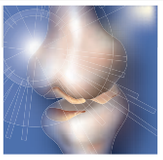
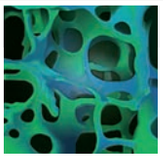




Bulletin Board

Are arthritis drugs associated with an increased risk of shingles?

Researchers in Germany have found that some arthritis drugs, specifically anti-tumor necrosis factor-α (TNF-α) agents, may be associated with an increased risk of developing shingles (herpes zoster).

It has already been suggested from previous studies that rheumatoid arthritis sufferers, who are treated with anti-TNF-α agents, are susceptible to bacterial infections. However, little is known regarding the risk of infection by viruses such as herpes zoster. A study conducted by Dr Anja Strangfeld and colleagues of the German Rheumatism Research Center in Berlin, examined data of over 5000 rheumatoid arthritis patients in an attempt to determine whether taking anti-TNF-α agents led to an increased risk of shingles.

In this study, the researchers looked at the records of rheumatoid arthritis patients who were registered with RABBIT, a German biologics register, between May 2001 and December 2006.

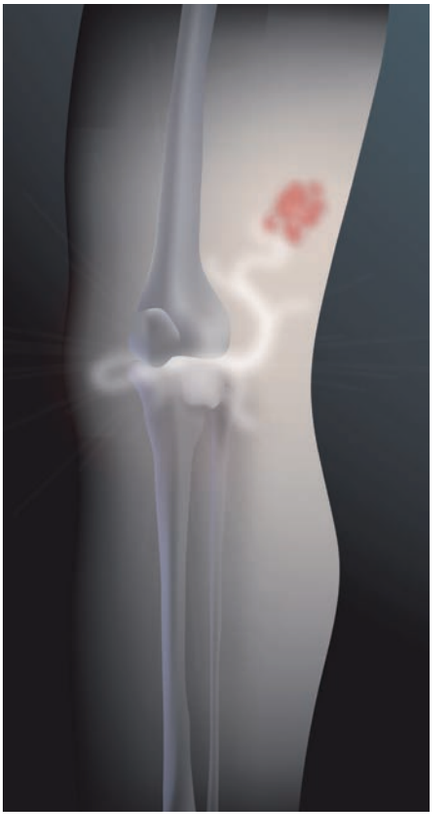
These patients enrolled on RABBIT once they began treatment with infliximab, etanercept, adalimumab or anakinra, or when they changed to a conventional disease-modifying antirheumatic drug (DMARD). Out of these, infliximab, adalimumab and etanercept function by inhibiting TNF-α. The clinical status, reports of adverse events and any changes in treatment regimen were all regularly assessed in each participant.

The objectives of the study by Strangfeld *et al.* was to determine the occurrence of shingles in patients treated with TNF-α inhibitors as a class or separately, thus seeing whether an association exists between shingles and the administration of these agents in patients with rheumatoid arthritis.

Upon analysis, it was seen that 86 episodes of herpes zoster were recorded among 82 patients. Among these, 39 occurrences were attributed to treatment with monoclonal anti-TNF-α antibodies, 23 to etanercept and 24 to conventional DMARDs. After adjusting for age, disease severity and glucocorticoid use, a significantly increased risk of using monoclonal anti-TNF-α antibodies was observed; however, this did not reach the threshold for clinical significance. Also, no significant association was found between the incidence of shingles and the use of etanercept or TNF-α inhibitors as a class.

> "Based on our data, we recommend careful monitoring of patients treated with monoclonal anti-TNF-α antibodies for early signs and symptoms of herpes zoster."

The authors concluded that: "Treatment with monoclonal anti-TNF-α antibodies may be associated with increased risk of herpes zoster, but this requires further study."



> "TNF-α inhibitors have revolutionized the management of a number of difficult diseases."

They added that: "Based on our data, we recommend careful monitoring of patients treated with monoclonal anti-TNF-α antibodies for early signs and symptoms of herpes zoster."

In an accompanying editorial, Drs Richard J Whitley and John W Gnann of the University of Alabama at Birmingham, AL, USA, commented on the findings:

"The TNF-α inhibitors provide tremendous benefit to a broad spectrum of patients with systemic inflammatory diseases. As with any therapy, time is required for all of the safety concerns related to these potent medications to become apparent. TNF-α inhibitors have revolutionized the management of a number of difficult diseases, especially inflammatory arthritis, but clinicians must continue to remain aware of the potential for serious infectious complications, which now include herpes zoster."

