseline variables	Mean (SD)	Frequency (yes, %)	HR (95% CI)* (age adjusted)	HR (95% CI) (multivariate analysis**)
MEN with incident gout (n=1014)	s-UA >405µmol/L (yes,%)		10.1%	5.4 (4.8-6.2)	4.1 (3.4-4.9)
	Age (years)	43.7 (6.6)	---	1.4 (1.3-1.5)	1.4 (1.2-1.5)
	Body mass index (kg/m²)	24.7 (3.3)	---	1.4 (1.4-1.5)	1.3 (1.2-1.4)
	e-GFR (ml/min)	79.1 (10.5)	---	0.9 (0.8-0.9)	0.9 (0.8-1.0)
	s-triglycerides (mmol/L)	1.5 (1.1)	---	1.1 (1.1-1.2)	1.1 (1.0-1.1)
	ESR mm/hour	5.9 (5.7)	---	1.0 (0.9-1.1)	1.0 (0.9-1.1)
	Hypertension (yes,%)	---	16.4%	1.7 (1.5-2.0)	1.3 (1.1-1.5)
	CVD at baseline (yes/no)	---	2.1%	1.7 (1.1-2.8)	1.4 (0.9-2.3)
	Smoking (yes/no)	---	19.2%	1.1 (1.0-1.3)	1.3 (1.1-1.6)
	Mm-MAST>2 (yes,%)	---	30.8%	1.5 (1.3-1.7)	1.3 (1.1-1.5)
WOMEN with incident gout (n=261)	s-UA > 405µmol/L (yes,%)		1.5%	12.5(8.6-18.1)	5.9 (2.2-15.9)
	Age (years)	49.7 (7.4)	---	1.7 (1.5-2.1)	1.3 (1.1-1.6)
	BMI (kg/m²)	21.4 (1.2)	---	1.6 (1.5-1.8)	1.6 (1.6-2.0)
	eGFR (ml/min)	75.6 (10.9)	---	0.8 (0.7-0.9)	0.8 (0.6-1.0)
	s-triglycerides (mmol/L)	1.1 (0.6)	---	1.3 (1.2-1.4)	1.2 (1.0-1.5)
	ESR (mm/hour)	9.6 (7.7)	---	1.3 (1.2-1.4)	1.2 (1.0-1.5)
	Hypertension (yes,%)	---	22%	2.0 (1.6-2.0)	1.1 (0.6-1.9)
	CVD at baseline (yes,%)	---	3.4%	2.1 (1.3-3.6)	3.0 (0.7-12.3)
	Smoking (yes,%)	---	34.9%	1.2 (0.9-1.5)	1.7 (1.0-2.8)
	Mm-MAST≥2 (yes,%)	---	2.8%	1.3 (0.6-2.6)	1.2 (0.6-2.4)

*HR is calculated per 1 SD or for dichotomous covariates (yes vs. no)
** baseline variables included in analysis: age, BMI, s-triglycerides, e-GFR, ESR, Hypertension (yes/no); CVD (yes/no); DM (yes/no); smoking (yes/no); Mm-MAST≥2(yes/no)

Conclusions
In this large cohort of middle-age individuals, hyperuricemia, higher age, hypertriglyceridemia and higher BMI were associated with incident gout in both sexes. Alcohol risk consumption predicted gout only in men. Higher ESR, as a possible marker of chronic inflammation, was a significant predictor only in women.

ABSTRACTNUMMER: 1516-A-1818 8

SUMMARY OF BARICITINIB EFFECT ON PATIENT-REPORTED OUTCOMES (PROS) IN METHOTREXATE–INADEQUATE RESPONDER PATIENT POPULATION

Maxime Dougodos[1], Bruno J Fautrel[2], Mart A.F.J. Van De Laar[3], Rieke Alten[5], Regina Cseuz[6], Josef Smolen[7], Juan Sanchez-Burson[8], Paul Bird[9], Morton Scheinberg[10], Filip Van Den Bosch[11], Jane Barry[12], Frederick Durand[13], Baojin Zhu[14], Francesco De Leonardis[6], Peter Taylor[16], Esbjörn Larsson Presenting on behalf of the authors

[1] Department of Rheumatology, Cochin Hospital, Paris, France
[2] Hôpital Pitié-Salpêtrière, Paris, France
[3]University of Twente, Twente, The Netherlands
[5]Schlosspark Klinik, University Medicine Berlin, Berlin, Germany
[6]Revita Clinic, Budapest, Hungary
[7]Medical University of Vienna, Vienna, Austria
[8]Hospital Infantaluisa of Sevilla, Sevilla, Spain
[9]University of New South Wales, Sydney, Australia
[10]Hospital Israelita Albert Einstein, Sao Paulo, Brazil
[11]UZ Gent, Reumatologie, Gent, Belgium
[12]Lilly UK, Eli Lilly and Company Ltd, Basingstoke, UK
[13]Lilly France, Neuilly-sur-Seine, France
[14]Eli Lilly and Company, Indianapolis, USA
[15]Eli Lilly Export S.A. Vernier - Geneva, Switzerland
[16]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom
[17] Eli Lilly Sweden

Background
Patient-Reported Outcomes (PROs) have become increasingly important in the evaluation of rheumatoid arthritis (RA) patients (pts). This is a summary of the effect of baricitinib (BARI) on PROs.

Materials and Methods
In RA-BEAM (NCT01710358), 1305 pts with inadequate response to MTX were randomised 3:3:2 to PBO QD, BARI 4mg QD, or ADA 40mg EOW. Post-hoc analyses focused on the impact of BARI on PRO measures such as the Pain visual analogue scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration of morning joint stiffness (MJS): i) the proportion of patients who achieved pain improvement of ≥50% of their baseline pain (VAS: 0-100mm) in each treatment arm; ii) differences in PROs, at week (Wk)24, among pts with DAS28-ESR defined low disease activity (LDA) and remission per treatment group.

Results
A significantly greater proportion of patients treated with BARI achieved ≥50% pain improvement as early as Wk1 compared to PBO (26% vs 13%; p≤0.001) and as early as Wk4 compared to ADA (48% vs 37%; p≤0.01); improvements were sustained through Wk24 (BARI 61% vs ADA 52%; p≤0.05). Patients in LDA at Wk24, treated with BARI, reported significantly greater improvements in pain and HAQ-DI than those with ADA and PBO . Among patients in remission at Wk24, significantly greater improvements in HAQ-DI scores were reported with BARI than with PBO; among patients with LDA, significantly greater improvements in morning joint stiffness duration were also observed with BARI and ADA than with PBO (data not shown).

Conclusions
BARI demonstrated rapid and sustained improvements in pain. Attainment of remission or LDA is associated with improvements in pain, physical functioning and health-related quality of life for patients treated with BARI, ADA or PBO but with most marked improvements on BARI and ADA.

ABSTRACTNUMMER: 1522-A-1818 9

SMOKING IS ASSOCIATED WITH LOW LEVELS OF SOLUBLE PROGRAMMED DEATH PROTEIN 1 LIGAND 1 IN RHEUMATOID ARTHRITIS

Caroline Wasén[3], Malin Erlandsson, Apostolos Bossios[1,2,4], Linda Ekerljung, Carina Malmhäll, Sofia Töyrä Silfverswärd, Rille Pullerits, Bo Lundbäck, Maria Bokarewa

[1] Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
[2] Department of Respiratory Medicine & Allergy, Karolinska University Hospital, Stockholm, Sweden
[3] Göteborgs universitet
[4] Krefting Research Centre, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, University of Gothenburg, Göteborg, Sweden

Background
Smoking is a risk factor for developing rheumatoid arthritis (RA), but the mechanism remains uncertain. We previously demonstrated that smoking lowers the T cell activation threshold by limiting programmed death protein 1 (PD-1) expression.

Aim
To investigate how smoking influence the levels of soluble PD-1 ligand 1 (sPD-L1).

Method
Serum levels of sPD-L1 were measured in 246 RA patients and in 168 healthy subjects; then analyzed with respect to inflammation, smoking, treatments and autoantibody status. Effect of therapeutic TNF-inhibiting antibodies (TNFi) on sPD-L1 was studied in 16 RA patients at their first infliximab infusion. The expression of Fcγ-receptor (FcγR) subclass IIB and IIIA were analyzed with qPCR in peripheral blood mononuclear cells (PBMC) from 12 RA patients and 15 healthy controls, and in healthy PBMC exposed to IgG containing antibodies to cyclic citrullinated peptides (aCCP).

Results
Smoking was associated with low levels of sPD-L1 in RA patients (p=0.016) and in healthy subjects (p=0.095). The RA patients with high IL-6 and IL-1β had higher sPD-L1 (p=0.0005 and p=0.0006). sPD-L1 depended on the disease activity in aCCP+ and TNFi treated patients, but low sPD-L1, due to smoking, dissociated from inflammation and disease activity. Infliximab repressed sPD-L1 (p=0.047) in TNFi-naive patients, and low levels were found in patients with short disease duration treated with TNFi (p=0.018). TNFi treatment in patients with long disease duration was associated with higher sPD-L1 (7-9 years, p=0.041). Importantly, TNFi could restore sPD-L1 levels in smokers. Similarly, in vitro exposure to aCCP+IgG inhibited sPD-L1 release (p=0.036) but aCCP+ patients with long disease duration had higher sPD-L1 (p=0.016).

High ratio of the inhibitory FcγR subclass IIB over the stimulatory IIIA resulted in low sPD-L1 release (p=0.029). Smoking was associated with lower expression of FcγRIIIA (p=0.0093), thereby increasing the IIB/IIIA ratio (p=0.0004) and repressing sPD-L1 in TNFi negative patients (p=0.0093).

Conclusion
In RA, high serum sPD-L1 was related to systemic inflammation and disease activity. Smoking altered the expression of FcγRs and limited sPD-L1 in RA patients, potentially allowing inappropriate T cell responses. Exposure to therapeutic antibodies regulated sPD-L1 production and levels were normalized in smokers by treatment with TNFi.

ABSTRACTNUMMER: 1524-A-1818 10

INSULIN-LIKE GROWTH FACTOR 1 RECEPTOR REGULATES THE PHENOTYPE AND FUNCTION OF CD21+ B CELLS

Malin Erlandsson[1,2], Caroline Wasén[1], Maria Bokarewa[1,2]

[1] Göteborgs Universitet, Sahlgrenska akademin, Avd för Reumatologi
[2] Sahlgrenska Universitetssjukhuset, Reumatologi

Background
Ligand to the inducible T cell costimulator (ICOSL) on B cells is essential for the ICOS-dependent follicular recruitment of activated T cells. In patients with rheumatoid arthritis (RA) the IGF1-IGF1R axis is altered. Inhibition of IGF1R alleviated arthritis by reducing IL-6-dependent formation of Th17 cells. Here we study the role of IGF1R on CD21+ cells in experimental arthritis.

Methods
Female Balb/c mice were immunized with methylated BSA or with CII. Consequences of the IGF-1R inhibition for arthritis were studied in mBSA and CII-immunised mice treated with NT157 compound promoting degradation of insulin receptor substrates (mBSA) or using shRNA producing construct (mBSA+CII). At termination three sub-populations of CD21+ cells were analyzed: follicular dendritic cells (FDc, CD21+CD19-CXCR5-); marginal zone B cells (MZBc, CD21+CD19+CXCR5-); follicular B cells (FBc, CD21+CD19+CXCR5+).

Supernatants of LPS-stimulated splenocytes were analyzed for production of cytokines, chemokines using Cytokine Array. Serum levels of antigen specific and autoantibodies were measured in an ELISA.

Results
In spleen of mBSA-immunised mice, ICOSL expression on CD21+ cells correlated to IGF1R (r=0.70, p=0.007). Inhibition of IGF1R induced a 20% reduction in ICOSL expression in all CD21+ subsets (p=0.007) followed by an increase in the number of MZBc (p=0.003), while FDc and FBc were unchanged. Inhibition of IGF1R had no effect on the expression of ICOS+ on CD4 T cells or the subset of CXCR5+ follicular T cells. Reduction of the ICOSL+CD21+ B cells was associated with lower production of IL -13. Inhibition of IGF1R signaling by NT157 and by shRNA, reduced production of CXCL13 and CXCL12, the chemokines essential for B cell migration towards follicules.

In contrast, the production of chemokines CCL5 and CXCL12 preventing intra-follicular migration was increased, which explains the increase of MZBc. Additionally, the insufficient ICOSL signalling significantly reduced the production of IL-7 and IL-4, regulating class switching of B cells in germinal centers and differentiation of B cells into plasma cells. The described disbalance in the cytokines aiding B cell development led to the reduced production anti-inflammatory IL-10 and of mBSA-specific IgM (p=0.005) and increased production of autoreactive RF-IgM levels (p=0.001).

Conclusion
The study shows that IGF1R controls B cell development through the expression of ICOSL on CD21+ cells. Insufficent ICOSL signaling disturbs a balance between antigen-specific response and autoantibody production in experimental arthritis.

ABSTRACTNUMMER: 1525-A-1818 11

SOLUBLE UROKINSE PLASMINOGEN ACTIVATOR RECEPTOR (suPAR) CORRELATES WITH DISEASE ACTIVITY IN EARLY RHEUMATOID ARTHRITIS AND REFLECTS JOINT DAMAGE OVER TIME

Helena Enocsson[1], Alf Kastbom[2], Tanja Lukic[2], Christopher Sjöwall[2], Thomas Skogh[2], Jonas Wetterö[2]

[1] Rheumatology/AIR, Department of Clinical and Experimental Medicin, Linköping University, Linköping, Sweden
[2] Rheumatology/AIR, Department of Clinical and Experimental Medicin, Linköping university, Linköping, Sweden

Background
The urokinase plasminogen activator receptor (uPAR) is expressed on various cell types and plays important roles in proteolysis, migration and adhesion. Receptor shedding yields a soluble form (suPAR) that has been intensively studied as a potential biomarker in several inflammatory diseases and malignancies. The previous few studies on suPAR in rheumatoid arthritis (RA) have shown an association with inflammation and swollen joints, but data on changes in suPAR levels in relation to early disease course are lacking. This study investigates whether suPAR levels predict or reflect disease activity and/or joint damage in early RA.

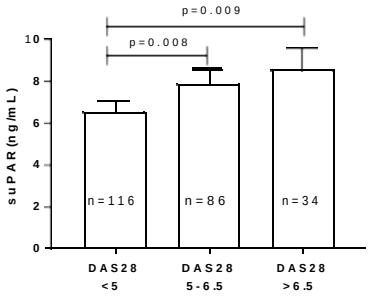


Figure 1. Serum levels of suPAR and in different categories of disease activity (DAS28) at study inclusion. P-values are from One-way ANOVA with Tukey's post hoc test. Error bars indicate 95% confidence interval.

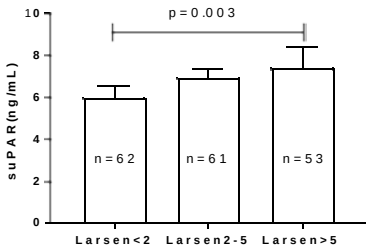


Figure 2. Serum levels of suPAR and the degree of joint damage (Larsen score) 36 months after study inclusion. P-values are from One-way ANOVA with Tukey's post hoc test. Error bars indicate 95% confidence interval.

Material and Methods
Serum suPAR was measured by ELISA at disease onset (0 months), after 3 months and after 36 months in 252 RA patients from the Swedish early RA cohort TIRA-2. suPAR levels were compared with disease activity (defined by DAS28) and joint damage (Larsen score) at baseline and up to 36 months after disease onset. Healthy individuals (n=100) served as controls.

Results
Circulating levels of suPAR were higher in RA patients at all three time points compared to healthy controls (mean suPAR = 3.62 ng/mL; p<0.001). The highest suPAR among patients was found at 3 months (mean = 8.47 ng/mL) and the lowest at 36 months (mean = 7.14 ng/mL). suPAR at inclusion correlated with baseline DAS28 (p<0.001, rho=0.25) whereas suPAR levels at 36 months correlated with Larsen score at 36 months (p=0.001, rho=0.24), and 24 months (p=0.002, rho=0.25), but not with DAS28 at any time point. No correlation was found between baseline suPAR and joint damage at any time point. Categorization of baseline DAS28 revealed higher baseline suPAR at high DAS28 (Fig. 1) whereas Larsen score at 36 month reveled higher suPAR (measured at 36 months) among patients with a high score (>5) compared to those with a low score (<2) (Fig. 2).

Conclusion
suPAR levels associate with disease activity in early untreated RA, but at later stages rather reflect joint damage. Since suPAR levels seem to increase at or after damage accrual, we speculate that suPAR reflects active inflammation and ongoing processes in the joint, rather than being a causative agent.

ABSTRACTNUMMER: 1527-A-1818 12

THE VALIDITY OF GOUT DIAGNOSIS IN PRIMARY AND SECONDARY CARE – RESULTS FROM A PATIENTS SURVEY

Anton Landgren[1], Lennart Jacobsson[1], Ulrika Bergsten[1], Mats Dehlin[1]

[1] Department of Rheumatology and Inflammation Research, Institution of medicin, Sahlgrenska Academy. University of Gothenburg, Sweden

Background
Gout affects 1-2 % of adults worldwide being the most common inflammatory arthritis and usually managed in primary care. The gold standard for definitive diagnosis of gout is the presence of monosodium urate crystals (MSU) in joints or tissues and the latest classification criteria from ACR-EULAR also have this as a central item. Microscopy is however seldom performed in primary care today. Although not intended as diagnostic there are several classification criteria, such as the Mexico and the Netherlands criteria that do not include microscopy.

The aim of this study was to validate the diagnosis of gout in primary and secondary care according to the Mexico and the Netherlands criteria and items thereof through a patient survey.

Table 1 Positive predictive values for different classification criteria, anchor points for gout diagnosis and common items of classification criteria

Definitions used for gout diagnosis	Primary care (n=786)	Secondary care (n=84)
Netherlands ≤4, n(%)	57 (7.7)	3 (3.8)
Netherlands ≥8, n(%)	522 (70.7)	62 (78.5)
Mexico score ≥4, n(%)	548 (74.2)	64 (82.1)
Self-reported gout diagnosis (%)	691 (90.2)	78 (94.0)
Selected items (self-reported) from classification criteria		
Hyperuricemia, n(%)	320 (41.8)	55 (66.3)
Men, n(%)	629 (80.2)	62 (73.8)
MI§ or Stroke or Hypertension, n(%)	598 (78.1)	70 (84.3)
Tophus, n(%)	107 (14.1)	26 (31.3)
Any MTP1 attack, n(%)	472 (62.4)	39 (47.6)
Swollen and red joint at attack, n(%)	583 (76.7)	77 (92.8)
Individual joints ever involved in attacks:		
1 joint, n(%)	205 (27.1)	3 (3.7)
>1 joints, n(%)	471 (60.1)	73 (86.9)

§ Myocardial infarction

Methods
All patients above 18 with an ICD10-diagnosis of gout at a visit in primary and secondary care (Jan 2015 through February 2017) were identified from 12 primary care centers and one rheumatology clinic within the Western Sweden Health Care Region. They were sent a questionnaire regarding comorbidities, demographics and gout characteristics. To test the validity of their gout diagnosis, questions of the two gout classification criteria Mexico and the Netherlands were posed. Self-reported knowledge about having gout, was included as an anchor point for the diagnosis. Positive predictive values (PPV) were calculated for these definitions. Structured telephone interviews collecting similar information were performed in 10% of non-responders. The ACR/EULAR criteria was not used, since it includes identification of MSU crystals and imaging as central items.

Results
1589 individuals with a gout diagnosis were identified. 868 (54.6%) individuals responded. Mean age was 71 years and the proportion of men was 80%. 89% of secondary care patients had ever been treated with Allopurinol compared to 71% in primary care. The PPVs ranged from 78.5 to 94%, in secondary care, being lowest for the Netherlands criteria and highest for self-reported gout (Table 1). Corresponding PPVs were marginally lower in primary care (but still over 70% for all criteria). Similar results were found among those interviewed by telephone (not shown).

Conclusions
The majority of patients diagnosed with gout in both primary and secondary care have had clinical symptoms compatible with the Netherlands and Mexico criteria for gout. Diagnoses of gout identified through health care registers is therefore a valid and useful tool for epidemiological research. Patients with gout in secondary care reported more features of gout than patients in primary care.

ABSTRACTNUMMER: 1528-A-1818 13

INFLAMMATORY MARKERS IN RELATION TO RISK FACTORS FOR CARDIOVASCULAR DISEASE IN THE PRE-SYMPTOMATIC PHASE OF RHEUMATOID ARTHRITIS

Heidi Kokkonen[2], Linda Johansson[2], Hans Stenlund[1], Solbritt Rantapää-Dahlqvist[2]

[1] Folkhälsa och klinisk medicin, Global hälsa och epidemiologi, Umeå Universitet
[2] Folkhälsa och klinisk medicin, Reumatologi, Umeå Universitet

Background
Individuals who later developed rheumatoid arthritis (RA) have increased levels and frequencies of risk factors for cardiovascular disease (CVD), years before onset of RA. The relationships between CVD risk factors and inflammatory markers, i.e., cytokines and chemokines, were analysed in individuals prior to onset of symptoms and compared with controls.

Methods
A case-control study was based on population surveys from The Medical Biobank of Northern Sweden with data collected on socioeconomic and lifestyle factors, BMI, waist, blood pressure, and blood samples by a nurse. The register of patients with RA (ARA criteria) was co-analysed with the registers from the Medical Biobank and 469 pre-symptomatic individuals (median age 50.2 years;

67.8% women, median predating time 5.0 (IQR;2.0-8.0) years), and 234 controls (median age 50.3 years; 67.1% women) were identified. CVD risk factors were defined as: hypertension (treatment or systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg), elevated ApoB/ApoA1 ratio (women ≥0.7, men ≥0.8, including lipid lowering treatment), BMI ≥25kg/m2, diabetes, and ever smoking. Concentrations of eotaxin, interferon gamma-induced protein (IP-10), monocyte-chemoattractant protein 1 (MCP1), macrophage derived chemokine (MDC), interleukin (IL) 2, IL-4, IL-6, IL-8, and IL-10, were analysed in plasma using assays from Meso Scale Discovery V-plex methods (Rockville, MD, USA).

Results

Pre-symptomatic individuals had significantly higher levels of IL-6 compared with controls, both in women and men. IL-10 was significantly higher in pre-symptomatic men compared with controls. Cytokines/chemokines were significantly associated with the CVD risk factors in the cases e.g. IL-6 with each of the risk factors, eotaxin with smoking, IP-10 with increased BMI, having diabetes or hypertension, whilst MDC was associated significantly with smoking and BMI≥25 kg/m2. After adjustments for sex and age only eotaxin concentrations were significantly associated with being ever smoker. In women, MDC was significantly associated with smoking, BMI≥25 kg/m2 and diabetes. Having the combination of several CVD risk factors was associated with significantly higher concentrations of MCP-1, MDC, and IL-6 in pre-symptomatic women. IL-6 further increased the relative risk for the combinations of CVD risk factors for the pre-symptomatic cases compared with controls.

Conclusions

Increased concentrations of cytokines/chemokines were associated with CVD risk factors to a higher extent among the pre-symptomatic RA cases compared with controls. The pattern of association varied between the risk factors and the sex of the cases.

ABSTRACTNUMMER: 1529-A-1818 14

MALE SEX PREDICTS A FAVOURABLE OUTCOME IN SERONEGATIVE EARLY RHEUMATOID ARTHRITIS

Giovanni Cagnotto[1,2], Emil Rydell[1,3], Lennart Jacobsson, Carl Turesson[1,3]

[1] Rheumatology, Department of Clinical Sciences, Malmö, Lund University
[2] Rheumatology, Skåne University Hospital Lund, Sweden
[3] Rheumatology, Skåne University Hospital, Malmö, Sweden

Background

Rheumatoid factor (RF) and antibodies against cyclic citrullinated peptides (anti-CCP) are universally recognized negative prognostic factors in rheumatoid arthritis (RA). The majority of studies of early RA have focused on RF and anti-CCP positive patients. Much less is known about prognostic markers in seronegative RA. Several studies report worse drug survival and worse patient reported outcomes in women with RA. This affects outcomes such as the 28-joint disease activity score (DAS28) and the health assessment questionnaire (HAQ). How these differences relate to autoantibody status is unknown. With this study we aim to investigate if the relation between sex and clinical outcomes varies by autoantibody status in patients with early RA.

Materials and methods

An inception cohort of patients with early RA (N=233; symptoms duration <= 12 months), recruited in 1995-2005, was studied. All the patients fulfilled the 1987 American College of Rheumatology criteria for RA. The patients were managed according to usual care, with no pre-specified protocol for pharmacotherapy or rehabilitation. In a structured follow-up program, all patients were examined by the same rheumatologist. In the present study we divided the patient population in three groups according to autoantibodies status: RF and anti-CCP seropositive (double positive), RF or anti-CCP seropositive, RF and anti-CCP seronegative (double negative). We examined the relation between sex and different outcomes at 12 months (EULAR good response, clinical remission (DAS28<2.6), HAQ <=0.5 and low pain score (VAS pain 0-100 of <20) by means of logistic regression.

Impact of sex on the chance of EULAR good response and clinical remission at the 1-year follow-up in patients with early RA. Logistic regression analysis.

		EULAR good response OR (95 % CI)		Clinical remission* OR (95 % CI)	
	Sex	Crude	Adjusted for baseline DAS28	Crude	Adjusted for baseline DAS28
All	Female (n=144)	(reference)	(reference)	(reference)	(reference)
	Male (n=57)	1.9 (0.9-3.7)	1.9 (0.9-3.7)	2.0 (1.0-3.9)	2.1 (1.0-4.1)
RF and anti-CCP negative	Female (n=42)	(reference)	(reference)	(reference)	(reference)
	Male (n=14)	4.7 (1.2-18.3)	6.0 (1.3-26.4)	6.4 (1.6-26.2)	6.3 (1.5-25.9)
RF or anti-CCP positive	Female (n=41)	(reference)	(reference)	(reference)	(reference)
	Male (n=13)	3.2 (0.6-17.2)	3.4 (0.6-20.6)	3.8 (0.8-17.7)	2.1 (0.3-12.3)
RF and anti-CCP positive	Female (n=61)	(reference)	(reference)	(reference)	(reference)
	Male (n=30)	1.3(0.4-4.5)	1.2 (0.3-4.2)	0.9 (0.3-2.9)	1.1 (0.3-3.7)

Results

Complete data on autoantibody status at baseline was available for 201 patients (mean age at inclusion 61 years, 72% female, 60% RF positive and 58% anti-CCP positive). Twenty-eight % of the patients were double negative, 27% were single positive and 45% were double positive. Mean baseline DAS28 was 4.53. All patients were treated with a conventional synthetic DMARD (48 % with methotrexate). Oral glucocorticoids were prescribed in 38% of patients. At the 1-year follow up, 19% had a EULAR good response, 21% were in remission, 40% had low pain and 53% low HAQ. Male patients in the double negative group were more likely to reach remission (odds ratio (OR) 6.40; 95% confidence interval (CI) 1.6-26.2) and EULAR good response (OR 4.67; 95% CI 1.2-18.3) compared to females. There were no such associations among the double positive patients (Table). Results were similar in analyses adjusted for DAS28 at baseline (Table). There was a similar pattern among double negative patients for low pain at 1 year (OR for male vs female patients 2.25; 95% CI 0.58-8.67 – adjusted for baseline pain), but no association between male sex and low HAQ at 1 year in double negative patients (OR 0.99; 95 % CI 0.23-4.22 – adjusted for baseline HAQ) or the other subgroups.

