

# Bulletin Board

## Number of sufferers disabled by arthritis is growing

A recent article from the American CDC and the US Census Bureau analyzed the most recent data from the Survey of Income and Program Participation (SIPP) and found that there has been an increase of over 3 million Americans with disability since 1999.

The three most common causes of disability continued to be arthritis or rheumatism (affecting an estimated 8.6 million persons), followed by back or spine problems (7.6 million) and heart trouble (3.0 million).

The authors speculated that “with the aging of baby boomers, the prevalence of arthritis is expected to rise by 40% – that is up to 67 million people – by the year 2030 ... These findings suggest a critical need to expand the reach of effective strategies aimed at disability prevention and management.”

The report also found that women (24.4%) had a significantly higher prevalence of disability compared with men (19.1%) at all ages, with women most likely to cite arthritis as the cause of their disability.

The study also saw a rise in the number of people who reported arthritis as being the primary cause of disability; by one million. The Arthritis Foundation believes that findings from this study must be taken into consideration and requires action, with arthritis research and prevention efforts strengthened to reduce and minimize the burden of arthritis.

All members of the sample frame of selected households were invited to participate in a voluntarily SIPP panel. Panels are active for 2.5–4 years, during which computer-assisted in-person interviews are conducted in 4-month intervals that include supplemental questionnaires. Participants were asked “Because of a physical or mental health condition, [do you] have difficulty doing any of the following by yourself?” Disability was defined as a ‘yes’ response to at least one

of the following limitation categories: use of an assistive aid (cane, crutches, walker or wheelchair), difficulty performing activities of daily living or instrumental activities of daily living, or specified functional activities, one or more selected impairments, or limitation in the ability to work around the house or at a job or business.

John Kippel, president and CEO of the Arthritis Foundation discussed: “Arthritis is a debilitating disease that profoundly impacts the lives of millions of Americans on a daily basis ... The effects of the 46 million Americans with arthritis on the economy are enormous; the direct and indirect medical costs of this disease are estimated to be US\$128 billion each year.”

Disability caused by arthritis often deprives people of the ability to live independently. Individuals with arthritis often report needing help with mobility and simple daily activities.

The Arthritis Foundation has recommended to Congress that funding for the CDC Arthritis Program be increased by US\$10 million for a total appropriation of US\$23 million.

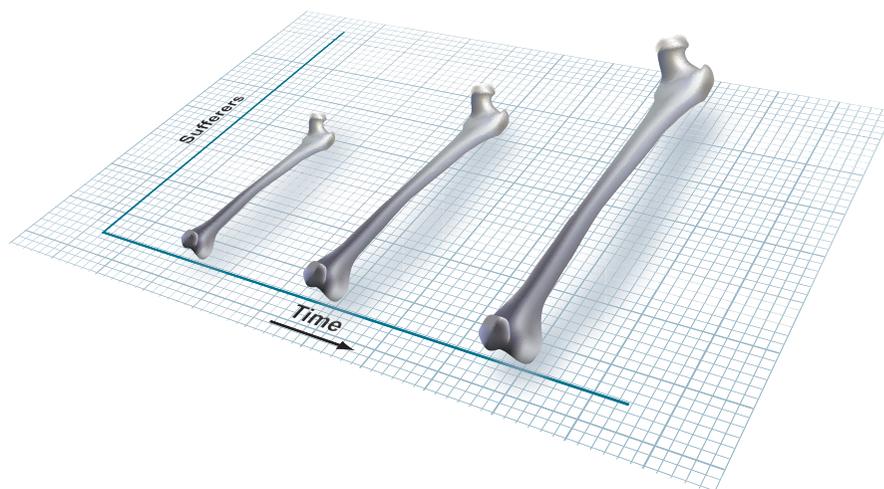
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Additionally, the Arthritis Foundation is working to curb the impact of arthritis through the Arthritis Prevention, Control and Cure Act (H.R.1210), which proposes strengthening public health prevention initiatives to ensure early diagnosis and appropriate management to help prevent permanent disability.

These findings are said to demonstrate that more investment is required so to avoiding paying for the burden of the disease.

