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fighting rheumatic & musculoskeletal
diseases together

PRESS REVIEW AND JOURNAL CLUB



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Dear Reader,

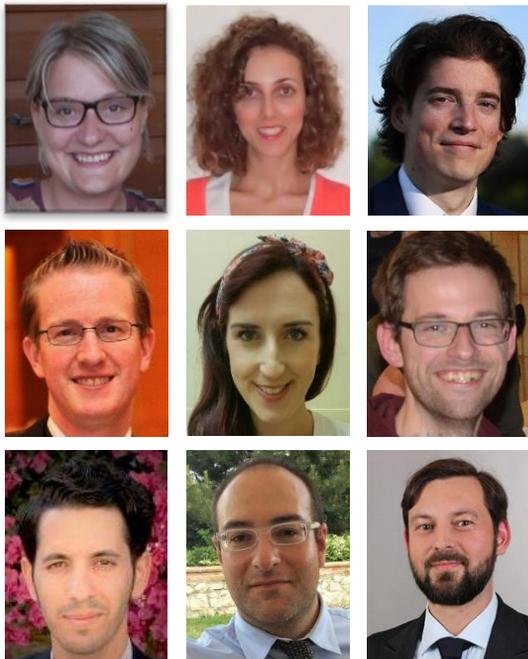
We are happy to present the second issue of the 'Press Review and Journal Club' Newsletter that is part of a new educational initiative from EULAR and the Emerging EULAR Network (EMEUNET). This newsletter includes a selection of the most relevant articles published both in top rheumatology journals and in the major general medicine journals in the last four months. For all articles, you will find a hyperlink that will redirect you to the journal page to read the article in full.

One of these articles has been selected by the School of Rheumatology faculty to be discussed in a few weeks in an online Twitter Journal Club. Another article, the 'EMEUNET paper of the month' has been selected by popular vote through a survey circulated among the rheumatology community.

The Journal Club aims to bring together rheumatologists, clinical researchers, basic scientists, and anyone else who might be interested in the subject, to participate in an online, lively discussion. These 'meetings' take place on Twitter at pre-specified times and dates, the next JC is planned on 4th October 2017 at 8:30 PM GMT (9:30PM CET). 'Save the date' reminders will be sent in advance. Where possible, key authors involved in selected articles will be invited to participate. The selected article will be freely accessible for a limited period of time on the journal website. Details of the article selected and of the Journal Club are included in page 3 of this issue.

We hope that you will enjoy reading this newsletter and look forward to 'seeing' you soon at our Twitter Journal Club meeting!

*Alessia Alunno, Elena Nikiphorou, Paul Studenic,
Richard Conway, Mary Canavan, Diederik De Cock,
Antonis Fanouriakis, Francesco Carubbi, Mike Becker
on behalf of the EMEUNET Newsletter and Social Media Subgroups*



DIRECTORY

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Hu Y, Sparks JA, Malspeis S, Costenbader KH, Hu FB, Karlson EW, Lu B.
Long-term dietary quality and risk of developing rheumatoid arthritis in women.

Ann Rheum Dis 2017;76:1357-1364 ([full text here](#))

The potential contribution of dietary factors to the development of rheumatoid arthritis (RA) has long been a topic of interest to physicians and patients alike. Conflicting evidence exists regarding the role of diet in RA pathogenesis. The authors propose that this lack of clarity may be due to the importance of dietary patterns rather than individual foods. They used the 2010 Alternative Healthy Eating Index (AHEI-2010) to analyse dietary patterns in the Nurses' Health Study and Nurses' Health Study II. Time-varying Cox proportional hazards models were employed to evaluate the association between AHEI-2010 and risk of RA. 1007 incident RA cases were identified during 3,678,104 person-years of follow-up in 169,989 women. Better quality diet was protective from RA among women ≤ 55 years old, HR 0.67, 95% CI 0.51 to 0.88, $p=0.002$), but no significant association was seen in those >55 years old. Stratification by serostatus revealed the strongest effect was seen in seropositive RA, HR 0.60, 95%CI 0.42 to 0.86, $p=0.003$. The results suggest that a healthy diet may reduce RA risk.



The online Journal Club will take place on:

Wednesday 4th October 2017 at 8:30PM GMT (9:30PM CET)

-duration 1 hour-

Follow the accounts **@EULAR_JC**, **@eular_org** and **@EMEUNET**

Use the hashtag **#EULARJC** to follow and join the discussion



EMEUNET PAPER OF THE MONTH

Alivernini S, Toluoso B, Petricca L, Bui L, Di Sante G, Peluso G, Benvenuto R, Fedele AL, Federico F, Ferraccioli G, Gremese E.

Synovial features of patients with rheumatoid arthritis and psoriatic arthritis in clinical and ultrasound remission differ under anti-TNF therapy: a clue to interpret different chances of relapse after clinical remission?

Ann Rheum Dis. 2017;76:1228-1236 ([free full text here](#))

This study aimed to define the synovial biopsy characteristics of patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) in clinical and ultrasound remission achieved by methotrexate and tumour necrosis factor inhibitor (TNFi) combination therapy. The authors found that RA patients in US remission and clinical remission or low disease activity had comparable synovial histological features. Both of these US remission groups had lower synovial histological scores (lining and sublining CD68+, CD20+, CD3+, CD31+ cells and collagen) than patients with US defined synovitis. In contrast PsA patients in US defined and clinical remission had a higher degree of residual synovial inflammation than RA patients in remission. The authors suggest that these findings may help identify which RA patients in remission may be suitable for tapering TNFi.



