My prog-MS ezine

For people with progressive MS and those interested in it

Issue number 10, October - December 2016

Hello and welcome to the 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 – which runs Oct- Dec 2016 - are six pages of news plus two features about issues that matter to prog-MSers. The first feature on page 4 is about a tongue neuro-modulatiom stimulator. On page 8 In the second feature I talk about taking high dose statins for my SPMS. And , yes I also have a website for 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.

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Novel 'tongue stimulator' helps in advanced MS

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London Cladribine trial for prog-MS will include wheelchair users

A clinical trial into the use of cancer drug cladribine for progressive MS is being planned by the MS team working at Barts Hospital in London led by Prof Gavin Giovannoni.

Following a trip to Lubin Poland where the local MS clinic reported "very promising results" after seeing 400 patients treated with the drug, Prof Giovannoni says he is seeking to get funding for a trial which would test cladribine in more advanced MS cases , including MSers in wheelchairs.

"Over the next few months Barts-MS will be making a strong case for getting this trial funded and started." Prof. Giovannoni said.

Cladribine works by killing cells in the immune system which are thought to attack the myelin sheath around nerves.

However in September 2010, the European Medicines Agency (EMA) rejected a licence application for cladribine for MS due to concerns about four cases of cancer observed during clinical trials.

In June 2011, makers Merck announced that they were discontinuing their applications for licences for cladribine for MS and withdrawing it in Australia and Russia where licences had been granted. However in September 2015, Merck announced that further research had not shown an increased risk of cancer and they were re-starting the licence application process.

Primary progressives may soon get Ocrelizumab

Results from a trial into Ocrevus (ocrelizumab) as a treatment for primary progressive MS have shown the drug stopped disease progression for more than two years in more patients than a placebo or dummy pill.

The findings, a highlight at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) 2016 Congress in London, raised hope that a treatment for patients with primary progressive MS may soon be available.

Ocrevus is an antibody targeting B-cells that express the CD20 molecule on their surfaces — something researchers believe contributes significantly to neuronal damage. Significantly more patients receiving Ocrevus had no evidence of progression at 120 weeks in comparison to placebo — 42.7 per cent and 29.1 per cent, respectively. A larger proportion of the treated patients with no disease activity also did better in additional tests. The U.S. Food and Drug Administration and the European Medicines Agency have both accepted marketing applications for Ocrevus.

Details of all news stories are on page 13

New drug for secondary progressives reduces three month risk of disability by 21%

Results of a trial into a new treatment for secondary progressive MS (SPMS) show that the once-daily pill called siponimod significantly reduced the risk of disability progression compared with a placebo or dummy pill.

The results presented at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), in London, UK showed that treatment with Siponimod reduced the risk of three-month confirmed disability progression by 21% compared with placebo or dummy pill.

There was a reduction in the risk of confirmed disability progression among SPMS patients without relapses. In addition there was a significant difference in favour of the drug compared to placebo in brain volume loss,. However the difference in the timed 25-Foot Walk test between those taking siponimod and those on the placebo was not significant

Siponimod (also called BAF312) was generally safe and well tolerated, with a profile comparable to other drugs in the same class. Makers Novartis say they will complete full analyses of the trial data and evaluate next steps in consultation with European and American health regulators.

Study shows vitamin D could help repair damage to myelin

A protein activated by vitamin D could help repair damage to myelin in MS, according to a study carried out at the University of Cambridge.

The study, published in the Journal of Cell Biology, offers significant evidence that vitamin D could be a possible treatment for MS. Researchers from the MS Society Cambridge Centre for Myelin Repair, found that the 'vitamin D receptor' protein pairs with an existing protein, called the RXR gamma receptor, already known to be involved in myelin repair,

By adding vitamin D to brain stem cells where the RXR gamma receptor protein was present, researchers found the production rate of oligodendrocytes (myelin making cells) increased by 80 per cent. When they blocked the vitamin D receptor to stop it working, the RXR gamma protein alone was unable to stimulate the production of oligodendrocytes. This work provides significant evidence that vitamin D is also involved in the regeneration of myelin once the disease has started. **More details of news stories on pages 13-15**

Tongue Neuro-Modulation Stimulation device may help in more advanced cases of progressive MS

