My prog-MS ezine

For people with progressive MS and those interested in it

Issue number 11, January-February 2017

Hello and welcome to the flu-delayed latest edition of my free ezine about progressive MS and MS progression in general. My name is Ian Cook. I'm a secondary progressive MSer who lives in Birmingham, UK.

In this issue are five pages of news plus two features about issues that matter to prog-MSers. The first feature on page 4 is about aids and adaptations that help me at home. On page 8 in the second feature I talk about an intriguing link between ageing, blood vessels and brain shrinkage.

Finally I also have a website where you can sign up for future editions of the ezine. It is at:

http://www.mymsprogblog.com Thanks to fellow prog-MSer Pete Joyce for helping me with the site.

So, please send this ezine to all other MSers, MS nurses and neurologists in your address book, and we can share our knowledge about what it's actually like to live with progressive MS.

Best wishes

Ian Cook

IN THIS ISSUE

SPMS patients taking high dose Simvastatin show better brain function

For the past two years it has been known that high dose Simvastatin significantly reduces the rate of whole brain atrophy when taken by patients with secondary progressive MS. Now there is more good news

A new analysis of the original trial data has shown that the statin drug significantly improved the function of the frontal lobe of the brain – the part of the brain which plays a key role in higher mental functions such as motivation, planning, social behaviour, and speech production.

Basically the results show that taking high dose simvastatin for two years significantly slowed down progressive cognitive impairment seen in SPMS.

At the start of the two year trial nearly half of SPMS patients showed they had impairment on frontal lobe function (45%) and in working memory (46%). There were also significant numbers of SPMS patients (up to 33%) with impairment on tests of verbal and nonverbal memory. However after two years , there was a significant difference in the simvastatin treated group and those receiving a placebo, with a 0.24 point increase in frontal lobe function score observed in the simvastatin-treated group, compared with a decline of 0.92 points in the placebo group

How simvastatin is doing this in unclear but researchers argue that it will make a compelling case for doing a definitive phase 3 trial of simvastatin in progressive MS to find out more.

Time to progression varies according to age at diagnosis

People diagnosed with MS at the age of 40 or over accumulate neurological damage more quickly than those diagnosed with MS at a younger age.

That's the finding of research published in the academic journal PLoS One. In the research scientists based in Kuwait compared the length of time it took older and younger relapsing remitting MS patients to reach the disability level of EDSS 6 (Requires a walking aid - cane, crutch - to walk about 100m with or without resting) usually regarded as the stage at which MS has become progressive. The researchers found people diagnosed over the age of 40 accumulate deficit more quickly than those diagnosed earlier in life . Other factors that led to a faster accumulation of disability were being male and spinal cord symptoms at MS onset.

More information on all stories on p11

Brain shrinkage in progressive MS associated with leak of blood haemoglobin

Haemoglobin leaking from damaged red blood cells may be linked to brain shrinkage in progressive MS. Stopping this leakage may slow progression.

That is the conclusion of a team from Imperial College London, whose research suggests treatments that lower levels of haemoglobin could slow progression of MS.

Haemoglobin carries iron and oxygen around the body in red blood cells and previous research has found high amounts of iron are deposited around MS affected blood vessels in the brain. Iron is toxic at high levels and scientists have suggested these toxic levels may trigger the death of brain cells in MS.

Normally haemoglobin is contained within red blood cells. However, red blood cells in MS patients are, for unknown reasons, more fragile than normal and break apart easily.

When red blood cells break apart they release haemoglobin into the blood stream. Normally, haemoglobin would be prevented from entering the brain by the blood-brain barrier – but in MS this barrier is weakened, allowing haemoglobin to enter. Once in the brain the destruction of haemoglobin causes iron to be released resulting in the cell damage and brain shrinkage which is a hallmark of secondary progressive MS.

In the study, the team found that the MS patients had high levels of a compound called serum lactate dehydrogenase, which is released when red blood cells disintegrate. They also found blood levels of "free" haemoglobin - haemoglobin that has escaped from the red blood cells - were significantly higher in MS patients with the greatest amount of brain shrinkage.

The researchers calculated that a 30 per cent increase in free haemoglobin levels resulted in an increased rate of brain shrinkage of 0.1 per cent – something which could make a significant difference to a patient's symptoms.