Dr Stefano Alivernini
MD PhD

Explore this paper in greater detail through an exclusive interview with study first author and EMEUNET member Dr Stefano Alivernini.

Interview available [here](#)

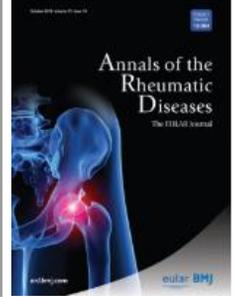
The EMEUNET Paper of the Month is selected by an online vote of selected articles from each of the rheumatology journal contributions. **Watch out for our next poll!**



ANNALS OF THE RHEUMATIC DISEASES

Volume 76 Issues 5-8

Francesco Carubbi, MD PhD

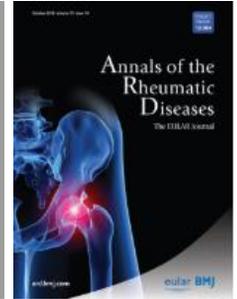


Francesco has completed his specialist training in Clinical Immunology and a PhD in Internal Medicine and Applied Immunology. He currently works as a consultant at the Department of Internal Medicine, ASL 1 Avezzano, L'Aquila, Sulmona, and research associate at the Rheumatology Unit, University of L'Aquila, Italy. He completed a 14-month research fellowship at the Centre for Experimental Medicine & Rheumatology, QMUL, UK. His main interests are Sjögren's syndrome, B-cell targeted therapies, salivary gland histopathology, spondyloarthritis, and musculoskeletal ultrasonography.

The efficacy and safety of novel therapeutic strategies in **rheumatoid arthritis (RA)** have been investigated in several studies. Ustekinumab is a monoclonal antibody (mAb) targeting the common p40 subunit of IL-12 and IL-23 which is currently employed for the treatment of plaque psoriasis and psoriatic arthritis, while guselkumab targets the p19 subunit and is selective for IL-23. Smolen et al reported in a phase 2 trial in active RA patients who failed methotrexate (MTX) that these two mAbs are not effective in RA ([pp 831-839](#)). Sarilumab is a mAb targeting the IL-6 receptor, Burmester et al found it to be superior to adalimumab in patients with active RA who had to stop MTX due to either lack of response or intolerance; the safety profile of sarilumab was comparable to adalimumab ([pp 840-847](#)). With regard to targeting the JAK-STAT pathway, several trials using tofacitinib have been published, hence, long term safety data are now available. Cohen et al. pooled the 6194 patients receiving tofacitinib for up to 8.5 years in clinical trials and demonstrated a stable adverse event profile with longer-term tofacitinib exposure ([pp 1253-1262](#)). Filgotinib is a selective JAK1 inhibitor that was investigated by Westhovens et al in RA patients who were MTX inadequate responders (DARWIN-1, [pp 998-1008](#)) and by Kavanaugh et al as monotherapy after MTX washout (DARWIN-2, [pp 1009-1019](#)). Both studies met the primary efficacy endpoint (percentage of patients achieving an ACR20 response at week 12) in all treatment groups (DARWIN-1: 50, 100 or 200 mg twice daily or once daily; DARWIN-2: 50, 100 or 200 mg once daily). Mavrilimumab is a human mAb targeting the GM-CSF receptor that demonstrated dose-dependent clinical efficacy in patients who failed MTX in a study by Burmester et al, with no evidence of safety concerns ([pp 1020-1030](#)). The influence of diet and lifestyle on the risk of RA development is of interest to both physicians and patients, Hu et al reported that a healthy diet reduces the risk of RA, particularly seropositive RA, occurring at 55 years of age or younger in a study of 170,000 women ([pp 1357-1364](#)). The contemporary improvement in RA management allows us to postulate that there may be a reduction in mortality over time. A population-based cohort study of 24,914 RA patients by Lacaille et al revealed an improvement in the mortality gap for cardiovascular, cancer, and all-cause mortality compared to the general population, excess mortality being higher in earlier (1996–2000) and lower in later (2001–2006) RA cohorts ([pp 1057-1063](#)). Peterfy et al pooled data from four randomized controlled trials in RA and demonstrated that early MRI detected changes in joint damage and inflammation predict subsequent damage seen on plain radiography, supporting the use of MRI for monitoring structural damage in short-duration trials ([pp 992-997](#)).

ANNALS OF THE RHEUMATIC DISEASES (CONTINUED)