Conclusions

In the subgroup of patients with seronegative early RA, male patients are more likely than female patients to reach DAS28 remission and EULAR Good Response after treatment with conventional synthetic DMARDs.

ABSTRACTNUMMER: 1530-A-1818 15

PREDICTORS OF DRUG SURVIVAL OF ABATACEPT IN RHEUMATOID ARTHRITIS – RESULTS FROM A LARGE NATIONAL QUALITY REGISTER COHORT STUDY

Giovanni Cagnotto[2,3], Minna Willim[2,4], Jan-Åke Nilsson[2,4], Saedis Saevarsdottir[1], Carl Turesson[2,4]

[1] *Karolinska Institutet, Stockholm, Sweden*
[2] *Rheumatology, Department of Clinical Sciences, Malmö, Lund University*
[3] *Rheumatology, Skåne University Hospital, Lund, Sweden*
[4] *Rheumatology, Skåne University Hospital, Malmö, Sweden*

Background
Abatacept is a biologic disease modifying anti-rheumatic drug (bDMARD) used to treat rheumatoid arthritis (RA). National registers are useful resources for investigation of long term real world outcomes. The purpose was to compare the effectiveness of abatacept in the treatment of RA between bionaïve patients and patients with previous bDMARD treatment and to investigate predictors of remaining on treatment with abatacept.

Methods
This was an observational cohort study, based on a national quality register database. Patients with a diagnosis of RA who initiated treatment with abatacept between April 1, 2006 and November 20, 2017, were included. Patients were censored at abatacept discontinuation, death, migration, or the end of the study period. Survival on drug, by previous exposure to bDMARDs, was estimated using the Kaplan-Meier method. Predictors of discontinuation of abatacept were investigated in Cox Proportional Hazards analyses, with significance-based backwards stepwise selection of variables for the final multivariate model.

Results
A total of 2716 patients with RA (80 % females, mean age 59 years, mean duration of RA 14 years) started abatacept during the study period. Seventeen percent had no previous bDMARD treatment (bionaïve patients), 27 % had received 1 bDMARD previously, and 56 % had been treated with ≥ 2 bDMARDs. Fifty percent each of the patients received intravenous and subcutaneous therapy. At the time of abatacept initiation, 57 % were on methotrexate (MTX), and 48 % were treated with glucocorticosteroids. There were significant differences in drug survival across categories of previous bDMARD exposure (p=0.002). The median survival time on treatment was 2.23 years for bionaïve patients (95 % confidence interval (CI) 1.69-2.79)), 1.68 years for those with 1 previous bDMARD (95 % CI 1.34-2.01) and 1.56 years for those with ≥ 2 previous bDMARDs (95 % CI 1.35-1.76). At 6 months, 88 % of bionaïve patients remained on abatacept, compared to 74 % at 12 months. The corresponding figures for those with 1 or ≥ 2 previous bDMARDs were 78 % and 61 %, and 76 % and 59 %, respectively. In bivariate analyses, bionaïve patients were less likely to discontinue treatment compared to those treated with ≥ 2 previous bDMARDs previously (Table). Bionaïve patients were more often male (28 % vs 18 %) and had lower pain scores (mean Visual analogue scale score 58 vs 62) compared to those previously exposed to ≥ 2 bDMARDs. Measures of disease severity were associated with reduced drug survival (Table), but age, RA duration and method of administration had no significant impact on discontinuation. In the final multivariate model, there was a positive association between pain score and abatacept discontinuation, whereas male patients and those on MTX had a reduced risk of stopping abatacept (Table).

Significant predictors for abatacept discontinuation. Cox regression analysis

		Unadjusted analysis HR (95 % CI)	Multivariate analysis – final model HR (95 % CI)
Sex	Male	0.85 (0.75-0.96)	0.86 (0.74-0.98)
No of previous bDMARDs	≥ 2 bDMARDs	reference (1.0)	*
	Bionaive	0.78 (0.68-0.90)	*
	1 bDMARD	0.94 (0.84-1.05)	*
Baseline clinical characteristics	DAS28-CRP (per SD)	1.11 (1.04-1.17)	*
	VAS pain (per SD)	1.14 (1.08-1.21)	1.14 (1.07-1.20)
	Current Methotrexate	0.86 (0.78-0.96)	0.85 (0.76-0.95)
	HAQ-DI (per SD)	1.10 (1.04-1.17)	*

*Not included in the final model

Conclusions
Survival on abatacept was significantly longer in bionaïve RA patients compared to those previously exposed to bDMARDs. In the bionaïve subset, 50 % of the patients remained on treatment after 28 months. Concomitant MTX therapy, male sex and low pain scores were associated with longer drug survival for abatacept.

ABSTRACTNUMMER: 1532-A-1818 16

SIBLINGS OF PATIENTS WITH RHEUMATOID ARTHRITIS ARE AT INCREASED RISK OF ACUTE CORONARY SYNDROME

Helga Westerlind[1], Marie Holmqvist[1], Lotta Ljung[1,2], Thomas Frisell[1], Johan Askling[1]

[1] *Karolinska Institutet*
[2] *Umeå Universitet*

Background
Patients with rheumatoid arthritis (RA) are at increased risk of cardiovascular disease such as acute coronary syndromes (ACS), which cannot entirely be explained by traditional cardiovascular risk factors. Studies have shown an association between RA disease severity and risk of ACS, speaking for a contribution of the RA disease per se to the excess ACS risk. In a recent report, however, we demonstrated that despite more efficient control of inflammation in RA during the recent years, the excess risk for ACS among patients with RA compared to the general population remains1. This finding suggests that besides effects related to the RA disease per se, there may be a shared susceptibility. If the excess risk of ACS in patients with RA were increased due to this, an increased risk of ACS would be observed also in individuals with a similar genetic set-up and background as the patients with RA, such as their siblings. This pro ect aimed at investigating any potential shared susceptibility between RA and ACS by estimating the risk of ACS in full siblings of patients with (vs. without) RA.

Methods
Methods e used the Swedish Rheumatology uality register (SR) to identify an early RA cohort diagnosed between 1996-2015, which was linked to the Swedish Multigeneration Register, Patient Register, the Cause of Death register, and the Total Population Register. Through this, we sampled five general population comparator sub ects to each patient with RA, matched by birth year and sex, and identified all full siblings to patients with RA and for their comparator sub ects born within five years of their index case. The comparators, and all siblings, were required to be alive and living in Sweden at the time of the index patient s RA diagnosis (start of follow-up). All unique individuals were then followed for ACS (defined as first ever hospitalization for ACS (ICD10 I21 or I20.0) or MI listed as the cause of death), and censored at death, migration, RA diagnosis (for non-RA sub ects) or the end of the study (Dec 31st 2015). e calculated hazard ratios (HR) using a Cox proportional hazards model, ad usting for age, sex and calendar period of diagnosis. Confidence intervals (CI) were estimated using a robust sandwich estimator.

Results
Results e identified 7492 patients with RA who had 10671 full siblings, and 35120 population comparator sub ects with 47137 full siblings. The HR for ACS was 1.44 (95%CI 1.25-1.66) and 1.23 (95%CI 1.09-1.40) for patients with RA and their siblings, respectively, compared to the comparator sub ects. A direct comparison ➤

between the RA patients and their RA-free siblings confirmed the familial association between RA and ACS, HR 1.19 (95%CI 1.02-1.38).

Conclusions

The increased risk of ACS in siblings of patients with RA a) provide evidence of shared susceptibility between RA and ACS, the nature of which needs to be further investigated, and b) suggests that to bring down the CV risk in RA to that in the general population, cardiopreventive measures must go beyond optimized RA disease control.

References

1. Holmqvist M, Ann Rheum Dis, 2017 PMID 28710095

ABSTRACTNUMMER: 1533-A-1818 17

LOW SERUM IGF1 IS ASSOCIATED WITH HIGHER CARDIOVASCULAR RISK IN WOMEN WITH RHEUMATOID ARTHRITIS

Rachelle Ann Espino, Caroline Wasén, Sofia Töyrä Silfverswärd, Mitra Nadali, Rille Pullerits, Maria I. Bokarewa

Department of Rheumatology and Inflammation Research, University of Gothenburg

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease. This is when the body's immune defense system attacks healthy tissues causing immense swelling and primarily affecting the joints. Imbalance in IGF1 receptor signaling has been described in RA. This study aims to investigate the relation between serum levels of IGF1 and cardiovascular risk (CVR) in women with RA. In a cohort of 184 RA women (mean age of 51.7 years), the risk of dying from CV disease within 10 years was calculated using the Framingham risk score computation. CVR and characteristics related to the traditional and RA-related CVR factors were analyzed with respect to levels of serum IGF1. The groups with serum IGF1 levels below and above the median of the total cohort were compared. Quantitative PCR was performed to measure transcription of parameters involved in the IGF1/IGF1R-signaling pathway. Women with low IGF1 (mean 106.1 pg/ml) had significantly higher CVR (mean 25.6 vs. 17.2, p=<10-4) in comparison to those with higher levels (mean 196.8 pg/ml). The main traditional CVR factors were associated with low IGF1. This included age (mean 56.8 vs. 46.5 years, p=<10-4), higher BMI (mean 26.6 vs. 24.5 kg/m2, p=0.002), higher prevalence of hypertension (p=0.005), higher body fat content (mean 39.5 vs. 34.7, p=<10-4); though smoking displayed no significance between the groups. Low IGF1 levels were also associated with adverse lipid profile, and high total cholesterol (TC, mean 5.6 vs. 5.1, p=0.001) consisting mainly of LDL (p=0.003) being present. Although HDL and triglycerides did not differ insignificantly, both tended to be higher in the low IGF1 group. Conversely, the atherogenic index (HDL/TC ratio) was similar (mean 0.34 vs. 0.35), which makes the impact of lipids in IGF1-related CVR in these RA women uncertain.

With exception of serum IL-6 (mean 8.3 vs. 6.1 pg/ml, p=0.047), which appeared to be high in low IGF1 group, the two groups presented no other significant difference in the RA-related CVR factors such as the disease activity measured by DAS28 (mean 3.3 vs. 3.0), disease duration (mean 11.9 vs. 8.8), serum IL-1β (mean 19.1 vs. 23.6 ng/ml) and the prevalence of autoantibodies (90% vs. 92%). Furthermore, low IGF1 group exhibited unfavorable balance in proteins of IGF1R signaling as revealed by high IGF1R (p=0.015) and low IRS1 (p=0.018) and IRS2 (p=0.009) transcription coincides to serum levels of IGF1. Low serum levels of IGF1 are associated with higher CVR in RA women. This increase in CVR seems to contain metabolic parameters and less dependent of the RA-related characteristics.

ABSTRACTNUMMER: 1534-A-1818 18

IMPACT OF SECUKINUMAB TREATMENT ON PSORIATIC ARTHRITIS PATIENTS WITH OR WITHOUT

J.K. Wallman[1], G. Schett[6], I. B. McInnes[7], E. Quebe-Fehling[3], L. Rasouliyan[5], L. Pricop[2], C. Gaillez[3], A. E. R. Fasth[4]

[1] Lund University
[2] Novartis Pharmaceuticals Corporation, East Hanover, United States
[3] Novartis Pharma AG, Basel, Switzerland
[4] Novartis Sverige AB, Täby, Sweden
[5] RTI Health Solutions, Barcelona, Spain
[6] University of Erlangen-Nuremberg, Erlangen, Germany
[7] University of Glasgow, Glasgow, United Kingdom

Background

Enthesitis is a common phenotypic manifestation of psoriatic arthritis (PsA) affecting approximately 70% of patients (pts) and may be associated with worse outcomes.1 Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralises IL-17A, provided significant and sustained improvement in the signs and symptoms of active PsA, with sustained resolution of enthesitis in Phase 3 studies.2,3 To report the impact of SEC treatment on efficacy outcome measures in active PsA pts with or without baseline (BL) enthesitis (defined by Leeds Enthesitis Index) using pooled data from the FUTURE 2 (NCT01752634) and FUTURE 3 (NCT01989468) studies over 2 years.

Material & Methods

SEC and placebo (PBO) were administered weekly during the first 4 weeks (wks) followed by subcutaneous maintenance dosing every 4 wks thereafter (PBO until Wk 16/24). The results are reported only for SEC 300 and 150mg (approved doses). Efficacy outcomes (ACR20/50/70, PASI 90, HAQ-DI, SF-36 PCS and DAS28-CRP) were analysed post-hoc in pts with enthesitis at BL (BLE; N=466) or without enthesitis at BL (No BLE; N=246). Observed data are presented for binary variables and least-square (LS) means from analysis of covariance for continuous variables.

Results

A total of 65% of pts had BLE. BL demographics were balanced between the BLE and No BLE groups except for a higher proportion of females and numerically higher tender joint count, disability (HAQ-DI) and lower physical function (SF-36 PCS) in BLE pts than No BLE pts. At Wk 16, improvements in ACR and PASI responses, HAQ-DI, SF-36 PCS and DAS28-CRP were similar in oth groups treated with SEC 300mg, but were lower (except for PASI) in BLE pts treated with SEC 150mg (Table). Improvements in these outcomes followed a similar trend to Wk 104 in SEC-treated pts (Table).

Table. Summary of Results with Secukinumab

	Wk	BLE			No BLE		
		300mg	150mg	PBO	300mg	150mg	PBO
ACR20[a,b]	16	53.5	46.5	19.8	53.7	64.6	18.1
	104	56.8	52.4	-	62.6	62.9	-
ACR50[a,b]	16	31.3	21.8	6.7	35.8	35.4	5.6
	104	44.7	34.8	-	47.3	34.3	-
ACR70[a,b]	16	16.9	9.2	1.8	20.1	16.5	1.4
	104	28.5	15.2	-	34.1	21.4	-
PASI 90[a,c]	16	58.0	36.6	7.9	62.1	57.0	6.9
	104	67.9	59.7	-	78.5	44.4	-
HAQ-DI[d]	16	-0.5	-0.3	-0.2	-0.5	-0.3	-0.2
	104	-0.5	-0.4	-	-0.5	-0.4	-
SF-36 PCS[d]	16	8.9	8.7	2.5	8.6	7.6	2.8
	104	7.4	4.3	-	8.6	6.9	-
DAS28-CRP[d]	16	-1.5	-1.05	-0.5	-1.35	-1.6	-0.5
	104	-1.7	-1.6	-	-2.0	-1.9	-

[a]Response, %; [b]At Wk 16/104, n=144/137 (SEC 300), 159/145 (SEC 150) and 163 (PBO) with enthesitis and n=95/91 (SEC 300), 79/70 (SEC 150) and 72 (PBO) without enthesitis at BL; [c]At Wk 16/104, n=66/56 (SEC 300), 82/63 (SEC 150) and 63 (PBO) with enthesitis and n=38/34 (SEC 300), 46/36 (SEC 150) and 30 (PBO) without enthesitis at BL (provisional cohort); [d]LS mean

Conclusions
Although pts with BLE had more severe BL clinical characteristics than pts with No BLE, SEC showed higher efficacy than PBO at Wk 16 and sustained efficacy over 104 wks in both groups with greater magnitude of improvement in pts treated with SEC 300mg than 150mg.

References
1.Schett G, et al. Nat Rev Rheumatol 2017;13:731–41; 2.Mease PJ, et al. N Engl J Med 2015;373:1329–39; 3. McInnes IB, et al. Lancet 2015;386:1137–46

ABSTRACTNUMMER: 1539-A-1818 19

ANKYLOSING SPONDYLITIS RELATED FACTORS PREDICT THE PRESENCE OF CARDIAC CONDUCTION DISTURBANCES – A SWEDISH LONGITUDINAL COHORT STUDY

Karin Bengtsson[2], Eva Klingberg[2], Anna Deminger[2], Lennart TH Jacobsson[2], Lennart Bergfeldt[1], Helena Forsblad-d'Elia[2,3]

[1] Avdelningen för molekylär och klinisk medicin, Institutionen för Medicin, Sahlgrenska Akademin vid Göteborgs universitet
[2] Avdelningen för reumatologi och inflammationsforskning, Institutionen för medicin, Sahlgrenska Akademin vid Göteborgs universitet
[3] Avdelningen för reumatologi, Institutionen för folkhälsa och klinisk medicin, Umeå universitet

Background
Despite a well-known association between ankylosing spondylitis (AS) and cardiac conduction disturbances (from here CCD), it's not clear which factors that predict their presence.

Objectives
To describe electrocardiographic (ECG) alterations in a cohort of patients with AS and if AS related factors at baseline predict the presence of CCD at 5-year follow-up.

Material and methods
In total 210 patients diagnosed with AS at 3 rheumatology clinics from Western Sweden participated 2009 in an observational longitudinal cohort study with a planned follow-up after 5 years. At follow-up 2014, physical examination, ECG, questionnaires, laboratory tests and radiographic examinations were repeated in 172 patients (82%). CCD was defined in the presence of AV block I (PQ duration ≥ 220 ms), AV block Ix (PQ duration 200-219 ms), AV block II-III, right and left bundle branch block (RBBB and LBBB)), left anterior and posterior fascicular block (LAFB and LPFB) and pacemaker. Descriptive statistics and logistic regression analyses were performed in order to find predictors at baseline for the presence of CCD at follow-up. Baseline characteristics with a p-value < 0.2 in univariate analyses (dependent variable present CCD (yes=1, no=0)) were included as independent variables in a forward stepwise multiple logistic regression analysis.

Table 1.

	Patients without CCD (n=149)	Patients with CCD (n=23)
BASELINE CHARACTERISTICS 2009		
Male sex	74 (49.7)	19 (82.6)
Age, years	48.5±12.3	58.7±11.4
Symptom duration, years	22.5±12.3	33.5±14.3
HLA-B27	127 (85.2)	22 (95.7)
ASDAS-CRP	2.0±0.8	2.7±1.0
History of anterior uveitis	69 (46.3)	19 (82.6)
Aortic regurgitation[#]	20 (13.4)	6 (26.1)
At least one syndesmophyte	63 (42.3)	17 (73.9)
Reported comorbidity		
a. Hypertension	36 (24.2)	11 (47.8)
b. Diabetes	5 (3.4)	0 (0.0)
c. Hyperlipidemia	7 (4.7)	4 (17.4)
Medications		
a. Anticoagulation	6 (4.0)	8 (34.8)
b. Potential antihypertensive	22 (14.8)	11 (47.8)
c. Lipid modulators	7 (4.7)	3 (13.0)
d. DMARDs	55 (36.9)	5 (21.7)
CCD 2014		
1. AV block Ix		10 (43.5)
2. AV block I		7 (30.4)
3. LAFB		3 (13.0)
4. RBBB		1 (4.3)
5. LBBB		2 (8.7)
6. Pacemaker		3 (13.0)

Data are expressed as mean ± SD or number (%). [#] Missing data in 13 patients (10 without CCD and 3 with CCD) who did not underwent echocardiography at baseline.

Results
In total 23 of the 172 patients (13.4%) had CCD at 5-year follow-up. Eight had developed a new CCD out of which 2 had required pacemaker implantation, 3 had a more aggravated CCD, whereas 10 patient had an unchanged and 2 a less pronounced CCD compared with 2009. CCD and some of the patient characteristics are presented in Table 1. (None had LPFB or AV-block II-III). According to multiple logistic regression analysis, male sex (Odds ratio (OR) (95 % CI) 4.7 (1.1-20.6)), increasing age (OR 1.1 (1.0-1.1) per 1 year), a history of anterior uveitis (OR 6.4 (1.1-36.2)), higher ASDAS-CRP (OR 3.6 (1.6-7.9)) and existing CCD at baseline (OR 42.4 (8.9-202.2)) were predictors for the presence of CCD at follow-up.

Conclusions
The presence of CCD in AS is dynamic. AS related factors, represented by baseline ASDAS-CRP and a history of anterior uveitis, predicted their presence at 5-year follow-up.

ABSTRACTNUMMER: 1545-A-1818 20

CASE FATALITY OVER 365 DAYS AFTER FIRST ACUTE CORONARY SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS

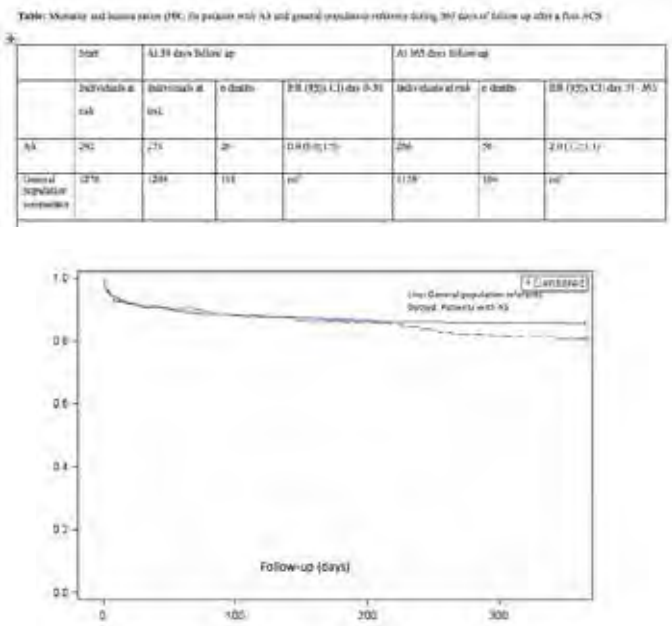
Anna Södergren[2], Johan Askling, Karin Bengtsson, Helena Forsblad D'Elia, Tomas Jernberg[4], Ulf Lindström[1], Lotta Ljung[3,5], Ängla Mantel[5], Lennart TH Jacobsson[1]

[1] Avd för reumatologi och inflammationsforskning vid Institutionen för medicin, Göteborgs universitet
[2] Inst för folhälsa och klinisk medicin/Reumatologi
[3] Inst för folhälsa och klinisk medicin/Reumatologi, Umeå Universitet
[4] Institutionen för Kliniska vetenskaper, Danderyds sjukhus, Karolinska Institutet
[5] Klinisk epidemiologi, Institutionen för medicin, Solna, Karolinska Institutet

Background
Ankylosing spondylitis (AS) is characterised by systemic and local inflammation of the axial skeleton, joints, and entheses. Studies have suggested a higher risk of acute coronary syndrome (ACS) among patients with AS compared with the general population, but whether patients with AS also have an increased fatality following ACS is not known.

Aim
Is AS associated with an increased case fatality after a first-time ACS compared with the general population?

Methods
From the Swedish National Patient Register (NPR) we identified ➤



all patients registered with AS Jan 2001 through Dec 2014 and a later registration of a first time ACS between Jan 2006 and Dec 2014 (n=292). As a general population comparator, we identified up to 5 individuals per index-patient (n=1276), matched on year of first ACS and birth, gender, and place of living. The follow-up period began at the date of admission for ACS and extended until death, emigration, 365 days of follow-up or 31 December 2014, whichever occurred first. Hazard ratios (HR) for death in the AS group vs. the general population comparator was assessed using Cox regression. We assessed HRs for death in two intervals: 30-day mortality (day 1 through 30), and mortality day 31 through 365.

Results
During the 365 days following the ACS, 56 (19%) of the 292 AS patients and 184 (14%) of the 1276 population controls died (Table). Whereas the 30-day mortality in the AS group was not elevated (HR=0.9), the mortality day 31 through 365 was doubled compared with the general population (HR=2.2, Table and Figure).

Conclusion
Patients with AS were at increased risk of death during the first year, though not during the first month, following ACS. It is yet not clear whether this could be due to factors associated with the AS disease per se, or differences in ACS characteristics or treatment.

ABSTRACTNUMMER: 1550-A-1818 21

THE DOSING OF INTRA-ARTICULAR TRIAMCINOLONE HEXACETONIDE FOR KNEE SYNOVITIS IN CHRONIC

Tomas Weitoft[1], Kajsa Öberg[2]

[1] Centrum för Forskning och Utveckling Uppsala Universitet/Region Gävleborg
[2] Reumatolologikliniken Falu Lasarett

Background
Intra-articular glucocorticoid (IAGC) injection treatment is an easy and effective way to treat signs and symptoms of arthritis and it has been used for decades. Serious adverse reactions are rare, but IAGC therapy has impact on endocrine balances. There is limited knowledge of the adequate dosing for different joints and dosing traditions vary all over world.

Objectives
To compare the relapse rate during 6 months after IAGC for knee synovitis, between two common doses (20 mg vs 40mg) of triamcinolone hexacetonide (THA).

Methods
A total of 159 adult patients with rheumatoid arthritis (RA) or psoriatic arthritis (Psoa) and active knee synovitis was randomized to IAGC injection with either 20 mg or 40 mg THA blinded to the participants. The primary endpoint was relapse of arthritis. When symptoms from the treated joint recurred and signs of arthritis could be confirmed on a following Clinical examination a relapse was recorded and days from injection to relapse was calculated. At the end of the observation period those without relapse had a phone call to verify persistence of good treatment response.

Results
In this material there was no significant difference in patient characteristics at baseline and the proportion of relapse after 6 months were equal in the treatment arms (30% versus 32%, p=0.822). Additionally no significant differences were found in the subgroups with RA and Psoa patients.

Conclusions
To reduce the risk for endocrine side effects and as no difference in treatment outcome between the compared doses was found the lower 20 mg THA dose should be preferred in IAGC treatment for knee synovitis in chronic polyarthritis.