Professor Charles Bangham lead author of the study explained that the findings were unexpected: "We were amazed by the results, and we were surprised by the size of the apparent effect of haemoglobin on brain shrinkage. Over a number of years it could significantly impact a patient's symptoms."

Existing trials are testing potential MS treatments that mop up excess iron. However, Professor Bangham questions whether this is the best approach. " It may be more effective to look at ways of removing excess haemoglobin from the blood, rather than iron. There are number of drugs that do this, although none have been used for multiple sclerosis," he added. **More information on stories on page 11**.

Perching stools, shower seats and grab rails – all to make your life easier

Progressive MS is challenging, and it's not just the physical challenges, there's also the mental challenge of working out what to do about them.

My MS has been secondary progressive for ten years but it wasn't until I had a fall in 2013 followed by a period of greatly reduced mobility that I realised I needed to get some help for my progression. I found the most practical and immediate help was, of course, aids and adaptations so my first port of call was my local Lloyds pharmacy where I picked up a catalogue entitled "Betterlife" www.betterlifehealthcare.com

The catalogue is more than 100 pages long and contains just about every aid and adaptation that someone with progressive MS might need. It is brilliant. Leafing through the catalogue I found three aids: a shower stool, a foldable walking stick and a device that helps you put on your socks called the Soxon stocking aid. (More about that later on)

The shower seat proved so useful that it made me think of other situations where I should sit down rather than stand such as cooking meals and a "perching stool" seemed like the obvious solution. I found a company called Aidapt www.aidapt.co.uk which had a perching stool with arms giving me maximum support which I think is important when cooking, so I bought one. I then looked at some other websites and discovered the Complete Care shop www.completecareshop.co.uk Here I went a bit wild and bought not one but six products: *Continued on page 5*

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a long shoe horn which helps me put on my shoes; a "button hook-zipper combo"; a pair of elastic shoe laces which means I don't need to actually tie shoe laces as they are already tied ; some easy grip cutlery, and a belt with a Velcro fastener. The Velcro belt got me thinking about Velcro as a way of putting on shoes without using laces, and when my trainers with laces needed replacing I went straight for the Velcro fastening type.

The one thing I have learned since I started buying aids and adaptations is that you can never really have enough. Progressive MS is, as its title suggests, progressive. It gets worse over time so helps not just to respond to progression, but to anticipate it. And if you don't need an aid right now the chances are you soon will. If you want another reason for starting sooner rather than later then think of the three letters PIP - Personal Independence Payments – the benefit that is replacing Disability Living Allowance (DLA)

The daily living component of PIP which replaces the care component of DLA is awarded on a points basis. You are awarded points because you have problems in specific areas such as washing and bathing, dressing/ undressing or preparing a simple meal. The presence of aids and adaptations provides evidence that backs up your claim.

A perching stool that you use in the kitchen can provide evidence that you really cannot stand for long periods preparing food, A shower stool and a grab rail can show you do really need help in the shower. A Velcro belt, trainers and the sock aid can show that you really do need help dressing. When I had my PIP assessment I scored eight points in the daily living category (two points each in the categories of preparing food, washing and bathing, managing my toilet needs- I self –catheterise - and dressing/undressing.)

This gave me entitlement to the standard rate of PIP for daily living. That rate is £55.10 a week.Of course, the benefit of aids and adaptations is far greater than any financial rewards. With aids you can do far more for yourself and maintain your independence for far longer. Who can put a price on that?

Continued page 6

So,my top five indoor aids and adaptations are

- Velcro fastening shoes – available from most shoe shops or online

- Height adjustable shower stool from Betterlife (Lloyds Pharmacy) (See pic on page 4) www.betterlifehealthcare.com

- Grab rail – mine was provided by the social services but there are other suction grab rails which can be found in the Betterlife catalogue www.betterlifehealthcare.com

- Perching stool with arm rest – pictured on left - Aidapt Independent Living Solutions https://www.aidapt.co.uk/homepage.aspx?tl=0&pg=0&com=help&pagename=about

- Elbow crutches. These were provided by my local social services but a range of elbow crutches can also be supplied by Betterlife from Lloyds Pharmacy www.betterlifehealthcare.com.