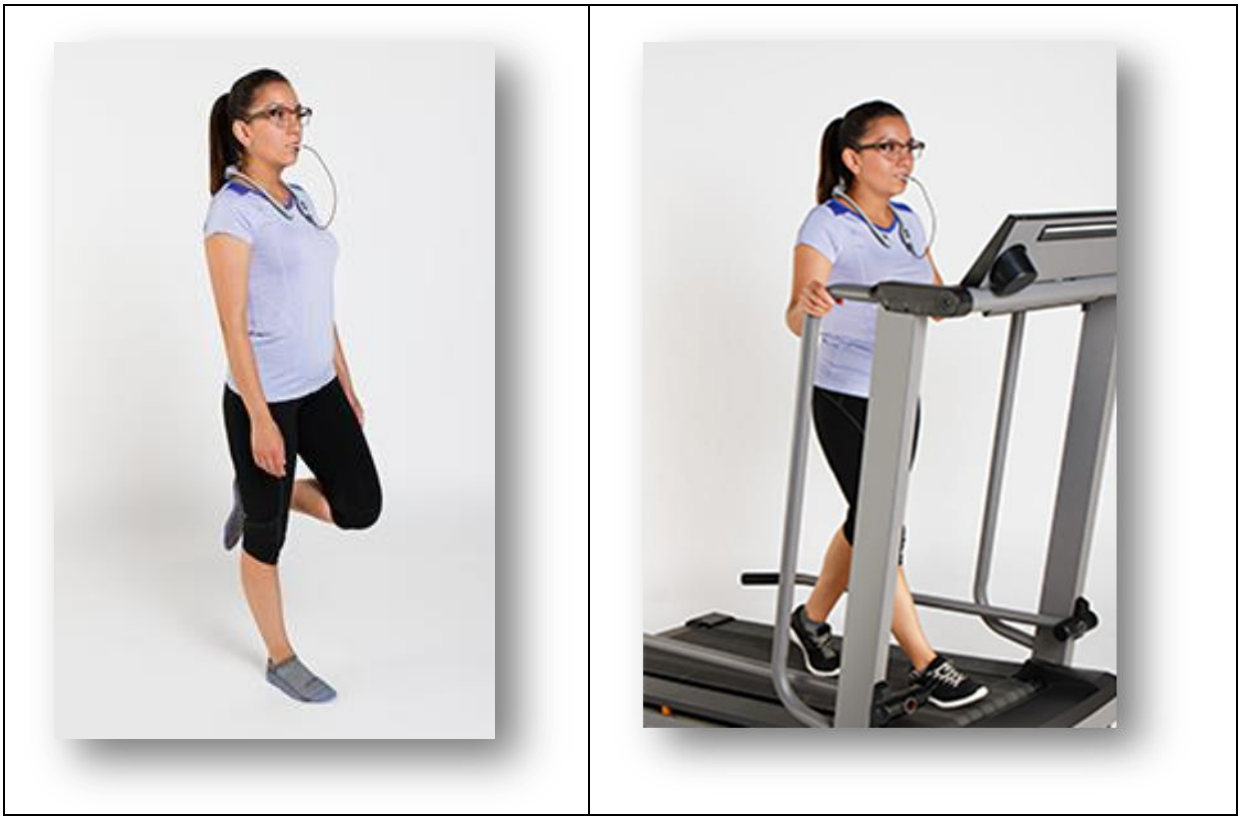
A study of a device called a Portable Neuro-modulation Stimulator (PoNS) – pictured left - has shown that those with advanced MS can improve when using it where its use is combined with physical therapy**.**

PoNS delivers neuro-stimulation when the large flat part (shown on the bottom left of the picture) is placed under patients' tongues for short periods. This has been shown in experiments to enhance the brain's ability to restructure itself in response to new experiences.

The flat part of the PoNS device is placed under the tongue while electrical impulses are generated by the controls operated with switches on the semi-circular band (picture top right) is worn round the neck.

For 20 minutes electrical stimulation is coupled with targeted functional therapy, called Cranial Nerve Non-Invasive Neuromodulation (CN-NINM). The electrical stimulation of the cranial nerves creates a flow of nerve impulses that are then delivered directly into the brain stem and cerebellum – the main control centres for many life functions including sensory perception and movement.

