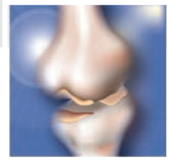
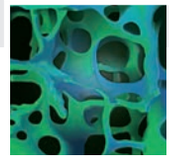




Bulletin Board

New study indicates link between obesity and the development of fibromyalgia

Recent results have indicated a link between obesity and the risk for fibromyalgia (FM). A longitudinal study was used to explore the risk of having FM at 11-years follow up; baseline assessment of engagement, frequency, duration and intensity of physical exercise, along with BMI was used to explore the risk of FM in a large unselected female population.

The study aimed to determine the relationship between levels of leisure-time physical exercise and future risk of FM and to observe if being overweight or obese was an independent risk factor for future development of fibromyalgia. Results were reported in the May issue of *Arthritis Care & Research.*

Data for the study were collected from the Nord-Trøndelag Health (HUNT) Study 1 (HUNT 1) from 1984 to 1986 and from HUNT 2 during 1995–1997. A total of 15,990 women provided data for the surveys. From this total, all of whom reported no FM or physical impairment at baseline, 380 later experienced incident FM during the 11 years between HUNT 1 and HUNT 2.

Compared with normal-weight women who exercised at least 1 h per week, overweight or obese women with a similar activity level had a 72% higher risk for FM, whereas data indicated that overweight or obese women, who exercised for less than 1 h a week or who were inactive, had more than double the risk for FM.

Lead author Paul Mork, from the Norwegian University of Science and Technology in Trondheim, Norway, commented, "Women who reported exercising four times per week had a 29% lower risk of FM compared with inactive women… Similar results were found in the analysis of the summary score combining information on frequency, duration, and intensity of exercise; women with the highest exercise level had a somewhat lower risk than inactive women."

Data demonstrated that women who reported the highest exercise level had a relative risk of 0.77 for the development of FM, and there was a weak dose–response association between the level of physical exercise and the risk for FM. Overweight or obese women had approximately a 60 to 70% higher risk for FM. The study also demonstrated that BMI was an independent risk factor for FM.

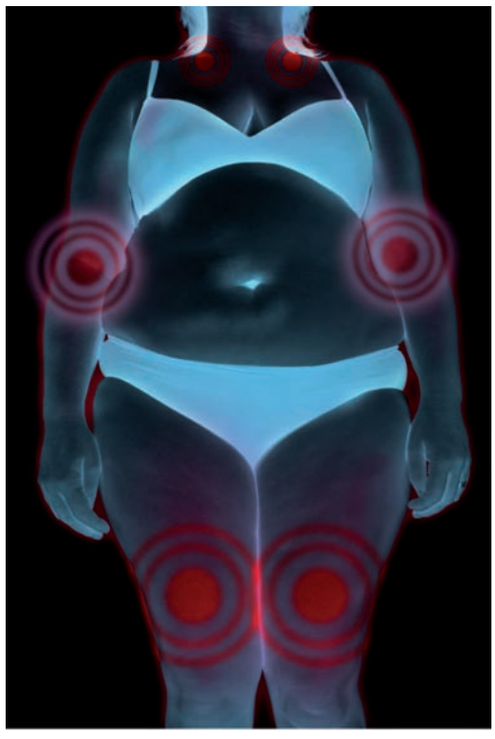
"The study further shows that a high BMI is a strong and independent risk factor for future development of FM," Mork stated. "Moreover, the higher relative risks for the combined effect of being overweight/obese and inactive, relative to being overweight/obese alone, point to a further disadvantage for overweight women who do not exercise."

Limitations of the study included the loss of contact with some women during follow-up, as well as possible misclarifications of the duration and intensity of physical exercise; the study was unable to differentiate between the different exercise types and the role this may play in FM risk.

The study concluded that these findings along with the current study indicate that increasing exercise and, hence, physical fitness may act as protection against the continued muscoskeletal symptoms that could eventually lead to the FM development.

Community-based measures that are aimed at reducing the incidence of FM should emphasize the importance of regular exercise and maintenance of normal body weight.

Source: Mork PJ, Vasseljen O, Nilsen TI: The association between physical exercise, body mass index, and risk of fibromyalgia: longitudinal data from the Norwegian HUNT study. *Arthritis Care Res. (Hoboken)* (2010) (Epub ahead of print).



in the news...

Intravenous immunoglobulin shows potential as treatment for pain syndrome

Research at the University of Liverpool (UK) has provided evidence for the efficacy of immunotherapeutic treatment of complex regional pain syndrome (CRPS).

