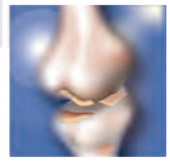
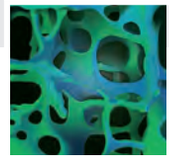




# Bulletin Board

## Study sheds light on B-cell disturbances in Takayasu arteritis offering hope for future therapy

A study carried out by researchers from the Charité Universitätsmedizin Berlin has been the first to extensively describe B-cell disturbances in Takayasu arteritis. The currently poorly understood disease "was previously thought to have a mainly T-cell-mediated pathogenesis," according to researchers.

The recent findings now suggest that a greater number of circulating plasmablasts coincided with increased disease activity in Takayasu arteritis, as in systemic lupus erythematosus (SLE). In addition, "it is hoped that B-cell depletion therapy may be an option for these patients," explained lead author of the study Bimba Hoyer.

The blood samples of 17 women with Takayasu arteritis were examined according to the American College of Rheumatology (ACR) disease criteria. A second cohort of nine women without Takayasu arteritis but with SLE was also studied, as was a control group of eight healthy women and one man. The expression of CD20, CD19, CD27 and HLA-DR were then analyzed.

"Unlike active SLE, which is characterized by lymphocytopenia, total lymphocyte and B-cell counts in patients with [Takayasu arteritis] were not significantly lower than those in healthy donors," explained the authors.

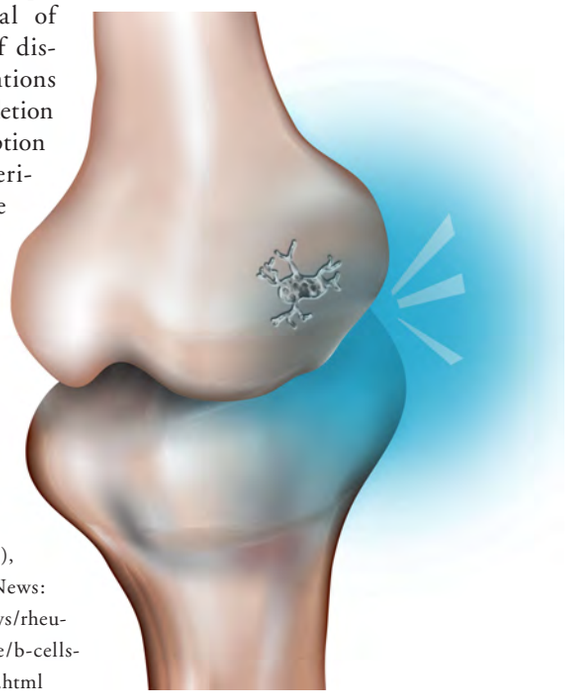
However, considerably altered B-cell subsets were found in active Takayasu arteritis. An increased number and frequency of $CD19^{+}/CD20^{-}/CD27^{high}$ antibody-secreting cells in patients with Takayasu arteritis compared with healthy donors (2800 vs 1200, respectively; p = 0.027), as well as a lower total number of naive B cells (28,000 vs 110,000; p = 0.012) and a higher number of memory B cells (78,000 vs 48,000; p = 0.049). They also found an increased number of plasmablasts among active Takayasu arteritis patients (11 out of 17 patients), both in relation to healthy donors (7800 vs 975; p = 0.027) and in relation to the inactive Takayasu arteritis cohort (n = 6), where the mean was 535 (p = 0.0056).

"This strongly resembles the findings in SLE, where plasmablast expansion serves as a marker of disease activity," explain the authors. Indeed, the number of plasmablasts in the active SLE patients was identical to that in the active Takayasu arteritis patients, at 7800.

Based on these findings, three patients who were refractory to other treatments were subsequently treated with rituximab, "so far successfully," commented the authors. "The observed correlation between the plasmablast numbers and active Takayasu arteritis, as well as the beneficial effects of B-cell depletion therapy, suggests a potential of plasmablasts as biomarkers of disease activity and for interventions targeting B cells … B-cell depletion therapy seems to be a useful option for refractory Takayasu arteritis, and its potential should be evaluated in controlled trials," concluded the authors.

– Written by Paolo Reveglia

Sources: Hoyer BF, Mumtaz IM, Loddenkemper K *et al.* Takayasu arteritis is characterised by disturbances of B cell homeostasis and responds to B cell depletion therapy with rituximab. *Ann. Rheum. Dis.* 71(1), 75–79 (2012); Internal Medicine News: www.internalmedicinenews.com/news/rheumatology-immunology/single-article/b-cells-key-in-takayasu-arteritis/00add7643b.html



## in the news...

# Multiple factors are predictive of knee pain in older women

Results of a 12-year study carried out in the UK, published online in the 19 December 2011 issue of *Arthritis and Rheumatism* has identified multiple factors that serve as predictors of persistent knee pain in women aged 50 years and older.