Source: MMWR May, 58(16), 421–426 (2009)  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5816a2.htm>



# Anakinra demonstrates a modest benefit for treating rheumatoid arthritis

The drug anakinra has a moderate beneficial effect for patients suffering from rheumatoid arthritis (RA), according to a recent *Cochrane Systematic Review*; however, the study warns of the possible risks of serious infections and discourages the use of anakinra with other biologic drugs.

Rheumatoid arthritis is a chronic inflammatory condition of the joints, estimated to affect up to 1% of the worldwide population. In RA sufferers, the immune system mounts an aberrant attack on the joints, causing them to become inflamed, stiff and painful.

Various treatments for the disease are available, including painkillers, anti-inflammatory drugs and steroids, which are used to suppress the symptoms, and disease-modifying antirheumatic drugs, which act to inhibit or halt the underlying immune process. In the past decade, a new breed of drugs – the biologics – has greatly improved and expanded treatment options for RA.

Anakinra is one such member of this newer class of medication that acts to dampen the inflammation associated with RA through blocking the biologic activity of the proinflammatory cytokine IL-1.

The recent review evaluated the clinical efficacy and safety of the drug for treating RA in adults. Data was compiled from five trials of anakinra,

involving 2876 patients in total, and the study concluded that the drug is a relatively safe and moderately efficacious biologic therapy for RA.

“On the basis of these results, we recommend that doctors avoid combining biologic medications with anakinra when treating patients with rheumatoid arthritis”

Nevertheless, the improvements observed were notably less than those demonstrated for other biologics, and the authors recommend using anakinra for RA with caution, owing to the increased rate of serious infections.

Moreover, one study in the review explored the combination of anakinra with etanercept – another biologic used for the treatment of RA – and found a significant increase in the number of serious adverse events. “On the basis of these results, we recommend that doctors avoid combining biologic medications with anakinra when treating patients with rheumatoid arthritis,” said lead researcher Marty Mertens.

Source: Mertens M, Singh JA: Anakinra for rheumatoid arthritis. *Cochrane Database Syst. Rev.* 1, CD005121 (2009).

## 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...

EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics.

Bertsias G, Ioannidis JPA, Boletis J *et al.*: *Ann. Rheum. Dis.* 67(2), 195–205 (2008)

The EULAR Task Force on SLE, comprising of 19 specialists and a clinical epidemiologist, used the Delphi technique to compile management questions regarding SLE. A systematic search of PubMed and Cochrane Library Reports was performed using McMaster/Hedges clinical queries' strategies for questions related to the diagnosis, prognosis, monitoring and treatment of SLE. Evidence was categorized based on sample size and type of design, and the categories of available evidence were identified for each recommendation. The strength of recommendation was assessed and agreement on the statements was measured across the 19 specialists. A total of 12 questions were generated regarding the prognosis, diagnosis, monitoring and treatment of SLE. Recommendations for the management of SLE were developed using an evidence-based approach followed by expert consensus, with high level of agreement among the experts.

Health-related quality of life, physical function, fatigue, and disease activity in children with established polyarticular juvenile idiopathic arthritis.

Ringold S, Wallace CA, Rivara FP: *J. Rheumatol.* (2009) (Epub ahead of print)

The study compares the child self-report and parent/proxy report of health-related quality of life, disability, and fatigue in children with active polyarticular juvenile idiopathic arthritis (JIA) with that of children with inactive polyarticular JIA, and previous data from healthy controls. A cross sectional survey of children with polyarticular JIA was used along with a variety of assessment questionnaires. The results indicated a 79% response rate. Overall, participants reported lower scores on the Pediatric Quality of Life Inventory (PedsQL) Generic Core Scales and the PedsQL Rheumatology Module than those with inactive disease. Participants also reported lower scores on the PedsQL Multidimensional Fatigue Scale than healthy controls, regardless of disease activity status. Thus, although children with polyarticular JIA and inactive disease reported HRQOL scores similar to those of healthy controls, children with polyarticular JIA tended to report more fatigue regardless of disease activity.

## US FDA approves golimumab for treating three types of immune-related arthritis

The US FDA has approved golimumab (Simponi™) for the treatment of immune-related arthritis including moderate-to-severe rheumatoid arthritis, active psoriatic arthritis and active ankylosing spondylitis.