Volume 76 Issues 5-8



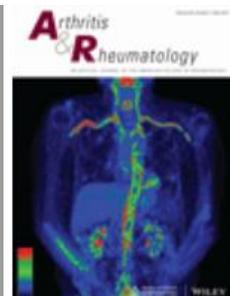
The definition of remission in RA has been a matter of debate due to the discrepancies arising from clinical and ultrasonographic (US) assessment. In recent years, the increasing application of synovial biopsy in clinical practice added another variable to the concept of remission. Alivernini et al demonstrated that RA patients in clinical (DAS28<1.6) and US remission (absence of power doppler signal) and patients with clinical low disease activity (1.6<DAS28<2.4) and US remission on anti-TNF therapy display lower histopathological scores compared to RA patients with moderate to high disease activity ([pp 1228-1236](#)). Interestingly, in **psoriatic arthritis**, despite US remission a higher degree of synovial inflammation was detected in biopsies. Tofacitinib was investigated by van der Heijde et al in active **ankylosing spondylitis** (AS); a significant improvement across most endpoints was seen after 12 weeks of treatment with minimal clinical differences between the different doses (2, 5 or 10 mg twice daily) ([pp 1340-1347](#)). Efficacy and safety data on secukinumab over 2 years of treatment were reported by Braun et al in AS patients either naïve to tumour necrosis factor inhibitors (TNFi) or who failed one TNFi ([pp 1070-1077](#)). Secukinumab demonstrated a sustained clinical response without major safety concerns. With regard to radiographic progression, the overall change in the modified Stoke Ankylosing Spondylitis Spine Score was 0.3 in secukinumab treated patients but this cannot be compared to those obtained in previous studies on anti-TNF agents due to differences in study design and populations. Moltó et al used data from the DESIR cohort to model disease trajectories in early **axial spondyloarthritis**; they found five distinct trajectories, with more than 30% of patients in a trajectory with persistent high disease activity, which was associated with negative work consequences ([pp 1036-1041](#)). Brito-Zerón et al used an international **Sjögren's syndrome** registry to demonstrate significant influences of geolocation and ethnicity on the presenting phenotype and autoantibody status ([pp 1042-1050](#)). In these issues, **criteria and recommendations** have also been published. The 2016 ACR/EULAR criteria for minimal, moderate, and major clinical response in juvenile dermatomyositis ([pp 782-791](#)) and in adult dermatomyositis and polymyositis ([pp 792-801](#)) have been defined. The same criteria items were chosen in both cases but with different thresholds for improvement. Diagnostic criteria for the cryopyrin-associated periodic syndrome (CAPS) have been defined and validated in a large cohort of patients ([pp 942-947](#)). EULAR and EFORT developed the first collaborative recommendations for the management of patients older than 50 years with a fragility fracture ([pp 802-810](#)). In the field of RA, recommendations for the management of early arthritis ([pp 948-959](#)) and for the management of RA with synthetic and biological disease-modifying antirheumatic drugs ([pp 960-977](#)) have been updated. The ASAS-EULAR recommendations for the management of axial spondyloarthritis ([pp 978-991](#)) as well as the EULAR recommendations for the treatment of systemic sclerosis have also been updated ([pp 1327-1339](#)). Finally, the first recommendations to standardise labial salivary gland histopathology in clinical trials in primary Sjögren's syndrome have been released ([pp 1161-1168](#)).



ARTHRITIS AND RHEUMATOLOGY

Volume 69 Issues 5-8

Mike Becker, MD MSc



Mike is a consultant rheumatologist and researcher at the University Hospital of Zürich, Switzerland. His research focuses on clinical and translational aspects of systemic sclerosis, and his major clinical interests include connective tissue diseases and vasculitis. He graduated from the Philipps University in Marburg, Germany and got a Master's degree from the University of Oxford, UK.

Solomon et al ([pp 1374–1380](#)) tested the effects of a 9-month multisite group-based learning collaborative on adherence to the treat-to-target (TTT) concept in a cluster-randomized controlled trial in **rheumatoid arthritis** (RA). Five sites were randomized to the intervention (320 patients) and 6 sites were randomized to the control (321 patients). The mean TTT implementation score rose from 11% in both arms to 57% in the intervention group and 25% in the control group. Hambardzumyan et al ([pp 953–963](#)) investigated whether the Multi-Biomarker Disease Activity (MBDA) score (including 12 serum biomarkers) predicts optimal add-on treatment in patients with early RA who were inadequate responders to methotrexate (MTX-IRs). Data was analyzed from 157 MTX-IRs in the SWEFOT trial who were randomized to receive triple therapy (methotrexate plus sulfasalazine plus hydroxychloroquine) versus methotrexate plus infliximab. Patients with post-methotrexate biochemical improvements (lower MBDA scores) were more likely to respond to triple therapy than to methotrexate plus infliximab. In **systemic lupus erythematosus** (SLE) nephritis, Fu et al identified podocyte activation of the NLRP3 inflammasome as a contributing factor to proteinuria in human samples and a mouse model ([pp 1636–1646](#)), thus indicating a new treatment approach. Tamirou et al reported that the Euro-Lupus regimen of low dose IV cyclophosphamide (cumulative dose <3g) does not impact the ovarian reserve of pre-menopausal SLE patients as measured by serum levels of the anti-Müllerian hormone ([pp 1267–1271](#)). Data from the Scleroderma Lung Study I and II were used to analyse the effect of mycophenolate mofetil (MMF) versus placebo on **systemic sclerosis** (SSc)-related interstitial lung disease (ILD) by Volkman et al ([pp 1451–1460](#)). The groups differed slightly in age and baseline diffusion capacity. After adjustment for baseline disease severity, treatment with MMF was associated with higher % predicted forced vital capacity ($P<0.0001$), % predicted diffusion capacity ($P<0.0001$), modified Rodnan skin score ($P<0.0001$), and dyspnoea ($P=0.0112$) over 2 years compared to placebo. Goh et al ([pp 1670–1678](#)) tested the prognostic significance of pulmonary function test trends at 1 year and 2 years for 15-year survival in patients with SSc-related ILD. The optimal definition of progression for trial purposes was an FVC and DLCO composite end point, consisting of either an FVC decline from baseline of >10% or an FVC decline of 5–9% in association with a DLCO decline of >15%.



