My prog-MS ezine

For people with progressive MS and those interested in it

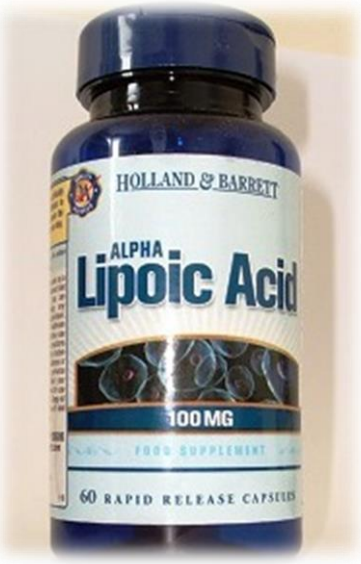
Issue number 15, September/October 2017 (free edition)

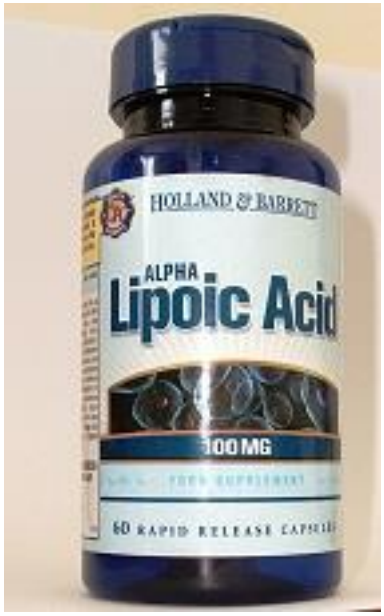
Welcome to issue 15 of my ezine about progressive MS and MS progression. My name is Ian Cook. I'm a secondary progressive MSer from Birmingham, UK.

In this issue are six pages of news plus a feature about issues that matter to prog-MSers. In news there's a story about research that asks whether a common stomach bug is linked to MS progression and a story about an experimental new diabetes drug that seems to have the potential to re-myelinate. The feature on page 6 looks at a recent seminar where top neurologists discussed treatment options at home and abroad for us progressives. The findings are surprising and well worth reading.

If there is any story you would like me to follow then I'm at iancookjournalist@yahoo.co.uk

IN THIS ISSUE





Over the counter anti-oxidant pill could slow SPMS brain shrinkage

A US study suggests large doses of lipoic acid, an over-the-counter anti-oxidant can slow down the rate of brain shrinkage in secondary progressive MS and also help prevent falls.

The research was published in Neuroimmunology and Neuroinflammation and carried out at Oregon Health & Science University(OHSU) in the US. In the study 27 people were given a 1,200-miligram (mg) daily dose of lipoic acid, and 24 people given a placebo for two years. "These are high doses," said lead author Rebecca Spain, M.D., M.S.P.H., an assistant professor of neurology in the OHSU School of Medicine. (Lipoic acid pills on sale in the high street are usually 300 or 600 mg)

She added: " While it seems safe, we won't know whether it actually improves the lives of people with MS until we can replicate the results in the pilot study through a much bigger clinical trial. Fortunately, we're going to be able to answer that question with the participation of kind volunteers."

The major finding of the pilot study involved measuring the degree to which lipoic acid arrested the rate of whole brain atrophy or shrinkage, as measured through magnetic resonance imaging (MRI). The study revealed a 68 percent improvement over the placebo in slowing the rate of whole brain atrophy in patients with secondary progressive MS.

These results are impressive. For the sake of comparison, a clinical trial involving the recent FDA-approved pharmaceutical Ocrevus (ocrelizumab) showed an 18 percent improvement over a placebo in slowing the rate of whole brain atrophy for patients with primary progressive forms of the disease.

In addition, the lipoic acid pilot study suggested slightly improved walking times and fewer falls among study participants who took a daily dose of lipoic acid compared with those who received the placebo. Researchers are eager to test these outcomes in the larger clinical trial.

More details of all stories on p9

Pancreas may provide potential drug candidate for regenerating myelin – a new drug is in clinical studies

A substance secreted by the pancreas may promote regeneration of myelin, the protective nerve coating that is damaged in multiple sclerosis.

In a study carried out on mice and titled "Peripherally derived FGF21 promotes remyelination in the central nervous system," scientists found that the substance, fibroblast growth factor 21, or FGF21, promotes remyelination in mice. Remyelination is the renewal of the myelin sheath and is seen as the key to repairing the nerve damage that has accumulated in progressive MS.

