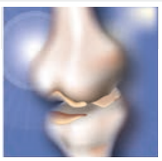
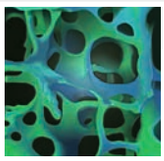




Bulletin Board

Approximately half of fibromyalgia patients have evidence of nerve damage

Damage to nerve fibers in the skin and evidence of small-fiber polyneuropathy (SFPN) were found in approximately half of a small group of fibromyalgia patients.

In contrast to fibromyalgia, which has no known causes and few effective treatments, the pathology behind SFPN is known as are the medical conditions that cause it, which can often be treated and sometimes cured.

"This provides some of the first objective evidence of a mechanism behind some cases of fibromyalgia and identifying an underlying cause is the first step towards finding better treatments," said Anne Louise Oaklander, corresponding author of the paper and director of the Nerve Injury Unit in the MGH Department of Neurology.

> "In 13 out of the 27 fibromyalgia patients, a marked reduction in nerve fiber density, abnormal autonomic function tests or both was observed, which demonstrates the presence of small-fiber polyneuropathy."

Fibromyalgia affects approximately 1–5% of the population in western countries, more commonly women. The term covers a set of symptoms that include chronic widespread pain, increased sensitivity to pressure and fatigue.

Although the diagnosis of fibromyalgia is accepted by the NIH and the ACR, the biological processes underpinning the disease are, as yet, unknown. Fibromyalgia and SFPN share many symptoms, but SFPN is a recognized cause of widespread pain for which there are accepted, objective tests.

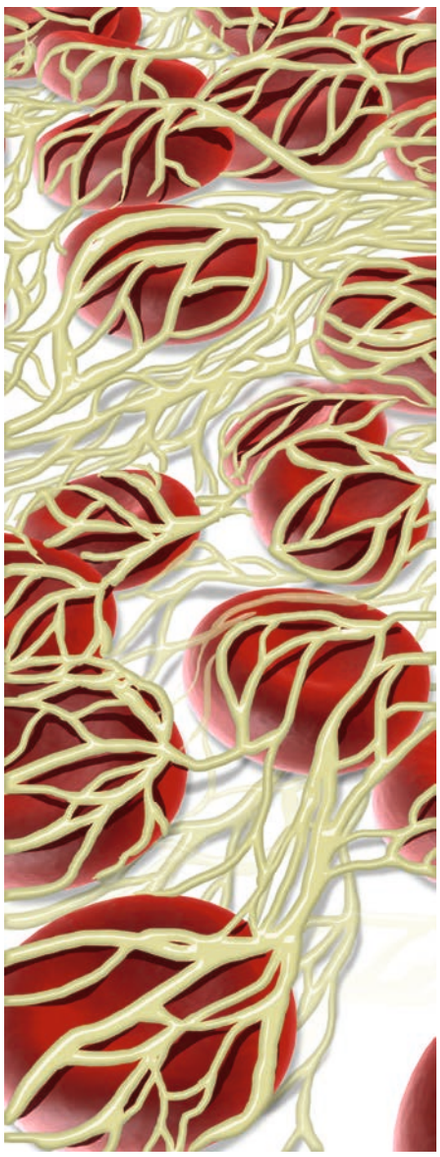
This study, which was recently published in *Pain*, involved 27 adult fibromyalgia patients and 30 healthy volunteers. All participants underwent a range of tests that are used in the diagnosis of SFPN, these included assessments of neuropathy based on physical examination and a questionnaire, skin biopsies that evaluated the number of nerve fibers in the lower leg, and tests of autonomic functions such as heart rate, blood pressure and sweating.

Significant levels of neuropathy were observed in the fibromyalgia group, but not the controls based on the questionnaires, examination assessments and skin biopsies. In 13 out of the 27 fibromyalgia patients, a marked reduction in nerve fiber density, abnormal autonomic function tests or both was observed, which demonstrates the presence of SFPN. Blood tests for known causes of the disorder were also performed on those who met criteria for SFPN. While none of those who met the criteria had evidence of diabetes, which is a common cause of SFPN, two patients were found to be suffering from hepatitis C virus infection, which can be treated, and over half showed signs of immune system dysfunction.