The drug is a new fully human monoclonal antibody (MAb) against TNF and is administered subcutaneously in combination with the immunosuppressant drug methotrexate in patients with rheumatoid arthritis. It also may be used with or without methotrexate for psoriatic arthritis and alone in patients with ankylosing spondylitis.

It will be used as a monthly treatment for adults with moderate-to-severe rheumatoid arthritis and is said to provide “another treatment option for patients with these three debilitating

disorders ... the steps we’re taking to minimise the risks will give patients the same level of safety protection required for other drugs in its class”, explains Bob Rappaport, Director of the Division of Anesthesia, Analgesia and Rheumatology Products, Center for Drug Evaluation and Research, US FDA.

“...the steps we’re taking to minimise the risks will give patients the same level of safety protection required for other drugs in its class”

The drug targets and neutralizes TNF- $\alpha$ , a protein that, when overproduced in the body owing to chronic inflammatory diseases, can cause inflammation and damage to bones, cartilage and tissue.

In clinical trials, patients who received golimumab for one of the three conditions showed improvements in the signs and symptoms common to their form of arthritis.

The US FDA warns of the potential risk associated with TB and invasive fungal infections, owing to the TNF- $\alpha$  blocking mechanism involved.

The most common adverse reactions to golimumab include upper respiratory tract infection, sore throat and nasal congestion. When treating a debilitating disease like rheumatoid arthritis, it is important to have several treatment options, and the safety and efficacy data that has been produced is very encouraging for golimumab.

Source: US FDA press release <http://www.fda.gov/bbs/topics/NEWS/2009/NEW02000.html>

## Neurotransmitter receptor may modulate inflammation in rheumatoid arthritis synovium

Recent evidence suggests that the  $\alpha 7$  nicotinic acetylcholine receptor ( $\alpha 7$ nAChR) could play a critical role in the regulation of inflammation in rheumatoid arthritis (RA) sufferers. The receptor is expressed in the synovium of patients with RA and is thought that it could be a potential new therapeutic target.

Paul Tak from the University of Amsterdam, The Netherlands, and colleagues explained, “accumulating evidence suggests that fibroblast-like synoviocytes (FLS) play a major role in the initiation and perpetuation of the chronic inflammatory process in RA synovial tissue.”

The receptor was identified by isolating and screening for FLS from arthroscopic synovial biopsy samples. The screening demonstrated that a specific  $\alpha 7$ nAChR potently modulated IL-8 and matrix metalloproteinase expression in FLS.

Current studies are indicative of the importance of neurotransmitters

as modulators of inflammation; the  $\alpha 7$ nAChR is expressed by various immune cells, including monocytes, macrophages, T and B lymphocytes and dendritic cells, and thus was already thought to have an important role in RA.

“Accumulating evidence suggests that FLS play a major role in the initiation and perpetuation of the chronic inflammatory process in RA synovial tissue.”

Further studies revealed that the  $\alpha 7$ nAChR was expressed in the inflamed synovium of RA patients, predominantly in the intimal lining layer and also, to a lesser extent, in the synovial sublining. The study then confirmed the expression of  $\alpha 7$ nAChR mRNA in cultured FLS from eight RA patients.

Functional studies examined the effects of  $\alpha 7$ -specific agonists on the production of IL-6 and IL-8 by activated FLS. The team found that the cholinergic agonists significantly decrease TNF- $\alpha$ -induced IL-6 and IL-8 production.

Tak and colleagues concluded “The data show that  $\alpha 7$ -specific agonists can modulate the inflammatory response of FLS, which suggests the importance of  $\alpha 7$ nAChR, and perhaps dup $\alpha 7$ , in the regulation of proinflammatory cytokines and chemokines...Targeting the  $\alpha 7$ nAChR could provide a novel anti-inflammatory approach to the treatment of RA,” they added.

Source: Maanen MA, Stoof SP, Zanden EP, Jonge WJ *et al.*: The  $\alpha 7$  nicotinic acetylcholine receptor on fibroblast-like synoviocytes and in synovial tissue from rheumatoid arthritis patients: a possible role for a key neurotransmitter in synovial inflammation. *Arthritis Rheum.* 60(5), 1272–1281 (2009).