ARTHRITIS CARE AND RESEARCH

Volume 69 Issues 5-8

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Mike is a consultant rheumatologist and researcher at the University Hospital of Zürich, Switzerland. His research focuses on clinical and translational aspects of systemic sclerosis, and his major clinical interests include connective tissue diseases and vasculitis. He graduated from the Philipps University in Marburg, Germany and got a Master's degree from the University of Oxford, UK.

Hammann et al investigated predictors of sustained remission in **rheumatoid arthritis** (RA) patients treated with tumour necrosis factor inhibitors (TNFi) ([pp 783–793](#)). By evaluating six clinical trials, the authors identified concomitant methotrexate (MTX) use as a factor associated with an increased likelihood of sustained remission. In contrast, greater baseline disease activity, tender joint count, age, disease duration, baseline functional impairment, and female sex were associated with a reduced likelihood of sustained remission. Rohr et al reported an underuse of MTX in RA, whether it be as a single therapy, or in combination with other drugs ([pp 794–800](#)). Their data come from a national analysis of prescribing practices from approximately 274 million patients in the United States. Of all patients with a 5-year follow-up, oral MTX was started in 35,640 in 2009, and 44% continued taking this dose during follow-up, with a mean dose of 15.365 mg/week prior to the start of a biologic agent. Akenroye et al ([pp 625–632](#)) concluded in their publication that implementing an electronic medical record-based reminder did not improve cardiovascular risk screening among RA patients in a tertiary referral centre. Yue et al investigated the effect of denosumab or oral alendronate on bony erosions in RA by high-resolution peripheral quantitative computed tomography ([pp 1156–1163](#)). After 6 months, the width, depth, and volume of erosions significantly decreased in the denosumab group, whereas they significantly increased in the alendronate group. Maas et al investigated the course of spinal radiographic progression over up to 8 years of follow-up in a large cohort of 210 consecutive **ankylosing spondylitis** patients from a single centre starting TNFi ([pp 1011–1019](#)). During the first 4 years, radiographic progression followed a linear course, which was then deflected at 6 and 8 years. The estimated mean 2-year progression rate was reduced at year 8. De Hooge et al investigated associations between magnetic resonance imaging lesions originating from either axial spondyloarthritis or from degeneration disease, and pain in patients with chronic back pain of <2 years duration ([pp 717–723](#)). Inflammatory lesions of the sacroiliac joint and erosions of the sacroiliac joint in patients <25 years were associated with buttock pain. Axial spondyloarthritis spinal lesions were not associated with pain. Modic type 1 lesions in patients >35 years, high-intensity zone lesions in females not fulfilling ASAS criteria, and herniation, were associated with pain.



ARTHRITIS RESEARCH AND THERAPY

Volume 19 Issues April-August

Diederick De Cock, PhD

Arthritis Research
& Therapy



BioMed Central

Diederik is a Belgian epidemiologist currently working in Manchester, UK. Aside of his full time job of being a father and professional sports enthusiast, Diederik is working at the University of Manchester as a post doctoral research associate in the field of rheumatic epidemiology. His specialties are investigator initiated randomized trials in early RA and the safety of biologic treatment in advanced RA and JIA.

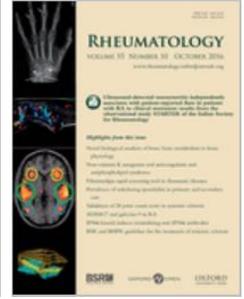
In **rheumatoid arthritis** (RA), Jamshidi et al undertook a phase III, randomized, two-arm, double-blind, parallel, active-controlled non-inferiority trial to compare efficacy and safety of biosimilar adalimumab (CinnoRA) to the reference product (Humira) and demonstrated non-inferiority at week 24 ([19:168](#)). Jin et al investigated factors associated with patterns of use of biologic disease-modifying anti-rheumatic drugs (DMARDs) for initial and subsequent RA treatment using claims data from a commercial health plan and Medicaid ([19:159](#)). In addition to previous use of steroids and non-biologic DMARDs, insurance type (commercial) and race (non-Hispanic white) were strongly associated with initial or subsequent treatment with biologic DMARDs. A large cohort study by Landgren et al investigated the overall incidence of nephrolithiasis in **gout** patients and general population controls, and the risk factors (common comorbidities and medications) for first-time nephrolithiasis. The risk of nephrolithiasis was increased by 60% in gout patients compared to the general population. No commonly used medications were found to increase the risk of nephrolithiasis ([19:173](#)). The impact of obesity on response to tumor necrosis factor inhibitors (TNFi) in **axial spondyloarthritis** (axSpA) was analyzed by Micheroli et al ([19:164](#)). A total of 624 axSpA patients starting a first TNFi were included. Significantly lower odds ratios for achieving an ASAS40 response were found in analyses in obese patients versus patients with normal BMI. Therefore, obesity seems to be associated with significantly lower response rates to TNFi in patients with axSpA as is seen in other rheumatic diseases. A small study by Zhang et al demonstrated sustained benefit after 12 months from combined plasmapheresis and allogeneic mesenchymal stem cells transplantation therapy in **systemic sclerosis** ([19:165](#)). A review by Olsen et al discussed the role of testing for **antinuclear antibodies** (ANAs) in systemic rheumatic diseases ([19:172](#)). Often ANAs are the only disease-specific serological markers available and have become part of the classification criteria for particular disease. Therefore, it is important to have an understanding of the proper use of ANA testing and its value and limitations.