ABSTRACTNUMMER: 1552-A-1818 22

URIC ACID MEASUREMENT IN ARTHRALGIA PATIENTS

Mathilda Mybeck[1], Maria Bokarewa[1,2], Malin Erlandsson[1,2], Li Bian[2], Sofia Silfverswärd[1], Rille Pullerits[1,2]

[1] Göteborgs universitet
[2] Sahlgrenska universitetssjukhuset

Background
Recent studies attracted attention to a potential connection between rheumatoid arthritis (RA) and uric acid. It has been shown that RA patients with hyperuricemia have a milder joint disease [1]. Furthermore, it is more common for patients who do not have rheumatoid factor (RF) to have monosodium urate crystal deposits in their joints [2]. Therefore, our objective was to examine the connection between uric acid and RA and to find out if there was a connection between uric acid, RA-specific autoantibodies and survivin.

Material and methods
A total of 338 patients were selected from the material of 1743 first-visit patients with arthralgia to the Rheumatology Clinic at the Sahlgrenska University Hospital, Gothenburg, during one year. All patients had at least one measure of serum uric acid levels, where >400 mol/l indicated hyperuricemia for females and >480 mol/L indicated hyperuricemia for males. The patients were divided into groups depending on gender, rheumatic diagnosis, autoantibody profile, survivin and uric acid level. The gout diagnostic rule was applied to 152 patients [3]. Statistical analysis was done using multiple Chi-square test and ANOVA.

Results
Hyperuricemia was found in 114 of 338 (34 %) patients, and in 35 of 42 (83 %) patients diagnosed with gout. As expected, the prevalence of hyperuricemia was higher in males than females (29/140 vs.

15/198, P<0.0005). There was no difference in uric acid levels in patients with rheumatic diagnoses except for gout, which had significantly higher levels of uric acid than RA (median 454 mol/l vs 281 mol/l, P<0.0001). Among females with hyperuricemia, RA was the most common diagnosis (40%). However, symptoms of gout, from gout diagnostic rule, was significantly less in RA patients compared to gout (Mann-Whitney, females P=0.011, males P=0.028.). The prevalence of hyperuricemia was similar among the patients stratified by autoantibody profile as sero-positive (aCCP and/or RF) and sero-negative (9/25 vs 44/114, P=0.82 for males and 11/33 vs 51/166, P=0.76 for females). We found no difference in prevalence of hyperuricemia between survivin-positive and survivin-negative patients (21/55 vs 32/84, P= 0.99 for males and 31/98 vs 31/101, P=0.89 for females).

Conclusions

Hyperuricemia was attributed to the diagnosis of gout and shows its specificity regardless of autoantibody and serum survivin profile. Our study supports the use of gout diagnostic rule for clinical diagnosis of gouty arthritis in primary care when joint fluid analysis is not available.

ABSTRACTNUMMER: 1558-A-1818 23

THE VON WILLEBRAND FACTOR-BINDING PROTEIN IS A MAJOR VIRULENCE FACTOR IN STAPHYLOCOCCAL SEPTIC ARTHRITIS

Tao Jin[1,5,6], Manli Na[1], Zhicheng Hu[1,2], Majd Mohammad[1], Abukar Ali[1], Ying Fei[1,2], Anders Jarneborn[1,5], Peter Verhamme[3], Olaf Schneewind[4], Dominique Missiakas[4],

[1] Department of Rheumatology and Inflammation Research, Institution of Medicine, Sahlgrenska Academy at University of Gothenburg, Sweden
[2] Department of Microbiology and Immunology, The Affiliated Hospital of GuiZhou Medical University, China
[3] Center for Molecular and Vascular Biology, Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium
[4]Department of Microbiology, University of Chicago, Chicago, Illinois, United States of America
[5]Department of Rheumatology, Sahlgrenska University Hospital, Swe
[6] Sahlgrenska universitetssjukhuset

Background

Septic arthritis is the most dangerous joint diseases due to its rapidly progressive and destructive disease character. Staphylococcus aureus (S. aureus) activates host coagulation cascade by two secreted enzymes, coagulase (Coa) and von- Willebrand factor-binding protein (vWbp). So far, the role of these clotting factors in septic arthritis is largely unknown.

Aims

To investigate the role of Coa and vWbp in staphylococcal septic arthritis in mice.

Methods

The induction and maintenance of septic arthritis by four different congenic S. aureus strains differing in expression of coagulases (WT newman, ΔCoa, ΔvWbp, and ΔCoa/ΔvWbp) were studied in a murine model for septic arthritis. Arthritis and bone destruction were evaluated clinically, histopathologically and radiologically. To understand the impact of interaction between vWbp and vWF in disease development, von Willebrand factor (vWF) deficient mice and their wild-type counterparts were inoculated intravenously with WT and ΔvWbp S. aureus strains.

Results

Both severity and frequency of septic arthritis were greatly ameliorated in wild type mice infected with ΔCoa/ΔvWbp and ΔvWbp, but not ΔCoa strains compared with wildtype strain, suggesting that vWbp rather than Coa is a major virulence factor in S. aureus septic arthritis. Importantly, no difference was found in arthritis severity between ΔvWbp and WT strains when vWF deficient mice were used.

Conclusion

vWbp expression enhances staphylococcal septic arthritis and this effect might be mediated through the interaction between vWbp and vWF.

ABSTRACTNUMMER: 1560-A-1818 24

UNMET NEEDS IN RHEUMATOID ARTHRITIS – A SUBGROUP OF PATIENTS WITH HIGH LEVELS OF PAIN, FATIGUE AND PSYCHOSOCIAL DISTRESS 3 YEARS AFTER DIAGNOSIS

Joakim Lindqvist[3], Lars Klareskog[3], Lars Alfredsson[1], Jon Lampa*[3], Helga Westerlind*[1,2]

[1] Institutet för Miljömedicin, Karolinska Institutet, Stockholm
[2] Institutionen för Medicin, Avdelningen för Klinisk Epidemiologi, Karolinska Institutet, Stockholm
[3] Institutionen för Medicin, Enheten för Reumatologi, Karolinska Institutet, Stockholm
* These authors contributed equally

Background

The wide range of effective treatment alternatives for rheumatoid arthritis (RA) makes treating the disease to inflammatory remission a feasible goal for a majority of patients. However, earlier studies have reported that symptoms other than inflammatory disease activity causes a substantial burden of illness for RA-patients. These unmet needs include persistent pain, fatigue, impaired physical function and mental health status (1). The aim of this project was to identify subgroups of early RA-patients based on pain, fatigue, sleep, physical and mental function and quality of life, 3 years after diagnosis and to investigate associations between subgroups and clinical presentation around the time of diagnosis.

Methods

Data was compiled from the early RA cohort Epidemiological Investigation of RA (EIRA) and linked to the Swedish Rheumatology Quality Register (SRQ). All patients were diagnosed with RA according to the 1987 ACR criteria. Early RA-patients with clinical data from diagnosis and 3 year follow-up questionnaire data were included (N=618; 74% women, median age at diagnosis 58 years). Measurements of pain, fatigue, physical and mental health related quality of life, physical functioning and sleep problems was entered into a hierarchical agglomerative clustering procedure using Ward's method of squared Euclidian distances. Associations between subgroups and clinical variables at diagnosis were calculated using Chi square, t-test or Wilcoxon, based on variable type and distribution. All statistical analysis was performed using jmp statistical software (SAS, US).

Results

The cluster analysis identified three subgroups. Subgroup 1 consisted of 178 patients (29%) doing significantly worse for all included variables. Subgroup 3 consisted of 209 patients (34%) doing very well and subgroup 2, consisting of 231 patients (37%), constituted an intermediate group doing fairly well. Subgroup 1 was associated with female sex (p=0.0007) and lower education level (p=0.0003)

compared to subgroup 3. Subgroup 1 was also associated to higher HAQ (p <0,0001), higher patient global assessment of health (p<0.0001), higher pain ratings (p<0.0001) and lower swollen/tender joint count ratio (STR) (p=0.0065) at the time of diagnosis compared to subgroup 3. Moreover, subgroup 1 was highly associated to pain problems before onset of RA (p <0.0001).

Conclusions
A subgroup of almost a third of the RA-patients had high levels of pain, fatigue, sleep problems and poor physical and mental health related quality of life 3 years after RA-diagnosis. These findings indicate that other factors than inflammatory disease activity causes a significant burden of illness also at an early stage of RA and that there is a need of additional intervention strategies for these patients.

References
1. Taylor PC, Moore A, Vasilescu R, Alvir J, Tarallo M. A structured literature review of the burden of illness and unmet needs in patients with rheumatoid arthritis: a current perspective. Rheumatol Int. 2016;36(5):685-95.

ABSTRACTNUMMER: 1562-A-1818 25

SJUKSKÖTERSKEMOTTAGNING

Madeleine Ericsson, Helena Björkesten, Anne-Charlotte Hoflin, Anne-Louise Jaregran, Karin Hjorton,

Reumatologmottagningen, Reumatologkliniken, Akademiska sjukhuset Uppsala

Bakgrund/problem
I Uppsala finns sedan många år en sjuksköterskemottagning i form av s.k. nydiagnosmottagning dit alla med nydiagnosticerad sjukdom kommer för information. Det har även gjorts försök med sköterskemottagning för återbesök i mindre skala. Vi har haft svårt att hinna med planerade återbesök till läkare i tid på reumatologkliniken. Mottagningen hade däremot efter flytt fått bättre lokaler samt blivit personalmässigt fulltalig med sjuksköterskor.

Syfte/mål
- Genom ny sjuksköterskemottagning för stabila patienter med RA förbättra kontinuiteten och tryggheten med tätare återbesökstider och därmed god kontroll av den antireumatiska behandlingen.
- Frigöra fler återbesökstider till läkare till de svårast sjuka och komplicerade patienterna.
- Öka sjuksköterskans kunskap och självständighet inom reumatologi.
- Förbättra registreringen av klinisk data i SRQ.

Metod/genomförande
1. Arbetet med bokningsunderlag hade tidigare skötts av sjuksköterskorna. Detta togs över av sekreterarna genom att planering efter läkarbesök började dikteras av läkarna fr.o.m. maj 2017.
2. Omfördelning av arbetsuppgifter för att frikoppla en sjuksköterska till de dagliga återbesöken.
3. Återkommande planeringsmöten.
4. Studiebesök i Västerås på Reumatologmottagningen.
5. Ny journalmall för sjuksköterskebesöket i journalsystemet Cosmic för att möjliggöra snabbt ifyllande.
6. Teoretisk och praktisk utbildning i ledstatus för sköterskorna med hjälp av läkare och patient-partner.
7. Patienter med en okomplicerad, stabil lågaktiv RA med syntetiska DMARD och eller TNF-hämmare valdes ut till sköterskemottagningen. Denna patientgrupp kallas till sjuksköterska vartannat år och till sin ansvariga läkare vartannat år.
8. Återbesöket hos sjuksköterskan inkluderar: Ledstatus och blodtryck, genomgång av läkemedelslistan, genomgång av provsvar och SRQ-registreringen, levnadsvaneenkät – samt livsstilsråd.
9. Egna mallar för besöket med sökord och bilder på lederna, för att snabbt kunna nedteckna under besöket viktiga detaljer.
10. Mottagningssjuksköterskans arbetsuppgifter: Återbesök, injektionsundervisning för nyinsatta antireumatiska läkemedel, uppföljande telefonsamtal med patient som är nyinsatta på ett antireumatikum.

Resultat
Vi startade 5 februari 2018. Under denna tid har vi genomfört ett 50-tal återbesök till sjuksköterska. För att kontinuerligt utvärdera våra resultat har en enkät gjorts för att mäta kvalitén på patientens återbesök genom frågor som belåtenhet, om dem saknade något, om vi kan förbättra något. Vi har hitintills fått mycket god respons av dessa patienter.

Slutsats/förbättringar
När större antal återbesök genomförts planeras en sammanställning av enkäten att presenteras vid en kommande posterpresentation. Patienternas belåtenhet med besöket tyder på att vi ökar patientens trygghet med tätare återbesök på reumatologmottagningen i Uppsala.

ABSTRACTNUMMER: 1564-A-1818 26

WEIGHT-LOSS TREATMENT WITH VERY LOW ENERGY LIQUID DIET IMPROVES DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY

Eva Klingberg[3], Annelie Bilberg, Sofia Björkman, Martin Hedberg, Björn Eliasson[1], Ingrid Larsson[2]

[1] Department of Endocrinology, Diabetology and Metabolism, Sahlgrenska University Hospital
[2] Department of Gastroenterology and Hepatology Sahlgrenska University Hospital
[3] Sahlgrenska Academy at the University of Gothenburg

Background
Obesity is over-represented in patients with psoriatic arthritis (PsA) and associated with increased risk of getting the disease, higher disease activity, poorer effect of treatment and in addition cardiovascular co-morbidity. Studies on the effects of weight-loss are however needed.

Objectives
This study aimed to determine the effects of weight-loss treatment with Very Low Energy liquid Diet (VLED) on disease activity in patients with PsA and obesity.

Methods
Patients with PsA (Caspar criteria) and obesity (body mass index BMI ≥33 kg/m2) where recruited. Treatment with DMARDs and biologics was held constant from 3 months before baseline until 6 months after baseline. VLED, which gives a daily energy intake of 640 kcal, was taken during 12-16 weeks, depending on BMI. An energy restricted diet was then successively introduced during 18 weeks. The treatment was given within a structured framework for support and medical follow-up during 12 months. The patients were assessed with 68/66 tender/swollen joints count, back-mobi-

lity tests, body surface area (BSA), questionnaires, ESR, CRP and BMI at baseline, 3 and 6 months. The number of patients reaching Minimal Disease Activity (MDA), Psoriatic Arthritis Response Criteria (PsARC) and American College of Rheumatology (ACR) 20, 50, 70 response criteria was calculated.

Results

Totally 41 PsA patients (63% women) with median age 54 (IQR 48-62) years completed the study. At baseline BMI was positively correlated with DAS28, DAPSA, ASDAS-CRP, tender joints count, CRP, patient global VAS, Leeds enthesitis index, HAQ and BASFI. (Spearman's rho ranged from rS= 0.312, p= 0.047 to rS= 0.497, p=0.001) The median weight loss was 18.7 kg (IQR 14.6-26.5, range 8.5- 40.2) or 18.6% (IQR 14.7-26.3, range 8-35) of the baseline weight. BMI decreased from median 35.2 (34.1-38.1) kg/m2 to 29.7 (26.2-31.5) kg/m2 (p<0.001). A majority of the disease activity parameters improved significantly, including 68/66 tender/swollen joints count, CRP, BSA, Leeds enthesitis index, HAQ, BASDAI, BASFI and patient VAS for global health, pain and fatigue. The number of patients with MDA increased from 29% (n=12) to 54% (n=22), between baseline and the 6 months visit (p<0.001). PsARC was reached by 46.3% (n=19) and the ACR 20, 50, 70 responses were 51.2% (n=21), 34.1% (n=14) and 7.3% (n=3) respectively. The VLED treatment was generally well tolerated and no serious adverse events occurred. When the patients were asked to score their experience of the VLED treatment between 1 (very easy to implement) to 10 (very hard to implement) the median score was 2 (IQR 1-3.5).

Conclusions

Weight-loss treatment with VLED had significant positive effects on disease activity in joints, entheses and skin in patients with PsA and obesity. The percentage of patients reaching ACR 20, 50, 70 responses was 51.2%, 34.1% and 7.3% respectively. The VLED treatment was effective, safe and well tolerated. At baseline increased BMI was associated with higher disease activity and poorer function.

ABSTRACTNUMMER: 1565-A-1818 27

TENOSYNOVITIS DETECTED BY ULTRASOUND PREDICTS ARTHRITIS ONSET IN INDIVIDUALS THAT ARE AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

Yogan Kisten[2], Hamed Rezaei[2], Erik af Klint[2], Guozhong Fei[1,2], Aleksandra Antovic[1,2], Aase Hensvold[1,2], Anca Catrina[1,2]

[1] Academic Specialist Center, Center for Rheumatology, Stockholm Health Service, Stockholm, Sweden
[2] Rheumatology Unit, Department of Medicine, Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden

Background

The pathophysiological processes leading from musculoskeletal (MSK) complaints to clinically manifest rheumatoid arthritis (RA) are not fully understood. We aim to explore ultrasound detected tenosynovitis as a marker of arthritis development.

Methods

Patients presenting with MSK complaints and a positive Anti-Citrullinated Protein Antibody (ACPA) test were referred from primary care centres to the Rheumatology Department of Karolinska University Hospital. Those lacking clinical signs of arthritis, confirmed by absence of synovial hypertrophy and Doppler activity on ultrasound, were recruited into the Risk-RA prospective program. A total of 66 patients with complete ultrasound records were included between years 2015 up to December 2016. Hands and feet, including symptomatic joints were ultrasound-evaluated for Doppler active synovitis according to the EULAR-OMERACT guidelines. The presence of wrist (compartments 1-6) and finger tenosynovitis was recorded in all patients. After retrospective review of medical journals, ultrasound detected tenosynovitis emerged as an interesting marker. Serum samples from inclusion were analysed on a multiplex immunoassay to detect specific ACPA reactivities.

Results

66 Risk-RA patients (85% female, median age 50 years, range 22-82) were included and followed up to arthritis onset (median 8 months, range 1-27), or to the end of year 2017 (median 25 months, range 11-43). Twenty-seven of the 66 patients (41%, 86% female, median age 52 years, range 22-74) developed arthritis. Of these, 7 had tenosynovitis detected by ultrasound at inclusion, and 7 more developed a tenosynovitis at follow-up (14 pre-arthritis in total). At the time of diagnosis, 20 out of 27 patients presented with both tenosynovitis and synovitis. A majority of patients with tenosynovitis (12 out of 14, 86%) and a minority without tenosynovitis (15 out of 52, 29%) developed arthritis, resulting in an increased relative risk (3.0[95% CI 1.8-4.8]) of arthritis development for patients with tenosynovitis present at baseline or follow-up visits (p=0.001). Concentrations of the anti-CCP antibodies, anti-CEP antibodies and anti-citrullinated vimentin (60-75) antibodies tended to be higher in patients with tenosynovitis developing arthritis (n=12, median of 70 AU/ml, range 2-175 for anti-CCP, median of 68 AU/ml, range 0-673 for anti-CEP, median of 53, range 0-644 for anti-vim) than those without tenosynovitis developing arthritis (n=15, median of 35 AU/ml, range 1-100 for anti CCP, median of 12, range of 0-1179 for anti-CEP, median of 29, range 0-332 for anti-vim). Same trend was observed when comparing patients with tenosynovitis developing arthritis to patients' without-tenosynovitis not-developing arthritis. The 2 patients with tenosynovitis not developing arthritis, had lower levels of antibodies, compared to tenosynovitis patients that developed arthritis. No significant differences in patient baseline characteristics were seen between those with, and those without tenosynovitis (86 vs 85 % female, median[range] 54yrs[29-71] vs 50yrs[22-82], mean visual analogue scale pain 34 vs 31, mean c-reactive protein 2.7 vs 3.2 and tender joint count 1.2 vs 0.7).

Conclusion

Ultrasound detected tenosynovitis in the context of ACPA positivity is a specific clinical predictor of rapid arthritis onset in individuals at risk of developing rheumatoid arthritis.

ABSTRACTNUMMER: 1567-A-1818 28

INFLIXIMAB LEVELS AND ANTI-DRUG ANTIBODIES IN PATIENTS WITH RHEUMATOID ARTHRITIS - A PILOT STUDY OF TREATMENT RESPONSE AND DRUG SURVIVAL DURING FIRST YEAR

Rille Pullerits[2], Boja Jovancevic, Egidija Sakiniene, Christine Wennerås [1], Rille Pullerits

[1] Department of Infectious Diseases, Institute of Biomedicine at the Sahlgrenska Academy, University of Gothenburg
[2] Sahlgrenska Academy at University of Gothenburg

Background

Even though most of patients with rheumatoid arthritis (RA) respond favorably to anti-TNF treatment, ca 30% of patients have primary response failure or experience decreased treatment effect over time (secondary response failure).

Objective
To analyse the clinical relevance of infliximab (IFX) concentration and the production of anti-drug antibodies (ADA) in patients with RA undergoing IFX treatment during the first treatment year.

Methods
Blood samples were obtained at 4 months and at 1 year from RA patients fulfilling the ACR 1987 RA criteria and included in the "Blood panel" study. They had not sufficiently responded to previous DMARD therapy and were treatment naïve for biologics. IFX was administered intravenously at a standard dose of 200 mg at weeks 0, 2, 6 and every 8 weeks thereafter. The trough drug concentrations and ADA were assayed with in-house ELISA methods and the levels analyzed in relation to clinical disease activity as assessed by disease activity score in 28 joints (DAS28), EULAR treatment response criteria (good, moderate or non-responder), and drug survival.

Results
Forty patients were included (8 male, 32 female; mean age 55±12 years; mean disease duration 11±12 years; 88% RF-positive, 65% ACPA-positive; mean DAS28 at inclusion 4.8±0.1; median methotrexate dose 20 mg, IQR 15-22.5 mg/week; median IFX dose 3.1, IQR 2.4-3.4 mg/kg;). The overall drug survival on infliximab was 85% at 4 months and 53% at 1 year. At 4 months, 45% of patients exhibited good EULAR treatment response (median decrease in DAS28 score 2.6, IQR 2.0-3.5; median IFX concentration 2.0, IQR 0.7-3.0 µg/ml) whereas 24% of patients were non-responders according to EULAR treatment response criteria (median IFX 0.3, IQR 0.2-3.0 µg/ml). At 4 months, 27% of patients had undetectable (<0.2 µg/ml) or very low (<0.5 µg/ml) circulating IFX concentration and all these patients presented moderate or high titres of anti-infliximab antibodies. At 1 year, 33% of patients remaining on IFX treatment displayed DAS28<2.6 (median DAS28 1.7, IQR 1.3-1.8; median IFX level 2.9, IQR 2.0-3.3 µg/ml) whereas 47% of patients at 1 year were non-responders as compared to DAS28 values at 4 months (median DAS28 3.3, IQR 3.0-3.9; median IFX level 0.5, IQR 0.2-1.9 µg/ml). Importantly, the change in DAS28 at 4 months inversely correlated with total IFX dose administered during first 6 weeks (rho -0.371, p=0.026). Moreover, the adequate dose escalation of IFX during the treatment initiation (3 doses vs 1-2 doses during 6 weeks) improved the drug survival at 4 months (96% vs 67%, p=0.012) and at 1 year (64% vs 33%, p=0.06).

Conclusion
The formation of anti-infliximab antibodies during treatment with infliximab is associated with a loss of clinical response, the appearance of infusion reactions and discontinuation of treatment. The adequate dose escalation during treatment initiation relates to better treatment response and improves the drug survival.

ABSTRACTNUMMER: 1569-A-1818 29

PHYSICAL ACTIVITY IN EARLY AND LONG-STANDING RA. RELATIONS TO DISEASE ACTIVITY, CARDIOVASCULAR RISK FACTORS AND SUBCLINICAL ATHEROSCLEROSIS

Kristina Hörnberg[1], Jeremy Pomeroy[2], Camilla Sandberg[1], Björn Sundström[1], Anna Södergren[1], Lars Ångström[1], Solveig Wållberg Jonsson[1]

[1] Institutionen för folkhälsa och klinisk medicin
[2] Marshfield Clinic Research Institute, Marshfield, USA

Background
The excess risk for cardiovascular disease (CVD) in Rheumatoid Arthritis (RA), is partly attributable to traditional cardiovascular risk factors for CVD and systemic inflammation, factors known to be modified by physical activity. The aim of this cross-sectional study was to objectively measure and compare the level of physical activity in patients with early and long-standing RA, and to investigate its associations with disease activity, risk factors for CVD and measures of subclinical atherosclerosis.

Methods
This study included 84 patients with early and 37 with long-standing RA (disease duration, mean [SD] 1.4 [0.4] and 16.3 [2.3] years respectively). Physical activity was measured using a combined accelerometer and heart rate monitor and included total physical activity (counts /min), proportion of moderate to vigorous physical activity (MVPA) and sedentary time. Further assessments were; disease activity (Erythrocyte sedimentation rate [ESR], Disease activity score [DAS28]), functional ability (Health Assessment Questionnaire [HAQ]), risk factors for CVD (blood lipids, i.e., triglycerides, high density lipoprotein [HDL], low density protein [LDL], blood glucose, blood pressure, waist circumference, body mass index [BMI]), body fat and subclinical atherosclerosis (pulse wave velocity [PWV], augmentation index [AIx] and carotid intima-media thickness [cIMT]).

Results
Physical activity variables did not differ between patients with early and long-standing RA. Thirty-seven % of the patients with early and 43% of the patients with long-standing RA did not reach WHOs recommended levels of MVPA. Univariate linear regression analyses with the two groups combined, showed associations between total physical activity and younger age, lower values for HAQ and ESR, as well as more beneficial values for blood glucose, triglycerides, waist circumference, BMI, body fat, sleeping heart rate (SHR), systolic and diastolic blood pressure, aortic blood pressure and pulse pressure (PP), AIx, PWV, and cIMT. After adjusting each variable for age, sex, disease duration and Actiheart wear time, associations remained for all variables except triglycerides, aortic PP, PWV, AIx and cIMT. In a final regression model, the association with ESR was no longer evident. More time spent in MVPA was associated with younger age and with more favourable values of blood glucose, HDL, LDL, waist circumference, SHR and PWV. After adjustments for age, sex, disease duration and wear time, associations remained for HAQ, HDL, blood glucose and SHR.

Conclusions
Physical activity behaviour was similar in patients with early and long-standing RA. Total physical activity as well as more time spent in moderate to vigorous physical activity were associated with more favourable risk factors for CVD and measures of subclinical atherosclerosis. Patients with lower functional ability were less physically active. These results stress the importance of promoting physical activity in patients with RA.

ABSTRACTNUMMER: 1570-A-1818 30

EULAR-RECOMMENDED MODIFICATIONS OF CARDIOVASCULAR RISK SCORES PERFORM BETTER THAN STANDARD RISK SCORES TO IDENTIFY ASYMPTOMATIC CORONARY ARTERY DISEASE AS CONFIRMED BY CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY IN PATIENTS WITH PSORIATIC ARTHRITIS

Agnes Szentpetery[4], Muhammad Haroon[2,3], Gerard M. Healy[1], Jonathan D. Dodd[1], Oliver FitzGerald[2]

[1] *Department of Radiology, St. Vincent's University Hospital, Dublin, Ireland*
[2] *Department of Rheumatology, St. Vincent's University Hospital, Dublin, Ireland*
[3] *Division of Rheumatology, Department of Medicine, University Hospital Kerry, Tralee, Ireland*
[4] *Reumatologavdelningen, Akademiska Sjukhuset, Uppsala*

Background

Psoriatic arthritis (PsA) patients have an increased prevalence of cardiovascular (CV) risk factors and are at greater risk for subsequent major CV events compared with the general population. We have recently reported accelerated coronary plaque formation in PsA as measured by coronary computed tomography angiography (CCTA), which was independent of metabolic disease. It has been shown that established CV risk scores underestimate the risk of carotid subclinical atherosclerosis in PsA, but their performance against coronary artery plaque burden assessed by CCTA in PsA patients without symptoms of coronary artery disease (CAD) has not been studied yet. EULAR recommends a multiplication factor of 1.5 to the calculated total CVD risk for RA patients. Our aim was to examine whether similar modifications improves the performance of CV risk scores and their association to coronary plaque burden in our PsA cohort.