And finally one that I never really got to grips with (literally) was a device that helps you put on your socks called the Soxon stocking aid. On reflection perhaps it would be more use putting on stockings and tights rather than socks. Either that or perhaps I wasn't using it properly!

Inactive lifestyle linked to brain volume loss in MS

Sedentary behaviour may be linked to brain volume loss in people with MS. This is according to researchers who found that less active MSers have a smaller brain. This is an important finding for progressive MSers because brain volume loss is more commonly seen as MS advances.

In the research which was published in Neurodegenerative Disease Management magazine researchers studied 36 people with MS who wore an accelerometer, a device that measures walking speed, and who underwent a brain MRI. Whole brain grey matter, white matter and deep grey matter structures were calculated from structural brain images.

The researchers found there were statistically significant and moderate or large associations between the number of sedentary bouts or sedentary days and brain volume measures. It was found that the more sedentary days an MSer had the smaller was their brain volumeand of course loss of brain volume increases as MS progresses.

According to Prof. Gavin Giovannoni 's MS Research blogspot the issue that needs to be resolved is whether the researchers' observation is simply an association ie do you exercise less because your MS limits your physical activity or is it a causal relationship ie does sedentary behaviour actually cause brain volume loss.

Prof. Giovannoni concedes it will be very difficult to resolve this question as it would require a large randomised-controlled trial, which for an exercise intervention is very difficult and some would say impossible to achieve.

The other approach, he says, is simple – just exercise! "There is enough evidence that exercise is good for you regardless of whether or not it is maintaining your brain volume. Exercise improves sleep, fatigue, mood and anxiety. Exercise helps maintain you metabolically, i.e. your weight, glucose levels, blood pressure, etc. Exercise outside of the MS space protects, or delays, you from developing age-related cognitive impairment. So why wouldn't you want to exercise? To quote one of my favourite clichés 'Just Do It'."

Umbilical cord blood may hold key to re-myelination

Umbilical cord blood cells taken from mice have been found to contain a substance that can accelerate re-myelination in a mouse version of MS. That is according to a study carried out at Duke University, North Carolina, USA.

The study shows that a substance in the umbilical cord blood cells has the characteristics of macrophages – a type of white blood cell, and microglia, (cells which protect and support neurons).

Researchers tested the substance which they called DUOC-01 on mice with chemical-induced demyelination. They found DUOC-01 induced rapid myelination, a higher proportion of fully myelinated neurons, and increased the differentiation of oligodendrocyte progenitor cells – cells which make myelin. **More information on all stories on page 11.**

PPMS drug Laquinimod shows new promise in mouse trials

An experimental drug called laquinimod has been found to disrupt the progression of multiple sclerosis (MS) in a mouse model of the disease. This finding may be especially promising, as the treatment is aleady being developed for people with progressive MS.

In a new study: "Treatment of spontaneous EAE by laquinimod reduces Tfh, B cell aggregates, and disease progression," published in the journal Neurology researchers wrote; "we found that laquinimod treatment not only prevented spontaneous MS but also was successful when treatment was initiated after mice developed paralysis."

Laquinimod is a novel drug with immunomodulatory properties that is being developed by Active Biotech and Teva to treat both MS and Huntington's disease. The drug has shown promising results in two phase 3 clinical trials, and is currently being tested in a Phase 2 trial in primary progressive MS patients (ARPEGGIO, NCT02284568). But the mechanisms behind its effects are not well understood.

The team behind the latest research have identified some possible mechanisms of action of laquinimod in progressive MS. In treated mice, they observed a 96 percent reduction in harmful clusters of B-cells — clusters only seen in patients with progressive MS as well as a 60 percent reduction in harmful antibodies.