RHEUMATOLOGY (OXFORD)

Volume 56 Issues 5-8

Antonis Fanouriakis, MD MSc



Antonis works as a consultant rheumatologist in "Attikon" University Hospital, Athens. He has completed a MSc program in Molecular Medicine and his thesis on neuropsychiatric systemic lupus erythematosus, both in the University of Crete, Greece. His scientific interests focus on systemic autoimmune diseases, mainly pathogenesis and treatment of systemic lupus erythematosus. Antonis is a member of the EMEUNET Newsletter and Country Liaisons Subgroups.

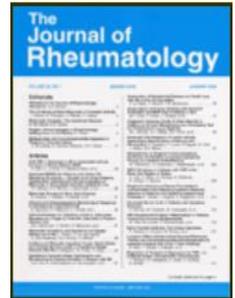
Abhishek et al performed a nationwide population-based cohort study to evaluate trends in the incidence and prevalence of **rheumatoid arthritis** (RA) over the past 25 years ([pp 736-744](#)). Interestingly, the authors found a decrease in the incidence of RA by 1.6% between 1990 and 2014, with respective decreases in prevalence during the past decade, albeit with significant geographic variations. Arida et al examined the hypothesis that accelerated atherosclerosis of RA can be halted by keeping the disease in remission ([pp 934-939](#)). Interestingly, RA patients in remission for 3 years showed no difference in any of the atherosclerosis indices, when compared to matched controls, suggesting that RA-specific effects on atherosclerosis may be arrested by adequate disease control. Janssens et al tested the performance of the 2015 ACR-EULAR classification criteria for **gout** in a cohort of patients with monoarthritis ([pp 1335-1341](#)). Having the presence of crystals as the gold standard, the criteria showed an excellent specificity and positive predictive value (both > 95%), albeit with relatively low sensitivity (68%). In **systemic lupus erythematosus** (SLE), Schneider et al performed a multicentre validation of the Lupus Impact Tracker (LIT, a patient-reported outcome) in five different European countries ([pp 818-828](#)). The LIT was found to have a strong association with the Short-Form-36 and various care satisfaction questionnaires, with negligible cross-cultural variations. Li et al examined the association between **giant cell arteritis** (GCA) and preexisting as well as incident cardiovascular diseases ([pp 753-762](#)). The study found patients with GCA to bear increased risk for all forms of incident vascular disease compared with controls, with hazard ratios ranging from 1.41 for stroke to 2.03 for venous thromboembolism. In **systemic sclerosis** (SSc), Markusse et al tested 287 SSc patients from the Leiden SSc cohort to determine associations between nailfold videocapillaroscopy (NVC) patterns and several anti-extractable nuclear antigens (ENA) and cardiopulmonary involvement ([pp 1081-1088](#)). The authors found that, independent of anti-ENA type, the NVC pattern correlated both with the presence of interstitial lung disease and with surrogate markers of pulmonary arterial hypertension. Finally, Zhong et al reported their single-centre experience regarding the outcome of pregnancy in **inflammatory myopathies** (IM) ([pp 1272-1275](#)). The authors evaluated a total of 142 pregnancies and found a significantly higher risk for adverse pregnancy outcomes (preterm birth, spontaneous abortion) in women who conceived after a diagnosis of IM (odds ratio 9.3), especially if the disease was active during pregnancy.



THE JOURNAL OF RHEUMATOLOGY

Volume 44 Issues 5-8

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Antonis works as a consultant rheumatologist in "Attikon" University Hospital, Athens. He has completed a MSc program in Molecular Medicine and his Thesis on neuropsychiatric systemic lupus erythematosus, both in the University of Crete, Greece. His scientific interests focus on systemic autoimmune diseases, mainly pathogenesis and treatment of systemic lupus erythematosus. Antonis is a member of the EMEUNET Newsletter and Country Liaisons Subgroups.

In **rheumatoid arthritis** (RA), Mary et al performed a systematic literature review to compare triple combination therapy with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) versus tumor necrosis factor inhibitors (TNFi) in methotrexate-inadequate responders ([pp 773-779](#)). With a limited numbers of studies, the authors found that TNFi treatment leads to better clinical and radiographic outcomes, when poor prognostic factors are present. Myasoedova et al assessed the trends in cardiovascular (CV) mortality in RA during 2000-2007, compared with previous decades ([pp 732-739](#)). Interestingly, a markedly decreased 10-year CV mortality in patients with incident RA during 2000-07 was noted (hazard ratio 0.43%) compared to 10-year CV mortality of patients diagnosed between 1990-99, attaining a level similar to matched non-RA controls. Kim et al examined 1274 Japanese RA patients for factors related to work and activity impairment ([pp 1112-1117](#)). The latter were reported by as many as 67.4% of patients and achievement of disease remission was associated with significantly less work impairment and absenteeism. In **systemic lupus erythematosus** (SLE) and **antiphospholipid syndrome** (APS), Orquevaux et al published a retrospective study regarding the use of in vitro fertilization (IVF) in SLE and/or APS ([pp 613-618](#)). In 97 procedures in 37 women, the authors found low rates of complications (disease flares and thromboembolic events, 4% each), suggesting that IVF may be used with relative safety in SLE/APS patients. In **systemic sclerosis** (SSc), Lazzaroni et al explored the risk of malignancy in SSc patients with anti-RNA polymerase III antibodies (anti-RNAP3) from the European League Against Rheumatism Scleroderma Trials and Research group (EUSTAR) ([pp 639-647](#)). Notably, anti-RNAP3 positive patients had an almost 8-fold increased risk for concomitant malignancy compared to anti-RNAP3 negative SSc controls, pointing to the need for vigorous cancer screening in the former group. In vasculitis, Seeliger et al reported a single-centre experience regarding the use of interferon- α in 30 patients with **eosinophilic granulomatosis with polyangiitis** (EGPA) ([pp 806-814](#)). The authors reported remission or partial response in 25 patients (83.3%) and significant reductions in glucocorticoid dose, albeit with frequent relapses and reversible side-effects. Finally, regarding **infectious complications of antirheumatic therapy**, Harada et al performed a nested case-control study within the Japanese Registry of Biologics in RA to identify associations between different medications and the occurrence of herpes zoster infection (HZ) ([pp 988-995](#)). In their analysis, use of TNF inhibitors and higher glucocorticoid doses were significantly associated with HZ (odds ratio 2.28 and 1.13 per mg increase of prednisone dose, respectively).



