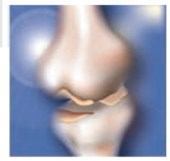
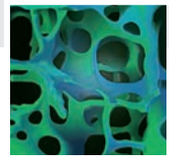




Bulletin Board

Neuromyelitis optica often misdiagnosed as multiple sclerosis, according to Mayo Clinic neurologist

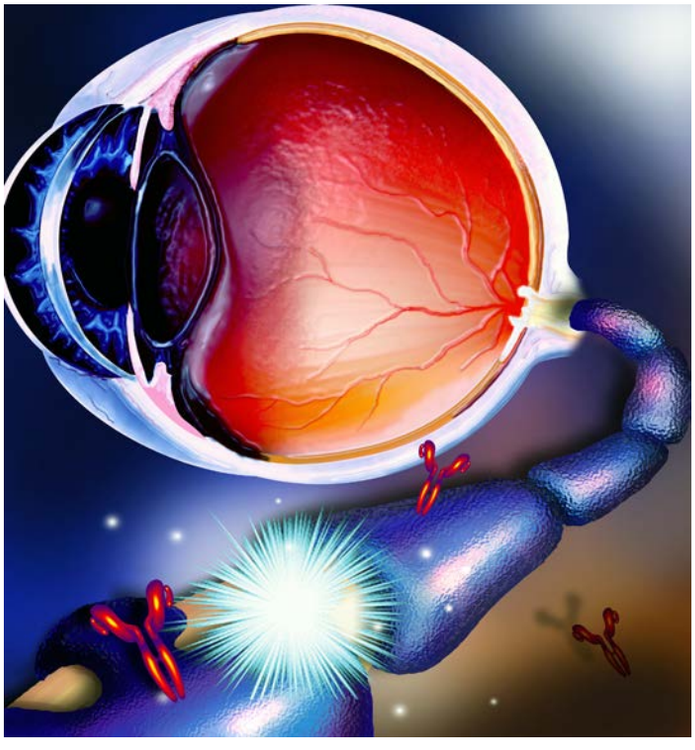
According to findings presented by Sean Pittock of the Mayo Clinic, MN, USA, thousands of neuromyelitis optica (NMO) patients could be misdiagnosed with multiple sclerosis (MS) owing to a lack of awareness of NMO within the medical community.

Neuromyelitis optica is a rare, debilitating disease that attacks the spinal cord and optic nerves, and can cause vision loss, paralysis of legs and arms, and sensory disturbances. Pittock arrived at his conclusion based on ongoing research at the Mayo Clinic. Out of approximately 1200 blood samples sent to the Mayo Clinic for NMO antibody (NMO-IgG) testing each month, approximately 70 new patients test positive for NMO – a high figure considering the disease is believed to be rare. Of the patients who have the NMO antibody, Pittock found that most were previously thought to have MS.

The Mayo Clinic's recent discovery of NMO-IgG has assisted in distinguishing MS and NMO, and this is the first biomarker shown to be sensitive and specific for a CNS inflammatory demyelinating disease. "It is important to differentiate NMO from MS as these disorders are treated differently," says Pittock. "The identification of this novel antibody marker will hopefully assist neurologists in making a correct diagnosis of NMO, rather than MS."

Pittock believes that the fact that until recently there was no biomarker is part of the reason for the lack of awareness of NMO, and, traditionally, NMO was considered by many in the medical community to be a form of MS, which itself is difficult to diagnose. Recent studies now support the idea that NMO is distinct from MS. "It is important for the neurologists to be aware that NMO is associated with symptoms other than optic neuritis and transverse myelitis. NMO patients can have intractable hiccups, nausea and vomiting, as well as problems with thermoregulation," says Bruce Cree of the University of California San Francisco Multiple Sclerosis Center (CA, USA). "It is important to test for the presence of the antiaquaporin 4 antibody, in the setting of neurological illness presenting with these symptoms as well as optic neuritis and myelitis, even in patients who have abnormal brain MRI findings. Some of these abnormalities can appear to be identical to those observed in MS, whereas others are more distinct of NMO." Mayo Clinic neurologist Dean Wingerchuk also reported at the conference that the prevalence and incidence of NMO have not been firmly established. Based on current data, the suggestion is that there are probably more than 4000 people with NMO in the USA. As a result of this, the Guthy-Jackson Charitable Foundation is launching a medical education campaign with the aim of increasing doctors' awareness of the differences between MS and NMO. It is hoped that by doing so, this will help patients get the appropriate treatments and will enable more researchers to collect the best data in their pursuit of a cure.