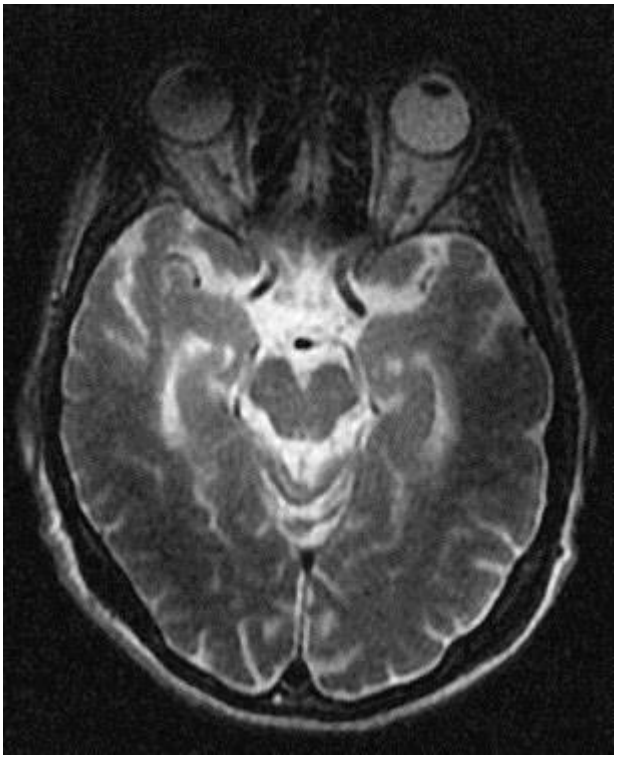
According to the MS Trust website Laquinimod is believed to work by affecting the levels of certain cytokines (substances released by immune cells) and reducing the passage of immune cells into the brain and spinal cord.

Laboratory investigations have suggested it may have both neuroprotective and anti-inflammatory actions. It is a tablet taken once daily**. Information on all stories is on page 11.**

TENS may be an option to treat MS related spasticity

TENS (Transcutaneous electrical nerve stimulation) might be an option for treating spasticity in progressive MS according to a review of research into the subject.

TENS is a therapy that relieves pain by delivering low-voltage electrical current to the body. It can be used to treat chronic pain and spasticity caused by neurological conditions such as MS where electrical signals travel along nerve pathways. The review was carried out at two Spanish universities - Universidad de Castilla la Mancha, Toledo, and Hospital Nacional de Parapléjicos de Toledo. The reviewers concluded that TENS might be a valid option to reduce spasticity and pain in multiple sclerosis thanks to its low cost, ease of use, and absence of adverse side effects.



Link found between blood vessels, ageing and MS progression

It has been known for longer than a century that MS is a chronic inflammatory demyelinating disorder of the central nervous system where, after an initial phase of relapse and remisssion, slow neurological deterioration due to progressive neuronal loss takes place.

More recently it has been suggested that age is a major determinant in this progression. Several mechanisms have been proposed to explain the key drivers of this age related neurodegeneration and disability accumulation in MS. However, the effect of commonly encountered age-related cerebral vessel disease, called small vessel disease (SVD), has been largely neglected until now.

A new review of age related small vessel disease (SVD) aims to look at its relevance in MS progression. The review notes SVD shares some features with MS, i.e. white matter demyelination and brain atrophy, and has been shown to contribute to the neuronal damage seen in vascular cognitive impairment. Several lines of evidence suggest that an interaction between MS and SVD may influence MS-related neurodegeneration.

SVD may contribute to hypoperfusion (poor blood flow), and hypoxia, (oxygen deficiency) all features seen in MS. Venule (small veins) and endothelium abnormalities have been documented in MS but the role of arterioles – a small branch of an artery and of other neurovascular unit structures, such as the pericyte – cells which help retain the blood brain barrier- have not been explored.

Vascular risk factors (VRF) have recently been associated with faster progression in MS though the mechanisms are unclear since very few studies have addressed the impact of VRF and SVD on MS imaging and pathology outcomes. Therapeutic agents targeting the microvasculature and the neurovascular unit may impact both SVD and MS and may benefit patients with dual pathology the authors say. **For more information go to page 11**

$6.1 m research project to track biomarkers of disability progression in MS

The International Progressive MS Alliance has awarded a $6.1 million grant to fund a research project identifying a biomarker of MS disability progression for use in clinical trials.

Using magnetic resonance imaging (MRI), researchers will work on identifying markers that signal MS progression in patients with progressive disease, a necessary step in the development of next-generation disease measurement tools.