Source: Strangfeld A, Listing J, Herzer P *et al.*: Risk of herpes zoster in patients with rheumatoid arthritis treated with anti-TNF-α agents. *JAMA* 301(7) 737–744 (2009); www.medicalnewstoday.com/articles/139394.php

in the news...

Clinical study shows that chondroitins can significantly improve the symptoms of osteoarthritis

Osteoarthritis (OA), also known as degenerative arthritis or degenerative joint disease, is the most common form of arthritis. In the USA, almost 21 million people are affected. OA can occur in any joint, but usually it affects the hands, knees, hips or spine.

There are three main features of OA: damage to cartilage; bone regrowth in areas of cartilage erosion (eburnation); and inflammation of the tissues around the joints (synovitis). Clinical symptoms include joint pain, tenderness, stiffness, inflammation and a grating sound in the joints.

A team of researchers led by Andre Kahan of the University of Paris Descartes in Paris, France, have examined the effects of chondroitins 4 and 6 sulfate (CS) on the radiographic progression and symptoms in sufferers of knee OA. The study conducted was an international, randomized, double-blind, placebo-controlled trial. A total of 622 sufferers of OA were recruited from France, Belgium, Switzerland, Austria and the USA. Patients were randomly assigned to receive either 800 µg CS (n = 309 patients) or placebo (n = 313 patients) once-daily for a period of 2 years. X-ray images of the target knee were obtained from all patients at the time of enrollment and at 12, 18 and 24 months. Digital image analysis was used to measure the minimum joint space width (JSW) of the medial compartment of the tibiofemoral joint.

The intent-to-treat analysis showed that minimum JSW loss was significantly reduced in the CS group. The percentage of patients with radiographic progression greater than or equal to 0.25 mm was also notably reduced in the CS group in comparison with the placebo group (28 versus 41%, respectively). Furthermore, the CS group showed a significantly faster improvement in pain than the placebo group. CS was shown to be well-tolerated and there were no significant differences in adverse effects between both groups.

The authors concluded that "long-term administration of CS over 2 years can prevent joint structure degradation in patients with knee OA."

This study certainly presents promising data suggesting that CS could be a future therapy for OA.

The authors commented that: "Further studies with longer follow-up and different outcome criteria are warranted to assess whether the beneficial structural changes associated with CS demonstrated in our study are predictive of improvement in the long-term clinical progression of OA."

Source: Kahan A, Uebelhart D, De Vathaire F, Delmas PD, Reginster JY: Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: The study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 60(2), 524–533 (2009); http://www.sciencedaily.com/releases/2009/01/090129131835.htm

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of rheumatology.

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in brief...

The effect of infliximab and timing of vaccination on the humoral response to influenza vaccination in patients with rheumatoid arthritis and ankylosing spondylitis.

Elkayam O, Bashkin A, Mandelboim M *et al.*: *Semin. Arthritis Rheum.* (2009) (Epub ahead of print)

This article investigated the effect of timing of vaccination in relation to administration of infliximab on the efficacy and safety of influenza vaccine in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS). A total of 38 patients with RA or AS treated with infliximab (mean dosage of 3 mg/kg) were compared with 23 control patients. Split-virion inactivated vaccine was administered. A total of 22 patients received the vaccination on the same day as infliximab was administered, the remaining 16 received the vaccination 3 weeks later. RA patients and controls had similar occurrence of protective levels of HI antibodies and geometric mean antibody titers (GMT), while AS patients had lower levels reflecting lower rates of previous vaccination. After 4 weeks, a significant increase in GMT for each antigen was observed in all groups except in the RA–infliximab group. Patients demonstrated an increase in GMT, independently of the time of vaccination.

Bone mineral density and risk of fractures in aging, obese post-menopausal women with type 2 diabetes. The GIUMO Study.

Sosa M, Saavedra P, Jódar E *et al.*: *Aging Clin. Exp. Res.* 1, 27–32 (2009).

This prospective study enrolled 111 patients with Type 2 diabetes mellitus (DM) and 91 control individuals aged over 65 years. The influence of DM in quantitative ultrasound measurements of the heel (QUS) and bone mineral density (BMD) measured by dual x-ray absorptiometry (DXA), in both lumbar spine (L2–L4) and proximal femur was also studied. Patients were found to have a higher BMD in the lumbar spine (L2–L4) compared with controls (0.979 g/cm^2 vs 0.927 g/cm^2, p = 0.035), but no statistically significant differences in the proximal femur were found. The authors conclude that Type 2 DM produces an increase in BMD of the lumbar spine in obese, postmenopausal, Caucasian women, without changes in BMD of the proximal femur or in QUS measurements of the heel. The prevalence of vertebral, hip and nonvertebral fractures did not increase in Type 2 DM patients.