Source: Guthy-Jackson Foundation press release (www.guthy-jacksonfoundation.org/pdf/Guthy-Jackson SymposiumRelease 11.11.09.pdf)



in the news...

Ocrelizumab appears to be promising, according to STAGE trial study results

Results from a Phase III study investigating the efficacy of ocrelizumab in treating the signs and symptoms in rheumatoid arthritis (RA) patients were recently announced. The Study of Ocrelizumab Compared to Placebo in Patients with Active Rheumatoid Arthritis Continuing Methotrexate Treatment (STAGE) trial was a Phase III, randomized, three-arm, parallel-group, placebo-controlled study. A total of 1015 patients with active RA and an inadequate response to previous treatment with methotrexate (MTX) were recruited. The primary end point of the study was to assess the number of patients with an American College of Rheumatology (ACR)20 response at weeks 24 and 48.

> "...(patients) treated with methotrexate and ocrelizumab demonstrated a notable improvement in the signs and symptoms of (rheumatoid arthritis)..."

Investigators randomized patients to receive either 200 or 500 mg ocrelizumab intravenously. Infusions of ocrelizumab or placebo were given on days 1 and 15, in addition to weekly MTX. Infusions were repeated after 6 months.

Compared with patients who received MTX plus placebo, those treated with MTX and ocrelizumab demonstrated a notable improvement in the signs and symptoms of the disease at weeks 24 and 48. Adverse events were comparable between the two treatment groups; however, serious infections were more common in the ocrelizumab-treated group in comparison to the placebo group. Further analyses of safety are being undertaken and will be presented at a forthcoming meeting.

> "...serious infections were more common in the ocrelizumab-treated group in comparison to the placebo group."

At present, there are three other Phase III studies investigating the use of ocrelizumab; FEATURE is investigating the effects of a single infusion of the drug. The SCRIPT and FILM studies are assessing the effects of ocrelizumab in patients with an inadequate response to TNF-α inhibitors and MTX-naive individuals, respectively. The results of these three trials are expected in the first half of 2010.

Source: Genentech, news (www.gene.com/gene/news/press-releases/display.do?method=detail&id=12487)

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...

Long-term improvement of lipid profile in patients with refractory systemic lupus erythematosus treated with B-cell depletion therapy: a retrospective observational study.

Pego-Reigosa JM, Lu TY, Fontanillo MF, Campo-Pérez VD, Rahman A, Isenberg DA: *Rheumatology (Oxford)* (2010) (Epub ahead of print).

Discusses the use of B-cell depletion therapy (BCDT) in patients with active SLE, who had failed standard immunosuppressive therapy, and the effect on lipid abnormality, which increases the risk of premature atherosclerosis. A total of 12 patients with refractory SLE treated with BCDT based on rituximab; lipid profile and lupus activity were measured before the infusions and again at 1-year follow-up. Results indicated a decrease in mean levels of total, high-density lipoprotein and low-density lipoprotein cholesterols from baseline at 1 year. The atherogenic index was 3.8 at baseline and decreased to 2.7. A decrease in triglyceride and global British Isles Lupus Assessment Group (BILAG) index score was also observed. The control group demonstrated no differences in any of the lipid determinations over a 1-year period. This study suggests a favorable long-term effect of BCDT on the lipid profile of patients with refractory SLE, which correlated with decreasing activity of the disease.

First-line DMARD choice in early rheumatoid arthritis – do prognostic factors play a role?

Rachapalli SM, Williams R, Walsh DA, Young A, Kiely PD, Choy EH; on behalf of the Early Rheumatoid Arthritis Network (ERAN). *Rheumatology (Oxford)* (2010) (Epub ahead of print).