Myelination is carried out by a specific type of nerve cell called an oligodendrocyte. In normal development, oligodendrocyte precursor cells (OPCs) differentiate into oligodendrocytes, which are required for myelination. OPCs will proliferate around the lesions of demyelination after injury and contribute to spontaneous remyelination, but the molecular mechanism of OPCs proliferation is not fully understood.

In Japan's Osaka University Associate Professor, Rieko Muramatsu focused on the blood leakage around demyelinating lesion. "Factors in the blood cannot reach the normal brain because the central nervous system has a blood-brain barrier. In demyelinatiing diseases like multiple sclerosis, the blood-brain barrier around the lesion is disrupted," she said.

Muramatsu suspected that with the breach, factors from peripheral organs secreted into the blood could now reach the brain.

To test her hypothesis she disrupted the vascular barrier and myelin structures in mice by injecting Lysophosphatidylcholine (LPC). " We looked for circulating factors that promote OPCs proliferation and found FGF21 as a candidate," she explained.

The results suggest that FGF21 has therapeutic potential for demyelinating diseases. FGF21 analogues are already being used for clinical studies on diabetes, which means its development for remyelination could go faster than had it been an untested compound.

"There are many drugs that inhibit demyelination, but none that promote remyelination. FGF21 is a new candidate that deserves more testing. The most important finding is that we show the peripheral milieu promotes central nervous system remyelination."

The study was published in the Journal of Clinical Investigation.

For further details of all news stories go to page 9

Resistance training may slow progression in MS

New research has revealed that resistance training protects the brains of people with MS, something which may delay the progression of the disease.

The research study was conducted in Denmark and Germany and published in Multiple Sclerosis Journal.

The study shows that resistance training has a number of positive effects on the brain, which go beyond what can be achieved through effective disease specific medication.

Researcher and Associate Professor Ulrik Dalgas from the Department of Public Health at Aarhus University, said: 'For the past 15 years, we have known that physical exercise does not harm people with MS, but instead often has a positive impact on, for example, their ability to walk, their levels of fatigue, their muscle strength and their aerobic capacity, which has otherwise often deteriorated. But the fact that physical training also seems to have a protective effect on the brain in people with MS is new and important knowledge.'

The study followed 35 people with MS for six months. Half of the group took part in resistance training twice a week, while the other half continued to live their lives normally without systematic training. Prior to and following the six-month period, the test subjects had their brains MRI scanned, and the researchers could see that there was a tendency for the brain to shrink less in those patients who undertook resistance training.

'Among persons with MS, the brain shrinks markedly faster than normal. Drugs can counter this development, but we saw a tendency that training further minimises brain shrinkage in patients already receiving medication. In addition, we saw that several smaller brain areas actually started to grow in response to training,' says Ulrik Dalgas.

More details of all news stories on page 9

Is stomach bug linked to MS progression?

Secondary progressive MS patients have larger quantities of antibodies to the stomach ulcer bug Helicobacter pylori (H.pylori) than those with relapsing-remitting MS, according to research published in the journal Scientific Reports.

The research, carried out at the University of Thessaly in Greece, suggests an immune response to H. pyolori produces large quantities of antibodies which might be linked to progression in MS and may also be connected to disease activity.

The study is "big news" according to the Barts Hospital MS website www.msresearchblogspot.com as it demonstrates that the antibody response to H. Pyolori infection differs between pwMS and controls, as well as between pwRRMS (Relapsing remitting MS) and pwSPMS (Secondary progressive MS). It also appears to be linked with disease activity.

The team behind the new research recruited 102 patients with RRMS, 37 with SPMS and 68 healthy people to determine whether antibodies to various proteins on the H. pylori microbe's surface might differ between MS patients and healthy people.

Reactivity against specific H. pylori immune-dominant antigens revealed several differences between people with MS and healthy controls (HCs) , and more importantly between people with RRMS and SPMS. Antibodies to anti Vac-A (a secreted bacterial protein) were four times more frequent in SPMS than in the control group. This is an intriguing finding as this was the only antigen (amongst 7 with different recognition between patients and controls) which is more common in MS patients than the control group.