From the brain stem, these impulses travel throughout the brain and activate or reactivate neurons and structures involved in potentially the entire central nervous system. In a pilot study researchers assessed the efficacy of PoNS Therapy in six people with progressive MS, who had Expanded Disability Status Scale (EDSS) scores of 6.5 (Requiring two walking aids) to EDSS scale 7.5 (Restricted to wheelchair) The study looked at balance, posture, stability and walking movement. *Continued on page 6*



Pictured above: neuro-modulation is tried out with different forms of physical exercise

Continued from page 5 Improvements were recorded in a number of areas including the ability to again use a walker for local trips, decreased fatigue, overcoming physical obstacles at home, increased independence with day-to-day activities, and greater community access.

“Those with greater functional ability at the beginning of the study (EDSS 6.5-7.0) made the most significant gains but all subjects could be qualified as improved.,” said Mitch Tyler, the study’s principal investigator.

The PoNS device was developed at The Tactile Communications and Neurorehabilitation Laboratory at the University of Wisconsin, Madison and licensed to a subsidiary of Helius Medical Technologies a medical technology company focused on neurological wellness which intends to file for FDA (Food and Drug Administration) clearance for the PoNS™ device in the US. Thanks to Helius for letting us use the pictures

For further information go to pages 13-15

Protein bio-marker may predict MS progression

Swedish researchers believe a newly discovered potential biomarker of MS may help to distinguish between people who will go on to have less severe disease and those in whom the disease will progress.

The biomarker's discovery came through an investigation into the immune system of MS patients carried out by researchers at Linköping University in Sweden. Biomarkers are naturally occurring substances, in the blood or elsewhere, that indicate likely disease progression.

In a series of experiments, researchers tested how large numbers of proteins interact with each other and sought to discover those proteins that are highly significant in MS, behaving differently in patients than in controls upon activation

Natural human enzyme might drastically reduce spasticity

Injections of a naturally occurring enzyme called hyaluronidase may drastically reduce spasticity in MS patients according to research carried out at New York University(NYU). Further trials are planned.

Muscle spasticity in MS can lead to damage to neurons that control muscle movement (motor neurons) and muscles. Existing treatments often cause muscle weakness, which can make movement even more difficult. The urgent need for new and better treatment led a team of scientists at NYU Langone Medical Centre to consider the possible involvement of a sugar molecule, called hyaluronan which accumulates in the joints and muscles after neurological damage.

The research team hypothesized that injections of an enzyme called hyaluronidase, which breaks down hyaluronan, would reverse its accumulation, reduce muscle stiffness, and increase joint movement. The team gave hyaluronidase injections to 20 patients with moderate or severe spasticity in the arms resulting from neurological damage, Results showed that before treatment the joints tested had between 44.4 per cent and 50.6 percent stiffness, after the treatment these values decreased to 5.8 percent, and 15.3 percent respectively, within two weeks..The team is planning another trial with a larger group of patients. If effective hyaluronidase may be an inexpensive option for patients with spasticity compared to other treatments (one vial of hyaluronidase typically costs $50, and the complete treatment may only require 4-8 vials. **More details on p14**

Fat molecules may play major role in progression

New work by researchers at Cornell University in the US (left) is unravelling the role of lipids in MS and its progression. The work may be key to developing more effective therapies.

Lipids are fat molecules which besides being major components of myelin are known to participate in signalling inside cells. Alterations in lipid stability may be involved in MS progression.

The Cornell researchers have been working on techniques that might allow the visualization of lipids within the cell, making it possible to understand the signalling pathways in which they are involved.

Dr Jeremy Baskin, the principal investigator, has recently carried out work showing lipids in myelin sheaths have a role in the development of leukodystrophy diseases - neurological disorders with similarities to MS, so there may be a link between myelin lipids and MS progression.

PPMS drug Laquinimod shows promise in animal trials

A drug being developed to treat primary progressive MS has shown promise in stopping a mouse model of the illness. The drug Laquinimod, is currently being tested in phase II clinical trials in humans and results of the trials are expected in October 2017.

In the mouse study, published in the journal Neurology: Neuroimmunology & Neuroinflammation, researchers from the University of California-San Francisco gave mice either a placebo or laquinimod . Less than one third (29%) of the mice that received the drug developed MS compared with more than half (58%) of those on the placebo. A reduction in harmful clusters of B cells, which play a key role in primary progressive MS was also seen in the mice given Laquinimod.