Oaklander said, "Until now, there has been no good idea about what causes fibromyalgia, but now we have evidence for some but not all patients. Fibromyalgia is too complex for a 'one size fits all' explanation. The next step of independent confirmation of our findings from other laboratories is already happening, and we also need to follow those patients who did not meet SFPN criteria to see if we can find other causes. Helping any of these people recieve definitive diagnoses and better treatment would be a great accomplishment."

Source: Oaklander AL, Herzog ZD, Downs HM, Klein MM. Objective evidence that small-fiber polyneuropathy underlies some illnesses currently labeled as fibromyalgia. *Pain* doi:10.1016/j.pain.2013.06.001 (2013) (Epub ahead of print).

in the news...



Risk of leg and lung blood clots increased in those with rheumatoid arthritis

A large nationwide study has produced evidence that rheumatoid arthritis (RA) causes an increase in the potential for developing dangerous blood clots in the leg and lungs. The research is published online in the *Annals of the Rheumatic Diseases*.

Evidence from the study indicates that, within 30 days of diagnosis, between 11 and 30% of those with a deep-vein thrombosis (DVT) or pulmonary embolism (PE) will have died.

Despite the fact that several studies have shown that chronic inflammation, a state associated with RA, is linked to an increased risk of thickened blood, RA is not commonly considered to be a risk factor for blood clots, say the researchers.

In order to discover whether RA increased the risk of potentially fatal blood clots, the researchers followed the health of the majority of Taiwan's population using the country's compulsory national insurance scheme from 1998 to 2009. A further monitoring period up to 2010 was also added.

During this time, just under 30,000 people were seen to develop arthritis, details of these cases were added into a national (catastrophic illness) registry of the National Health Insurance Database. For analysis purposes, the RA group were matched with just under 117,000 healthy individuals of the same age and sex.

Women made up just over three-quarters (77%) of those who developed RA, with 52 years being the average age at diagnosis. Those over 65 years made up approximately one-fifth of the total patients.

RA patients were more likely to have additional underlying conditions than the control group. These included high blood pressure, diabetes, high cholesterol, heart failure and fractures.

Analysis demonstrated that patients with RA were significantly more likely to develop potentially fatal blood clots when the effect of underlying condition and age were taken into account.

Figures revealed that when compared with those without RA, those with the condition were three-times as likely to suffer a DVT and twice as likely to suffer a PE.

In addition, RA was seen to have the greatest effect in the under 50s, who, when compared with either middle aged or older adults, were nearly six-times as likely to develop a DVT and three-times as likely to develop PE.

> "...within 30 days of diagnosis, between 11 and 30% of those with a deep-vein thrombosis or pulmonary embolism will have died."

Source: Chung WS, Peng CL, Lin CL *et al.* Rheumatoid arthritis increases the risk of deep vein thrombosis and pulmonary thromboembolism: a nationwide cohort study. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2013-203380 (2013) (Epub ahead of print).

Children with chronic arthritis show premature aging of immune cells in joints

Children suffering from the most common form of inflammatory arthritis have immune cells in their joints that resemble those from 90 year olds, new research from the Children's Hospital of Pittsburgh of UPMC (PA, USA) and the University of Pittsburgh School of Medicine (PA, USA) has shown.

The results may mean that premature aging of immune cells could be prevented through the use of innovative treatment approaches. Senior researcher Abbe de

Vallejo, associate professor of medicine and immunology at Pitt School of Medicine said that juvenile idiopathic arthritis (JIA) affects one in 1000 children in the USA and is the most prevalent rheumatic condition in the world. A swollen ankle, knee or wrist is often the first sign and this is usually put down to a minor injury picked up while playing.

de Vallejo said, "Untreated JIA has devastating consequences. It can slow growth and, in extreme cases, the child can be physically disfigured. It's a degenerative disease that eats up the joints."