Examines prognostic factors to predict the choice of first disease-modifying antirheumatic drugs (DMARD) for patients with rheumatoid arthritis (RA). Details of 616 patients with early RA were collected from 16 centers in the UK Early Rheumatoid Arthritis Network (ERAN). Logistic regression was used to identify whether Health Assessment Questionnaire (HAQ) score, swollen joint count, nodules, rheumatoid factor, erythrocyte sedimentation rate, C-reactive protein and erosions on radiographs were associated with the choice of first DMARD treatment. A total of 547 patients were started on a DMARD therapy, 253 on methotrexate, 230 on sulfasalazine, 47 on other DMARD monotherapies and 17 on combination DMARD therapy. The authors conclude that rheumatologists in ERAN appear to preferentially prescribe methotrexate for patients with a poor prognosis and sulfasalazine for patients with good prognosis as monotherapy in early RA; no DMARDs were used in older patients or in those with a low HAQ score.

Lupuzor™ demonstrates promising results in the treatment of systemic lupus erythematosus

Results from a Phase IIb trial assessing the efficacy of Lupuzor™ for the treatment of systemic lupus erythematosus (SLE) have demonstrated statistically significant superiority over placebo.

> "We are pleased to have the opportunity to further develop Lupuzor and potentially bring a new medication to the lupus patients who have waited 50 years for new therapy."

The Phase IIb study was a randomized, double-blind, placebo-controlled, dose-ranging study conducted in 150 patients suffering from SLE. The aim of the trial was to evaluate the efficacy of Lupuzor over a period of subcutaneous injections of either Lupuzor 200 µg once a month, Lupuzor 200 µg twice a month or placebo.

The primary end point was defined as a decrease of at least four points in the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score – an assessment of the clinical activity of lupus patients, where a lower score reflects lower disease activity.

It was found that 53 and 45% of patients were SLEDAI score responders in the Lupuzor once-a-month and twice-a-month groups, respectively, in comparison to 38% in the placebo group. In the moderate-to-severe subgroup, 62 and 48% of patients were responders in the Lupuzor once-a-month and twice-a-month groups, respectively, in contrast to 41% in the placebo group. Lupuzor was well tolerated and its safety profile was better than placebo.

> "Lupuzor was well tolerated and its safety profile was better than placebo."

Lupuzor is now licensed to Cephalon Inc., PLC, UK, and is in preparation for Phase III clinical trials. Frank Baldino Jr, Cephalon's Chairman and CEO, stated: "We are pleased to have the opportunity to further develop Lupuzor and potentially bring a new medication to the lupus patients who have waited 50 years for new therapy."

Source: ImmuPharma PLC, UK (www.immupharma.com)

New study demonstrates efficacy of shock-wave therapy in repairing bone

Data from a study recently published in the *Journal of Bone and Joint Surgery* have suggested that the technique of shock-wave therapy may be as effective as surgery in the treatment of long-bone nonunion.

> "The research team is optimistic that shock-wave therapy will be a welcome addition to a treating physician's options for repairing fractures that do not heal naturally."

In the study, 126 patients with non-unions in the femur, tibia, ulna or radius were randomized to one of three groups. Of the three groups, two received shock-wave therapy while the third received surgical treatment. The two shock-wave groups were treated with different energy flux densities during four treatments, each of 4000 shock-wave impulses. The primary outcome for the study was radiographic results, with clinical results as a secondary outcome; subjects were evaluated at 3, 6, 12 and 24 months following the procedure.

At the 6-month evaluation point, there was no significant difference in the primary outcome for all three of the treatment groups, but a significant difference was found in the secondary outcome at the 6-month evaluation, with both shock-wave treated groups demonstrating improved clinical outcomes compared with the patients treated surgically.

It is thought that shock-wave therapy induces the regeneration of bone through the activation and stimulation of specific growth factors, and that this may induce a metabolic response that is similar to the natural bone-healing process.

The research team is optimistic that shock-wave therapy will be a welcome addition to a treating physician's options for repairing fractures that do not heal naturally.

> "...shock-wave therapy induces the regeneration of bone through the activation and stimulation of specific growth factors..."

Sources: Cacchio A, Giordano L, Colafarina O *et al.*: Extracorporeal shock-wave therapy compared with surgery for hypertrophic long-bone nonunions. *J. Bone Joint Surg. Am.* 91(11), 2589–2597 (2009); American Academy of Orthopaedic Surgeons (www.aaos.org)