Materials and methods

50 PsA patients without symptoms of CAD underwent CCTA. Segment involvement score (SIS), the total number of segments with plaque per patient (0-15); stenosis severity score (SSS), the sum of the stenosis severity scores over 15 segments (0-60); and total plaque volume (TPV) in mm3 were calculated. We applied 4 commonly used risk algorithms in predicting CV events: the Framingham risk score (FRS), Systematic Coronary Risk Evaluation (SCORE), QRISK2 and the Atherosclerotic Cardiovascular Disease (ASCVD). PsA patients with "high risk" of CVD were identified using cut-off values for the general population: FRS>10%, SCORE>5%, QRISK2>20%, and ASCVD>7.5%, respectively. Similar to EULAR recommendations for CVD risk assessment in RA, we used a multiplication factor of 1.5 for CV risk scores. Differences between PsA patients with high and low risk of CVD for the presence/absence of coronary plaques and for quantitative plaque scores (SIS, SSS and TPV) were compared using Chi-square and Mann-Whitney tests. Rank correlation was used to study the relationship between the risk scores and SIS, SSS and TPV.

Results

50 patients (23 female/27 male) with mean age of 58.3 (±8.2) years were assessed. Patients' metabolic profile, quantitative plaque scores and clinical characteristics are described in Table 1. We found that only 38%, 26%, 24%, and 54% of the PsA patients were at "high risk" of CVD disease, defined as FRS, SCORE, QRISK2, and ASCVD, respectively; however, after applying a multiplication factor of 1.5, the percentage of high risk patients was 48%, 44%, 44% and 72%, respectively. Table 2 and Table 3 show the suboptimal performance of 4-CV risk scores against coronary plaque burden using CCTA; however, their performance significantly improved after applying the multiplication factor of 1.5. We found a significant linear relationship between TPV and CV risk scores: FRS, r=0.31, p=0.02; SCORE, r=0.34, p=0.01; QRISK2, r=0.21, p=0.13; ASCVD, r=0.33, p=0.02.

Conclusions

Established CV risk scores showed suboptimal performance in our cohort, however applying multiplication factor of 1.5 accurately categorised PsA patients at "high risk" of CVD. As recommended by EULAR for RA, we would suggest that a similar multiplication

Table 1. Cardiovascular risk factors, quantitative plaque scores and disease characteristics of PsA patients

	PsA (n=50)
Age (years)	58.3 (±8.2)
Males n(%)	27 (54)
Cardiovascular risk factors	
Ever smoker n(%)	21 (42)
Smoking pack/year	7.6±13.9
BMI>30 n(%)	23 (46)
BP >135/85 n(%)	40 (80)
TG >1.7 n(%)	19 (38)
HDL-C <1 n(%)	18 (36)
GLU >5.6 n(%)	19 (38)
HOMA-IR >2.5 n(%)	11 (22)
Quantitative plaque scores	
Segment Involvement Score (0-15)	2.04±2.02
Segment Stenosis Score (0-60)	3.90±4.84
Total Plaque Volume (mm^3)	1.32±2.03
Joint related	
Age of onset PsA (years)	37.1 (±12.1)
PsA duration (years)	18.7 (±7.8)
TJC max (0-68)	13 (±7.1)
SJC max (0-68)	9.2 (±4.9)
ESR max (mm/h)	25 (±21.6)
CRP max (mg/L)	21.3 (±24.1)
No of deformed joints (0-68)	7.3 (±9.2)
Dactylitis n(%)	24 (48)
Enthesitis n(%)	22 (44)
Sacroiliitis n(%)	14 (28)
Skin related	
Age of onset Psoriasis (years)	32.2 (±13.8)
PASI max ever (0-72)	4.7 (±4.8)
BSA max ever (0-100%)	8.8 (±11.1)
DLQI (0-30)	2.8 (±4.1)
Nail involvement n(%)	42 (84)
Medications	
DMARD n(%)	32 (64)
Biologic n(%)	33 (66)
Combination n(%)	16 (32)

Results are presented as mean±SD or percentage.

Table 2. Comparative performance of cardiovascular risk scores against the presence or absence of coronary artery plaques

Risk Scores		Plaque presence	No plaque	p-value
FRS	High Risk	17	2	0.100
	Low Risk	21	10	
m-FRS	High Risk	22	2	0.013
	Low Risk	16	10	
SCORE	High Risk	11	1	0.248
	Low Risk	27	11	
m-Score	High Risk	20	2	0.029
	Low Risk	18	10	
QRISK2	High Risk	10	2	0.705
	Low Risk	28	10	
m-QRISK2	High Risk	18	4	0.393
	Low Risk	20	8	
ASCVD	High Risk	23	4	0.099
	Low Risk	15	8	
m-ASCVD	High Risk	31	5	0.023
	Low Risk	7	7	

Chi-square and Fisher's exact tests. Results are presented as number of patients. The EULAR recommended modifications (multiplication factor by 1.5) was applied for 4 CV risk scores and labelled as m-FRS, m-SCORE, m-QRISK2 and m-ASCVD.

Table 3. Comparative performance of cardiovascular risk scores against quantitative measurement of coronary artery plaques

Risk Scores	Segment Involvement Score			Segment Stenosis Score			Total Plaque Volume		
	High Risk	Low Risk	p-value	High Risk	Low Risk	p-value	High Risk	Low Risk	p-value
FRS	2.7±2.2 (n=19)	1.6±1.8 (n=31)	0.050	5.1±6.4 (n=19)	3.2±3.4 (n=31)	0.39	1.7±2.6 (n=19)	1.07±1.5 (n=31)	0.22
m-FRS	2.9±2.0 (n=24)	1.2±1.6 (n=26)	0.001	5.5±5.8 (n=24)	2.3±3.0 (n=26)	0.03	1.8±2.4 (n=24)	0.8±1.5 (n=26)	0.009
SCORE	2.9±2.2 (n=13)	1.7±1.8 (n=37)	0.07	6.0±7.1 (n=13)	3.1±3.5 (n=37)	0.22	2.2±2.9 (n=14)	0.9±1.4 (n=36)	0.08
m-SCORE	3.1±2.1 (n=22)	1.2±1.4 (n=28)	<0.001	5.8±5.9 (n=22)	2.3±3.1 (n=28)	0.01	2.1±2.6 (n=22)	0.7±1.07 (n=28)	0.003
QRISK2	3.0±2.3 (n=12)	1.7±1.8 (n=38)	0.06	6.6±7.2 (n=12)	3.0±3.5 (n=38)	0.09	1.4±1.4 (n=12)	1.3±2.2 (n=38)	0.30
m-QRISK2	2.7±2.1 (n=22)	1.5±1.7 (n=28)	0.01	5.3±5.9 (n=22)	2.8±3.5 (n=28)	0.06	1.5±1.4 (n=22)	1.2±2.4 (n=28)	0.04
ASCVD	2.3±2.0 (n=27)	1.6±1.9 (n=23)	0.12	4.7±5.7 (n=27)	2.9±3.5 (n=23)	0.28	1.7±2.5 (n=27)	0.8±1.0 (n=23)	0.20
m-ASCVD	2.5±2.1 (n=36)	0.85±1.0 (n=14)	0.007	4.7±5.3 (n=36)	1.7±2.0 (n=14)	0.04	1.6±2.2 (n=36)	0.4±0.7 (n=14)	0.001

Mann-Whitney test. Results are presented as mean±SD. The EULAR recommended modifications (multiplication factor by 1.5) was applied for 4 CV risk scores and labelled as m-FRS, m-SCORE, m-QRISK2 and m-ASCVD.

factor of 1.5 be used in PsA patients in order to improve the performance of CV risk scores.

ABSTRACTNUMMER: 1572-A-1818 31

FACTORS RELATED TO HEALTH RELATED QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS, OVERALL AND STRATIFIED BY SEX

Helena Forsblad-d'Elia[1], Lucy Law[1], Jeanette Beckman Rehnman[1], Anna Deminger[2], Eva Klingberg[2], Lennart Jacobsson[2]

[1] Department of Public Health and Clinical medicine/Rheumatology, Umeå University
[2] Department of Rheumatology and Inflammatory Research, University of Gothenburg

Background
Ankylosing spondylitis (AS) begins early in life and often leads to reduced physical function, but less is known about the impacts it has on health related quality of life (HRQoL). The aims of this study were to assess HRQoL by short form-36 (SF-36) in a cohort of patients with AS compared with controls and to examine associations between SF-36 and spinal radiographic changes, physical function, disease activity and demographic data overall and stratified by sex.

Methods
A cohort of patients with AS from Western Sweden were assessed with spinal radiographs for mSASSS, clinical examination and questionnaires, including BASMI, BASFI, ASDAS-CRP, BASDAI, BASG and SF-36. Each patient's SF-36 results were compared with 5 age- and sex-matched persons (n=1055) from the SF-36 Swedish normative population database. Associations between SF -36 physical component summary (PCS) and mental component summary (MCS) scores and disease related and demographic factors were investigated with univariate and multiple logistic regression analyses with PCS and MCS below/above their respective median values as dependent variables.

Results
210 patients, age (median, IQR) 49.0 (40.0, 61.2) years, symptom duration 24.0 (13.0, 34.0) years, men 57.6%, HLAB27 87.1% were included. AS patients scored significantly lower ($p<0.001$) compared to controls in all SF-36 domains and component summaries. Both men and women with AS scored significantly lower in PCS compared with MCS. Multiple logistic regression analyses revealed that living without a partner (OR 2.38, 95%CI 1.00-5.67), long symptom duration (year in decade OR 1.66, 95% CI 1.16-2.37), higher BASFI (OR 1.98, 95%CI 1.46-2.70) and ASDAS≥2.1 (OR 3.32, 95%CI 1.45-7.62) were associated with worse PCS while living without a partner (OR 3.04, 95%CI 1.34-6.91), fatigue (VAS global fatigue >median (OR 6.36, 95%CI 3.06 -13.19) and ASDAS≥2.1 (OR 2.97, 95%CI 1.41-6.25) with worse MCS. Some differences between sexes were revealed.

Conclusions
The patients with AS had significantly lower HRQoL compared with controls. PCS was more affected compared to MCS in both sexes. Both disease related and demographic factors were associated with HRQoL, partly overlapping for PCS and MCS. Factors associated with HRQoL showed some differences between sexes. By modifying factors, such as ASDAS-CRP and fatigue, HRQoL may potentially be improved.

ABSTRACTNUMMER: 1574-A-1818 32

THE INFLUENCE OF SEX AND THE PROGRESSION OF REUMATOID ARTHRITIS IN DIFFERENT AGE GROUPS

Inger Gjertsson[2], Jenny Nilsson[2], Maria Andersson[1], Monica Leu Agelii[2]

[1] Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden
[2] Göteborgs Universitet

Background
More than 50 % of the patients with rheumatoid arthritis (RA) are >65 years of age. With an ageing population it becomes more important to understand how factors such as the age of onset affects the outcome of the disease.

Methods
This study included 2825 patients (68 % females) from the BARFOT (Better Anti-Rheumatic PharmacOTherapy) early RA cohort. The patients were divided into male and female and into four age groups based on age of RA at inclusion in the study: <40 years (yr) n=415, 40 –54 yr n=658, 55 – 69 yr n=986 and ≥70 yr n=766 .The following parameters were assessed at 3, 6 months and 1, 2, 5, 8 years after inclusion: DAS28, VAS pain, VAS global health, 28 joint count of tender and swollen joint, respectively, and rheumatoid factor (RF) and antibodies to citrullinated proteins (APCA). Mann-Whitney U-test and Wilcoxon Rank test were used to compare groups, $p<0.01$ was considered as significant due to multiple comparisons. At inclusion, the status of smoking and hormones (menopause and hormonal contraceptives), respectively, civil status and disease duration before inclusion, were compared between groups using Pearson's chi-squared test ($\alpha = 0.05$) and the Wilcoxon Rank test.

Results
At inclusion, there were no significant differences in DAS28, VAS global health, VAS pain or tender and swollen joint counts in any group. DAS28 were significantly lower for men compared to women in all age groups, except for 40 – 54 yr, from 3 months and onward. The lowest score was seen for RF and ACPA positive men <40 yr, the highest for RF positive women ≥70 yr and men ≥70 yr irrespective of RF. VAS pain and VAS global health were significantly lower for men compared to women from 3-6 month and onward in all age groups except for 40 – 54 yr. For both sexes, there was a significant association between age group and civil status and smoking, respectively. There was no significantly difference observed between sexes in disease duration before inclusion in respective age group; though the duration was significantly shorter for women ≥70 yr compared to younger women but not compared to men in any age group.

Conclusions
The course of the disease, measured as DAS28, was affected by the age of onset, where seropositive men < 40 yr have the most favourable prognosis and women ≥70 yr the worst. The difference between sexes in respective age groups does not seem to be explained by smoking, civil status or disease duration before inclusion. No differences in DAS28, VAS global health or pain were found between men and women aged 40-54 yr.

ABSTRACTNUMMER: 1575-A-1818 33

B-CELL SUBPOPULATIONS IN NEWLY DIAGNOSED EORA AND YORA PATIENTS

Inger Gjertsson, Katrin Thorarinsdottir, Alessandro Camponeschi, Lennart Jacobsson, Inga-Lill Mårtensson

Göteborgs Universitet

Background
B-cells are thought to have an important role in rheumatoid arthritis (RA). This is demonstrated by the success of B-cell depleting therapy as well as the negative prognostic value of anti-citrullinated protein antibodies (ACPA). However, the pathogenesis of the disease is unclear. Studies have suggested that there are differences in disease characteristics between elderly-onset RA patients (EORA, defined by disease onset at ≥ 60 years of age) and younger-onset RA patients (YORA, with disease onset <60 years of age).

Objectives
Our aim was to study the B-cell subpopulations in newly diagnosed EORA and YORA patients. We investigated whether there were differences in B-cell subpopulations between the groups and whether there was a correlation between B-cell subpopulations and disease activity, autoantibody profile and inflammatory parameters in these two RA patient groups.

Methods
Treatment-naive EORA (n=29) and Yora (n=31) patients with newly diagnosed RA were included at their first visit to the Rheumatology clinic. The patients' clinical response (DAS28), autoantibodies and B-cells were assessed. Flow cytometry was used for the analysis of cellular surface markers on leukocytes in peripheral blood: CD19, CD27, CD24, CD27, CD38, PD-1, PDL -1, IgG, IgD and IgM. Non-parametric tests were used for comparing groups and Spearman's test was used for correlation.

Results
We found a correlation between the ACPA titers and the frequency of the CD27+ and CD27- memory B cell populations in EORA patients but not in YORA patients. This was further supported by a correlation of the ACPA titer and IgG+ B cells in the EORA patients (r=0.7, p=0.003) and not in the YORA patients. There was neither a correlation between age and ACPA titer nor between age and memory B cell populations. We did not find any significant difference between the B cell subpopulations in the two patient groups.

Conclusions
Our results suggest that the memory B cell compartment in peripheral blood in EORA patients reflects the ACPA titer. This was not seen in the YORA patients. The mechanisms behind these findings need to be further elucidated.

ABSTRACTNUMMER: 1578-A-1818 34

HYDROXYCHLOROQUINE IMPROVES THE BLOOD LIPID PROFILE IN RA AND SLE AFTER FOUR AND EIGHT WEEKS OF TREATMENT. A RANDOMIZED INTERVENTIONAL STUDY

Christine Bengtsson[1,4], Bengt Wahlin[1,2], Antje Braune[1], Elias Jönsson[1,3], Solveig Wållberg-Jonsson[1]

[1]Institutionen för Folkhälsa och Klinisk medicin/Reumatologi, Umeå Universitet
[2] Reumatologi Kliniken, Umeå Universitetssjukhus
[3] Reumatologimottagningen, Östersunds sjukhus
[4] Reumatologimottagningen, Medicinkliniken, Centralsjukhuset, Kristianstad

Objectives
Cardiovascular co-morbidity is increased in Rheumatoid arthritis (RA) and in systemic lupus erythematosus (SLE). In both RA and SLE, retrospective studies have shown an association between treatment with chloroquine and a positive impact on cardiovascular risk factors. However, interventional studies are scarce. We therefore aimed to investigate the effects of hydroxychloroquine (HCQ) (Plaquenil ®) treatment on the blood lipid profile and vascular function, after 4 and 8 weeks in patients with RA and SLE.

Method
Patients with RA (n=25) or SLE (n=7) (mean age 53 years) and low-medium disease activity (DAS-28 <4.6 resp SLEDAI -2k <6) were included. Twelve patients with RA and 4 with SLE were randomized to start HCQ treatment after 4 weeks to exclude the impact of care on the results. Total cholesterol (CHOL), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), apolipoproteins, blood-glucose, HbA1c, blood pressure and the vascular function, as measured with pulse wave analysis (Arteriograph®), were investigated before, and after 4 and 8 weeks of treatment with HCQ.

Results
Thirty patients completed the study period of 8 weeks with HCQ medication. At the point of 4 weeks the CHOL levels decreased (mean 5.43 mmol/L-5.1 mmol/L) and remained significantly decreased at 8 weeks (p=0.005). This was also seen in LDL levels, that decreased from 3.03 mmol/L at inclusion to 2.68 mmol/L after 4 weeks and stayed significantly decreased after 8 weeks (p=0.002), as well as ApoB that decreased after 4 weeks from 0.95g/L to 0.90g/L and remained significantly lowered after 8 weeks (p=0.033). Also HbA1c-levels decreased, however not with statistical significance. No significant changes were seen in the vascular function. There was no significant difference in the results of the two treatment groups implicating a genuine impact of HCQ.

Conclusion
Hydroxychloroquine treatment in 8 weeks improved the lipid profile in patients with low –medium active RA and SLE. A numerical improvement of HbA1c-levels was seen. No influence on vascular function was noticed.

ABSTRACTNUMMER: 1579-A-1818 35

DETECTION OF INFLIXIMAB LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS - A COMPARISON OF THREE DIFFERENT ASSAYS

Boja Jovancevic[4], Egidija Sakiniene[4], Christine Wennerås[2], Rille Pullerits[1,3,4]

[1] Department of Clinical Immunology and Transfusion Medicine, Sahlgrenska University Hospital
[2] Department of Infectious Diseases, Institute of Biomedicine at the Sahlgrenska Academy, University of Gothenburg
[3] Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at University of Gothenburg
[4] Rheumatology Clinic, Sahlgrenska University Hospital

Background
Monitoring infliximab (IFX) concentrations and anti-drug anti- ➤

body (ADA) titres against IFX might allow more precise decision making in clinical practice, better patient-centred treatment and increased patient safety if patients with high ADA levels and therefore in risk for allergic reactions would be identified in time. However, the heterogeneity of different commercially available and in-house methods has made it difficult to compare individual study results and to establish recommendations with regard to therapeutic trough drug concentrations.

Objective
The objective was to compare three commonly used, principally different analytical techniques for measuring IFX concentrations in patients with rheumatoid arthritis.

Methods
Blood samples were obtained at 4 months and at 1 year from 40 RA patients fulfilling the ACR 1987 RA criteria and included in the "Blood panel" study. They were treatment naïve for anti-TNF drugs. IFX was administered intravenously at a standard dose of 200 mg at weeks 0, 2, 6 and every 8 weeks thereafter. The trough drug concentrations were assayed in with 3 different methods: 1) an in-house direct ELISA method developed and currently in routine clinical use in several immunological laboratories in Sweden; 2) a commercially available capture ELISA (Promonitor®-IFX; Progenika Biopharma, Spain); 3) a cell-based reporter gene bioassay (iLite™-IFX Bioassay, Biomonitor AS, Galway, Ireland).

Results
IFX level was analysed in a total of 60 samples. The quantitative median IFX concentration differed significantly between the assays and was 1.5, 0.86 and 8.45 µg/ml as obtained respectively with in-house ELISA, Promonitor®-IFX andiLite™-IFX kits. The respective detection ranges for these assays were 0.2-56 µg/ml, 0.035-14.4 µg/ml and 0.65-31 µg/ml. IFX levels were undetectable in 27% of samples with in-house ELISA, in 43% with iLite™-IFX and in 24% with Promonitor®-IFX method. In 29% of samples, Promonitor®-IFX kit detected the drug levels >14.4 µg/ml. The inter-test agreement was good for in-house ELISA and iLite™-IFX Bioassay (Spearman's rho 0.946, weighted kappa coefficient moderate 0.6) whereas Promonitor®-IFX kit detected in general higher IFX levels as compared to in-house method (rho 0.871, weighted kappa coefficient fair 0.29) and to iLite™-IFX Bioassay (rho 0.804, weighted kappa coefficient poor 0.19), respectively. The mean estimate difference between in-house and iLite™-IFX was -0.8 and the limits of agreement (LoA) estimate an interval of -4.2 to 2.7. The corresponding estimate between in-house and Promonitor®-IFX was 5.2 and LoA interval of -4.2 to 14.7.

Conclusion
Performances of assays for IFX are relatively good and comparable. However, IFX quantitative concentrations show systematic differences, and in individual patients, only the same assay should be used to monitor therapy in the same patient.

ABSTRACTNUMMER: 1580-A-1818 **36**

THE SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (SRAGE) LEVELS ARE DECREASED AND ASSOCIATED WITH INFLAMMATION IN MALE PATIENTS WITH RHEUMATOID ARTHRITIS

Mitra Nadali, Rille Pullerits, Malin Erlandsson, Sofia Töyrä Silverswärd, Karin Andersson, Maria Bokarewa

Sahlgrenska Academy at University of Gothenburg

Background
Receptor for advanced glycation end products (RAGE) is a membrane-bound molecule expressed on a variety of cells and upregulated at sites of inflammation. Soluble RAGE (sRAGE), a truncated soluble form of the receptor, might act as a decoy and prevent the inflammatory response mediated by activation of membrane-bound RAGE. Soluble RAGE has recently emerged as a biomarker in inflammation and has been implicated in the pathogenesis of rheumatoid arthritis (RA) through its ability to amplify inflammatory pathways. We aimed to study the levels of sRAGE in RA patients in relation to traditional cardiovascular risk factors and the association of sRAGE with circulating adipokines.

Material and methods
In this cross-sectional study we measured sRAGE in 253 patients with RA who fulfilled the ACR 1987 RA criteria: 184 women (mean age 51.6±11.9, disease duration 10.3±8.7 years), and 69 men (54.2±10.7; 12.5±8.7 years, respectively). Serum levels of sRAGE were analysed by ELISA. The serum levels of adipokines, inflammatory cytokines, inflammatory parameters and lipid profile were analysed in relation to sRAGE.

Results
Median sRAGE level was significantly higher in women (1418, 25th-75th percentiles 1118-1749 pg/ml, $p<0.0001$) compared to men (1207, 852-1469 pg/ml). The male RA patients displayed undesirable lipid profile with significantly higher triglycerides (median 1.0 (0.8-1.8) vs 0.9 (0.7-1.2) mmol/L; $p<0.0007$), total cholesterol/HDL index (3.6 vs 2.9, $p<0.0001$) and lower HDL-cholesterol levels (median 1.4 (1.1-1.6) vs 1.7 (1.5-2.1) mmol/L; $p<0.0001$). In addition, the majority of men (75%) had overweight with BMI>25. The male patients with RA also presented significantly higher levels of inflammation related adipokines such as resistin (109 (61-143) vs 21 (13-39) ng/ml; $p<0.0001$) and visfatin (3.4 (1.5-6.8) vs 2.6 (1.1-4.6) ng/ml; $p<0.05$) whereas adiponectin levels were significantly lower (2.4 (1.3-4.4) vs 5.2 (3.2-8-3) ng/ml; $p<0.0001$) as compared to female RA patients, respectively. No association was found between sRAGE levels with blood lipids and adipokines, neither in the whole cohort, nor in female or in male RA patients. Interestingly, in male patients, a significant inverse correlation was found between sRAGE level with ESR (rho -0.366, $p=0.01$) and DAS28-ESR (rho -0.308, $p<0.05$). Of male RA patients, 45% had medication for hypertonia, 13.5% for diabetes and 14.5% for hypercholesterolemia whereas in female RA patients, 14.6% had medication for hypertonia, 3.8% for diabetes and 3.8% for hypercholesterolemia.

Conclusions
Male RA patients presented significantly lower levels of sRAGE that were inversely associated with inflammation. Frequency of traditional cardiovascular risk factors such as obesity, hypertension, diabetes, and hypercholesterolemia were significantly higher in men compared to women which could contribute to lower levels of sRAGE.

Systemsjukdomar

ABSTRACTNUMMER: 1477-A-1818 **37**

GIANT CELL ARTERITIS- SYSTEMATIC PERIPHERAL VASCULAR EVALUATION AND LARGE VESSEL INVOLVEMENT AS A PROGNOSTIC RISK FACTOR, REAL LIFE DATA

Nazanin Naderi[1]

[1] Danderyds sjukhus

Distribution of the patients with high flare frequency on high dose GC and the GC dose at flares

The entire cohort 17/26 (65%)	LV-GCA 13/15 (87%)	C-GCA 4/11 (36%)
Median dose (mg/d)	27.5	25.0
Interquartile range (mg/d)	17.5-40.0	19.4-38.1
Range (mg/d)	15 – 52.5	17.5- 42.5

Background
Large vessel involvement (LVI) as a prognostic factor with regard to flare frequency and glucocorticoid (GC) demand has not been investigated in giant cell arteritis (GCA). LVI may indicate a complicated disease course. No specific diagnostic or activity biomarker exists, neither ESR nor CRP separately or combined are infallible. Periodic imaging is not an accepted norm of reexamination in this disease and data on the findings of vascular damage at follow-up with clinical vascular assessment in GCA is scarce. This study was conducted to: 1. test the value of the often taught but rarely applied teaching of bilateral brachial measurement in conjunction with this disease, 2. test the potential merit of adding ankle pressure measurement to the clinical evaluation, 3. evaluate if eventual fluctuations in pressure measurements could serve as a reliable disease activity indicator, 4. investigate whether periodic peripheral vascular evaluation can be a useful tool to identify LVI, and 5. find out whether LVI predicts frequent flares on high dose GC.