RMD OPEN

Volume 3 Issue 1

Francesco Carubbi, MD PhD

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Musculoskeletal
Diseases

Francesco has completed his specialist training in Clinical Immunology and a PhD in Internal Medicine and Applied Immunology. He currently works as a consultant at the Department of Internal Medicine, ASL 1 Avezzano, L'Aquila, Sulmona, and research associate at the Rheumatology Unit, University of L'Aquila, Italy. He completed a 14-month research fellowship at the Centre for Experimental Medicine & Rheumatology, QMUL, UK. His main interests are Sjögren's syndrome, B-cell targeted therapies, salivary gland histopathology, spondyloarthritis, and musculoskeletal ultrasonography.

EULAR and OMERACT established an ultrasound taskforce to develop a standardised, consensus-based scoring system for ultrasound synovitis in **rheumatoid arthritis** (RA) ([e000428](#)) and to establish its reliability and applicability to multiple joints ([e000427](#)). This score, ranging from 0 to 3, is based on the extent of synovial hypertrophy in grey-scale and on power doppler signal. It demonstrated moderate-good reliability in metacarpophalangeal (MCP) joints and is equally applicable in non-MCP joints. Strand et al reported on the effect of sarilumab, a monoclonal antibody targeting the IL-6 receptor, in addition to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) on patient reported outcomes ([e000416](#)). These data have been extrapolated from the TARGET trial conducted in RA patients stopping tumour necrosis factor inhibitors (TNFi) due to failure or intolerance. Patient global assessment (PtGA), pain and morning stiffness visual analogue scales, Health Assessment Questionnaire Disability Index (HAQ-DI), Short Form-36 Health Survey (SF-36), FACIT-Fatigue (FACIT-F), Work Productivity Survey-Rheumatoid Arthritis (WPS-RA) and Rheumatoid Arthritis Impact of Disease (RAID) improved after 12 weeks of treatment and were maintained at week 24. Using data from the British Society for Rheumatology Biologics Register in RA (BSRBR-RA) Jani et al found that treatment with TNFi does not increase the risk to develop lupus-like and vasculitis-like events compared to patients treated with csDMARDs ([e000314](#)). In the field of **axial spondyloarthritis** (axSpA), Braun et al reported long term data about the effects of certolizumab pegol on the spine and sacroiliac joints ([e000430](#)). Certolizumab was superior to placebo in improving MRI inflammation in both radiographic and non-radiographic axSpA and this effect was maintained at 96 weeks. A consensus group aimed at selecting and defining echostructural abnormalities in salivary glands in **primary Sjögren's syndrome** concluded that echogenicity and homogeneity are the two most reliable items for use in clinical practice with a fair interobserver reliability ([e000364](#)). Heijl et al explored long-term survival in patients with **ANCA-associated vasculitis** (AAV) in a Swedish population-based cohort ([e000435](#)). Clinical features at disease onset, were found to be the major determinants of the overall increased mortality of patients with AAV compared to the general population. In particular, the highest mortality was observed in patients with cardiovascular and gastrointestinal manifestations.



MISCELLANEOUS

Mike Becker, MD MSc, and Mary Canavan, PhD



Mike is a consultant rheumatologist and researcher at the University Hospital of Zürich, Switzerland. His research focuses on clinical and translational aspects of systemic sclerosis and his major clinical interests include connective tissue diseases and vasculitis. He graduated from the Philipps University in Marburg, Germany and got a Master's degree from the University of Oxford, UK.

Mary is a postdoctoral researcher in Molecular Rheumatology in Trinity College Dublin. She completed her PhD in Immunology in Dublin City University and is now completing her second postdoctoral research fellowship. Her research interests include examining the immune infiltration in particular dendritic cells and T cells in inflammatory arthritis and examining the effects of the joint microenvironment on immune cell activation. Mary is co-leader of the Social Media Group and leader of the ARD – EMEUNET Social media collaboration.