Among the factors shown to be significant predictors ($p < 0.05$) of persistent knee pain in both univariate and multivariate models were higher BMI, previous knee injury and radiographically confirmed osteoarthritis (OA). Senior author Nigel Arden, from the University of Oxford (Oxford, UK) and colleagues also noted that BMI was predictive of knee pain incidence in both models. "Understanding the prevalence and predictors of knee pain is the first step in developing comprehensive pain assessment plans that could lead to more targeted treatment options for those burdened by OA," explained Arden.

In order to aid clarification of risk factors, the investigators studied the natural history, prevalence and predictors of knee pain over a 12-year period. Information from various time points was acquired in the hope of helping to describe the pain fluctuations. Participants in the study were chosen from the Chingford Study, a prospective population-based study of osteoporosis and OA among 1003 women aged 44–67 years. Fully extended x-rays of the knees were taken and the Kellgren–Lawrence grading was completed.

Self-reported pain information was acquired by questioning the participant whether or not she experienced any pain in either knee over the last month and how many days during that time period the pain had been present. Pain data was again assessed in years 3, 5, 6, 10 and 15.

Higher BMI predicted persistent (OR: 1.14; 95% CI: 1.05–1.25) and incident pain (OR: 1.10; 95% CI: 1.02–1.18). The presence of OA on x-rays predicted persistent pain (OR: 3.82, 95% CI: 1.02–10.68; $p = 0.01$). Knee injury reports were predictive of both persistent (OR: 4.25; 95% CI: 1.38–1.12; $p = 0.012$) and intermittent pain patterns (OR: 4.21; 95% CI: 1.80–9.89; $p = 0.001$).

However, the authors did add a note of caution highlighting that the results can only be generalized to females in the community between certain ages and that they only assessed knee pain, leaving out other symptoms such as stiffness and other functional limitations.

"This study highlights the value of the temporal pattern of pain, even when using quinquennial assessments, in identifying different subgroups of pain, and may explain the heterogeneity in the literature when pain is measured at only one point," concluded the authors.

– Written by Paolo Reveglia

Sources: Soni A, Kiran A, Hart D *et al.* Reported knee pain prevalence in a community-based cohort over 12 years. *Arthritis Rheum*. doi:10.1002/art.33434 (2011) (Epub ahead of print); Medical News Today: www.medicalnewstoday.com/articles/239489.php

# Research shows that joint damage could still occur in rheumatoid arthritis patients in remission

In recent research published in *Arthritis & Rheumatism*, scientists report that rheumatoid arthritis (RA) patients who meet the 'Disease Activity Score in 28 joints (DAS28)' criterion for remission, could still possibly have advancing joint damage.

In their report, authors explain that the DAS28 has been criticized owing to the fact that certain amounts of disease activity can be observed in patients even though they have achieved remission according to DAS28. They state that the objective of the study was "to investigate the significance of residual inflammation in remission in relation to radiographic progression."

Investigators pooled 1-year clinical data taken from methotrexate monotherapy groups in pivotal clinical trials carried out recently. The analysis covered a total of 864 patients and researchers looked for patients who had achieved "persistent DAS28 remission" from the 6th through to the 12th month – that is a DAS28 of <2.6 in the specified time period. Once these patients were identified, researchers examined radiographic progression in total Sharp/van der Heijde scores in this group from baseline to 12 months; specifically between patients who had residual joint swelling, and patients without residual joint swelling. Investigators used a swollen joint count (SJC) from the 6th to the 12th month of ≥2 ($SJC_{6–12}$ ≥2) to define patients with residual joint swelling and an $SJC_{6–12}$ <2) to define those without.

Results demonstrated that 114 had a DAS28 of less than 2.6. Out of the 114 patients, 80.7% did not have residual joint swelling and demonstrated less radiographic progression across 1 year than the 19.3% of patients who did have residual joint swelling. Additionally, amongst other results, analysis revealed that there was a significantly lower proportion of patients with a "total Sharp/van der Heijde score progression" of >0.5 per year in those without joint swelling, than in those with joint swelling.

Daniel Aletaha (Medical University of Vienna, Austria) explains, "Our findings were that joint damage progresses even in DAS28 lower that 2.6, and that this continuing damage is driven by residual swollen joints." He goes on to say, "The implications are that from a structural perspective (i.e., joint damage), it is not sufficient for clinicians to rely on the presence of DAS28 remission. If clinicians wish to

use the DAS28, they will also need to look at the number of swollen joints separately."

In conclusion, the report states that only when patients in DAS28 remission have no persistent residual joint swelling, is there minimal radiographic progression with nonbiologic treatment. Authors explain that, "under these conditions, progression is comparable to that in patients with disease in remission according to other disease activity indices."

– Written by Roshaine Gunawardana

Sources: Aletaha D, Smolen JS. Joint damage in rheumatoid arthritis progresses in remission according to the Disease Activity Score in 28 joints and is driven by residual swollen joints. *Arthritis Rheum.* 63(12), 3702–3711 (2011); Medscape News: www.medscape.com/viewarticle/756191

# Study shows that abatacept is ALLOWed to be withdrawn in patients with rheumatoid arthritis

Abatacept was approved for the treatment of RA in patients who have an inadequate response to anti-TNF-α therapy in December 2005.