Complex regional pain syndrome is a chronic pain condition that causes burning pains in a limb and usually develops after an injury but then continues after the injury has healed.

The discomfort caused by CRPS can be severe and there are instances of patients requesting amputations in an attempt to alleviate the pain. It is estimated that long-term CRPS affects approximately 1 in 5000 in the UK.

> *"The discomfort caused by CRPS can be severe and there are instances of patients requesting amputations in an attempt to alleviate the pain."*

The study was a randomized double-blind placebo-controlled trial that enrolled individuals who had suffered from CRPS for between 6 and 30 months and had not benefited from previous treatment or had pain intensity greater than four out of ten on a numerical rating scale. The researchers treated the patients with 0.5 g/kg IVIG, and then normal saline, in different treatment sessions that were separated by at least 28 days.

The results of the intervention demonstrated that, in the 12 patients that completed the trial, average pain intensity was reduced by 1.55 units after IVIG treatment compared with placebo (95% CI: 1.29–21.82; $p < 0.001$) and that in 25% of the patients, pain intensity after IVIG treatment was reduced by more than 50%.

> *"...in CRPS, the real effect of this treatment in [the] clinic may turn out to be even greater than what we have already seen..."*

The authors recognize that the small size of the study is a major limitation but suggest that this finding has the potential to prompt further research into novel pain relief for CRPS. Andreas Goebel, who headed the Liverpool CRPS treatment research, explains: "In CRPS, the real effect of this treatment in [the] clinic may turn out to be even greater than what we have already seen, because IVIG can be given in higher doses, and repeated treatment may have additional effects. IVIG is normally repeated every 4 weeks and we are working to develop ways which would allow patients to administer the treatment in their own home".

Sources: Goebel A, Baranowski A, Maurer K *et al.*: Intravenous immunoglobulin treatment of the complex regional pain syndrome. A randomized trial. *Ann. Int. Med.* 152 (3), 152–158 (2010); National Health Service – Complex regional pain syndrome: www.nhs.uk/Conditions/Complex-Regional-Pain-Syndrome/Pages/Introduction.aspx

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...

Hydroxychloroquine and glycemia in women with rheumatoid arthritis and systemic lupus erythematosus.

Penn SK, Kao AH, Schott LL et al.: *J. Rheumatol.* (2010) (Epub ahead of print).

Determines the relationship between current hydroxychloroquine (HCQ) use and two indicators of glycemic control, fasting glucose and insulin sensitivity, in nondiabetic women with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA). Nondiabetic women with SLE were characterized by HCQ usage status. Unadjusted and multivariately adjusted mean fasting glucose, median insulin, and insulin resistance were compared among HCQ users and nonusers for disease-specific groups. Results indicated that more women with SLE were taking HCQ than those with RA. After adjustment for several factors, serum glucose was lower in HCQ users than in nonusers. Also in women with SLE, HCQ was associated with lower HOMA-IR, but no difference was observed in RA patients. The authors conclude HCQ use was associated with lower fasting glucose in women with SLE or RA. The use of HCQ may be beneficial for reducing cardiovascular risk by improving glycemic control in these patients.

Clinical improvements in proliferative vs membranous lupus nephritis following B-cell depletion: pooled data from two cohorts.

Jónsdóttir T, Gunnarsson I, Mourão AF, Lu TY, van Vollenhoven RF, Isenberg D: *Rheumatology (Oxford)* (2010) (Epub ahead of print).

Compares clinical results following treatment with B-cell depleting therapy in patients with membranous versus proliferative lupus nephritis (LN). Data from two European centers on all patients with LN who were treated with intravenous rituximab (RTX) in a combination protocol with intravenous cyclophosphamide and steroids, were collected. A total of 43 patients, 28 with proliferate and 15 with membranous LN by renal biopsy, were evaluated. 6 months following treatment both LN groups demonstrated significant reduction in proteinuria and an increase in serum albumin, with the main improvement observed in the first 6 months following treatment. Membranoud LN patients had lower anti-dsDNA titres and higher complement C3 levels at baseline, but in both groups a significant reduction in anti-dsDNA titer and improvements in complement C3 levels were seen. Further studies are needed to confirm the efficacy of B-cell depleting therapy in proliferative nephritis, but clinicians may reasonably consider such therapy in membranous LN.

FDA approves Vimovo™ for treatment of arthritis

The US FDA has approved Vimovo™ delayed-release tablets to alleviate the symptoms of ankylosing spondylitis, osteoarthritis and rheumatoid arthritis, as well as decreasing the risk of NSAID-associated gastric ulcers in those patients prone to developing them.