Why VacA is responsible for this is not clear. It could be that infection with H. pylori could initiate antibody (or T cell)-responses against VacA in genetically prone individuals, which in turn could cross-recognize myelin antigens leading to demyelination in SPMS. Nobody seems to know for certain although there appears to be consensus that these findings are important. What is known is that H. pylori is more common in middle age as is SPMS and there may be a link here. There are other possibilities as the above website www.msresearchblogspot.com points out:

"Many people think that MS is triggered by exposure to infectious agents in our environment. The most well-known putative trigger is EBV, (Epstein Barr virus) but there has also been debate surrounding the role of H. Pylori, an enteric pathogen better known for its role in causing peptic ulcers. Epidemiological evidence has been conflicting on whether H. Pylori infection protects against MS, increases the risk of MS, or has no association at all." **For further details of all news stories go to page 9**

Top doctors discuss drug options for progressive MSers

Neurologists, health researchers, an MS Society representative and a few progressive MSers met recently at Barts Hospital in London to discuss treatments for advanced or progressive MS.

Dr. Klaus Schmierer, a neurologist at London's Barts Hospital, who organised the meeting said real promise lies in cladribine, a drug used for the past 25 years to treat hairy cell leukaemia, but which has also proved effective in relapsing remitting MS. Cladribine is safe, easy to use, is an injectable but also comes in tablet form - and it's cheap as it's a generic drug. Intriguingly, there is also evidence, dating from the early 1990s, that cladribine may slow advanced (progressive) MS. At the moment, about 100 patients at the Royal London Hospital with advanced MS - who have failed other therapies - are using it and finding it effective.

The conference was told that another MS drug which offers hope is rituximab, an injectable, which works in a similar fashion to ocrelizumab (recently licensed by the EMA (European Medicines Agency) in the US for primary progressive MS. Though the NHS has declined to fund rituximab for the treatment of MS in the UK - citing insufficient trial results - Swedish neurologists have been using the drug for RRMS (relapsing remitting MS) and advanced or progressive MS for more than a decade.

"It fulfilled an unmet need and there were fewer options available for advanced MS," said Frederik Piehl, a neurologist from the Swedish Karolinska Institute. In Sweden, he said rituximab has been found to have been highly effective and well tolerated. However in the UK, neurologists are not allowed to prescribe it for their patients. The final drug discussed was ocrelizumab – the drug currently being assessed for licensing by the EMA for RRMS and PPMS (Primary Progressive MS) . There are high hopes for this drug and although it is only licensed for PPMS and not SPMS (Secondary Progressive MS) it does at least present a treatment option for one section of the community of progressive MSers.

For more details see page 9

Unknown B-cell toxin may cause MS progression

B-cells in progressive MS patients' blood secrete toxic substances that cause neurons and myelin-forming cells (oligodendrocytes) to die, according to a new study published in the Journal of Neuro-immunology. Researchers are now seeking to discover more about the link between this cell death (called apoptosis) and the progressive stage of MS.

A research a team led by Dr. Robert Lisak of Wayne State University in Detroit, and Dr. Amit Bar-Or of McGill University in Montreal looked at the blood of MS patients and discovered that B-cells in their blood killed lab-grown neurons and oligodendrocytes - cells which form myelin. Deterioration of myelin and the death of neurons are hallmarks of MS.

The researchers said B-cells trigger apoptosis – a process that tells the cell to die when exposed to stressful factors or toxins. Although the research team screened around 40 inflammation-related substances they were unable to identify which substance caused this apoptosis. Finding this substance is crucial as it may pinpoint the trigger that starts the disease process in MS and leads to its progression. In the next phase of the study the teams plan to learn more about the working process of this toxin, what it is and what causes it to be produced.

B cells, also known as B lymphocytes, are a type of white blood cell that along with T cells form part of the body' immune system.

Disappointing results of trial into new drug for SPMS

A one-year clinical trial of MIS416, a naturally occurring agent derived from bacteria that can potentially alter immune responses in secondary progressive MS, has produced disappointing results.

The recently completed trial involved 93 people with secondary progressive MS in Australia and New Zealand. None of the clinical or MRI measures suggested benefit of MIS416 compared to those taking the placebo.

In spite of the trial outcome the study's sponsor, Innate Immunotherapeutics Limited, have announced plans to continue analysing data to see if there were any subgroups of participants who responded to therapy.

