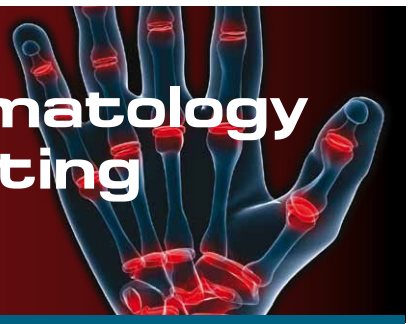
American College of Rheumatology 2011 Annual Scientific Meeting

Conference Review



Making Education Easy

November 4–9, 2011; Chicago, Illinois, USA

In this review:

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Welcome to this review of the American College of Rheumatology (ACR) 2011 Annual Scientific Meeting, a locally focused summary of some of the latest and most exciting developments in rheumatology.

This Review has been created to allow those unable to attend, but with a keen professional interest in research in rheumatic diseases, such as rheumatoid arthritis (RA), osteoarthritis (OA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS) and psoriatic arthritis, to access a summary of significant abstracts presented that are likely to affect current practice. Review of the research has been carried out independently by Paul Healy, who attended the ACR 2011 Annual Scientific Meeting during November 4–9, 2011, in Chicago, Illinois, USA.

Abstracts from the meeting have been published in Arthritis Rheum 2011;63(10 Suppl) and can be downloaded from http://www.rheumatology.org/education/annual/2011_abstract.pdf.

I hope you find this conference review stimulating, and I look forward to your feedback.

Kind regards,

Dr Chris Tofield

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Antiphospholipid syndrome

The review on antiphospholipid (aPL) syndrome was well attended and finally in a room that could hold the numbers. I found the most useful was the talk considering primary prophylaxis. The speaker asked who is most at risk? When considering individual tests, those with lupus anticoagulant seem at highest risk along with anticardiolipid (ACL)>40IU, while ACL <20IU are not really at risk. Raised anti-β2 glycoprotein shows risk, but there is no nominated cutoff. When comparing single vs. >1, the obvious is confirmed with triple positive having a greater risk of clotting. What is the incident rate with positive blood tests? Depending on the data (which are retrospective), the range is 0–3.8%, but probably close to 0% if there are no other risk factors. A recent prospective study followed 105 patients for 4.5 years. This compared one versus double versus triple positive, and found the risks of clots were 0.4%, 1.4% and 5.3%, respectively [Pengo V et al. Blood 2011;118(17):4714–8]. How would you manage these people? The advice was to eliminate the non-aPL syndrome risks such as diabetes, obesity, hypertension, smoking, hypercholesterolaemia, inactivity and stopping the oral contraceptive pill. In patients with asymptomatic aPL syndrome and no risk factors, there is no evidence for prophylaxis. In asymptomatic aPL syndrome with SLE, aspirin and hydroxychloroquine may be beneficial based on observational data.

Antimalarials

A review of hydroxychloroquine, chloroquine and quinacrine was presented by Daniel Wallace. He discussed the basic pharmacology and potential mechanisms of action. These include raising cell pH to slow receptor site production and thereby prevent activation and cytokine production. More recent thoughts include blocking tumour necrosis factor (TNF), interleukin (IL)1-β and IL6. Hydroxychloroquine also blocks Toll-like receptor (TLR)-7 and -9 in immature dendritic cells that are activated by self proteins and potentially lead to an autoimmune condition. He then reviewed the data on beneficial use in RA, the effects on lipids and other effects such as venous thromboembolism in SLE. Mention was made of the potential for quinacrine to be used in patients where hydroxychloroquine was contraindicated. It is thought to be useful for severe fatigue and refractory skin disease. It requires a compounding pharmacy in order to be manufactured (there is one in Auckland).

Independent commentary by Paul Healy.

Paul Healy is a Consultant General Physician and Rheumatologist at Hutt Hospital. Current interests include psoriatic arthritis, gout management and education and the application of outcome measures to clinical practice.