Material and Methods
A portion of all consecutive newly diagnosed patients with GCA and polymyalgia rheumatica or referrals for second opinion or initiation of GC-sparing drug in patients with these diagnosis between July 2011 and May 2015 were evaluated and followed on regular intervals by one rheumatologist. Only those with GCA were included in this study. Patients were evaluated at follow-ups with auscultation of the heart and peripheral vessels, palpation of the peripheral pulses and pressure measurement of the brachial and dorsal pedal arteries. Imaging was done if: new vascular bruit or pressure asymmetry, frequent flares, long standing disease or rise in inflammatory markers without any other explanation.

Results
Imaging revealed LVI in 58% of the patients (LV-GCA). Sixty-five percent developed pressure asymmetry, 65% of them had LV-GCA. With pressure measurements 73% of those with LV-GCA could be found. Six patients exhibited a relapsing and remitting course of pressure asymmetries as a sign of disease activity.

Thirty-one percent of the ankle pressure asymmetries (APA) at baseline were due to vasculitis. APA occurred significantly higher in LV-GCA patients (p=0.0017). Sixty-five percent of the patients had flares on high dose GC, 76% of them were LV-GCA patients (p=0.014).

Conclusions
Periodic vascular assessment is a simple and reliable method to I) use as an independent activity marker, II) evaluate treatment efficacy, III) detect LVI and smouldering inflammation. LVI predicts a complicated disease course. Imaging at the time of diagnosis is needed to identify the LV-GCA patients, since LVI may impact follow-up and treatment.

ABSTRACTNUMMER: 1498-A-1818 38

CIGARETTE SMOKING IS A RISK FACTOR FOR DEVELOPING PRIMARY SJÖGREN'S SYNDROME WITH RO/SSA AND LA/SSB AUTOANTIBODIES

Albin Björk[1], Johannes Mofors[1], Marika Kvarnström[1], Helena Forsblad-d'Elia[4], Sara Magnusson Bucher[6], Jan Hillert[1], Per Eriksson[2], Thomas Mandl[3], Gunnel Nordmark[5], Lars Alfredsson[1], Marie Wahren-Herlenius[1]

[1] Karolinska Institutet
[2] Linköpings Universitet
[3] Skånes Universitetssjukhus
[4] Umeå Universitet
[5] Uppsala Universitet
[6] Örebro Universitet

Background
Cigarette smoking is a well-established risk factor for several systemic autoimmune disorders, including rheumatic diseases. However, only a limited number of studies have investigated the effect of smoking on the risk of developing primary Sjögren's syndrome (pSS), reporting contradictory results. This may relate to factors such as them being conducted before development of current classification criteria, including few patients or using sicca controls for comparison. The aim of this study was therefore to investigate the impact of smoking on the development of pSS in a large, clinically well characterized cohort of patients with pSS.

Methods
A case-control study using prevalent cases of pSS classified according to the American-European Consensus Criteria (606 cases and 5,925 population controls) was performed. Smoking habits prior to diagnosis were obtained from questionnaire data and cases and controls were classified into ever-smokers or never-smokers. The impact of ever-smoking on pSS was assessed by calculating odds ratios (OR) with 95% confidence intervals (CI) employing logistic regression. Estimates were adjusted for age, sex, time period and area of residence.

Results
Ever-smokers had an increased risk of developing pSS (OR 1.3, 95% CI 1.1-1.5). The risk of ever-smokers to develop pSS was somewhat higher for men (OR 2.0, 95% CI 1.0 – 4.1, compared to OR 1.2, 95% CI 1.0 – 1.5 for women). Stratifying the analysis according to Ro/SSA and La/SSB autoantibody positivity revealed that the increased risk of pSS associated with smoking was limited to individuals with autoantibodies; both in pSS positive for Ro/SSA and La/SSB autoantibodies (OR 1.5, 95% CI 1.2 – 2.0) as well as in Ro/SSA and/or La/SSB positive pSS (1.4, 95% CI 1.1 – 1.7), but not in pSS negative for these autoantibodies (OR 1.1, 95% CI 0.8 – 1.6).

Conclusions
We observed a significantly increased risk for ever-smokers of both sexes to develop pSS in the largest study to date. The increased risk was only evident for development of Ro/SSA and/or La/SSB positive pSS, and not for pSS negative for these autoantibodies. The data indicate that underlying genetic factors predisposing for autoantibody positivity may be of importance for the increased risk.

ABSTRACTNUMMER: 1500-A-1818 39

AUTOIMMUNE LIVER DISEASE AMONG WELL- CHARACTERIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Rebecca Heijke[3], Martina Frodlund[1], Stergios Kechagias[2], Christopher Sjöwall[1]

[1] Institutionen för klinisk och experimentell medicin, avdelning för neuro-och inflammationsvetenskap. Linköpings universitet
[2] Institutionen för medicin och hälsa, avdelning för kardiovaskulär medicin. Linköpings universitet
[3] Medicinkliniken, Länssjukhuset Ryhov

Objective
The clinical spectrum of systemic lupus erythematosus (SLE) is exceedingly heterogeneous as virtually any organ system may be affected. Liver test abnormalities are commonly found in SLE with a wide range of possible causes. Regarding co-existence of SLE and autoimmune liver diseases, the literature is scarce. This study aimed to describe the prevalence of autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC) among Swedish SLE cases. We further aimed to test whether anti-C1q and anti-ribosomal P (anti-ribP) antibodies associated inversely with AIH [1].

Methods
The study population consisted of 287 cases (86% females) included in a regional Swedish SLE cohort. All patients met the 1982 ACR classification criteria and/or the Fries' diagnostic principle with involvement of ≥2 organ systems in combination with a positive ANA test at the time of diagnosis. With support from an experienced hepatologist, different strictness for the diagnoses of AIH and PBC were applied.

Results
Applying the diagnostic AIH criteria [2] combined with persistent elevation of alanine aminotransferase to our study population, 25 (8.7%) cases reached at least "probable AIH". However, merely 5 of these patients (1.7%) had a clinical diagnosis of AIH and liver biopsy had been performed in only 3/5 cases. None were anti-ribP or anti-C1q positive. The requirement of elevated alkaline phosphatase (ALP) in combination with typical PBC associated antibodies (M2/sp100/gp210) yielded 7 (2.4%) cases, but only 4 had a clinical diagnosis of PBC (1.4%). In 2/4 cases, PBC was confirmed by liver biopsy; 3 cases showed PBC associated antibodies, and in 1 case PBC diagnosis was based on elevated ALP combined with histopathology. None had anti-ribP or anti-C1q antibodies.

Conclusion
Clinical diagnoses of AIH and PBC were strongly overrepresented in SLE compared to prevalence figures from the Swedish population [3]; AIH: 1.7% vs. 0.018%, and PBC: 1.4% vs. 0.016%. Using the AIH criteria, even higher numbers were achieved but the specificity of these criteria among an SLE population is uncertain. Liver biopsy and specific autoantibodies, which associates with autoimmune liver diseases, could aid in the search for AIH and PBC in SLE.

References
1) Ohira H, Takiguchi J, Rai T, Abe K, Yokokawa J, Sato Y, Takeda I, Kanno T. High frequency of anti-ribosomal P antibody in patients with systemic lupus erythematosus-associated hepatitis. Hepatol Res 2004;28:137-39
2) Hennes EM, Zeniya M, Czaja AJ, Parés A, Dalekos GN, Krawitt EL, Bittencourt PL, Porta G, Boberg KM, Hofer H, Bianchi FB, Shibata M, Schramm C, Eisenmann de Torres B, Galle PR, McFarlane I, Dienes HP, Lohse AW; International Autoimmune Hepatitis Group. Simplified criteria for the diagnosis of autoimmune hepatitis. Hepatology 2008;48:169-76
3) http://svenskgastroenterologi.se/wp-content/uploads/2017/06/utredning_av_patologiska_leverprover_bakgrundsdokument.pdf. Page 22-24.

ABSTRACTNUMMER: 1511-A-1818 40

MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SOUTHERN SWEDEN

Ragnar Freyr Ingvarsson[1], Andreas Jönsen[2], Anton Landgren[2], Anders Bengtsson[2]

[1] Lunds Universitet
[2] Lunds Universitet avd. Reumatologi

Objective
The objective of the study was to ascertain the mortality rate and causes of death in patients with Systemic Lupus Erythematosus (SLE) within a defined region in Southern Sweden during the time period 1981-2014 and to determine whether these have changed over time.

Methods
In 1981, a prospective observation study of patients with SLE was initiated in Southern Sweden. All patients living with a defined geographic area were identified using diagnostic and immunology registers. Patients with a confirmed SLE diagnosis were then followed prospectively at the Department of Rheumatology in Lund. Clinical data were collected at regular out-patient visits. Patients were recruited from 1981 to 2006 and followed until 2014. The patient cohort was split into two groups based on the year of diagnosis in order to examine secular trends. Causes of death were collected from medical records and from the cause of death registry at The National Board of Health and Welfare in Sweden.

Results
In all, 175 patients were diagnosed with SLE during the study period. A total of 60 deaths occurred during a total of 3053 years of follow up. In the first half of the study period 46 patients died, compared to 14 in the latter. The majority of patients died of cardiovascular disease, 52,4%. Infections caused 15% of the deaths and malignancy was the cause of death in 13,3% of patients. Active SLE was the main cause of death for 6,7% of the patients and as a contributing factor for half of the patients. Standardized mortality ratio (SMR) was increased in patients by a factor of 2,54 compared to the general population. Deaths occurred at an even rate through the whole observation period. No significant difference in death rates was observed between either gender or different age groups.

Conclusions
Patients diagnosed with SLE in southern Sweden have a substantially raised mortality rate compared to the general population. The mortality rates have not changed significantly in the past three decades. The main cause of death was due to cardiovascular disease and this trend was consistent over the observation period.

ABSTRACTNUMMER: 1513-A-1818 41

RO/SSA AUTOANTIBODY EXPOSED NEONATES HAVE AN EXPANSION OF NK CELLS AND A DISCERNIBLE TYPE II IFN SIGNATURE WITH HIGH IFNγ IN PERIPHERAL BLOOD

Margarita Ivanchenko[2,4,5,7], Malin Hedlund[2,4,5,7], Gudny Ella Thorlacius[2,4,5,7], Vijole Ottosson[2,4,5,7], Karine Chemin[1,2,5], Sven-Erik Sonesson[3,4,5,6], Marie Wahren-Herlenius[2,4,5,7]

[1] Center for Molecular Medicine
[2] Department of Medicine
[3] Department of Women vs and Children vs Health
[4] Karolinska Institutet
[5] Karolinska University Hospital
[6] Pediatric Cardiology Unit
[7] Unit of Experimental Rheumatology

Background
Congenital heart block (CHB) may develop in the fetus of women with Ro/SSA autoantibodies. During pregnancy, the antibodies are transported across placenta and induce inflammation in the fetal

heart, resulting in fibrosis and calcification that cause the permanent disruption of impulse propagation. The mechanism by which the antibodies initiate inflammation is however not understood. In the mothers, Ro/SSA antibodies may induce type I IFN production, and we recently described an upregulation of type I IFN-regulated genes in PBMC and increase in circulating IFNα also in the Ro/SSA exposed newborns. IFNα is known to expand and activate NK cells. In this study, we analyzed the immune cell populations and evaluated levels of IFNα (as a main cytokine produced by NK cells) in cord blood of anti-Ro/SSA exposed neonates who did not develop CHB.

Methods
Maternal and cord blood was sampled at birth from healthy donor (HD, n=9) and Ro/SSA positive mother-neonate pairs (n=13). PMBC were prepared and used for microarray analysis and for flow cytometry to define CD19+ B cell (CD27-IgD+ naïve, CD27+IgD- memory, CD27+IgD+ marginal zone), CD3+ T cell (CD8+, CD4+) subpopulations and CD16+CD56+ NK cells. High-sensitivity ELISA kit was used to evaluate plasma levels of IFNα.

Results
In the Ro/SSA positive mothers, an increase in naïve B cells, but decrease in memory and marginal zone cells was observed, confirming previous reports for non-pregnant women with Sjögren's syndrome and SLE. Surprisingly, Ro/SSA exposed neonates presented an expanded population of NK cells (p=0.02), which was influenced by immunomodulatory treatment of the mother (neonates of non-treated mothers p=0.002, neonates of treated mothers p=ns compared to HD). No other differences in the T or B cell subsets analyzed were observed. Microarray modular analysis of PBMC revealed, in addition to type I, a type II IFN signature in Ro/SSA exposed neonates, and high IFNα was detected in four out of twelve subjects.

Conclusion
Our data demonstrate an expansion of NK cells, IFNα signature and IFNα production in Ro/SSA exposed neonates, indicating that cytotoxic effector mechanisms may be central in CHB. The expansion of NK cells and type II IFN signature in neonates at risk for CHB are a novel observation and implicates fetal innate immune mechanisms in the pathogenesis.

ABSTRACTNUMMER: 1519-A-1818 — 42

PERFORMANCE OF POTENTIAL DEFINITIONS OF REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) VERSUS QUALITY-OF-LIFE OVER 5 YEARS IN SWEDISH PATIENTS WITH RECENT-ONSET SLE

Rebecca Heijke[1], Mathilda Björk[2], Martina Frodlund[2], Sreeram Ramagopalan[3], Evo Alemao[3], Christopher Sjöwall[2]

[1] Internmedicinska kliniken, Ryhov, Region Jönköping
[2] Linköpings universitet
[3] Bristol-Myers Squibb

Background
Remission constitutes a desirable goal in the management and treatment of patients with systemic lupus erythematosus (SLE), but no universally accepted definition exists. Based on established disease activity measures (e.g. clinical SLE Disease Activity Index [cSLEDAI], physician's global assessment [PhGA] and British Isles Lupus Assessment Group [BILAG] index), serology (anti-double-stranded DNA antibodies and low complement) and ongoing therapy, an international task force recently suggested four preliminary definitions of remission in SLE (DORIS) [1]. However, the definitions did not include any patient-reported outcome measures (PROMs).

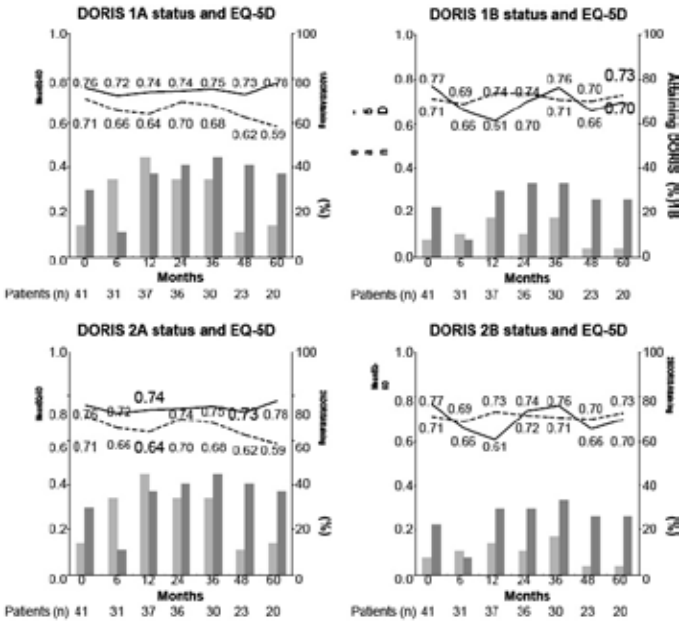


Figure legend: Months since SLE diagnosis. Bars represent % pts attaining remission (on vs. off treatment) and lines represent mean EQ-5D (QoL) for pts (meeting vs. not the definition of remission) at each time-point since onset of SLE.

Objectives
Using data from well-characterized Swedish patients with recent-onset SLE included in the KLURING (Clinical Lupus Register In Northeastern Gothia) cohort, we aimed to describe the performance of the four definitions over 5 years in relation to PROMs and quality-of-life (QoL) as defined by EuroQoL-5 Dimensions (EQ-5D).

Methods
Patients with SLE who met the 1982 ACR and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria were included and followed prospectively from the time-point of SLE diagnosis. Patients were (at least) seen by a rheumatologist at Months 0 (inclusion), 6, 12, 24, 36, 48 and 60, with collection of disease activity measures, damage accrual, serology, therapy and PROMs such as fatigue, pain intensity, well-being (all visual analogue scale) and QoL (EQ-5D). Definitions of remission were: DORIS 1A: cSLEDAI 0, PhGA <0.5; DORIS 1B: cSLEDAI 0, PhGA <0.5, serology normal; DORIS 2A: PhGA <0.5, BILAG D/E only; DORIS 2B: PhGA <0.5, serology normal, BILAG D/E only. Each definition could be reached either on or off treatment (maintenance with antimalarials only was allowed) [1]. The effect on QoL of achieving versus not achieving remission was assessed using multilevel regression modelling.

Results
A total of 41 patients were included in the study: median (interquartile range) age at baseline 39 years (18–77), 33/41 (81%) female, 35/41 (85%) white and 18/41 (44%) former/current tobacco smokers. The median number of fulfilled 1982 ACR criteria was 4 (range 3–9) and 15/41 (37%) had lupus nephritis. Using DORIS 1A or 2A, patients with SLE achieving versus not achieving remission had higher QoL (p=0.01), whether on or off treatment (Figure). This association remained significant after adjusting for sex, tobacco smoking and treatment in a multivariable analysis. Achieving ➤

remission according to DORIS 1B (p=0.93) or 2B (p=0.86) was not significantly decisive for QoL (Figure).

Conclusions
This pilot study demonstrates the first real-life performance of the suggested preliminary definitions of remission in SLE. Higher QoL was associated with achieving remission as defined by DORIS 1A or 2A. However, further evaluation of the accuracy of DORIS in larger longitudinal studies of recent-onset SLE is required before introduction in routine clinical practice.

Reference
1) van Vollenhoven R, et al. Ann Rheum Dis 2017;76:554–61.

ABSTRACTNUMMER: 1523-A-1818 43

NOVEL RISK LOCI IN JUVENILE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Johanna K. Sandling[5], Lina Hultin Rosenberg[9], Fabiana H.G. Farias[9], Andrei Alexsson [5], Dag Leonard[5], Sergey Kozyrev[9], Eva Murén[9], Åsa Karlsson[9], Argyri Mathioudaki[9], Daniel Eriksson[2], Gerli Pielberg [9], Jennifer Meadows[9], Jessika Nordin[9], Johanna Dahlqvist[9], Matteo Bianchi[9], Christine Bengtsson[7], Andreas Jönsen[8], Leonid Padyukov[6], Maija-Leena Eloranta[5], Christopher Sjöwall[3], Iva Gunnarsson[6], Elisabet Svenungsson[6], Solbritt Rantapää-Dahlqvist[7], Anders A. Bengtsson[8], Ann-Christine Syvänen[4], Kerstin Lindblad-Toh[1,9], Lars Rönnblom[5], the DISSECT consortium[5]

[1] Broad Institute of MIT and Harvard, Boston, MA, USA
[2] Center for Molecular Medicine, Department of Medicine (Solna), Karolinska Institutet, Stockholm, Sweden; Department of Endocrinology, Metabolism and Diabetes Karolinska University Hospital, Stockholm, Sweden
[3] Department of Clinical and Experimental Medicine, Rheumatology/Neuro and Inflammation Sciences, Linköping University, Linköping, Sweden
[4] Department of Medical Sciences, Molecular Medicine and Science for Life Laboratory, Uppsala University, Uppsala, Sweden
[5] Department of Medical Sciences, Rheumatology, Uppsala University, Uppsala, Sweden
[6] Department of Medicine, Rheumatology unit, Karolinska Institutet, Stockholm, Sweden
[7] Department of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden
[8] Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden
[9] Science for Life Laboratory, Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Sweden
[10] Uppsala University, Department of Medical Sciences

Background
Systemic lupus erythematosus (SLE) is a systemic autoimmune disease affecting mainly women. Disease diagnosis typically occurs between the ages of 15 and 45, but childhood onset SLE is commonly associated with a more aggressive disease course and higher mortality risk than adult onset SLE. It has been suggested that juvenile onset SLE cases could have a more genetically determined disease. To identify genetic risk loci in juvenile onset SLE we performed targeted DNA resequencing in Swedish SLE patients and control individuals.

Materials and methods
Coding and regulatory regions of 1853 genes selected from pathways involved in immunological diseases were resequenced in 958 patients with SLE and in 1030 healthy individuals. All patients fulfilled at least four American College of Rheumatology 1982 classification criteria for SLE. For 117 of the SLE patients the disease onset was before the age of 18, 105 of whom were women and 12 men. Capturing of the targeted genes was performed with a Roche NimbleGen custom-made liquid capture library followed by Illumina HiSeq2500 sequencing. 97,264 single nucleotide variants (SNVs) which passed quality control and had a minor allele frequency of at least 1% were included in genetic association testing using logistic regression.

Results
Single variant case-control association analysis revealed that 40 SNVs were associated with juvenile onset SLE (false-discovery rate <5%). These 40 SNVs were enriched for missense variants (8% vs 1.8% for all SNVs) and were annotated to 15 genes. Two coding SNVs on chromosome 1q25 in the NCF2 gene showed the strongest evidence of association with juvenile onset SLE (best SNV p-value= 1E-10, OR=3.9, 95% CI [2.6-5.9]), one of which results in a predicted deleterious amino acid change. Interestingly, this association exceeded the signal from the human leukocyte antigen (HLA) region on chromosome 6 in statistical significance (best HLA SNV was in TNXB, p-value=6E-08, OR=2.5 [1.8-3.5]). In order to identify genetic variants unique to childhood onset SLE, a case-case association analysis comparing childhood and adult onset SLE cases was also performed. Association signals at four loci reached our suggestive significance threshold in this analysis, two of which have previously been associated with inflammatory disorders.

Conclusion
Using targeted sequencing we have identified coding SNVs in novel candidate risk loci in juvenile onset SLE. Our finding suggests differences in the genetic risk factors for childhood and adult onset SLE and provides insight into the genetic etiology of juvenile onset SLE.

ABSTRACTNUMMER: 1531-A-1818 44

INTERFERON- MODULATES THE EFFECT OF THE STAT4 SLE RISK ALLELE RS7574865[T]

Niklas Hagberg, Lars Rönnblom

Institutionen för Medicinska Vetenskaper, Uppsala Universitet

Objectives
Intronic single nucleotide polymorphisms in STAT4 are associated with an increased susceptibility to SLE and other rheumatic diseases. Recently, we demonstrated that T cells from SLE patients carrying the STAT4 risk allele rs7574865[T] have an augmented response to IL-12 [1]. Since the majority of risk allele carriers do not develop disease, we asked whether the STAT4 risk allele exerts the same effect in cells from healthy individuals.

Methods
Peripheral blood mononuclear cells (PBMCs) were isolated from 24 homozygous protective (G/G), 24 heterozygous (G/T) and 24 homozygous risk (T/T) age-matched female healthy individuals. Phosphorylation of STAT4 (pSTAT4) and IFN-γ production following IL-12 stimulation was determined in subsets of T cells using flow cytometry and compared to that previously reported in SLE patients [1]. The IL-12-response was assessed with or without pre-activation of cells with 100 U/ml IFN-alpha. CD8 + memory T cells were isolated from 11 homozygous protective and 15 homozygous risk healthy individuals and mRNA expression of STAT4alpha and STAT4beta was determined before and after PHA/

IL-2-stimulation using qRT-PCR. Statistical comparisons were performed using Spearman's correlation test, Mann-Whitney U test or Wilcoxon matched-pairs signed rank test.

Results

In contrast to SLE patients, healthy donors carrying the STAT4 risk allele displayed a decreased IL-12-induced pSTAT4 in CD8+ (median-MFI(G/G)=494 vs median-MFI(T/T)=937, p=0.004) and CD4+ T cells (median-MFI(G/G)=544 vs median-MFI(T/T) =1047, p=0.06), which resulted in a decreased IFN-γ production in CD8+ T cells (median frequency IFN-γ+: CD8+(G/G)=0.87% vs CD8+(T/T)=0.37% , p=0.009; CD4+(G/G)=0.25% vs CD4+(T/T)= 0.07%, p=0.13). The reduced IL-12-response was confined to the CD57– T cells, i.e. the CD45RA+CD57– naïve and CD45RA–CD57– memory T cells. Mechanistically, STAT4 risk allele carrier-ship was associated with a lower induction of STAT4alpha mRNA in CD8+ memory T cells following PHA/IL-2-stimulation (p=0.004), whereas levels of STAT4beta were normal (p=0.57).

When comparing healthy donors and SLE patients, homozygous protective individuals phosphorylated STAT4 to the same extent. However, with increasing numbers of risk alleles, SLE patients displayed an augmented IL-12 response. Pre-activation of healthy donor cells with IFN-γ augmented the IL-12-induced pSTAT4 in STAT4 risk allele carriers (fold increase=1.8x, p=0.02), but did not affect homozygous protective individuals (fold increase=1.1x, p=0.58).

Conclusions

The STAT4 risk allele rs7574865 has opposite directional effects in SLE patients compared to healthy donors. We identify IFN-α as an environmental modulator of the STAT4 risk allele. These findings may have implications for why the majority of risk allele carriers do not develop disease.

Reference

[1] Hagberg et al. "The STAT4 SLE risk allele rs7574865[T] is associated with increased IL-12-induced IFN-gamma production in T cells from patients with SLE." Ann Rheum Dis. Feb 2018

ABSTRACTNUMMER: 1535-A-1818 45

VARIATIONER I GENERNA ITGA1, BANK1 OCH BACH2 ÄR ASSOCIERADE TILL PROLIFERATIV NEFRIT VID SLE

Karin Bolin[1], Dag Leonard [1], Malena Loberg Haarhaus[2], Christopher Sjöwall[3], Andreas Jönsen[4], Anders A Bengtsson[4], Juliana Imgenberg-Kreuz[1], Andrei Alexsson[1], Solbritt Rantapää-Dahlqvist[5], Elisabet Svenungsson[2], Iva Gunnarsson[2], Ann-Christine Syvänen[6], Lars Rönnblom[1], Johanna K Sandling[1], Gunnel Nordmark[1]

[1] Institutionen för medicinska vetenskaper, reumatologi och Science for Life Laboratory, Uppsala universitet, Uppsala
[2] Institutionen för medicin, Karolinska Institutet, Stockholm
[3] Institutionen för klinisk experimentell medicin, Linköpings universitet, Linköping
[4] Institutionen för klinisk medicin, Skånes universitessjukhus, Lunds universitet, Lund
[5] Institutionen för folkhälsa och klinisk medicin, Umeå universitet, Umeå
[6] Institutionen för medicinska vetenskaper, molekylärmedicin och Science for Life Laboratory, Uppsala universitet, Uppsala

Bakgrund

SLE-nefrit är en allvarlig sjukdomsmanifestation som drabbar ca 30 % av patienterna med SLE. Proliferativ nefrit är den vanligaste och mest allvarliga subtypen med sämst prognos. Studier av den genetiska bakgrunden till SLE-nefrit har visat en association till variationer i ett tiotal genregioner, bland annat integrin subunit alpha M (ITGAM), interferon regulatory factor 5 (IRF5) och signal transducer and activator of transcription 4 (STAT4), där STAT4 även associerar till ökad risk för utveckling av njursvikt. Någon studie som analyserat den genetiska bakgrunden till proliferativ nefrit finns inte. Syftet med denna studie var att i större skala studera den genetiska bakgrunden till SLE-nefrit och mer specifikt till proliferativ nefrit.