Results from a Phase II trial suggest that ustekinumab may be a potential treatment for psoriatic arthritis

Recent results from a Phase II clinical trial, published in the *Lancet*, have shown ustekinumab to be effective in treating psoriatic arthritis. In this Phase II study, researchers assessed the efficacy and safety of ustekinumab in patients suffering from psoriatic arthritis. The trial was conducted at 24 sites in North America and Europe and was a double-blind, randomized, placebo-controlled, crossover study. Patients were randomly assigned to receive either ustekinumab (90 or 63 mg) every week for 4 weeks followed by placebo at weeks 12 and 16 (n = 76; group 1) or placebo and ustekinumab (63 mg) at weeks 12 and 16 (n = 70; group 2).

An intention-to-treat analysis revealed that 42% of patients in Group 1 and 14% in Group 2 achieved the primary end point of an ACR20 response at week 12. Furthermore, out of 124 participants who had psoriasis affecting 3% or more body surface area, 52% in group 1 and 5% in group 2 had an improvement of 75% or more in psoriasis area and severity index score at week 12.

A rise in adverse events was observed during the placebo-controlled period; 61% of patients in group 1 and 63% in group 2. Serious adverse events were reported in 4% of group 2 patients, none were reported in group 1.

These results indicate that ustekinumab was well-tolerated and can effectively reduce the signs and symptoms of psoriatic arthritis in comparison to placebo. Skin lesions were also seen to be significantly reduced.

Alice Gottlieb, MD, Chairperson of the Department of Dermatology at Tufts Medical Center (MA, USA) and lead author of the study, commented: "This is a positive development for patients living with the joint pain and swelling that characterizes the disease, even as more research is needed to further test the efficacy of this treatment in psoriatic arthritis."

Since some psoriatic arthritis sufferers do not respond to typical drug treatments, alternatives are needed. The results from this study certainly suggest that ustekinumab can be a potential therapy against this type of inflammatory arthritis.

Source: Gottlieb A, Menter A, Mendelsohn A *et al.*: Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. *Lancet* 373(9664), 633–640 (2009); http://www.sciencedaily.com/releases/2009/02/090211193813.htm

Increased burden and impaired functioning in elderly patients with rheumatoid arthritis

A new study has demonstrated that functioning is worse in elderly rheumatoid arthritis (RA) patients compared with the general aging population. Approximately 12,000 people are diagnosed with the disease annually, with a high prevalence in people in their 70s.

The study, published in the *Journal of Rheumatology* attempted to assess disability levels and physical functioning in elderly RA patients compared with age-matched controls who were disease free.

The study aimed to link the items included in the self-report Multidimensional Health Assessment Questionnaire (MDHAQ) with components of the WHO International Classification of Functioning, Disability and Health (ICF) instrument, to assess disability and functioning of elderly patients with rheumatoid arthritis.

Data from 1439 RA patients with an average age of 66 years were compared with data from 957 age-matched controls. The questionnaires gathered information on education, employment, physical exercise, self-reported pain and joint tenderness, comorbidity and general health. Patients were also asked how long they had had the disease.

The study was able to use a large patient and control population and was able to cover a wide spectrum of functioning. The results indicated that in all areas of assessment RA patients had lower levels of functioning, compared with the control group. The results also revealed that male patients and controls showed similar levels of functioning when it came to general tasks and daily demands.

"In patients, disease activity, education, exercise frequency and comorbidities were expectedly associated with lower functioning in the body structure and function component, while male sex and subjectively perceived health were associated with more favorable functioning."

"In the activity and participation components, disease activity, exercise frequency and comorbidities were associated with impaired functioning, while better health on self-report was associated with better functioning … Elderly patients with RA, in comparison to population controls, encounter more difficulties in daily activities and their social life."

Over all the researchers concluded that white male sex and subjectively perceived health were associated with more favorable functioning. There is an extra burden of disability in elderly patients with RA compared with the reference population.

Source: Häkkinen A, Arkela-Kautiainen M, Sokka T, Hannonen P, Kautiainen H: Self-report functioning according to the ICF model in elderly patients with rheumatoid arthritis and in population controls using the multidimensional health assessment questionnaire. *J. Rheumatol.* 36(2), 246–253 (2009).