FREE PAPERS AND POSTERS

Gout

Dual energy CT (DECT) is a relatively new technique that has been modified to detect monosodium urate (MSU) crystals. It has potential to diagnose gout by a method other than joint aspiration. Abstract 1617 reported the outcome of two questions – what is the diagnostic accuracy?, and is it clinically useful? Based on a cohort of 43 patients with aspiration-confirmed gout and 40 with no history of gout, the diagnostic accuracy appears to be good, with sensitivity and specificity of 93% and 95%, respectively. The false-negative results were in patients with a short duration of disease and small joint involvement, suggesting the amount of crystal burden might be an important limiting factor. The false positives were in patients with advanced knee OA. The clinically usefulness question was tested in a cohort where aspiration had failed to confirm clinically suspected disease. DECT was used to confirm crystal presence and site. If present, ultrasound-guided aspiration was performed. This confirmed MSU crystals in 14 of 30 patients, suggesting DECT may be useful to firm up a diagnosis. This is potentially useful in patients where therapy may cause significant morbidity. A further poster (213) from this group evaluated the presence of gouty enthesopathy. It was frequently present when the clinical picture was suggestive and the joint aspirate negative (11 of 19 cases). In 8 of these 11, the only site of crystal deposition was the enthesis or peritendinous area. DECT is still a research tool, but it may yet have clinical utility.

Along this theme, Nicola Dalbeth presented data (abstract 1618) on DECT determination of tophus size and a comparison with tape measure and vernier callipers. DECT proved superior, but this measurement is probably more applicable to a research context. The interesting observation was that similar sized tophi showed variable amounts of MSU, suggesting that tophus volume may not relate to the overall urate load.

How do MSU crystals induce the osteoclastogenesis that is critical for tophus development? Abstract 1620 showed MSU crystals induce IL1, IL6, tumour necrosis factor (TNF) and RANKL, and this expression is more marked in synovial fluid monocytes than peripheral blood monocytes. *In vitro* osteoclastogenesis in synovial fluid monocytes was inhibited by T-cell depletion. It is uncertain if it is the local milieu that induces the T-cell RANKL production or whether those with tophaceous gout have a higher number of circulating RANKL-expressing T-cells.

Tony Merriman reported the NZ data on sugar-sweetened beverages and gout in abstract 1622. He showed a plausible mechanism with fructose being metabolised through ATP to uric acid, along with the effect of fructose on tubular secretion. There is an association of gout with intake of >4 sugar-sweetened beverages across all population groups, with an odds ratio of 4. The nonlinear association may relate to rate of ingestion. The question surrounding a lack of association with fruit intake and gout has several potential answers. The type of fruit could be important, and these data were not captured, while there may be a protective effect of vitamin C present in fruit.

Abstract 1617: Bongartz T et al. Diagnosis of gout using dual-energy computed tomography: an accuracy and diagnostic yield study

Poster 213: Wang H et al. Gouty enthesopathy: an important pattern of uric acid deposition in difficult to diagnose gout

Abstract 1618: Dalbeth N et al. Assessment of tophus size; a comparison between physical measurement methods and dual energy computed tomography scanning

Abstract 1620: Lee S-J et al. Bone destruction by RANKL-expressing T cells in chronic gouty arthritis

Abstract 1622: Merriman TR et al. Association between sugar-sweetened beverage consumption and gout in the New Zealand population

RA

Glucocorticoids appear to increase the risk of infection in patients with RA, although there is still some debate about the level of risk. It is uncertain how different doses and length of exposure to a dose might affect the final risk. Abstract 2463 used a weighted cumulative dose model to estimate the effect on infection risk of different dosing over time and used a number of other models as comparators. All models found an association of glucocorticoids with infections. As might be expected, current and recent doses had the greatest impact on risk. The interesting result was that doses given up to 2.5 years ago seemed to have some ongoing influence on current risk. The length of time a stable dose was used also appeared to influence risk, with longer times increasing the risk of infection. Their data suggested a similar risk for a patient using 5mg for 3 years vs. 30mg for a month.

Lisa Stamp presented data from her work on red-cell methotrexate (MTX-Glu) and folate polyglutamates (FPG) in abstract 2467. She compared her data with that of a US cohort to help determine the contribution of MTX-Glu and FPG to disease activity. A lower MTX-Glu seemed to be associated with higher disease activity score (DAS); however, there was no cutoff for an ideal level. A higher FPG is associated with higher DAS with ROC, suggesting an RBC folate level of >1000 nmol/L as an important cutoff. The level of FPG seems more important than MTX-Glu in determining disease activity, suggesting we need to pay attention to the level of folate supplementation we supply.