JIA has long been assumed to be an autoimmune disease. However, de Vallejo has shown that signs of abnormal cell division and premature aging are present in a population of cells found in the joint synovial fluid in young adults with rheumatoid arthritis. de Vallejo and his team have been investigating whether this is true in pediatric arthritis.

Synovial fluid and blood from 98 children aged 1–17 years with a diagnosis of JIA was taken in order to examine T cells – immune cells that protect the body by eradicating infection and responding to other dangerous agents to which an individual is exposed. The results were compared with 46 blood samples from children without the disease.

In children with JIA, one-third of T cells were found to have shortened telomeres with a reduced, or completely absent, ability to proliferate. Telomeres are found at the end of chromosomes and do not code for proteins. As they are not fully copied by enzyme mechanisms, they become slightly shorter during each DNA replication cycle. Aging is thought to occur when normal DNA replication and cell division can no longer proceed as the telomeres have become too short.

"The T cells of the children with JIA had very short telomeres, about the level we see in a 90 year old or a young adult with rheumatoid arthritis. Those same T cells express unusually high levels of several classic protein markers of cell aging and exhaustion," de Vallejo said. "These kids haven't lived long enough to have cells that look that old. This is the first indication that premature aging is occurring in this childhood condition."

The immune activity of the T cells could also be stimulated through atypical cell surface receptors as the cells had become dysregulated. Although these findings could lead to novel treatments, much more need to be discovered about the unusual cells and the genetic mechanisms that might contribute to the development of JIA.

de Vallejo added, "JIA is typically treated with broad-spectrum drugs such as steroids and biologics that essentially paralyze the entire immune system, but only one-third of cells are affected and their abnormality seems to be premature aging rather than autoimmune activity. This study suggests cell-targeted treatments could be developed to prevent this premature immune aging."

"This study suggests cell-targeted treatments could be developed to prevent this premature immune aging."

Source: Dvergsten JA, Mueller RG, Griffin P *et al.* Premature cell senescence and T cell receptor-independent activation of CD8 T cells in juvenile idiopathic arthritis. *Arthritis Rheum.* 65(8), 2201–2210 (2013).

Targeted treatment of childhood arthritis in the future?

The discovery of potential markers for the severity of childhood arthritis by researchers at the University of Adelaide (Adelaide, Australia) and Women's and Children's Hospital (Adelaide, Australia) could lead to children with this disease receiving targeted therapy.

Changes in the levels of a set of molecules known as prostanoids, which are formed from essential fatty acids, have been shown in a study of 115 children with juvenile arthritis. Detection of these changes in the blood could allow the course of the disease to be more accurately monitored and could lead to more individualized treatment.

One in every 500 children are affected by juvenile arthritis, a condition that is as common as juvenile diabetes. However, although many treatments are available, a

significant proportion of children do not respond to standard treatments.

Christina Boros, Senior Lecturer in the University of Adelaide School of Pediatrics and Reproductive Health, researcher in the Robinson Institute (Adelaide, Australia) and Head of Rheumatology at the Women's and Children's Hospital said, "Juvenile arthritis can present at any age, with some children diagnosed as early as 6–9 months. The longer children go without treatment, the more likely they are to have permanent joint damage."

Boros added, "So far we've been able to determine relationships between the blood levels of molecules called prostanoids and disease activity in childhood arthritis. These appear to be more accurate than traditional blood markers of inflammation. This is promising research. We are now expanding our study to look at a larger group of children with arthritis, and how prostanoids may predict arthritis disease activity over time as well as how the use of medications affects prostanoid levels."

As well as changing treatment of juvenile arthritis, having confirmed biomarkers could reduce the physical, emotional and financial burden of the disease, Dr Boros said.

"There are many medications available for juvenile arthritis but unfortunately there is still no cure. Anything that can improve treatment and prevent joint damage is welcome."

Source: Potential markers for severity of childhood arthritis. www.sciencedaily.com/releases/2013/07/130712102443.htm

– All stories written by Sarah Jones

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of rheumatology. If you have newsworthy information, please contact: Sarah Jones, Commissioning Editor, *International Journal of Clinical Rheumatology*, Future Medicine Ltd, s.jones@futuremedicine.com