During therapy, RA patients may need to terminate treatment owing to events such as surgery. This termination can cause an immunogenic antibody response causing antibody-mediated drug clearance hence reducing levels of the drug in the body and hence reducing its therapeutic effect. The recent Phase III ALLOW study has shown that withdrawing abatacept treatment could be safe.

Jeffrey Kaine (Sarasota Arthritis Research Center, FL, USA) and colleagues enrolled 167 patients with RA into a trial to assess the effect of withdrawing abatacept treatment temporarily. The study was carried out in three phases, during which the patients were administered a loading dose of abatacept followed by a 125-mg fixed dose per week for 12 weeks. The patients were then randomized 2:1 in a double-blind format to either subcutaneous abatacept or subcutaneous placebo for 12 weeks. The primary end point of the study was immunogenicity rate. This was detected by ELISA as the proportion of patients with an immunogenic response after period 2. A secondary more sensitive electrochemiluminescence immunoassay was also used. Following period 2 the patients receiving abatacept stayed on the drug and the patients who were given the placebo were then reintroduced to abatacept.

Immunogenicity rates were low at the end of Phase II of the study in both groups, 0% of patients receiving subcutaneous abatacept and 9% of patients receiving placebo subcutaneously were positive for immunogenicity. Of this 9%, one patient was positive for anti-abatacept antibodies and six patients were positive for anti-CTLA4-T antibodies. Of these seven patients only three remained seropositive after the reintroduction of abatacept.

At the commencement of the study all patients had a DAS28 of 4.8, by the end of period 1 the DAS28 had reduced to an average of 1.925 in all patients. The score then rose slightly in the placebo group although by the end of the trial the DAS28 was 2.22 in both the abatacept group and 2.32 in the placebo group.

The results of the trial show that withdrawal of abatacept for 3 months does not compromise its overall efficacy in RA patients. These results may give confidence to clinicians who are prescribing the drug to RA patients requiring surgery at a later stage.

– Written by Claire Attwood

Sources: Kaine J, Gladstein G, Strusberg I *et al.* Evaluation of abatacept administered subcutaneously in adults with active rheumatoid arthritis: impact of withdrawal and reintroduction on immunogenicity, efficacy and safety (Phase Iiib ALLOW study). *Ann. Rheum. Dis.* 71(1), 38–44 (2012).

# A mindfulness intervention can potentially reduce symptoms of arthritis

A mindfulness program has been used as an intervention to help people accept the pain and disability associated with RA. It was thought that this intervention could block the negative thoughts and anxiety associated with the disease and hence reduce depression among these patients and improve the way that they cope with the disease.

A recent study was carried out by Heidi Zang (National Resource Center for Rehabilitation in Rheumatology, Diakonhjemmet Hospital, Oslo, Norway) and colleagues to assess the efficacy of this intervention on patients with inflammatory rheumatoid joint diseases. Seventy three patients, with a mean age of 56 years and a disease duration of 16 years, were enrolled in the study and were randomized to either a vitality training program (VTP) (ten sessions over 4 months and a booster session at 6 months) or to routine care plus a compact disk with instructions on mindfulness exercises for use at home.

The primary outcome of the study was psychological distress, which was measured by the general health questionnaire-20; further primary outcomes were self efficacy and emotion-focused coping. Secondary outcomes included pain, fatigue, patient global disease activity, self-care ability and well being.

Patients receiving the VTP saw a decrease in psychological distress of 4.7 points and maintained a 3.7 point reduction over the 12-month follow-up period. Over 12 months the number of patients who qualified for having psychological distress fell from 36 to 6%, a 30% reduction compared with only a 5% reduction in the control group from 29 to 24%. The additional primary end points such as self efficacy, pain and symptoms, emotional processing, fatigue, self-care ability and overall well being also saw significant improvements. However, no improvement was seen in emotional expression, pain or disease activity.

This study shows that the VTP, a psychological intervention, can be beneficial to RA patients as it has enabled people to incorporate mindfulness strategies into their daily lives in order to cope with their disease.

– Written by Claire Attwood

Sources: Medpage today: www.medpagetoday.com/Rheumatology/Arthritis/30307; Zangi HA, Mowinckel P, Finset A *et al.* A mindfulness-based group intervention to reduce psychological distress and fatigue in patients with inflammatory rheumatic joint diseases: a randomised controlled trial. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2011–200351 (2012) (Epub ahead of print).

**in brief...**

A randomized, controlled, trial of rituximab for treatment of severe cryoglobulinemic vasculitis. De Vita S, Quartuccio L, Isola M *et al. Arthritis Rheum.* doi:10.1002/art.34331 (2011) (Epub ahead of print).

Results of a study has shown rituximab to be 'a very good option' for severe cryoglobulinemic vasculitis according to the study investigators. The primary end point of the controlled randomized trial was the proportion of patients remaining on their assigned treatment at 12 months after randomization. The authors noted that the Birmingham Vasculitis Activity Score did not alter in the conventional treatment group but declined from 11.9 at baseline to 7.1 at month 2 and to 5.4 at month 12 with rituximab treatment.