In the experiments the scientists noted that the “MS mice” that had begun to develop paralysis, had a slower rate of progression after taking the medicine.. Laquinimod is a once daily tablet.

Information on all stories is on pages 13-15

I take high dose Simvastatin for my SPMS – but has it had any effect over the past year?

I see my neurologist once a year and the meeting is usually fairly short. After greeting me and asking me how I am he generally reminds me there are no disease modifying drugs for my type of MS - secondary progressive (SPMS). We then have a brief chat about my latest symptoms and I leave saying: "See you next year".

Last year's visit in October 2015 was completely different. My neurologist grinned broadly the moment I walked in. He said for once he might be able to help me with something more than symptom relief. There was a drug called simvastatin that I could try out for my SPMS. He explained this drug belongs to a class of cholesterol lowering drugs called statins.

At this point I vaguely remembered reading that simvastatin had been tried out on a group of secondary progressive MS patients in 2014. I recall the results had been quite positive. My neuro, who of course is far better informed than me, told me that high doses of simvastatin (80 mg daily) had been given to a group of 70 SPMS patients in a stage 2 clinical trial which had been published in the medical journal The Lancet. *Continued on page 9*

Continued from page 8. The trial showed a big reduction in brain shrinkage among the patients who took simvastatin.

Their annual rate of whole-brain shrinkage was reduced by 43%.There were also improvements in EDSS scores (a scale measuring disability levels) and better MSIS-29 scores (a scale used to measure the impact of MS on daily life.) To cap it all there were very few side effects.

So how is this possible? One theory is that statins protect nerve cells. Another theory is that statins stop immune cells migrating through the blood-brain barrier.

A third theory is that simvastatin improves vascular (blood vessel) function. Vein problems, are common in progressive MS, and may be linked to higher cholesterol which statins lower. In this sense statins may not be hitting the MS disease process directly but rather a factor involved in its progression.

To add to the list of theories one new one is one I read over the Summer and put forward by Danish scientists. This is the theory that when swallowed simvastatin binds to an immune structure known as complement receptor (CR)3, and blocks immune cells from binding to the receptor stopping the cells triggering auto- immune attacks.

No one really knows which of these theories is true but my hope is that after two years my EDSS and MSIS-29 scores will, like the trial patients, be much improved . I can at least be certain of one thing – my cholesterol levels, which were a bit high - 6.1 at the start - will be much lower.

More information on this feature in page 14

Breast cancer drug tamoxifen can treat myelin loss in MS

Tamoxifen, a widely used treatment for breast cancer, can also treat myelin loss in MS according to a new study titled "Tamoxifen accelerates the repair of demyelinated lesions in the central nervous system".

Researchers from the University of Cambridge used lab cultures and a mouse model of reduced myelin to analyse how Tamoxifen might affect the repair and recovery of oligodendrocytes -cells able to produce myelin. The research is published in the journal Scientific Reports. The scientists discovered Tamoxifen can enhance myelin repair in MS by encouraging the brain's own stem cells to regenerate myelin."

The team found Tamoxifen, could stimulate stem cells in the body to become oligodendrocytes, the brain cells responsible for producing myelin.

Investigators also observed that mice with reduced myelin levels, when treated with Tamoxifen, had increased numbers of brain oligodendrocytes, showing that in a living organism Tamoxifen may well induce remyelination in the brain.

"The use of Tamoxifen has several advantages over the development of new drugs.

"For example, it has an excellent safety profile that has undergone the test of time by exhaustive application in the clinic," the researchers wrote.

Parkinson's drug may help MSers to walk better

A pill approved to treat Parkinson's disease and also the flu virus may be able to help people with progressive -MS to walk better.

That is the finding of a Phase 2 proof-of-concept clinical trial evaluating ADS-5102 (amantadine HCl), an extended-release version of amantadine, in MS patients with difficulties walking.

Findings indicated that ADS-5102 had a positive impact on walking speed, with a nearly 15 percent improvement seen in a timed 25 foot walk test .