Using these markers, the researchers will explore MRI as a tool capable of identifying the brain damage characteristic of progressive MS before it is evident to doctors. The work may also be used in evaluating proactive treatments for people with progressive MS whose symptoms are not yet clinically evident.

"There is an urgent need for effective therapies for progressive MS," said Dr. Douglas Arnold of the Montreal Neurological Institute Hospital (MNI) at McGill University who is leading the research.

"This project will use sophisticated computerised MRI analysis techniques to develop MRI markers that can be used in early phase (phase II) clinical trials for progressive MS. This will enable more efficient, less expensive clinical trials, lower the financial risk for drug companies to test potential therapies, and in so doing, facilitate the development of new drugs for progressive MS." he added..

Four of six prog MSers improve after stem cell treatment

Four out of six patients with progressive MS showed "measurable clinical improvement" after they were treated with their own stem cells injected into their spinal canal.

This is the finding of research carried out at Tisch MS Research centre in New York. In the research patients received MSC-NP cells (Mesenchymal stem cells which then become Neural Progenitor cells).

The cells were cultured from patients' own stem cells

The patients were followed for an average of 7.4 years after initial injection.

There were no safety concerns noted, no serious adverse events, and the multiple dosing regimen was said to be "well tolerated".

More information on all stories on page 11.

References contact details etc

Page 2

Simvastatin story

Source: D Chan, S Binks, J Nicholas, A Alsanousi, N Fox… - 2016. Effect of high-dose simvastatin on cognition in secondary progressive multiple sclerosis (MS-STAT cognitive): a randomised, placebo-controlled, phase 2 trial

Time to progression varies with diagnosis age story

Source: Alroughani R, Akhtar S, Ahmed S, Behbehani R, Al-Hashel J.Is Time to Reach EDSS 6.0 Faster in Patients with Late-Onset versus Young-Onset Multiple Sclerosis?PLoS One. 2016 Nov 1;11(11):e0165846. doi: 10.1371/journal.pone.0165846**.**

Page 3 haemoglobin story

Source: Medical News Today
http://www.medicalnewstoday.com/releases/314748.php

Pages 4-6 Aids and adadptations

Details of where I got all the aids and adaptations are in the feature itself

http://www.ncbi.nlm.nih.gov/pubmed/26269928

page 7 Inactive lifestyle/ brain volume loss story

Klaren et al. Objectively measured sedentary behavior and brain volumetric measurements in multiple sclerosis. Neurodegener Dis Manag. 2017 Jan 11. doi: 10.2217/nmt-2016-0036.

Page 7 umbilical cord blood and remyelination

Source: Source: https://multiplesclerosisnewstoday.com/cell-therapy-for-ms-using-cord-blood-derived-cells-promotes-remyelination-in-mice?utm_source=Multiple+Sclerosis&utm_campaign=7fa8e19b23-

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P8 laquinimod story

https://multiplesclerosisnewstoday.com/2016/10/12/potential-progressive-ms-drug-laquinimod-shows-promise-in-mouse-study+?utm_source=Multiple+Sclerosis&utm_campaign=53d4a25377-RSS_MONDAY_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_b5fb7a3dae-53d4a25377-71290133

page 8 TENS story

Source , Transcutaneous Electrical Nerve Stimulation For Spasticity: A Systematic Review, Jordi Serrano-Muñoz, Juan Avendaño Coy, Julio Gómez-Soriano, and E. Fernández-Tenorio, Neurologia.

page 9 blood vessels, age and progression

Source: Geraldes R, Esiri MM, DeLuca GC,Palace J. Age-related small vessel disease: A potential contributor to neurodegeneration in multiple sclerosis. Brain Pathol. 2016 Nov 19. doi: 10.1111/bpa.12460. [Epub ahead of print]

Page 10 MS biomarkers

Source https://multiplesclerosisnewstoday.com/2016/09/28/mcgill-researcher-awarded-6-million-grant-to-id-progressive-ms-markers+

Page 10 stem cells

Harris VK, Vyshkina T, Sadiq SA. Clinical safety of intrathecal administration of mesenchymal stromal cell-derived neural progenitors in multiple sclerosis.Cytotherapy. 2016 Oct 7. pii: S1465-3249(16)30496-0. doi: 10.1016/j.jcyt.2016.08.007

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