For details of all news stories go to page 9

Survival rates of MSers have increased dramatically in past 50 years

Three studies from Scandinavian countries show people with MS are living longer and the difference in life expectancy between MSers and the general population is narrowing.

The first study, from Sweden, looked at all Swedes with a diagnosis of MS between 1968 and 2012. For each MSer identified, ten individuals without MS but with the same age, gender, county of residence were also selected. The study found there was a 3.5 fold reduction in the risk of death in MSers relative to the general population comparing 1968-1980 to 2001-2012.

The second study used the Danish MS nationwide registry from 1950 to 1999, looked at the survival rates of 12,847 MSers whose mortality was compared to known Danish mortality rates for the general population. This study found that comparing the years 1950-1959 to 1990-1999 there was a 5-fold reduction in lives lost to MS. Survival for MSers increased by an average 15 years.

The third study looked at MSers in Norway from 1953-2012. The risk of death for MSers compared to the general population reduced three- fold from 1953-1974 to 1997-2012.Collectively, these studies with exceptionally long study periods and complete sampling of their source population (thus, making generalizations easier to their target population) demonstrate significant improvements to survival in people with MS.

More than one third of Sativex patients stop taking it in first year

Nearly 40% of MS patients given Sativex, the cannabis based spray for treating MS related spasticity, stopped taking it in the first year of treatment according to research carried out in Italy. During the observation period (January 2014 to February 2015) 631 out of 1,597 (39.5%) patients discontinued the drug with 333 patients (20.8%) discontinuing treatment at 4 weeks while 422 patients (26.4%) discontinued at 6 weeks. Reasons given for discontinuation during the whole observation period were lack of effectiveness for 23.2% of patients and “adverse events” for 16.3% of patients.

For more details of all news stories go to page 9

References contact details etc

Page 2

Lipoic acid story

sources:

http://nn.neurology.org/content/4/5/e374.abstract

https://medicalxpress.com/news/2017-06-patients-multiple-sclerosis-benefit-over-the-counter.html#jCp

Page 3 Pancreas/MS story

http://resou.osaka-u.ac.jp/en/research/2017/20170822_1

https://multiplesclerosisnewstoday.com/2017/08/29/study-reports-that-pancreas-produced-factor-can-renew-ms-related-neuron-sheath/

page 4 Resistance training and progression

Source; MS-UK http://www.ms-uk.org/resistance-training-may-slow-progression-ms

P5stomach bug and MS progression link

Source: https://www.nature.com/articles/s41598-017-07801-9

P6 New drugs seminar

Source: http://multiple-sclerosis-research.blogspot.com/ 21/7/17

Page 7 B-cell toxin

Source: https://www.ncbi.nlm.nih.gov/pubmed/28601295

Page 7 MIS416 study

http://www.ms-uk.org/phase-ii-trial-mis416-secondary-progressive-ms-suggests-no-benefit-060717

Page 8 Longevity story

Sources: Original feature at https://www.acceleratedcure.org/sites/default/files/images/Briggs%20article_073117%20Final%20with%20images.pdf

The three pieces of research are at:

1. https://www.ncbi.nlm.nih.gov/pubmed/28687718

2. https://www.ncbi.nlm.nih.gov/pubmed/28705951

3. https://www.ncbi.nlm.nih.gov/pubmed/28365589

Page 8 Sativex story

Source: Source: Messina S, Solaro C, Righini I, Bergamaschi R, Bonavita S, Bossio RB, Brescia Morra V, Costantino G, Cavalla P, Centonze D, Comi G, Cottone S, Danni MC, Francia A, Gajofatto A, Gasperini C, Zaffaroni M, Petrucci L, Signoriello E, Maniscalco GT, Spinicci G, Matta M, Mirabella M, Pedà G, Castelli L, Rovaris M, Sessa E, Spitaleri D, Paolicelli D, Granata A, Zappia M, Patti F; SA.FE. study group. PLoS One. 2017:12(8):e0180651. doi: 10.1371/journal.pone.0180651. eCollection 2017.

DISCLAIMER:

This ezine is strictly a news and information ezine/website about MS . It does not provide medical advice, diagnosis or treatment. This content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your doctor or other qualified health provider with any questions you may have regarding MS or any a medical condition. Don't disregard professional medical advice or delay in seeking it because of something you have read in this ezine.

To Contact me email iancookjournalist@yahoo.co.uk or via twitter@iancookMSer