Material och metoder

Totalt 1155 patienter med SLE genotypade på Illumina® ImmunoChip innefattande 200 000 genvarianter (singelnukleotidpolymorfier, SNP) inkluderades i studien. Kliniska data avseende kön, ålder vid sjukdomsdebut, ålder vid nefritdebut, sjukdomsduration, American College of Rheumatology (ACR)-kriterier, njurbiopsi samt njurfunktion insamlades från patienternas journaler. SLE-nefrit definierades som förekomst av proteinuri > 0,5 g/dygn eller patologiskt urin-sediment enligt ACR-kriteriet, alternativt biopsiverifierad SLE-nefrit med ANA eller anti-dsDNA enligt Systemic Lupus International Collaborating Clinics (SLICC)-kriteriet. Efter kvalitetskontroll kvarstod 1091 patienter med SLE från Stockholm (n=346), Umeå (n=232), Uppsala (n=188), Linköping (n=172) och Lund (n=153) samt 134 000 SNP. Totalt 377 av 1091 patienter (34,6 %) hade haft nefrit. Allelfrekvenserna jämfördes mellan SLE-patienter med (n=377) och utan (n=714) nefrit samt mellan SLE-patienter med (n=153) och utan (n=649) proliferativ nefrit (WHO/ISN-RPS klass III-IV). Kön och sjukdomsduration inkluderades som kovariater och analyserna utfördes i PLINK. Okorrigerade p-värden presenteras.

Resultat

Patienterna med SLE-nefrit var signifikant oftare män (23,1 % respektive 8,8 %, p=8,0 x 10-11), yngre vid SLE-diagnos (30,7 år respektive 38,5 år, p=6,5 x 10-17) och uppfyllde fler ACR-kriterier (6,2 respektive 5,3, p=3,5 x 10-24) jämfört med SLE-patienterna utan nefrit. Information om njurbiopsi fanns för 247 patienter varav 153 (61,9%) uppvisade proliferativ nefrit. Av de 290 patienterna med tillgänglig uppföljning av njurfunktionen utvecklade 37 patienter (12,8%) terminal njursvikt. Vi identifierade flera genvarianter med association till nefrit. Starkast association sågs till ett flertal SNPar belägna i intronen till generna integrin subunit alpha 1 (ITGA1, p=3,7x10-5; OR 0,68; 95% CI 0,56-0,81) och B cell scaffold protein with ankyrin repeats 1 (BANK1, p=9,6x10-5; OR 0,66; 95% CI 0,54-0,81). När analysen begränsades till patienter med proliferativ nefrit jämfört med SLE-patienter med annan nefrit-typ och SLE utan nefrit, kvarstod association till ITGA1 och BANK1 (båda p<1x10-3). Vi identifierade även BTB domain and CNC homolog 2 (BACH2, p=3,1x10-3) som ett risklokus för proliferativ nefrit.

Slutsats

Variationer i gener kodande för proteiner av betydelse för inflammation bidrar troligen till utvecklingen av nefrit per se, liksom till den svårare subtypen proliferativ nefrit. ITGA1 kodar för en enhet av integrinreceptorn involverad i cell-celladhesion, BANK1 kodar för ett B-cellsrelaterat protein med tidigare association till SLE och BACH2 har betydelse för både B-cells- och T-cellsfunktion och är associerad till andra autoimmuna sjukdomar. Vidare studier av dessa geners epigenetiska reglering, genuttryck och funktion kan bidra till förståelsen för uppkomsten av nefrit hos patienter med SLE.

ABSTRACTNUMMER: 1536-A-1818 46

BEHÇETS SJUKDOM I REGION UPPSALA 2009-2016

Hanna Lindberg, Ann Knight

Reumatologen, VO Specialmedicin, Akademiska Sjukhuset

Bakgrund
Behçets sjukdom är en kronisk kärlinflammatorisk sjukdom med okänd etiologi. Sjukdomens prevalens är högst i länder runt Medelhavet och i Mellanöstern, men är beskriven från alla världsdelar. HLA B51 predisponerar den orientaliska populationen till sjukdomsutveckling men motsvarande genetiska koppling ses inte i Europeisk befolkning. Med ökad invandring, inte minst från Mellanöstern, kan prevalensen av Behçets förväntas stiga i Sverige. Avsikten med denna studie var att kartlägga Behçets-populationen i Region Uppsala avseende härkomst, symptombild och behandling och ge ett underlag för optimering omhändertagandet och prognosen för personer med denna potentiellt mycket allvarliga sjukdom.

Material och metoder
Ur journaldatasystemet Cambio Cosmic® plockade vi fram alla patienter som registrerats med diagnosen Behçets (ICD M35.2) på Akademiska sjukhuset mellan åren 2009-01-2016-12. Samtliga patienters diagnos validerades gentemot International Study Group(ISG) diagnoskriterier och endast patienter som uppfyllde dessa kriterier inkluderades i den fortsatta studien. Ur journalerna extraherades uppgifter om ålder, kön, debutålder, ursprungsland och kliniska symptom, liksom givna behandlingar.

Resultat
Av de initialt 36 identifierade patienterna som fått diagnosen Behçets exkluderades 4 patienter, samtliga svenska kvinnor, då de inte uppfyllde ISG diagnoskriterier. Av de återstående 32 patienterna var 72 % (23/32) av icke-svensk härkomst, samtliga utom en från Mellanöstern och Medelhavsländerna. 44 % (14/32) var kvinnor och medelålder vid insjuknandet var 31 år; medianålder 22,5 år. Under sjukdomsförloppet har 100 % utvecklat orala sår, 97 % genitala sår, 56 % hudmanifestationer, 38 % ögonsymptom (36% kvinnor/64%män), 40 % artrit/artralgi, 22 % tarmsymptom och 19 % trombo-embolisk sjukdom. Tre patienter (1%) hade haft CNS engagemang. Avseende diagnostik var Patergi-testet registrerat som utfört på fem patienter och positivt på två. HLA B51 var kontrollerat på 10 av patienterna men förelåg hos endast tre. Alla patienter hade behandlats med peroralt kortison, enstaka med intravenös SoluMedrol. Övriga behandlingar fördelades på kolkicin (22 st), Azatioprin (10 st), Cyklosporin (9 st), Metothrexate (2 st), Cyklofosfamid (1 st). Fem patienter hade haft någon form av antikoagulation eller trombocythämning, och sex patienter TNFα blockerare. De sex patienter som behandlats med TNFα blockad hade antingen tarm-, ögon- eller CNS-symptom.

Slutsats
Med så relativt få studerade patienter är det svårt att dra långtgående slutsatser. Patientgruppen tycks ändå väl avspegla en typisk Behçets -population avseende ålders och könsfördelning samt symptombild. Även i ett litet ”svenskt” patientmaterial är det tydligt att sjukdomen är betydligt vanligare bland personer som kommer från Medelhavsområdet eller Mellanöstern och att man hos en svensk patient kanske i första hand ska överväga andra vanligare orsaker till orala- och genitala sår. Patergi-testet bör sannolikt också användas mer konsekvent som diagnostiskt hjälpmedel, då det ingår i diagnoskriterierna, medan värdet av HLA-testning kanske är mer begränsat. Vad gäller behandlingsarsenalen är det tydligt att kolkicin har en etablerad plats vid mukokutana symptom. Att endast en patient erhållit behandling med cyklofosfamid kan antas bero på att flertalet patienter hade haft sina allvarligaste sjukdomssymptom innan ankomst till Sverige, eller att patienten debuterade med allvarliga symptom, dvs innan fastställd Behçets-diagnos.

ABSTRACTNUMMER: 1537-A-1818 47

SHARED AND UNIQUE PATTERNS OF DNA METHYLATION IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

Juliana Imgenberg-Kreuz[5], Dag Leonard[5], Jonas Carlsson Almlöf[5], Solbritt Rantapää-Dahlqvist[4], Anders A Bengtsson[3], Andreas Jönsen[3], Leonid Padyukov[1], Iva Gunnarsson[1], Elisabet Svenungsson[1], Christopher Sjöwall[2], Ann-Christine Syvänen[5], Lars Rönnblom[5], Gunnel Nordmark[5], Johanna K Sandling[5]

[1] Karolinska Institutet
[2] Linköping University
[3] Lund University
[4] Umeå University
[5] Uppsala University

Background
Epigenetic modifications, such as DNA methylation, have emerged as contributing factors in the pathogenesis of chronic autoimmune rheumatic diseases, including primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE). In the current study we investigated genome-wide DNA methylation in healthy controls and in patients with pSS and SLE with the aim of identifying methylation patterns that are shared between the two diseases and those that are unique to one of them.

Materials and methods
DNA extracted from blood from 100 patients with pSS, 347 with SLE and 400 healthy blood donor controls were analysed on the Illumina HumanMethylation 450k BeadChip, which targets 485,000 CpG sites across the genome. Signal intensities were parsed into the Minfi R package for quality control and normalisation. Blood cell type proportions were estimated based on publicly available reference DNA methylation signatures from flow sorted cells. To determine differential methylation, a logistic regression model was fitted including age, sex and cell type distribution as covariates. Significantly differentially methylated CpG sites (DMCs) were defined as $p<1.3\times10-7$ for association based on experiment-wide Bonferroni correction and an absolute average difference in methylation beta values of $|\Delta\beta|>0.05$.

Results
We identified differential DNA methylation between patients with pSS compared to SLE at 2,227 CpG sites, where the vast majority of DMCs showed increased methylation levels in pSS compared to SLE (89%; 1,985 DMCs). In patients with pSS we typically found average methylation levels which were intermediary to those of healthy individuals and patients with SLE. This pattern was in particular observed at type I interferon (IFN) induced genes; for example at the CpG site cg21549285 located in the promoter region of the MX1 gene on chromosome 21, where healthy controls exhibited an average methylation level of 0.83, patients with SLE showed distinctly decreased methylation with an average level of 0.40, whereas in-between levels were observed for patients with pSS with an average beta of 0.57. We further noted, that the signature of promoter hypomethylation at IFN induced genes in pSS was mainly driven by patients which were positive for SSA/SSB-antibodies (average beta at cg21549285 in MX1 of 0.49 compared to 0.79 for SSA/SSB-antibody negative patients with pSS).

Analysis of methylation variation unique for pSS identified a DMC at the proteasome subunit beta type 8 gene (PSMB8, p=1.8x10-9), which exhibited decreased methylation in pSS compared to both SLE and healthy controls, whereas no differential methylation between patients with SLE and healthy controls was observed at this CpG site. PSMB8 encodes a subunit of the immunoproteasome involved in processing of class I MHC peptides.

Conclusion
Comparative analyses of DNA methylation between pSS and SLE facilitates identification of shared and unique molecular patterns across systemic inflammatory autoimmune diseases. Our results suggest variation in DNA methylation in pSS as a starting point for development of pSS-specific biomarkers.

ABSTRACTNUMMER: 1538-A-1818 48

INFECTIONS PREDISPOSE TO DEVELOPING PRIMARY SJÖGREN'S SYNDROME

Johannes Mofors[1], Elisabeth V Arkema[1], Linnea Westermark[2], Albin Björk[1], Marika Kvarnström[1], Helena Forsblad-d'Elia[3], Sara Magnusson Bucher[4], Per Eriksson[5], Thomas Mandl[6], Gunnel Nordmark[2], Marie Wahren-Herlenius[1]

[1]Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Sweden
[2]Department of Medical Sciences, Uppsala University, Sweden
[3]Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Sweden
[4]Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Sweden
[5]Department of Clinical Experimental Medicine, Linköping University, Sweden
[6]Department of Rheumatology, Skåne University Hospital, Sweden

Background
Environmental insults are believed to trigger primary Sjögren's syndrome (pSS) in genetically susceptible individuals, and infectious agents have long been suspected as etiologic factors. This has been further supported by the discovery of an association between pSS and upregulation of the type I and II interferon pathways. In the present study, we therefore investigated the association between infections and future risk of developing pSS.

Methods
We performed a case-control study including well -characterized and validated cases with pSS (n=945) and controls from the Swedish population matched on age, sex and area of residence (n=9,048). Data including ICD10 codes were extracted from the population-based National Patient Register to identify infections occurring before the date of pSS diagnosis. Conditional logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) of the association between infections and pSS. Infections occurring in the year before pSS diagnosis were excluded to minimize the risk of reversed causality.

Results
Preceding infections were more common in pSS cases compared to controls (21% vs 12%) , and were associated with an increased risk of pSS (OR 2.0, 95% CI 1.7 – 2.4). Infections were more prominently related to pSS positive for both Ro/SSA and La/SSB autoantibodies (OR 2.7, 95% CI 2.0 – 3.5), than pSS without these autoantibodies (OR 2.1, 95% CI 1.5 – 2.9). Stratifying the analysis by organ system infected, we observed that respiratory infections were associated with pSS (OR 2.5, 95% CI 1.9 – 3.4), both with and without Ro/SSA and La/SSB autoantibodies. Interestingly, preceding skin infections were only associated significantly with Ro/SSA and La/SSB positive pSS (OR 3.2, 95% CI 1.8 – 5.5), and the relationship could not be established in pSS patients without such autoantibodies (OR 1.7, 95% CI 0.8 – 3.6). Notably, gastrointestinal infections were however not associated with an increased risk of pSS (OR 1.5, 95% CI 0.9 – 2.5). Considering the long time-interval that may occur between symptom onset and pSS diagnosis, we also applied models only including infections occurring at least 3 or 7 years prior to pSS diagnosis. These analyses confirmed pulmonary and skin infections as risk factors for developing pSS associated with autoantibodies, but failed to confirm an association between infections and seronegative pSS. The robustness of the observations was further tested by analyzing data among hospitalized patients only, or infections listed as primary diagnosis only, as well as correcting for previous health care consumption. Such parameter variation did not greatly influence the results.

Conclusions
We observed a significant and consistent association between infections and the subsequent development of pSS with autoantibodies, suggesting that external triggers of immunity influence the development of the disease. The risk was dependent on the location of the infection, indicating that the route of infection and/or immunoenvironment of the primarily affected organ may modulate outcome.

ABSTRACTNUMMER: 1541-A-1818 49

CYTOKINE PRODUCTION BY ACTIVATED PLASMACYTOID DENDRITIC CELLS AND NK CELLS IS SUPPRESSED BY AN IRAK4 INHIBITOR

Karin Hjorton[2], Niklas Hagberg[2], Elisabeth Israelsson[1], Lisa Jinton[1], Olof Berggren[2], Johanna K Sandling[2], Kristofer Thörn[1], John Mo[1], Maija-Leena Eloranta[2], Lars Rönnblom[2]

[1] Respiratory, Inflammation and Autoimmunity, iMED Biotech Unit, AstraZeneca, Göteborg
[2] Uppsala universitet, Inst med Vet, reumatologi

Background
In SLE, immune complexes containing self-derived DNA or RNA (RNA-IC) trigger the synthesis of several pro-inflammatory cytokines by immune cells. Treatment with anti-malarials, such as hydroxychloroquine (HCQ), which through endosomal TLR inhibition effectively blocks IFN-α, is standard of care. However, few patients experience complete remission.

Objective
We asked how an IL-1 receptor associated kinase 4 (IRAK-4) inhibitor I92 (ND-2158, Nimbus Discovery) 1, acting downstream of TLR 7/9, affects RNA-IC-induced cytokine production compared to hydroxychloroquine (HCQ).

Methods
Plasmacytoid dendritic cells (pDCs) and natural killer (NK) cells were isolated from peripheral blood mononuclear cells (PBMCs) of healthy individuals. PBMCs from 15 SLE patients were depleted of monocytes. Cells were stimulated with RNA-IC, consisting of IgG from SLE patient sera and U1snRNP particles, in the presence or absence of I92 or HCQ. Cytokines were measured by immunoassays or flow cytometry. RNA-sequencing was performed on RNA-IC stimulated pDCs from four healthy individuals and the effect of I92 and HCQ was assessed.

Results
RNA-IC induced IFN-α, TNF-α, IL-6, IL-8, IFN-γ, MIP1-α and MIP1-β production in pDC and NK cell co-cultures. I92 reduced the pDC and NK cell derived cytokine production by 74-95%. HCQ interfered with cytokine production in pDCs, but not in NK cells. In monocyte-depleted SLE PBMCs I92 blocked TNF-α, IFN-γ, MIP1-α and MIP1-β production more efficiently than HCQ. Following RNA-IC activation of pDCs, 975 differentially expressed genes were observed (FDR<0.05), many connected to cytokine pathways, cell regulation and apoptosis. The IRAK4 inhibitor significantly changed more RNA-IC induced genes than HCQ (492 vs. 65 genes). Several top upregulated genes were reversed by both I92 and HCQ, including IFNA2, IFIT2-3, OASL, CXCL10, CD274, TNFSF10, APOL6. Genes such as DKK4, LAD1 and EAF2 were significantly more downregulated by I92 than by HCQ.

Conclusions
Whereas both HCQ and the IRAK4 inhibitor block important pro-inflammatory cytokines, the IRAK4i I92 exhibits a broader inhibitory effect than HCQ on pathways triggered by RNA-IC, which suggests that IRAK4 inhibition could be a future therapeutic option in SLE and possibly other systemic autoimmune diseases characterized by the presence of ICs containing nucleic acid.

ABSTRACTNUMMER: 1547-A-1818 50

REGULATION OF CYTOKINE PRODUCTION BY PLASMACYTOID DENDRITIC CELLS AND B CELLS STIMULATED WITH TOLL-LIKE RECEPTOR 7 AGONISTS DSR-6434 OR RNA-CONTAINING IMMUNE COMPLEXES

Olof Berggren, Lars Rönnblom, Maija-Leena Eloranta

Dept. of Medical Sciences, Rheumatology, Science for Life Laboratory, Uppsala University, Uppsala, Sweden.

Background and objective
Activated B cells and type I interferon (IFN) produced by plasmacytoid dendritic cells (pDCs) are prominent features in many systemic inflammatory rheumatic diseases. Both cell types express Toll-like receptor (TLR) 7, and B cell/pDC interaction enhances the production of IFN-alpha by stimulated pDCs (1). The study was undertaken to further investigate activation of cytokine production and gene expression in pDCs and B cells stimulated with two different TLR7 activators.

Methods
B cells and pDCs were isolated from peripheral blood of healthy individuals and stimulated alone or in co-cultures with a small molecule TLR7 agonist DSR-6434 or RNA containing immune complex consisting of U1snRNA particles and SLE-IgG (RNA-IC). Levels of IFN-alpha, IL-6, IL-8, IL-10 and TNF-alpha were measured at 20h by immunoassays and expression of 600 immunological important genes were analyzed by a Nanostring nCounter expression array.

Results
IFN-alpha production by pDCs stimulated with DSR-6434 was approximately 3 times lower than with RNA-IC, but was increased when the pDCs were cultivated in presence of IFN-alpha2b ("priming"), (mean IFN-alpha: 1045 IU/ml without priming vs. 2521 IU/ml with priming, n=12, p<0.001). Co-cultivation of pDCs and B cells in presence of DSR-6434 did not enhance the IFN-alpha production. Furthermore, neutralizing antibodies to CD31 that effectively reduces the RNA-IC-induced IFN-alpha response (1), did not had any significant effect on DSR-6434-stimulated IFN-alpha production. The DSR-6434 also induced production of IL -6, IL-8 and TNF-alpha. Especially, the IL-6 levels were strongly enhanced (5-8 fold) in pDC/B cell co-cultures compared with the single cultures. Again, antibodies to CD31 did not affect the IL-6, IL-8 or TNF-alpha levels when using DSR-6434 as stimulus while RNA-IC-induced cytokine production was strongly inhibited. A mRNA expression analysis of co-cultured pDCs and B cells from four individuals confirmed the high levels of IL-6, and showed that DSR-6434 induced >4 2log fold increase (adj. p-value <0.01) of IFN-beta and several chemokine transcripts compared with unstimulated cells. In comparison with RNA-IC, DSR-6434 induced significantly higher expression of IL-6, CD80, CD44 and the transcription factor BATF (p<0.001).

Conclusion
The TLR7 ligands, a small molecule DSR-6434 and RNA-containing ICs, activate pDCs and B cells to produce several inflammatory cytokines, but the regulation of their synthesis differs. Thus, a relevant immune cell activator is necessary in order to identify possible targets for modulation of the immune response in patients with an IFN driven autoimmune disease, such as SLE.

Reference
(1) Berggren O, Hagberg N, Weber G, Alm GV, Rönnblom L, Eloranta ML. B lymphocytes enhance interferon-α production by plasmacytoid dendritic cells. Arthritis Rheum. 2012;64:3409-19.

ABSTRACTNUMMER: 1551-A-1818 51

MICROPARTICLES AS BIOMARKERS OF SYSTEMIC LUPUS ERYTHEMATOSUS: THE INFLUENCE OF SIZE AND MITOCHONDRIAL CONTENT

Fariborz Mobarrez[4], Enrico Fuzzi[4], Iva Gunnarsson[4], Anders Larsson[2], Susanna Eketjäll[1], David Pisetsky[3], Elisabet Svenungsson[4]

[1]Cardiovascular and Metabolic Diseases, Innovative Medicines and Early Development Biotech Unit, AstraZeneca, Integrated Cardio Metabolic Centre, Karolinska Institutet, Huddinge, Sweden.
[2] Department of Medical Sciences, Uppsala University, Akademiska Hospital, Uppsala, Sweden.
[3] Department of Medicine, Duke University Medical Center; Medical Research Service, Durham VA Hospital.
[4] Unit of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Karolinska University Hospital, Sthlm, Sweden

Objective
Microparticles (MPs) are small membrane-surrounded vesicles that can form immune complexes (ICs) in the blood of systemic lupus erythematosus (SLE) patients. Because MPs can contain DNA we hypothesized that MPs contain mitochondria, and together with immunoglobulins, forming ICs larger than conventional MPs. We therefore assessed the size, mitochondria content and IgG expression in MPs in the blood of SLE patients and controls.

Methods
We investigated 327 well-characterized SLE patients and 304 controls divided into two sets (280/280 and 47/24). We measured MPs by flow cytometry using a gating strategy to encompass both small (0.2 to 0.7 μm) and large (0.7 to 3.0 μm) MPs. Nucleic acids were labeled with SYTO 13 and mitochondria with MitoTracker deep red. Expression of mitochondria markers TOM-20 and Hexokinase 1 (HK1) and the presence of IgG was also investigated.

Results
MPs staining with SYTO 13 revealed higher concentrations of MPs

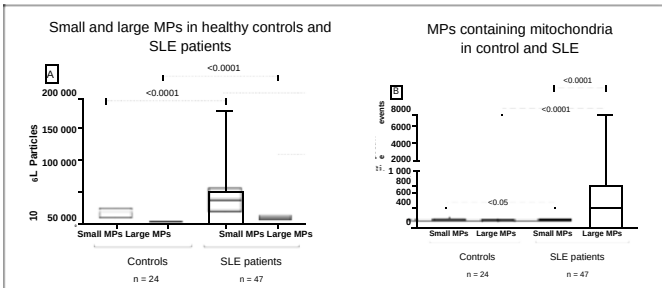


Figure 1. Small and large MPs and mitoMPs in healthy controls and patients with systemic lupus erythematosus (A) Number of small and large MPs defined by size, analyzed by flow cytometry (B) Number of mitoMPs i.e. large MPs containing mitochondria, defined by size and MitoTracker positivity. Bars represent median values and line indicates min and max values.

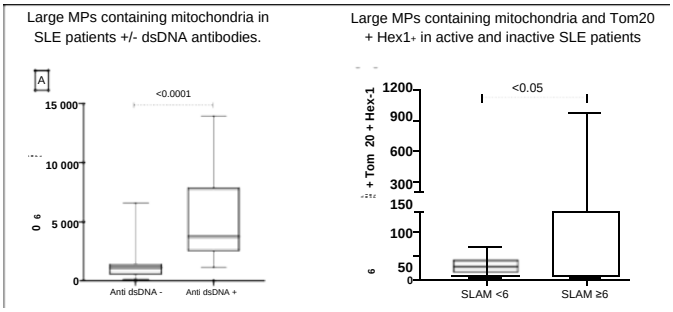


Figure 2. (A) Number of mitoMPs in 47 SLE patients negative or positive for dsDNA antibodies. (B) Number of mitoMPs expressing TOM20 and hexokinase-1 in 47 SLE patients with and without active disease, as measured by SLAM (equal or above 6). Bars represent median values and line

containing DNA in 280 SLE patients compared to 280 controls. Moreover, MPs measured in 47 SLE patients revealed a subset of large MPs (> 0.7 µm) compared to healthy controls (Figure 1A). The majority of large MP population contained mitochondria (mitoMPs) and exposed mitochondria markers TOM-20 and HK1 on the surface (Figure 1B). Furthermore, majority of the mitoMPs were studded with immunoglobulins suggesting IC formation. Interestingly, mitoMPs were more common in patients with high levels of anti-dsDNA antibodies and high disease activity (SLAM ≥6) (Figure 2 A-B). Moreover, MitoMPs were associated with pro-inflammatory cytokines. Patients with signs of ongoing renal lupus activity had higher levels of mitoMPs and IgG positive mitoMPs.

Conclusion

We demonstrate that SLE patients contain higher levels of large MPs than controls. These large MPs are rich in mitochondria (mitoMPs) and levels of mitoMPs are related to disease activity in SLE. These structures may be pivotal for SLE pathogenesis and they are promising novel biomarkers for surveillance of lupus activity.