The discontinuation of biological agents has both patient and fiscal appeal. Abstract 2468 presented a small study that discontinued adalimumab after a period of 24 weeks in DAS remission (<2.6). The primary outcome was DAS <3.2 at 6 months. One hundred and fifty-six were started and 40 discontinued with DAS <2.6. Twenty-two patients reached the outcome of DAS <3.2 at 6 months while 17 had a DAS <2.6. There was no radiological or functional progression at 1 year in those that achieved the outcome. The primary predictor was a low DAS at the time of discontinuation, with a cutoff of 2.16. These data are from a Japanese cohort, and may not be generalisable to the NZ population. Joseph Smolen presented a poster of PRESERVE trial data that showed reduction of etanercept from 50mg weekly to 25mg weekly had no effect on remission, but discontinuation resulted in loss of remission in 60%. The numbers remaining in remission off-drug were similar, and further work is required to predict those patients in whom this could work. There may be a difference in results when considering early versus established disease.

Abstract 2513 presented another matrix model to try and predict rapid radiological progression (RRP). Using data from a Swedish cohort, C-reactive protein level (<10, 10–35 and >35 mg/L), smoking and baseline erosions were predictive of RRP when used in the model. Other models were not predictive in this population. One of the odd things noted was for males to have more aggressive disease. The findings need validation in other cohorts.

Abstract 2515 looked at predicting work disability. A number of expected measures predict sick days. These include baseline HAQ, DAS28, VAS global, VAS pain and tender joint count, along with age and education level. Work disability was heavily influenced by baseline working status. Partial work (1–29 days off in the previous month) versus full time showed the greatest potential for intervention.

Does clinical remission equal patient expectations and therefore mean good quality of life (QOL)? Abstract 2516 presented 712 patients who were assessed with standard forms and examinations. They were grouped in to ACR/EULAR, DAS28 or CDAI remission, and compared with healthy controls on a number of QOL scores. ACR/EULAR remission showed similar scores to healthy controls. CDAI showed comparable scores, while DAS remission showed worse scores. Lowering DAS to 2 produced similar outcomes to the ACR/EULAR score. Aiming for remission appears a sensible target.

There were swathes of posters analysing the new RA criteria. Poster 314 presented data from a general rheumatology clinic. 126 were recruited and 112 analysed. The cohort included patients with SLE and psoriatic arthritis. Sensitivity and specificity were 97% and 55%, respectively, and the positive and negative predictive values were 44% and 98%, respectively. The authors make the comment that physicians should be aware of the limitation when applying the new criteria. This is something the authors of the new criteria may have been aware of when they noted synovitis 'should not be better explained by another diagnosis'. Other posters showed similar results and confirmed the score of 6 as sensible.

Poster 719 presented data on the abrogation of cardiovascular risk with the use of methotrexate or tumour necrosis factor (TNF)-α inhibitors. An inception cohort of 1829 patients with RA was analysed for incident cardiovascular disease and controlled for the expected variables. Ever-use of methotrexate or TNF-α inhibitors had a hazard ratio (HR) of 0.54. Use of these medications for 24 months gave methotrexate an HR of 0.33 and TNF-α inhibitors an HR of 0.24. Further to this theme, Fred Wolfe presented data (abstract 2589) from 23,328 patients on the cardioprotective effects of bisphosphonates, calcium and vitamin D in RA and SLE. Those on bisphosphonates had more severe disease. He adjusted for the usual confounders and showed that for myocardial infarction, bisphosphonates had an odds ratio (OR) of 0.75 and calcium and vitamin D an OR of 0.57. The three-drug combination had an OR of 0.38.

Obesity seemed to be the focus of a number of posters. Poster 416 presented a post-hoc analysis of the BeST data looking at response to infliximab treatment by BMI. BMI was an independent predictor of failure to respond, with ORs of 2.9 for overweight and 3.6 for obese patients. This finding was in keeping with a theme of obesity being associated with decreased response to both DMARDS and biological DMARDS in RA (posters 410 and 1310) and AS (poster 530).

Abstract 2463: Dixon WG et al. Immediate and delayed impact of oral glucocorticoid therapy on risk of serious infection in patients with rheumatoid arthritis: a nested case-control analysis using a weighted cumulative dose model

Abstract 2467: Stamp LK et al. Red blood cell folate polyglutamates are an important determinant of RA disease activity in patients on methotrexate – implications for folic acid supplementation

Abstract 2468: Tanaka Y et al. Discontinuation of adalimumab without functional and structural progress after attaining remission in patients with rheumatoid arthritis

Abstract 2513: Saevarsdottir S et al. Development of a matrix risk model to predict rapid radiographic progression in early rheumatoid arthritis: results from a randomized trial population

Abstract 2515: Olofsson T et al. Predictors of work disability during the first 3 years after diagnosis in a national rheumatoid arthritis inception cohort

Abstract 2516: Patel AM et al. Do rheumatoid arthritis patients meeting American College of Rheumatology/European League Against Rheumatism remission have improved functional ability, quality of life and work productivity compared to those with low disease activity?