Vimovo is a fixed-dose combination of enteric coated naproxen and the proton pump inhibitor (PPI), esomeprazole, which is designed to help prevent the development of gastric ulcers, a problem that half of all chronic NSAID users experience.

The approval was based on the results of the pivotal PN400–301 and 302 studies, comparing the results in patients receiving either Vimovo, or 500 mg enteric-coated naproxen twice daily, over a 6-month period. Data from the PN400–301 study showed that patients receiving Vimovo experienced significantly fewer gastric ulcers than those just receiving enteric-coated naproxen (4.1 vs 23.1%) and similar results were seen in the PN400–302 study (7.1 vs 24.3%).

Howard Hutchinson, Chief Medical Officer, AstraZeneca, commented: "In a single pill, Vimovo provides a proven pain reliever with a built-in PPI for arthritis patients at-risk for NSAID-associated gastric ulcers. The approval also demonstrates the commitment of AstraZeneca and POZEN to provide a new pain relief option that addresses the unmet medical needs of these patients."

Many osteoarthritis patients choose NSAIDs as a treatment option, but with 50% at risk of developing gastric ulcers, many patients will be relieving the symptoms of one condition at the expense of developing another. The approval of Vimovo offers hope that their symptoms can be alleviated, without a high risk of developing gastric ulcers as a result.

Source: www.astrazeneca.com/media/latest-press-releases/FDA-VIMOVO-Approval?itemId=9315643

Potential therapeutic target of colitis identified

Researchers at St Jude's Children's Research Hospital (Memphis, TN, USA) have demonstrated that Nlrp3, a protein already linked to an array of human inflammatory immune diseases, is involved in protecting the intestinal tract from colitis.

Colitis is a chronic inflammatory bowel disease with an estimated prevalence in the USA of 246 cases per 100,000 people per year. Inflammation in the lining of the large intestine and rectum leads to abdominal pain, diarrhea, bleeding and weight loss.

Nlrp3 is involved in the anchoring of the Nlrp3 inflammasome, a multiprotein complex that produces the cytokine IL-18. The team at St Jude's, led by Thirumala-Devi Kanneganti, demonstrated that IL-18, produced by the Nlrp3 inflammasome, triggered the production of epithelial cells in the colon. These helped to compensate for those cells damaged or destroyed by colitis and enabled mice to maintain a healthy colon.

The group also demonstrated the temporal and spatial location of these beneficial events; the Nlrp3 inflammasome is activated in the epithelial cells and produced IL-18 in response to colitis.

"This paper provides the basis for more effective, potentially disease-modifying approaches to treatment," said Kanneganti of her team's work.

Kanneganti and her colleagues developed their research and established that IL-18 is required to protect the colon from colitis. They found that, when it was injected into mice lacking the molecule, IL-18 eased the symptoms of colitis and Kanneganti commented, "I believe if we target molecules that are part of the innate immune response, we can find cures for many diseases, including cancer."

Sources: St Jude's Children's hospital: www.stjude.org; National digestive disease information clearinghouse (NDDIC): http://digestive.niddk.nih.gov/statistics

Identification of possible new genetic link to scleroderma

In research published in the May issue of *Nature Genetics*, scientists report the discovery of a new genetic link to systemic sclerosis (SSc).

Maureen D Mayes (The University of Texas Medical School, Houston, TX, USA) explains, "With our latest discovery, we are probably a quarter of the way to finding the genes and pathways responsible for SSc. Once most of the important genes are found, we will be able to focus on developing interventions to block their activity."

Investigators conducted the first genome-wide association study in 2296 SSc patients and 5171 control patients of Caucasian ancestory. Both this study and replication testing 'in an independent case–control set of European ancestry' including 2753 SSc patients and 4569 control patients, discovered the CD247 region of the genome as a new susceptibility locus for SSc. According to Mayes, "This region contains a gene that is central to immunity, which makes this very exciting." The study was also able to confirm the link between three other known areas of the genome, namely MHC, IRF5 and STAT4, and SSc.

Mayes says that scientists plan a second study in which patients will be recruited from ten scleroderma centers in the USA and Canada.

Sources: Radstake TR, Gorlova O, Rueda B *et al.*: Genome-wide association study of systemic sclerosis identifies CD247 as a new susceptibility locus. *Nat. Genet.* 42(5), 426–429 (2010); The University of Texas Health Science Center at Houston News Room www.uthouston.edu/media/newsreleases/nr2010/index.htm?id=1963629