ABSTRACTNUMMER: 1555-A-1818 52

MICROPARTICLES AS POTENTIAL BIOMARKERS OF DISEASE ACTIVITY IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY – ASSOCIATED VASCULITIS

Aleksandra Antovic[4], Milena Kostic[1], Fariborz Mobarrez[2], Annika Nordin[2], Jelena Vojinovic[1], Annette Bruchfeld[3], Iva Gunnarsson[2]

[1] Department of Pediatrics, Medical Faculty, University of Niš, Nis, Serbia
[2] Dept. of medicine Solna, Rheumatology unit, Karolinska Institutet
[3] Deptartment of Renal Medicine, Karolinska Institutet, Stockholm, Sweden
[4] Karolinska Institutet

Background

Microparticles (MPs) are submicron particles, which are released from plasma membrane upon cell activation and during the early phase of apoptosis. Increased levels of circulating MPs, mainly of endothelial cell origin, but also platelet derived, have been shown to correlate with autoinflammatory disease activity, such as anti-neutrophil cytoplasm antibody (ANCA) – associated vasculitis (AAV).

Objectives

The aim was to evaluate levels of activity markers expressed on MPs from patients with AAV, during active disease and remission, compared to healthy control subjects.

Methods

Our study included 46 AAV patients and 23 healthy age and gender matched control subjects. We analyzed the concentration of MPs in plasma by flow cytometry. MPs were phenotyped by expression: CD142 (tissue factor-TF), anti-H3cit (citrulinated Histone 3 directed against neutrophil extracellular traps - NETs), antipentraxin3 (pentraxin3), HMGB1 (high mobility group box 1 protein-HMGB1), anti-TWEAK (tumor necrosis factor-like weak inducer of apoptosis-TWEAK), anti-plasminogen (plasminogen), anti-C3a (C3a) and anti-C5a (C5a). The assessment of vasculitis disease activity was performed using the Birmingham Vasculitis Activity Score (BVAS), where active disease was defined as BVAS ≥1 and inactive (remission) as BVAS=0.

Results

Half of the patients group (23) had active vasculitis (13 male/10 female, mean age 61±14years) and 23 had inactive disease (12 male/11 female, mean age 64±13years). Concentration of MPs expressing TF, H3cit, pentraxin-3 and HMGB1 in active patients were significantly higher than in those in remission and healthy controls ($p<0.01$, $p<0.0001$, respectively). MPs expressing C5a andC3a were significantly higher in both active and inactive patients compared to controls ($p<0.001$). Additionally, levels of MPs expressing C5a and C3a strongly correlated with BVAS in patients with active disease ($r=0.78$, $p<0.0001$; $r=0.5$, $p<0.01$, respectively), while there was no significant correlation between other explored markers and BVAS.

Conclusions

Our results support recently postulated role of the complement system in AAV pathogenesis and disease activity. Evaluated proteins expressed on MPs, especially C5a and C3a, could be used as potential biomarkers which might reflect inflammation and disease activity in AAV patients. Further investigations are necessary to confirm our preliminary results and to validate the most promising biomarker in AAV.

ABSTRACTNUMMER: 1557-A-1818 53

GENETIC BASIS AND CLINICAL EVIDENCE FOR TWO DISEASE VARIANTS OF PRIMARY SJÖGREN'S SYNDROME WITH DISTINCT OUTCOMES

Gudny-Ella Thorlacius[3], Lina Hultin-Rosenberg[9], Johanna Sandling[9], Juliana Imgenberg-Kreuz[9], Elke Theander[5], Marika Kvarnström[3], Helena Forsblad-d'Elia[7], Sara Magnusson Bucher[10], Katrine Brække Norheim[6], Svein Joar Johnsen[6], Daniel Hammenfors[2], Kathrine Skarstein[2], Malin Jonsson[8], Eva Baecklund[9], the DISSECT consortium, Thomas Mandl[5], Per Eriksson[4], Roald Omdal[6], Roland Jonsson[8], Kerstin Lindbladh-Toh[1,9], Lars Rönnblom[9], Marie Wahren-Herlenius[3], Gunnel Nordmark[9]

[1] Broad Institute of MIT and Harvard
[2] Haukeland University Hospital
[3] Karolinska Institutet
[4] Linköping University
[5] Skåne University Hospital
[6] Stavanger University Hospital
[7] Umeå University
[8] University of Bergen
[9] Uppsala University
[10] Örebro University

Background
The classification of primary Sjögren's Syndrome (pSS) is based on fulfilment of internationally accepted criteria. However, patients with pSS present heterogeneous phenotypes, with varied outcomes, making optimal treatment and long-term outcome prediction challenging. In the current study we therefore aimed to identify markers for potential clinically relevant subsets of pSS.

Methods
DNA sequencing was performed of 1853 selected genetic loci including their regulatory regions, targeting 32Mb of the genome. The regions are selected to contain genes from pathways known to be involved in immunological diseases. A clinically well characterized cohort of 1016 pSS patients from Sweden and Norway, as well as 1350 Norwegian and Swedish controls were included. After quality control, 918 pSS cases, 1264 controls and 312 853 gene variants remained for analysis. Clinical data was extracted from patient records.

Results
We confirmed previous associations with the HLA region (p=1.4E-46, OR 3.9, 95% CI [3.2-4.7]) and IRF5 (p=1.9E-06, OR 0.72 [0.62-0.82]), and identified two novel associations with loci containing the genes GOT-1 (p=1.1E-06, OR 0.70 [0.61-0.81]) and MAP2K2 (p=1.7E-06, OR 0.55 [0.43-0.70]). Variants in or around 80 genes in the HLA region passed an experiment-wide Bonferroni correction (p<8.7E-07), while step-wise adjustment by conditioning on the top associated variants revealed three independent signals within the HLA, two in the MHC class II and one in the MHC class I. The top variant of each independent signal was near the HLA-DQA1, HLA-DRA and HCP5 genes, respectively. Principal component analysis of the clinical data collected revealed two distinct subgroups of patients, best identified by the presence of the pSS autoantibodies anti-SSA and/or SSB. Stratifying the patients based on SSA/SSB autoantibody status, we found significant clinical differences in SSA/SSB positive versus negative patients, including age at symptom onset, age at diagnosis, purpura, major salivary gland swelling and development of lymphoma. Based on these differences in clinical features, we compared only the patients positive for SSA and/or SSB autoantibodies (n=663, 72%) to controls, and observed a strengthened genetic association to HLA (p=2.2E-62, OR 6.1 [4.9-7.5]) and IRF5 (p=7.5E-08, OR 0.66 [0.56-0.77]). Notably, there was no association with variants in the HLA region or IRF5 in patients without these autoantibodies.

Conclusions
These data suggest a genetic basis and clinical evidence for two variants of primary Sjögren's syndrome with distinct outcomes, distinguishable by genetic associations to polymorphisms in HLA and IRF5 and SSA/SSB autoantibody positivity.

ABSTRACTNUMMER: 1566-A-1818 **54**

CARDIOVASCULAR DISEASE IN SLE AT ONE CENTER BETWEEN 1981 AND 2016. A POPULATION BASED STUDY HIGHLIGHTING THE IMPORTANCE OF DISEASE DURATION AND AGE AT DIAGNOSIS

Andreas Jönsen[1], Ragnar F Ingvarsson[1], Anna Jöud[2], Petrus Linge[1], Helena Tydén[1], Anders A Bengtsson[1]

[1] Department of Clinical Sciences, Rheumatology, Lund University
[2] Department of Laboratory Medicine, Occupational and Environmental Medicine, Lund University

Background
Active inflammatory processes characterize early SLE disease, while later morbidity to a considerable extent consists of consequences of organ damage, particularly cardiovascular disease (CVD). In this study, we report on the frequency of acute myocardial infarctions and stroke in incident SLE cases in a defined population over an extended time.

Methods
The current study includes SLE patients followed at the Department of Rheumatology in Lund diagnosed 1981 through 2006. First, we compare incidence rates of acute myocardial infarctions (AMI) and cerebrovascular incidents (CVI) between all incident SLE cases within 8 counties, through the years 1998-2016, with the population. This time constraint is due to the availability of reliable electronic health care information from 1998 and forward. Second, we describe AMI and stroke incidence patterns in SLE patients 1981-2016 and third we study risk factors of CVD development in an extended SLE cohort. Only the first events of AMI and CVI respectively, both among SLE patients and in the population, were used for calculations. Risk factors studied included hypertension, smoking, dysregulated lipids, renal dysfunction, as well as disease activity, anti-CL positivity and glucocorticoid treatment.

Results
In all, 276 SLE patients were included in the study. From the defined 8 counties 175 SLE patients were studied and thus 101 patients from outside this region were included. Overall, 38 AMI and 44 CVI were recorded in 72 SLE patients, thus 10 patients had suffered both from an AMI and a CVI. The incidence rate-ratio for AMI was 3.02 in SLE overall (CI 1.3-6.9 (99.9%) p<0.001). Significantly increased rate-ratios of AMI were seen in women <40 and between 40-59 years of age, while for males only the age group 40-59 years had an increased incidence of AMI.

SLE patients with a higher age at diagnosis (>54 years) had a shorter disease duration before suffering an AMI compared to SLE patients diagnosed at a younger age (median 7 years vs 18 years, p<0.05) The incidence rate-ratio for CVI in SLE overall was 3.2 (CI 1.6-6.6 (99.9%) p<0.001). An increased CVI incidence was only significant for women in the age group 40-59 years. Males were few and had only 2 events in the higher age group. Among the risk factors studied, renal dysfunction was associated with future AMI development (p<0.05) and presence of anti-CL with CVI (p<0.05). Although disease activity did not correlate with AMI development overall, the subset of patients with an AMI before the age of 55 displayed an increased yearly disease activity from diagnosis and onwards up to first AMI compared to patients without AMI and the same disease duration (p<0.001). This this association was not evident for patients developing CVI.

Conclusions
SLE patients are at risk of developing early myocardial infarctions

and cerebrovascular incidents compared with the population. Patients with a younger age at diagnosis may develop AMI after a longer disease duration compared to older patients. Increased SLE disease activity could be important preferably in early AMI development.

ABSTRACTNUMMER: 1571-A-1818 55

HÖGT GENETISKT RISKSCORE VID SLE ÄR ASSOCIERAT TILL ORGANSKADA OCH FÖREKOMST AV ANTIFOSFOLIPIDANTIKROPPAR MED ISCHEMISK HJÄRTSJUKDOM

Sarah Reid[2], Andrei Alexsson[2], Martina Frodlund[1], Elisabet Svenungsson[3], Andreas Jönsen[5], Christine Bengtsson[4], Iva Gunnarsson[3], Anders Bengtsson[5], Solbritt Rantapää-Dahlqvist[4], Johanna K Sandling[2], Maija-Leena Eloranta[2], Ann-Christine Syvänen[2], Christoffer Sjöwall[1], Dag Leonard[2], Lars Rönnblom[2]

[1] Dept of Clinical and Experimental Medicine, Linköping University
[2] Dept of Medical Sciences, Science for Life Laboratories, Rheumatology, Uppsala University
[3] Dept of Medicine, Karolinska Institutet
[4] Dept of Public Health and Clinical Medicine/Rheumatology, Umeå University
[5] Dept of Rheumatology, Skåne University Hospital

Bakgrund
Systemisk Lupus Erythematosus (SLE) är en autoimmun sjukdom med multifaktoriell etiologi. Idag har >100 genvarianter med association till sjukdomen identifierats, men deras sammanlagda effekt på sjukdomens svårighetsgrad är okänd. Vi har därför undersökt sambandet mellan ett genetiskt riskscore (GRS) och kliniska manifestationer kopplade till en svårare sjukdom.

Metod
1001 patienter med SLE som uppfyllde 4 ACR kriterier, samt 2802 friska blodgivare, genotypades med en 200K Immunochip SNP Array (Illumina). 57 singel nukleotid polymorfier (SNPs) belägna utanför HLA-regionen med association (p<5x10-8) till SLE i den europeiska populationen1, inkluderades i ett genetiskt riskscore (GRS). För varje patient multiplicerades den naturliga logaritmen av odds ratio (OR) för SLE för respektive SNP med antal alleler av riskvarianten. Summan av samtliga 57 produkter utgjorde GRS. Information om organskada enligt Systemic Lupus International Collaborating Clinics Damage Index (SDI), förekomst av hjärtinfarkt samt mortalitet och ålder vid diagnos sammanställdes via journalgenomgång. För 947 av patienterna sammanställdes även information om förekomst av antifosfolipidantikroppar (APL), vilket innefattade lupus antikoagulans (LAC), anticardiolipin (aCL) och anti-beta2glycoprotein (aB2GP). Vid jämförelse mellan grupper användes en logistisk regressionsmodell och för analys av organskada och GRS användes en ordinal regressionsmodell. En Kendall-Tau-modell användes för korrelation mellan GRS och antikroppar och för överlevnadsanalyser användes en Kaplan-Meier-modell (SPSS version 25, IBM). Justering gjordes för ålder vid analys av organskada samt för ålder, kön, hypertonibehandling och rökning vid analys av hjärtinfarkt.

Resultat
GRS var högre hos patienter jämfört med kontroller (OR 2,44 (2,26–2,63), p=9,0×10-99) och patienter med ett GRS över medel var yngre vid diagnos jämfört med patienter med ett GRS under medel (32 repsektive 36 år, (hazards ratio (HR) 1,24 (1,09–1,41), p=1,2×10-4). Patienter med ett GRS över medel avled tidigare än patienter med ett GRS under medel (HR 1,71 (1,10–2,64), p=1,6×10-2), och ett högt GRS var dessutom associerat med organskada, definierat som antal poäng på SDI (OR 1,12 (1,02– 1,23), p=2,1×10-2) och nefrit (OR 1,29 (1,16–1,44) p=7,0×10-6). GRS korrelerade med antalet positiva antikroppstyper av aCL-IgG, aCL-IgM, aB2GP1 och LAC (T=0,061, p=1,3×10-2)

ABSTRACTNUMMER: 1576-A-1818 56

VALIDITY OF POLYMYALGIA RHEUMATICA DIAGNOSES, AND CLASSIFICATION CRITERIA, IN PRIMARY HEALTH CARE

Charlotta Fors[2], Ulf Bergström[2], Minna Willim[1], Eva Pilman[4], Carl Turesson[2,3]

[1] Reumatologi, Institutionen för Kliniska Vetenskaper, Lund, Lunds Universitet
[2] Reumatologi, Institutionen för Kliniska Vetenskaper, Malmö, Lunds Universitet
[3] Sektionen för Reumatologi, Skånes Universitetssjukhus, Malmö
[4] Vårdcentralen Landborgen, Helsingborg

Background
Polymyalgia rheumatica (PMR) is an inflammatory disorder that mainly affects elderly women, and usually is diagnosed in primary health care (PHC). A number of classification criteria have been proposed. The American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) criteria (Dasgupta 2012) were developed in a cohort of patients recruited from rheumatology clinics. The objective was to examine the validity of PMR diagnoses in primary care, and to validate the use of classification criteria for PMR in a retrospective survey of a PHC cohort.

Methods
Patients were recruited from two PHC centers. All patients with a registered diagnosis of PMR between 2000 and 2013 were identified. Electronic case records were reviewed through June 2015. Patients with a diagnosis of PMR prior to 2000, or at another care facility, and those with an incorrectly registered PMR diagnosis code, were excluded. In a structured review of the case records, information required for classification according to the ACR/EULAR criteria, the Bird criteria, the Healey criteria, the Chuang&-Hunder criteria and the Jones&Hazelman criteria was extracted. For the ACR/EULAR criteria, a modified version, in which patients who had never been tested for rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) only required 2 points to be classified as having PMR, was used. As duration of morning stiffness (MS) was usually not recorded, criteria components for MS were considered to be fulfilled whenever MS was mentioned in the records. The reference method was an independent review, with assessment of the long term disease course and differential diagnoses, by an experienced rheumatologist with access to all electronic records.

Results
A total of 305 patients with a registered diagnosis of PMR were reviewed. Of these, 117 were excluded. Among 188 with an incident PMR diagnosis at the study sites during the study period, 49 (26 %) fulfilled the modified ACR/EULAR criteria, whereas 145 (77 %) fulfilled the Bird criteria and 93 (49 %) fulfilled the Healey criteria. Patients could not be classified according to the Chuang&Hunder or the Jones&Hazelman criteria due to missing data in most patients for several components. RF and ACPA were tested in only 42 cases (4 positive) and 29 cases (none positive), respectively. The PMR diagnosis was verified using the reference method in 113 cases (60 % of total; 68 % female, mean age at diagnosis 75 years). Among ➤

those fulfilling the modified ACR/EULAR criteria, the diagnosis was verified in 84 % of the patients. The corresponding proportion for the Bird criteria was 66 %, and for the Healey criteria 74 %.

Conclusions
In this study of patients with PMR diagnosed in PHC, the diagnosis could be verified in 60 % of the patients. This underlines the heterogeneity of PMR patients and related diagnostic procedures in PHC. A modified version of the ACR/EULAR criteria can be used to identify patients with a valid PMR diagnosis in retrospective surveys, but does not capture all PMR patients. The modified ACR/EULAR criteria appear to be more stringent than some of the older criteria sets.

ABSTRACTNUMMER: 1577-A-1818 57

PRIMARY SJÖGREN'S SYNDROME INCREASES THE RISK OF CARDIOVASCULAR EVENTS, WITH THE HIGHEST RISK IN SSA/SSB AUTOANTIBODY POSITIVE PATIENTS

Johannes Mofors[3], Linnea Westermark[2], Albin Björk[3], Marika Kvarnström[3], Helena Forsblad-d'Elia[4], Sara Magnusson Bucher[5], Per Eriksson[1], Thomas Mandl[6], Marie Holmqvist[3], Marie Wahren-Herlenius[3], Gunnel Nordmark[2]

[1] Department of Clinical Experimental Medicine, Linköping University, Sweden
[2] Department of Medical Sciences, Uppsala University, Sweden
[3] Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Sweden
[4] Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Sweden
[5] Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Sweden
[6] Department of Rheumatology, Skåne University Hospital, Sweden

Background
An increased risk of cardiovascular disease is well-established in autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. Studies examining cardiovascular morbidity in primary Sjögren's syndrome (pSS) are however few and inconclusive to date. In the present study, we therefore examined the incidence of cardiovascular events in patients with pSS using population-based national health registers.

Methods
A cohort of clinically well-characterized pSS patients fulfilling the American-European Consensus Group criteria, (n=962, 93% females) and matched controls from the Swedish population (n=9,189) was established. Data from the National Patient Register during 1987-2014 was extracted to identify cardiovascular events occurring after pSS diagnosis. Cox proportional hazard modeling was used to estimate the relative risk of cardiovascular events.

Results
The mean age at pSS diagnosis was 55 years. Patients with pSS had a significantly increased risk of acute coronary syndrome (HR 1.5, 95% CI 1.1-2.0). However, this risk first became evident after 5 years with pSS diagnosis. Stratifying the analysis by sex, female pSS patients had an increased relative risk of acute coronary events (HR 1.6, 95% CI 1.2-2.1), while male patients did not (HR 1.1, 95% CI 0.5-2.5). Furthermore, venous thromboembolism was more frequent in pSS patients compared to controls (HR 2.2, 95% CI 1.7-3.0). Notably, an increased risk of venous thromboembolism was also evident before pSS diagnosis (OR 1.7, 95% CI 1.1-2.8), as well as during the first 5 years with pSS diagnosis (HR 2.3, 95% CI 1.4-3.8). An increased risk was also prevalent in pSS patients under the age of 50 years (HR 5.6, 95% CI 2.1-15.3). pSS patients with SSA and/or SSB autoantibodies presented a more prominent association to venous thromboembolism (HR 2.5, 95% CI 1.8-3.5), compared to pSS patients without SSA and SSB autoantibodies (1.7, 95% CI 1.0-3.1). Moreover, pSS patients had an increased risk of cerebral infarctions occurring after 10 years from diagnosis (HR 1.7, 95% CI 1.1-2.6). This association was observed in SSA and/or SSB positive pSS (HR 2.1, 95% CI 1.3- 3.4), while the risk in SSA and SSB negative pSS was in parity with the general population (HR 0.9, 95% CI 0.3-2.4).

Conclusions
We observed a significantly increased risk for both arterial and venous cardiovascular events occurring after pSS diagnosis, compared to matched population controls. Patients with pSS positive for SSA and/or SSB autoantibodies were at higher risk, suggesting that autoimmune disturbances influence the risk of cardiovascular complications.

ABSTRACTNUMMER: 1583-A-1818 58

THE IMPACT OF BIOLOGICS ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Ioannis Parodis[1], Angie Heliana Lopez Benavides[1], Agneta Zickert[1], Susanne Pettersson[1,2], Sonia Möller[1], Elisabet Welin Henriksson[3,4], Anne Voss[5], Iva Gunnarsson[1]

[1] Rheumatology Unit, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
[2] Division of Physiotherapy, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden
[3] Division of Nursing, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden
[4] Division of Nursing Science, Department of Medical and Health Sciences, Linköping University, Linköping, Sweden
[5] Department of Rheumatology, Odense University Hospital, Odense, Denmark

Objective
Accumulating evidence supports an impaired health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE). We investigated the effects of two biologic treatments on SLE patients' HRQoL.

Methods
Patients with SLE from the Karolinska University Hospital treated either with belimumab (n=34) or rituximab (n=35) were included. Data were collected prospectively at treatment initiation and at months 3, 6, 12 and 24; these included the short form 36 (SF-36), functional assessment of chronic illness therapy (FACIT)-Fatigue, EuroQol research foundation 5-dimension (EQ-5D) health questionnaire, and Stanford health assessment questionnaire disability index (HAQ-DI). Comparisons with age- and gender-matched Swedish normative values for SF-36 – derived from a large Swedish population-based sample comprising 8930 subjects – were performed.

Result
Substantial decrements compared to Swedish norms were observed across all SF-36 domains at baseline. Belimumab-treated patients reported gradual improvements in the SF-36 physical component summary (significant from month 12; P=0.023) and FACIT-Fatigue (significant by month 24; P=0.001), no changes in EQ-5D scores, and improvements in HAQ-DI by month 6 (P=0.014).

Rituximab-treated patients showed rapid improvements in the SF-36 mental component summary and FACIT-Fatigue by month 3 (P=0.031 and P=0.007, respectively), which declined at month 12, as well as improvements in EQ-5D at month 6 (P=0.016) and HAQ-DI at month 3 (P=0.033), which were not maintained at later time points. Patients who were on antimalarial agents (n=33) performed better in SF-36 social functioning (P=0.022) and mental health (P=0.023) compared to patients who were not (n=36).

Conclusion

HRQoL was considerably impaired in SLE patients compared to population-based norms at baseline. Patients' perceptions of HR-QoL showed treatment-specific patterns over time, and could provide additional information along with the clinical evaluation of biologics in SLE. Antimalarial agents may have favourable effects on mental HRQoL in patients with active SLE.

ABSTRACTNUMMER: 1585-A-1818 59

UNSUPERVISED CLUSTERING OF PLASMA PROTEINS REVEALS MOLECULAR SUBGROUPS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Arash Zandi[1], Helena Idborg[2], Iva Gunnarsson[2], Elisabet Svenungsson[2], Peter Nilsson[1], Per-Johan Jakobsson[1,2]

[1] Affinity Proteomics, SciLifeLab, School of Biotechnology, KTH - Royal Institute of Technology, Stockholm, Sweden
[2] Karolinska Institutet and Karolinska University Hospital, Rheumatology Unit, Stockholm, Sweden

Background

Systemic Lupus Erythematosus (SLE) is a heterogeneous systemic autoimmune disease that is currently lacking specific diagnostic biomarkers. The diversity within the patients obstructs clinical trials and could reflect differences in underlying pathogenesis. Our objective was to obtain protein profiles to identify molecular subgroups within SLE for patient stratification subjected to different treatment.

Method

We have performed protein profiling of plasma samples from SLE patients (n=379) and matched controls (n=316) in a cross-sectional study, utilizing an antibody suspension bead array targeting 281 proteins. Proteins differentiating SLE and controls were selected for validation by additional antibodies towards these proteins. To investigate the differences between SLE and controls, Mann-Whitney U-test (Bonferroni correction), generalized linear modelling and receiver operating characteristics (ROC) analysis were performed. K-means clustering was used for unsupervised clustering of molecular SLE subgroups.

Results

IRF5, SLC22A2 and S100A12 were the top three proteins with the largest median fold change among the proteins differentially expressed in SLE patients compared to control. By unsupervised clustering we identified three molecular subgroups of SLE: one subgroup characterized by increased levels of E-selectin, SLC22A2, CERS5 and ITGB1, a second subgroup with lower levels of IRF5, ISG15, NOS3 and SLC22A2, and a third subgroup with higher levels of IRF5, ISG15, NOS3 and IL2RA.

Conclusion

We detected differential protein profiles in SLE compared to controls and identified three molecular subgroups of SLE suggesting differences in pathogenesis and treatment perspectives in different subgroups. This work will add new information to today's view of classifying the heterogeneous groups of SLE patients and improve diagnosis.

ABSTRACTNUMMER: 1586-A-1818 60

COMPARATIVE ANALYSIS OF THE TOTAL PROTEOME OF SKIN LESIONS FROM CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) AND DERMATOMYOSITIS (DM)

T. B. Niewold[1], A Meves[2], J Lehman[2], K. Popovic-Silwerfeldt[3], J. M. Dorschner[4], M. Wahren-Herlenius[5], E. Svenungsson[5], V. Oke (presenting author)[5]

[1] Colton Center for Autoimmunity, New York University, USA
[2] Department of Dermatology, Mayo Clinic, Rochester, MN, USA
[3] Dermatology Clinic, Danderyds Hospital
[4] Division of Rheumatology & Department of Immunology, Mayo Clinic, Rochester, MN, United States
[5] Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

Introduction

Cutaneous lupus erythematosus and dermatomyositis are autoimmune diseases. The histopathological pattern of skin involvement can be similar, i.e. interface dermatitis, but the systemic manifestations are very different. While dermatomyositis commonly affect muscles, lupus erythematosus may affect any organ system. Autoantibodies against intracellular targets are common in both conditions, but the specific targets of the autoantibodies differ between the two conditions. Our aim was to investigate a whole proteome of inflammatory foci of the CLE and DM lesions in a comparator manner and identify disease unique mechanisms of inflammation.

Material and Methods

Patients with CLE (n=6), DM (n=5) and controls (n=6) were included and biopsied at diagnosis or disease exacerbation. Skin biopsies were examined by a pathologist, and selected inflammatory foci were laser microdissected. The total protein content of the microdissected tissue was then analyzed using mass-spectrometry.