Wechsler et al ([N Engl J Med 2017;376:1921-1932](#)) investigated the effect of an add-on therapy with the anti-IL5 inhibitor mepolizumab in patients with relapsing or refractory **eosinophilic granulomatosis with polyangiitis**. Mepolizumab treatment led to significantly more accrued weeks of remission than placebo (28% vs. 3% had ≥ 24 weeks of accrued remission; OR 5.91; 95% CI 2.68 to 13.03; $P < 0.001$) and a higher percentage in remission at both week 36 and week 48 (32% vs. 3%; OR 16.74; 95% CI 3.61 to 77.56; $P < 0.001$). Saper et al ([Ann Intern Med 2017;167:85-94](#)) found 12 weekly yoga classes to be non-inferior to 15 visits of physical therapy for **chronic low back pain** (cLBP). However, yoga was not superior to education (an educational book and newsletters) for either outcome (back-related function and pain). A meta-analysis of 3 studies by Juch et al ([JAMA 2017;318:68-81](#)) evaluated the effect of radiofrequency denervation on pain intensity among patients with cLBP originating in the facet joints, sacroiliac joints, or intervertebral disks. Radiofrequency denervation combined with a standardized exercise program resulted in no clinically important improvement in pain compared with a standardized exercise program alone. A randomized clinical trial by McAlindon et al investigated the effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in 140 patients with knee **osteoarthritis** ([JAMA 2017;317:1967-1975](#)). Intra-articular triamcinolone every 3 months resulted in significantly greater cartilage volume loss than saline (between-group difference, -0.11 mm; 95%CI -0.20 to -0.03 mm); and no significant difference in pain (between-group difference, -0.6 ; 95%CI -1.6 to 0.3). A network meta-analysis by da Costa et al ([Lancet 2017;390:e21-e33](#)) compiled data on the effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis. For six interventions (diclofenac 150mg/day, etoricoxib 30mg, 60mg, or 90mg/day, and rofecoxib 25mg or 50mg/day), the probability that the difference to placebo is at or below a prespecified minimum clinically important effect for pain reduction (effect size [ES] -0.37) was at least 95%. Among maximally approved daily doses, diclofenac 150mg/day and etoricoxib 60mg/day had the highest probability to be the best intervention, both with 100% probability to reach the minimum clinically important difference.

MISCELLANEOUS (CONTINUED)

Anti citrullinated protein antibodies (ACPA) can be detected several years before the clinical onset of **rheumatoid arthritis** (RA). To date autoantibodies against several citrullinated proteins have been identified however limited evidence exists on how ACPAs trigger joint inflammation. An article by Ge et al ([JCI Insight 2017;2:e93688](#)) investigated the C1 epitope of collagen type II, which is commonly found in RA. A monoclonal antibody against citrullinated C1 was shown to cross-react with many non-citrullinated epitopes on collagen type II. This cross-reactivity led to cartilage degradation and the development of arthritis in mice, highlighting a potential mechanism for ACPA in joint destruction. Pianta et al used a proteomics based approach to identify autoantigen peptides presented by HLA-DR in RA synovium ([J Clin Invest 2017;127:2946-2956](#)). This led to the discovery of two peptides, N-acetylglucosamine-6-sulfatase (GNS) and filamin A (FLNA), which were presented by HLA-DR and induced T and B cells responses in 52% and 56% of patients respectively. Both of these peptides had high sequence homology to specific species of gut commensals; patients with T cell reactivity with each self-peptide also had responses to the corresponding microbial peptides thus linking the microbiome and synovial inflammation. Hong et al explored the therapeutic efficacy of selectively inhibiting synovial fibroblast proliferation in RA ([Nat Commun 2017;8:146](#)). The authors induced fibroblast cell death using a novel apoptosis-inducing gene therapy approach whereby the pro-apoptotic protein PUMA was successfully transduced into synovial fibroblasts. The authors approach builds on previous publications which were hampered by low transduction efficiencies. This resulted in apoptosis of fibroblasts, a decrease in joint inflammation, and joint damage in an adjuvant-induced rat model of RA. Dai et al explored the role of the IL-23/IL-17 pathway in **systemic lupus erythematosus** (SLE) ([J Immunol 2017;199:903-910](#)). IL-23 was significantly elevated in the sera of patients with active compared with inactive disease. To explore the direct effect of IL-23 on T cell and IL-17 responses, the authors treated SLE T cells with exogenous IL-23 in vitro. Results indicated that IL-23 induced IL-17 and limited IL-2 production from T cells, in addition to doubling the percentage of T cells that expressed T follicular helper cell markers, and increasing double negative T cell numbers.

EDUCATIONAL EVENTS

SEPTEMBER-OCTOBER 2017

SEPTEMBER 2017

36th Annual Meeting of the European Bone and Joint Infection Society

- o When and Where: 7 – 9 Sep 2017, Nantes, France
- o Website: <http://ebjis2017.org/>

2017 meeting of European Society for Immunodeficiencies: Autoimmunity & Inflammation in PID; Beyond The Paradox

- o When and Where: 11 – 14 Sep 2017, Edinburgh, United Kingdom
- o Website: <http://esid2017.kenes.com/>

PReS 2017

- o When and Where: 14 – 17 Sep 2017, Athens, Greece
- o Website: <http://www.pres.eu/>

Irish Society for Rheumatology Autumn Meeting 2017

- o When and Where: 21 – 22 Sep 2017, Galway, Ireland
- o Website: <http://www.isr.ie/events/78/isr-autumn-meeting-2017>

23rd Congress of the Polish Society of Rheumatology

- o When and Where: 21 – 23 Sep 2017, Szczecin, Poland
- o Website: <http://www.termedia.pl/Konferencje?Intro&e=612&p=4156>

OCTOBER 2017

27th International Musculoskeletal Ultrasound Conference

- o When and Where: 15 – 18 Oct 2017, Tel Aviv, Israel
- o Website: <https://www.musoc.com/musculoskeletal-ultrasound-conference.html>

THE EULAR ON-LINE COURSES

All EULAR courses, as electronic ways of continuous medical education in rheumatology, are managed by a scientific course committee responsible for the structure and content of the courses and for ensuring regular quality control and advancement. Teams of expert authors are regularly reviewing and updating the courses to keep up with the newest developments in the field.