"We are excited by these positive MS walking data, which represent our fourth successful controlled clinical trial with ADS-5102," Gregory T. Went, PhD, chairman and chief executive officer of Adamas Pharmaceuticals, said "We are now ready to speak with the US Food and Drugs Administartion (FDA) about a pivotal registration program ." **More information on news stories on p13-15.**

Exercise film shows why being active is so important

A film showing why exercise is so important for MSers has been made by filmmaker, Khurrum M Sultan. The film features the Windmill Exercise Group in Redditch, Worcestershire, and highlights the benefits of a regular exercise class demonstrating why some form of exercise is better than none. The class has been going for 8 years. Visit the following YouTube link to see the 14 minutes long film showing the exercise class 'in action': https://youtu.be/pcqJaFiNdFs

Scientists discover new way to make human immune cells

A group of UK, US and French scientists have found a new way to make human microglial-like cells from a type of highly versatile adult stem cell called induced pluripotent stem cells (iPS cells)

Microglial-like cells are a type of cell located throughout the brain and spinal cord which act as the first and main form of active immune defence in the central nervous system. They are also key cells in overall brain maintenance —constantly scavenging the nervous system for plaques, damaged nerve cells and infectious agents.

Defects in microglia are thought to be central to the generation of progressive MS and so the capacity to make human microglia is going to be of value in the search for treatments for people with progressive MS.

For details of all news stories go to page 13-15.

Changes afoot at this ezine

The times they say are a changing and from January 2017 we will be delivering the ezine in a new improved format –it will still be free and delivered electronically but will look more like a traditional magazine.

Plans are still at an early stage so I will email you all again with further details once these have been worked out.

In the meantime do please send me your stories, air your views, and give me hints and suggestions for things you would like to see covered. Finally, please send this ezine to all other progressive MSers in your address book

Finally If you want to get regular copies of this "ezine" directly then either fill in the relevant boxes at http://www.mymsprogblog.com or email me at iancookjournalist@yahoo.co.uk

IN THE NEXT ISSUE (Jan-Feb 2017)

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

References contact details etc

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Cladribine story

Source: : http://multiple-sclerosis-research.blogspot.com/ 02/10/16

Ocrelizumab story

Source: www.roche.com + Multiple Sclerosis News Today (26/09/16

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siponimod story

Source: https://www.novartis.com/news/media-releases/novartis-baf312-reduces-risk-disability-progression-pivotal-phase-iii-study?hootPostID=cfa242079cd3be03006662ed67970b9c

Vitamin D story

Source: Source: Guzman de la Fuente, A et al. Vitamin D receptor–retinoid X receptor heterodimer signaling regulates oligodendrocyte progenitor cell differentiation. Journal of Cell Biology; 7 Dec 2015)

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pages 4-6 Feature on tongue neuro-stimulator

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page 7 lipids story

Source: https://multiplesclerosisnewstoday.com/2016/08/03/work-to-tag-and-track-lipid-signaling-in-cells-of-relevance-in-ms/?utm_source=Multiple+Sclerosis&utm_campaign=c6ceda0fe3-RSS_MONDAY_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_b5fb7a3dae-c6ceda0fe3-71290133 Photo credit Shaogeng Tang / Cornell University

Page 7 laquinimod story

Source: International Business Times, 22/09/16, By Léa Surugue

P8-9 statins

Effect of high-dose simvastatin on brain atrophy and disability in secondary progressive multiple sclerosis (MS-STAT): a randomised, placebo-controlled, phase 2 trial.

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page 10 tamoxifen

Sourcehttps://multiplesclerosisnewstoday.com/2016/09/07/breast-cancer-drug-tamoxifen-shows-potential-to-repair-myelin-in-ms?utm_source=Multiple+Sclerosis&utm_campaign=7c090975db-RSS_MONDAY_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_b5fb7a3dae-7c090975db-71290133

Page 10 parkinsons/ flu drug

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Also look at:

http://onlinelibrary.ectrims-congress.eu/ectrims/2015/31st/116142/jack.nguyen.amantadine.ameliorates.gait.deficits.and.disease.severity.in.an.html

Source: http://www.buffalo.edu/ubreporter/stories/2016/06/zivadinov-microbleeds.html

Page 11 microglia story

Source: Source:Muffat J, Li Y, Yuan B, Mitalipova M, Omer A, Corcoran S, Bakiasi G, Tsai LH, Aubourg P, Ransohoff RM, Jaenisch R. Efficient derivation of microglia-like cells from human pluripotent stem cells. Nat Med. 2016. doi: 10.1038/nm.4189. [Epub ahead of print]

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