Results

In DM, there were 25 highly upregulated proteins, while CLE infiltrates were more protein rich and there were 88 proteins with up to 9-fold upregulation. Protein expression comparison between CLE and DM identified 22 differentially upregulated proteins, and all had higher abundance in CLE than in DM. A protein network analysis was performed by STRING platform (string-db.org). The network of interferon (IFN)-regulated proteins was abundant in both CLE and DM, including: IFIT, MX, OAS, STAT gene families and also EIF2AK2. Also, proteins involved in oxidative stress and antigen processing: IL4I1, TAP1 and TAP2 were highly upregulated in both CLE and DM. Proteins expressed differentially in CLE covered complement proteins (C1b), including membrane attack complex (C5, C6, C7, C8A and B) and complement regulators (CFHR1, CFHR2, CFHR5). Also, regulators of coagulation: thrombospondin 2 (THBS2), thrombin (F2) and annexin A3 (ANXA3) were highly abundant in CLE.

Discussion

Inflammatory foci in the interface dermatitis in CLE and DM contain high abundance of IFN-regulated proteins, as well as regulators of oxidative stress and antigen processing. The proteomics technique allowed identification of pathways differentially activated in CLE, including complement activation products and regulators of coagulation. Our study identified multiple pathways ➤

activated at the site of inflammation which will be of interest in further search of new therapeutic targets.

ABSTRACTNUMMER: 1587-A-1818 — 61

HIGH LEVELS OF CIRCULATING TYPE I, II AND III INTERFERONS DEFINE DISTINCT PATIENT SUBSETS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

V. Oke[1], I. Gunnarsson[1], A. Zickert[2], T. B. Niewold[3], E. Svenungsson[1]

[1] Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden
[2] Division of Rheumatology & Department of Immunology, Mayo Clinic, Rochester, MN, United States
[3] Colton Center for Autoimmunity, New York University, New York, NY, United States

Background
Interferons (IFN) play a major role in SLE pathogenesis. IFNs type I (predominately IFN-αs) are of major importance, but IFN type II (IFN-γ) and IFNs type III (λ) have also important roles. How the levels of circulating IFNs type I, type II and type III relate to each other in SLE, and if they associate with any particular disease manifestations is not known.

Objectives
We investigated serum levels of type I, type II, and type III IFNs and explored how these measurements relate to each other and to specific organ manifestations in patients with SLE.

Methods
We studied 497 well-characterized SLE patients and 322 controls. Functional type I IFN-activity (IFN-activity) was measured by WISH cell assay. IFN-α and IFN-λ1 were measured by ELISA, and IFN-γ by MSD 30-plex assay. High IFN-activity/levels were defined as value over 3rd quartile of the measurement.

Results
SLE patients had higher levels of all investigated IFNs. IFN-activity correlated with IFN-α and IFN-γ. High functional IFN-activity associated with active SLE in most domains: weight loss, fatigue, fever, rash, lymphadenopathy, arthritis and nephritis. The IFN-γ high group had active disease with higher rates of nephritis, arthritis, leuko-, lymphopenia and Sm, SmRNP, RNP68, Ro52 and Ro60 autoantibodies. A higher proportion of the IFN-α high group had active rash, lymphadenopathy, Ro52 and La autoantibodies, while rates of antiphospholipid antibodies/syndrome, vascular events and renal affection were lower. High IFN-λ1 associated with anti-nucleosome autoantibodies and lymphopenia.

Conclusions
High type I IFN functional activity is associated with active SLE in the majority domains. A severe SLE phenotype, including active nephritis, arthritis and anti-Sm/SmRNP autoantibodies associate with high IFN-γ, while rash and a benign cardiovascular profile are linked to high serum IFN-α. Isolated increase in IFN-λ1 is only coupled to lymphopenia and antinucleosome antibodies. Our findings demonstrate that several IFNs can be elevated at the same time in SLE and the importance of IFN-γ has so far been underscored. Sub-setting of SLE patients might be important when planning future clinical trials.

Verksamhetsutveckling

ABSTRACTNUMMER: 1526-A-1818 — 62

STRUKTURERAD UPPFÖLJNING AV PATIENTER MED MYOSIT VID AKADEMISKA SJUKHUSET

Dag Leonard, Christina Emilsson, Carin Holmer, Lowe Pellby, Rezvan Kiani, Elisabeth Lindbom, Maija-Leena Eloranta, Maria Lidén

Reumatologi, Science for Life Laboratory, Institutionen för Medicinska Vetenskaper, Uppsala Universitet

Bakgrund
Inflammatorisk myopati eller myosit är en heterogen grupp av autoimmuna systemsjukdomar som karaktäriseras av muskelinflammation och muskelsvaghet. Förutom musklerna påverkas andra organ såsom hud, leder, hjärta, lungor och magtarmkanalen. Incidensen är ca 2-11 per miljon och sjukdomen drabbar både vuxna och barn. Traditionellt har man delat in de kroniska myositerna i tre grupper, polymyosit, dermatomyosit och inklusionskroppsmyosit. Vid Akademiska sjukhuset har sedan 2010 patienter med myosit följts vid reumatologklinikens myositmottagning. En viktig del av denna uppföljning utgör skattning av Myosit Core Set Measures (Rider 2018). Under det senaste året har vi utvecklat denna verksamhet vilket beskrivs nedan.

Material och metoder
Myositteamet vid Akademiska sjukhuset inkluderar arbetsterapeut, fysioterapeut, sekreterare, sjuksköterska och läkare. Patienter som insjuknat i myosit tillfrågas om de vill delta i klinikens myositmottagning kopplad till forskningssamarbetet inom nätverken SweMyoNet och EuroMyositis. Vid inklusionen registreras patienten i SRQ-SweMyoNet samt i EuroMyositisregistret. Vid varje besök träffar patienten under samma dag arbetsterapeut, fysioterapeut, forskningssjuksköterska och läkare. Arbetsterapeuten undersöker och skattar muskelstyrkan i handen via testet GRIPPIT. Fysioterapeuten undersöker och mäter muskelkraft via testet Functional Index 2. Läkare skattar global sjukdomsaktivitet, muskelkraft via testet Manual Muscle Test 8 (MMT8), sjukdomsaktivitet via Myositis Disease Activity Assessment Tool (MDAAT) samt organskada via Myositis Damage Index (MDI). Vidare skattar patienten funktion via Health Assessment Questionnaire (HAQ) och global sjukdomsaktivitet. Blodprover tas inklusive rutinprover, CK, ASAT, ALAT och LD. Forskningssjuksköterskan tar prover för forskning inkluderande plasma, serum samt prov för analys av RNA och DNA. Den kliniska informationen inkluderas i SRQ och överförs därefter automatiskt till EuroMyositisregistret för de patienter som deltar i EuroMyositis.

Resultat
Sedan 2010 då Akademiska sjukhusets myositmottagning startade har sammanlagt 58 patienter med myosit inkluderats och följts via mottagningen. Idag följs 36 patienter vid mottagningen och under det senaste halvåret har 18 patienter inkluderats i EuroMyositisregistret.

Slutsats
Genom att följa upp patienter med myosit med ett strukturerat program inkluderande skattning av bland annat Myositis Core Set Measures av arbetsterapeut, fysioterapeut och läkare hoppas vi kunna erbjuda en bra vård och omhändertagande av patienterna. Vidare är förhoppningen att i framtiden förbättra behandling för patienterna genom att delta i forskningsprojekt inom forskningsnätverken SweMyoNet och EuroMyositis.

Referens
Rider et al, Update on outcome assessment in myositis. Nat Rev Rheumatol. 2018.

ABSTRACTNUMMER: 1549-A-1818 63

SCREENING FÖR TUBERKULOS: UPPSALAMODELLEN - HÖG KVALITET OCH AVLASTNING FÖR REUMATOLOGEN

Eva Baecklund, Anna Gillman, Johan Back

Enheten för reumatologi, Akademiska sjukhuset, Uppsala

Bakgrund
Patienter som börjar sitt första biologiska DMARD ska enligt riktlinjer screenas för tuberkulos (TB). För att få en samstämmig handläggning av alla aktuella patienter och bedömnings- och behandlingsstöd från TB-expert har vi sedan våren 2015 utvecklat en särskild TB-screeningverksamhet i samarbete med infektionskliniken på Akademiska sjukhuset, Uppsala.

Metod
Modellen innebär att läkare på reumatologen skriver kort standardiserad remiss till screeningmottagning på infektionskliniken och remiss för lungröntgen (om sådan inte är gjord sista 6 månaderna) inför start av första biologiska DMARD. Screeningsköterska kallar patienten för Quantiferon-TB Gold Plus (QFT)-test och kartläggning av TB-riskfaktorer via standardiserat protokoll och kompletterande intervju. Vid svårbedömt QFT-test tas i första hand nytt QFT, i andra hand tas TB spot eller görs tuberkulin skin test. Patienterna grupperas baserat på sannolikhet för att vara exponerad för aktiv lungtuberkulos (mycket låg, låg, möjlig, hög sannolikhet). Infektionsläkare går igenom enkät och övriga svar och kallar utvalda patienter till besök (de som sannolikt ska starta behandling samt svårbedömda resultat/patienter). Behandling för latent TB startas och följs upp på infektionsmottagningen. Biologisk DMARD behandling startas i normalfallet ca 1 månad efter start av TB-terapi.

Resultat
Mer än 95% av alla som startat första bDMARD-behandling har passerat TB-screeningmottagningen perioden mars 2015-december 2017, totalt 393 patienter. Av dessa var 21 (5%) positiva för QFT (>35 IU/ml), 22 (6%) hade svårbedömbart QFT-resultat, 28 (7%) hade någon typ av lungröntgenförändring varav 1 säkert representerade TB-förändringar (känd TB på 1940-talet), sannolikheten för TB-exposition bedömdes som mycket låg hos 66 (17%), låg hos 157 (40%), möjlig hos 122 (31%) och hög hos 40 patienter (10%). Totalt 46 (12%) av patienterna kallades för bedömning av infektionsläkare och 32 (8%) startade TB-behandling. Inga fall av aktiv TB har diagnostiserats hos screenade patienter.

Slutsats
En strukturerad och delvis sjuksköterskebaserad screeningverksamhet där TB-expert har ansvar för bedömning och TB-behandling ger högkvalitativ och samstämmig handläggning av alla patienter och fungerar avlastande för reumatologen. Ett problem kan vara växlande behov av screening över tid vilket kräver flexibilitet när det gäller tillgängliga tider för att hålla handläggningstiden kort.

ABSTRACTNUMMER: 1568-A-1818 64

TEAMOMHÄNDERTAGANDE VID SYSTEMISK SKLEROS

Christina Emilson[3], Vivianne Ekenberg[2], Anna Hillered Hultman[3], Gertrud Sedin[3], Karin Holmer[3], Ellinore Svensson[2], Erik Hellbacher[2]

[2]Reumatologkliniken, Akademiska sjukhuset
[3]Rehabilitering och Smärtcentrum, Akademiska sjukhuset

Bakgrund
Systemisk skleros är en komplex kronisk systemsjukdom där engagemang av olika organsystem såsom kärl, hud, lungor, hjärta, mag-tarmkanal och njurar ofta leder till allvarliga konsekvenser för allmän hälsa, aktivitets- och arbetsförmåga samt livskvalitet hos den drabbade individen. Ett multidisciplinärt, teambaserat omhändertagande för att tillgodose patienternas vårdbehov på bästa sätt är av stor vikt. Vid reumatologkliniken, Akademiska Sjukhuset (AS) i Uppsala, har en modell tagits fram för att kunna erbjuda patienter med systemisk skleros i regionen ett strukturerat, samlat teamomhändertagande.

Material och metod
Teamsammansättning: I det nystartade multidisciplinära teamet för systemisk skleros ingår två reumatologer, en sjuksköterska, två arbetsterapeuter, två fysioterapeuter/sjukgymnaster samt en dietist. Vid behov konsulteras kurator till teamet. Två lungläkare med särskilt intresse för interstitiell lungsjukdom vid reumatisk sjukdom är också engagerade och kommer att bedöma patienter med lungengagemang som del i teambedömningen efter behov.

Patienturval
Vid reumatologkliniken på AS följs ca 50 patienter med systemisk skleros. I nuläget, under uppstarten av teamverksamheten, kommer samtliga att erbjudas möjlighet att bedömas av teamet liksom alla nydiagnostiserade patienter. Framöver planeras en individuell bedömning av behovet av fortsatt uppföljning inom teamverksamheten utifrån sjukdomsyttringar och patientens eget önskemål.

Struktur för omhändertagande
Två patienter träffar teamet individuellt under två dagar enligt ett schemalagt program (tabell 1). Under dag 1 görs en första bedömning av alla i teamet och dag 2, efter avstämning i en teamrond, görs slutbedömningar och planering för den fortsatta vården. Läkaren gör en strukturerad bedömning av sjukdomsaktivitet inkluderande kapillärmikroskopi och bedömning av hudengagemang med modifierad Rodnan skin score, går igenom utförda undersökningar och provresultat samt bedömer eventuellt behov av läkemedelsförändringar. Inkludering i register planeras även ingå vid läkarbesök. Sjuksköterskan har en samordnande funktion i teamet samt utför provtagning och vid behov sårvård och instruktioner om egenvård av huden. Arbetsterapeuten kartlägger patientens aktivitetsförmåga och bedömer handfunktionen. Patienten får strategiråd rörande såväl aktivitetshinder som Raynauds fenomen, samt instruktioner för att förbättra och/ eller bibehålla greppfunktion vilket kan

Tabell 1. Översiktsschema för strukturerat teamomhändertagande av patienter med systemisk skleros på reumatologkliniken vid akademiska sjukhuset.

Dag 1		**Dag 2**	
Patient 1	Patient 2	Patient 1	Patient 2
9.30 Sjuksköterska	9.30 Läkare	*8.15-8-45 Teamrond*	
10.00 Läkare	10.00 Sjuksköterska	9.00 Fysioterapeut	9.00 Fysioterapeut
11.15 Arbetsterapeut	11.15 Fysioterapeut	10.00 Arbetsterapeut	10.00 Arbetsterapeut
13.15 Dietist	13.15 Arbetsterapeut	13.30 Läkare	14.15 Läkare
14.45 Fysioterapeut	14.45 Dietist		

innefatta rörlighetsövningar och ortosbehandling. Fysioterapeuten undersöker stramhet i hud- och muskler samt ledrörlighet och funktionellt status. Dessutom görs ett 6-minuters gångtest och en kartläggning av fysisk aktivitet. Patienten får också råd och instruktioner om stretching- och rörlighetsövningar för att bibehålla rörlighet och funktion. Dietisten screenar för hälsosamma matvanor och bedömer behov av behandling utifrån kostindex, kostanamnes och eventuella ätsvårigheter. Nutritionsbehandlingen innefattar kostråd vid undernäring eller risk för undernäring, anpassning av kost vid olika ätsvårigheter samt kostråd för hälsosamma matvanor i syfte att förbättra kostindex.

Resultat
Verksamheten startade under våren 2018 och har ännu inte hunnit utvärderats. Hittills har 6 patienter genomgått en samlad teambedömning enligt modellen. Uppföljning avseende patienternas upplevelse av teamverksamheten planeras via patientenkäter framöver.

Slutsats
Vi presenterar här den modell för ett multidisciplinärt, teambaserat omhändertagande av patienter med systemisk skleros som startats vid reumatologkliniken på AS under våren 2018. Vår förhoppning är att därigenom kunna förbättra och effektivisera vården av patienter med systemisk skleros samt stärka kompetensen kring diagnosen genom förbättrat kunskapsutbyte mellan professionerna.

Vårdforskning

ABSTRACTNUMMER: 1540-A-1818 **65**

SIGNIFICANT OTHERS AS BOTH BARRIERS AND FACILITATORS FOR PARTICIPATION IN DAILY ACTIVITIES IN PERSONS WITH RHEUMATOID ARTHRITIS

Maria Bergström[1], Annette Sverker[1,3], Åsa Larsson Ranada[1], Eva Valtersson[3], Ingrid Thyberg[3], Gunnel Östlund[2], Mathilda Björk[1,3]

[1] Linköpings universitet
[2] Mälardalens högskola
[3] Region Östergötland

Background
Restrictions in participation in persons with rheumatoid arthritis (RA) have been reported to be closely connected with more pain, fatigue and difficulties in performing daily activities. In addition, support and positive interactions with others have been considered important. We therefore need to understand how significant others of persons with RA can be facilitators or barriers, in participation in daily activities. This becomes of even greater importance in the sensitive and adapting phase of early RA. The aim of this study is therefore to describe the meaning of significant others in relation to participation in daily activities, in persons with early RA.

Materials and methods
This interview study is part of the multicenter project TIRA (Tidiga Insatser vid Reumatoid Artrit). Fifty-nine persons (58% women) participated. Inclusion criteria were a diagnosis of RA during at least three years and being in working age, <64 years of age. Semi-structured interviews were conducted using Critical Incidence Technique (CIT) [1] and the material was analyzed using content analysis [2]. The study was approved by the Regional Ethics Committee.

Results
Four categories were revealed: (1) Emotions in relation to activities with others, where participants would feel like being someone's burden, taking out aggression on others, and express anxiety about how relationships and activities would function in the future. (2) Interactions that include physical contact, referring to both the problematic and manageable impact RA could have on intimate life, as well as body contact in the form of hugging. (3) A balance between shortfalls and participation, where participants distinguished getting help they had not asked for, from helping each other out. The first being experienced as degrading, and the latter as feeling more involved in the activity. (4) Adaptation of daily activities, referring to how the person and significant others consciously modified their activities and activity choices when needed

Conclusions
Significant others can be either a barrier or facilitator for participation in daily activities, for persons with early RA. From a clinical point of view it is important to further involve significant others in the rehabilitation process, in order to enhance participation in daily activities for persons with RA.

References
1. Flanagan, C. The critical incidence technique. Psychol Bull 1954;51(4):327-58.
2. Graneheim, UH. & Lundman, B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today 2004;24(2): 105-12.

Övrigt

ABSTRACTNUMMER: 1573-A-1818 **66**

LOW LEVELS OF NATURAL ANTIBODIES TO PHOSPHORYLCHOLINE: A NOVEL PARADIGM IN AUTOIMMUNE AND CHRONIC INFLAMMATORY DISEASES AND AN EXTENSION OF THE OLD FRIENDS/HYGIENE HYPOTHESIS

Johan Frostegård

Karolinska Institutet

Background
Atherosclerosis is a chronic inflammatory disease process, which leads to cardiovascular disease (CVD) which is increased in rheumatic diseases, especially in SLE. IgM antibodies to phosphorylcholine (anti-PC) constitute a significant part of the circulating IgM pool. We reported that anti-PC are protection markers for atherosclerosis and CVD, and asked if this applies also to rheumatic and autoimmune diseases.

Material and methods
We use a combination of ex vivo studies and cohort studies. Dendritic cells (DC) and T cells from patients with SLE, and from atherosclerotic plaques, are studied, and anti-PC is determined by ELISA.

Results
Having low levels of anti-PC (below tertile or quartile) was associated with SLE, with CVD and atherosclerosis in SLE, and with being a non-responder to biologics in Rheumatoid arthritis. Anti-PC promoted polarization of T cells from SLE patients into T regulatory cells, and from a lower level than among controls, T regs normalized in SLE patients after anti-PC exposure. Other potential

underlying mechanisms include an antiinflammary property (inhibition of proinflammatory lipids which are raised in SLE); inhibition of uptake of Oxidized LDL in macrophages; increased clearance by phagocytosis of dead cells. Anti-PC levels were very high in New Guinea among people living a traditional "stone age" life, and where rheumatic diseases and chronic inflammatory conditions are virtually unknown and also anti-PC were associated with some infectious agents there.

Conclusions

Low anti-PC could contribute to development of autoimmune and rheumatic disease, in addition to atherosclerosis and CVD. One underlying cause could be lack of exposure to some microorganisms. These findings could have therapeutic implications, including immunization to raise anti-PC levels.

ABSTRACTNUMMER: 1584-A-1818 **67**

THE ROLE OF ANTI-INFLAMMATORY LIPID MEDIATORS ON VASCULAR MAINTENANCE IN HUMAN RESISTANCE SIZED ARTERIES UPON MPGES-1 INHIBITION

Julia Steinmetz[1], Samsul Arefin[2], Neja Mudrovcic[2], Filip Bergqvist[1], Karin Larsson[1], Marina Korotkova[1], Karolina Kublickiene[2], Per-Johan Jakobsson[1]

[1] Unit of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden
[2] Unit of Renal Medicine, Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska University Hospital, Stockholm, Sweden

Background

Non-steroidal anti-inflammatory drugs (NSAIDs) selectively inhibiting cyclooxygenase2 (COX-2), reduce prostaglandin E2 (PGE2) levels, thereby affecting pain and inflammation are widely used for the treatment of rheumatic diseases. But the cardiovascular side-effects such as myocardial infarction, stroke, pulmonary hypertension and heart failure limit their use. Peripheral resistance vasculature is considered to be a primary affected site due to cardiovascular complications, and the underlying mechanisms leading to related pathological conditions are diverse. A decrease in prostacyclin (PGI2) levels mediated by COX-2 inhibition is associated with increased cardiovascular side-effects. Thus, the inhibition of mPGES-1, the terminal synthase of PGE2 introduces an attractive approach for novel anti-inflammatory treatment leading besides the reduction of pro-inflammatory PGE2 to a redirection of excess PGH2 into the PGI2 pathway.

Methods

Here we use wire-myography in combination with immunological and mass-spectrometry based techniques to elucidate the effects of mPGES-1 inhibition on arterial functionality in patients with chronic inflammation and controls. We expose isolated subcutaneous resistance arteries to novel mPGES-1 inhibitors, COX-2 inhibitor or vehicle control, and asses their contractility and/or relaxation using a wire-myography technique.

Results

Our preliminary results showed a reduced adrenergic vasoconstriction after 30min incubation with mPGES-1 inhibitors at concentrations relevant to an in vivo situation. No adverse effects by means of reduced sensitivity to NO donors or changes in endothelium-dependent dilatation were observed, but tested mPGES-1 inhibitors induced acute dilatation in a concentration dependent manner in preconstricted arteries. PGE2, 6-ketoPGF1α and PGF2α were detectable in supernatants of IL-1β stimulated cultured arteries, and the treatment with mPGES-1 inhibitors resulted in a reduction of PGE2 levels.

Conclusion

Further studies are warranted to assess the role of PGI2 signaling upon mPGES-1 inhibition in these diseased arteries. However, we believe that our ex-vivo model system is well suited and of high interest for studies on the cardiovascular safety profile of mPGES-1 inhibitors in humans.

Register · Abstracts

Förstaförfattare	Abstraktnr.	Sida
Artritsjukdomar		
Brink	1463-A-1818	18
Porsdal	1503-A-1818	18
Ljung	1504-A-1818	19
Dehlin	1508-A-1818	20
Scheepers	1509-A-1818	23
Johansson	1512-A-1818	23
Kapetanovic	1514-A-1818	24
Dougodos	1516-A-1818	25
Wasén	1522-A-1818	25
Erlandsson	1524-A-1818	26
Enocsson	1525-A-1818	26
Landgren	1527-A-1818	27
Kokkonen	1528-A-1818	27
Cagnotto	1529-A-1818	28
Cagnotto	1530-A-1818	28
Westerlind	1532-A-1818	29
Espino	1533-A-1818	30
Wallman	1534-A-1818	30
Bengtsson	1539-A-1818	31
Södergren	1545-A-1818	31
Weitoft	1550-A-1818	32
Mybeck	1552-A-1818	32
Jin	1558-A-1818	33
Lindqvist	1560-A-1818	33
Klingberg	1564-A-1818	34
Kisten	1565-A-1818	35
Pullerits	1567-A-1818	35
Hörnberg	1569-A-1818	36
Szentpetery	1570-A-1818	36
Forsblad-d'Elia	1572-A-1818	38
Gjertsson	1574-A-1818	38
Gjertsson	1575-A-1818	39
Bengtsson	1578-A-1818	39
Jovancevic	1579-A-1818	39
Nadali	1580-A-1818	40
Systemsjukdomar		
Naderi	1477-A-1818	40
Björk	1498-A-1818	41
Heijke	1500-A-1818	41
Ingvarsson	1511-A-1818	42
Ivanchenko	1513-A-1818	42
Heijke	1519-A-1818	43
Sandling	1523-A-1818	44
Hagberg	1531-A-1818	44
Bolin	1535-A-1818	45
Lindberg	1536-A-1818	46
Imgenberg-Kreuz	1537-A-1818	46
Mofors	1538-A-1818	47
Hjorton	1541-A-1818	47
Berggren	1547-A-1818	48
Mobarrez	1551-A-1818	48
Antovic	1555-A-1818	49
Thorlacius	1557-A-1818	49
Jönsen	1566-A-1818	50
Reid	1571-A-1818	51
Fors	1576-A-1818	51
Mofors	1577-A-1818	52
Parodis	1583-A-1818	52
Zandi	1585-A-1818	53
Niewold	1586-A-1818	53
Oke	1587-A-1818	54
Verksamhetsutveckling		
Ericsson	1562-A-1818	34
Leonard	1526-A-1818	54
Baecklund	1549-A-1818	55
Emilson	1568-A-1818	55
Vårdforskning		
Bergström	1540-A-1818	56
Övrigt		
Frostegård	1573-A-1818	56
Steinmetz	1584-A-1818	57

Reumakalender

2018

5 sept **The 37th Scandinavian Congress of Rheumatology**
5-8 september
Helsingfors, Finland

19 sept **Reumadagarna 2018**
19-21 september
Uppsala

25 sept **European Forum on Antiphospholipid Antibodies**
25-26 september
Maastricht, Holland

1 okt **SK-kurs Reumatologisk farmakoterapi**
1-5 oktober
Lund

10 okt **RUCh Modul 1**
10-11 oktober
Göteborg

19 okt **ACR/ARHP Annual Congress 2018**
19-24 oktober
Chicago, USA

19 nov **SK-kurs Ovanliga Inflammatoriska systemsjukdomar**
19-22 november
Umeå

29 nov **SRF:s Utvecklingsdag**
29 november
Stockholm

30 nov **Post-ACR**
30 november

2019

17 jan **RUCh Modul 2**
17-18 januari
Uppsala

23 jan **SRQs Registerdag**
23 januari
Stockholm

24 jan **SRFs Riktlinjedag**
24 januari
Stockholm

16 maj **RUCh Modul 3**
16-17 maj
Lund

12 juni **EULAR 2019**
12-15 juni
Madrid, Spanien

8 nov **ACR 2019**
8-13 november
Atlanta, USA

14 nov **RUCh Modul 4**
14-15 november
Stockholm