REGISTRATION IS NOW OPEN

Course	Duration	Registration and More Information
12 th EULAR On-line Course on Rheumatic Diseases	2 years	https://www.eular.org/edu_online_course.cfm
9 th EULAR On-line Course on Connective Tissue Diseases (CTD)	9 months	https://www.eular.org/edu_online_course_ctd.cfm
7 th EULAR On-line Course on Systemic Sclerosis (SSc)	9 months	https://www.eular.org/edu_online_course_ssc.cfm
6 th EULAR On-line Introductory Ultrasound Course	7 months	https://www.eular.org/edu_online_course_msus.cfm
4 th EULAR / PRoS On-line Course in Paediatric Rheumatology	9 months	https://www.eular.org/edu_online_course_paediatric.cfm
3 rd EULAR On-line Course for Health Professionals	9 months	https://www.eular.org/edu_online_course_hpr.cfm



The EULAR On-line Courses on Rheumatic Diseases, CTDs, SSc and US are also available as APP



PARTICIPANT FEEDBACK:

"Ultrasonography is essential for the training of Rheumatologists and represents a key aspect of patient's evaluation. The EULAR On-line Introductory Ultrasound Course offers theoretical basic skills on musculoskeletal ultrasound in rheumatic diseases as well as in healthy subjects. The high quality of contents as well as the experience of the Faculty are the two main reasons to join this course. Moreover, the website is straightforward and very easy to use. Upon passing the final examination, EULAR releases a certificate. This course is very useful for Rheumatologists who would like to acquire a basic theoretical knowledge on musculoskeletal ultrasound."

"I attended the EULAR On-line Introductory Ultrasound Course. It is a well structured basic course on ultrasonography that is divided in different modules according to the different anatomical sites. Each module includes specific exercises and the final test. I found this course very interesting and it provided me with a complete overview of ultrasonography in rheumatology. I would recommend this course as to me it was overall more useful and formative compared to some different on-site courses I previously attended."

2ND EULAR IMMUNOLOGY COURSE

Understanding the immunologic background of autoimmune-mediated rheumatic diseases is a fundamental prerequisite for both clinicians to make wise decisions in complex medical settings and researchers to develop effective and tolerable targeted therapies. The ambition of this course is to bring both parties together for working on challenges in immunology and accelerating the translation of basic findings into clinical practice.

The main goal of the course is to increase the knowledge and skills of young researchers in immunology and stimulate critical thinking in the design of experimental studies. This course is designed as the perfect complement to the EULAR online course on rheumatic diseases and the EULAR postgraduate course, by consolidating your knowledge in immunology in a more interactive way. However, previous participation of these courses is not mandatory.

Furthermore, this course brings together clinicians and scientists, thereby facilitating interaction, discussion, and collaboration in translating basic immunology findings into clinical practice. People participating in this course can enter an immunology and translational rheumatology network to facilitate communication between European groups working in the field of immunology and translational research dedicated to rheumatic diseases.

This is a selective course, with competitive admission, for young rheumatologists and rheumatology researchers with a confirmed interest in immunology. The course is a compact, one and a half day event on immunology and translational research with a special emphasis on hot immunology topics and on the design, interpretation and analysis of basic or translational research projects. The course is designed to facilitate problem- and case-oriented learning to enhance the interactions among participants and between participants and the faculty.

Next EULAR Immunology Course will take place on

6-7 April 2018 in Lisbon, Portugal

REGISTRATION OPENING SOON, TRAVEL BURSARIES ALSO AVAILABLE

For information and to register visit:

http://www.eular.org/eular_course_on_immunology.cfm

18th EULAR Postgraduate Course

Belgrade, Serbia
22 – 25 October 2017



With its postgraduate course, EULAR seeks to update the professional knowledge of young rheumatologists from around the world, whilst giving the participants the opportunity to meet and exchange ideas and experiences. Target participants are fellows/residents in rheumatology, clinician scientists in rheumatology, and newly certified rheumatologists, as well as more experienced rheumatologists who need to remain up-to-date in rheumatology and immunology. The EULAR postgraduate course is a unique 3 day refresher, "crash course", in clinical and experimental rheumatology taught by a selected faculty of European experts in a very interactive and cordial environment. Participants have the opportunity to meet experts in an informal setting, and to network with trainees and rheumatologists from all over the world. The course includes a number of interactive workshop sessions and participants can choose which to attend.

Next EULAR Postgraduate Course will take place on

22-25 October 2017 in Belgrade, Serbia

REGISTRATION IS NOW OPEN

EULAR will grant 20 **bursaries** for this course, covering participation as well as hotel cost and all meals – everyone under the age of 40 is welcome to apply.

For more information and to register: http://www.eular.org/edu_course_postgraduate.cfm



SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we appreciate any suggestions and welcome new ideas to expand on what we currently offer to EMEUNET members. Make your voice heard and share your ideas with us!

It is easy, just write down some lines to summarize your proposal and send it either via email at emeunet@eular.ch or through our website (http://emeunet.eular.org/contact_us.cfm). Don't forget to provide your contacts so we can come back to you for additional details!

We look forward to hearing from you!!!

More information about EMEUNET can be found at <http://emeunet.eular.org>
You can also reach us through the following email emeunet@eular.ch



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