Poster 314: Kennish LM et al. 2010 American College of Rheumatology/European League Against Rheumatism Rheumatoid Arthritis criteria classifies 67% of systemic lupus erythematosus and 38% of psoriatic arthritis as rheumatoid arthritis: implications for real world use

Poster 719: Bozaite-Gluosniene R et al. Reduced cardiovascular risk with use of methotrexate and tumor necrosis factor-α inhibitors in patients with rheumatoid arthritis

Abstract 2589: Wolfe F et al. Reduction in the risk of myocardial infarction in bisphosphonate and calcium/vitamin D treated rheumatoid arthritis and lupus patients: a longitudinal cohort study

Poster 416: Heimans L et al. Body mass index is associated with decreased response to initial and delayed treatment with dose escalated infliximab in patients with recent onset rheumatoid arthritis

Poster 410: Smolen JS et al. Impact of body mass index on response to etanercept therapy in subjects with moderately active rheumatoid arthritis in the PRESERVE trial

Poster 1310: Greenberg JD et al. Effect of weight, body mass index and weight-based dosing on persistency of anti-TNFs in psoriatic arthritis

Poster 530: Ottaviani S et al. Body mass index influences the response to infliximab in ankylosing spondylitis

OA

Abstract 722 presented remarkable data on intensive weight loss and exercise in managing both pain and function in OA. The researchers enrolled 454 obese or overweight patients with pain and radiographical OA of the knee. OA at other sites was present, but not examined. Patients were randomised to diet, exercise or diet plus exercise. The diet was supported with meal replacement shakes and regular (weekly) counselling. Exercise was conducted under supervision in a wonderful (at least from the pictures) indoor arena in a regimen of 20 min walk, 20 min weights, 20 min walk. Weight loss was 8kg for diet, 2kg for exercise and 11kg for diet plus exercise. There were good functional outcomes in all groups at 6 months, but by 18 months the diet plus exercise group had better pain and function scores.

OA prevalence was examined in poster 877. Using the National Health Interview Survey data, the researchers were able to show that, despite anecdote, there was no increase in symptomatic OA from 2002–2009 except in patients aged 45–64 years who were nonobese. There was a marked difference in OA prevalence in obese (15.2%) versus nonobese (6.6%).

Abstract 722: Messier SP et al. The Intensive Diet and Exercise for Arthritis trial: 18-month clinical outcomes

Poster 877: Reichmann et al. Trends in the prevalence of symptomatic knee osteoarthritis from 2002 to 2009

Seronegative spondyloarthropathies

Can we prevent progression in AS? Poster 1303 presented a small cohort from the Toronto AS clinic. They compared 20 patients using tumour necrosis factor (TNF) inhibitors who continued NSAIDs with 20 using TNF inhibitors who had discontinued NSAIDs. There was a trend towards slower progression in the NSAID group versus nonusers, despite the NSAID group having higher baseline BASDAI. This replicates data from a similar sized cohort presented by Poddubnyy at EULAR.

There is considerable interest in screening patients with psoriasis in dermatology clinics for psoriatic arthritis. There are three questionnaires competing for the honours. Poster 1307 presented what seemed the most sensible analysis, suggesting that Psoriatic Epidemiology Screening ProjecT (PEST) and Toronto Psoriatic Arthritis Screen (ToPAS) were probably the most useful. They were also likely to be superior when patients had less active symptoms at the time of assessment. This may be a way to engage with our dermatology colleagues, given psoriatic arthritis is thought to be prevalent in 15–20% of the psoriasis population.

Poster 1303: Haroon N et al. Continuance of non-steroidal anti-inflammatory drugs may reduce radiographic progression in ankylosing spondylitis patients on biological therapy

Poster 1307: Walsh J et al. Comparison of screening instruments for psoriatic arthritis in patients with psoriasis

New Zealanders at ACR

NZ was well represented at ACR as noted above. There were other oral presentations by Lisa Stamp (her third with abstract 2579) and Peter Jones (abstract 1720). Posters were also presented by Tony Merriman, Nicola Dalbeth and Ashika Chhana on behalf of many NZ collaborators.

Abstract 2579: Stamp LK et al. Starting dose, but not maximum maintenance dose, is a risk factor for allopurinol hypersensitivity syndrome: a proposed nomogram for safe starting dosing of allopurinol

Abstract 1720: Jones PBB et al. Health Outcomes from a residential multidisciplinary rehabilitation program for musculoskeletal conditions: a ten year observational study

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