



My prog-MS e-zine

For people with progressive MS
and those interested in it

Issue number 9, August/ September 2016

Hello and welcome to the latest edition of my free e-zine 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 important prog-MS news plus two features about issues that matter to prog-MSers. The first feature on page 4 is about days out in the country if you can't walk. In the second feature on page 9 we read

about sunshine and why it might be better for you than vitamin D tablets. And , yes I also have a website for the e-zine. It is at <http://www.mymsprogblog.com> Thanks to fellow prog-MSer Pete Joyce for helping me with the site.

So, please send this e-zine 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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Feature

My great day in the country with the disabled ramblers

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Adding mix of three proteins to stem cells may make them work better in prog-MS patients

A cocktail of three proteins added to neural stem cells may make them more effective in treating progressive MS, according to laboratory research carried out by UK, US and Chinese scientists.

The “triple cocktail” contains three proteins – interleukin 10 (IL-10,) neurotrophin 3 (NT-3,) and LINGO-1-Fc.

Interleukin 10 (IL-10) targets persistent inflammation, neurotrophin 3 (NT-3) helps support oligodendrocytes (myelin making cells) and neurons, while LINGO-1 targets the accumulation of demyelination debris preventing neuro-regeneration.

Using an Experimental Autoimmune Encephalomyelitis model of MS the scientists genetically engineered neural stem cells and transplanted them into tissue samples along with the cocktail of drugs. The neural stem cells were then found to migrate into demyelinated areas and bring about effective recovery through encouraging the growth of

macrophages/microglia immune cells which drive oligodendrocyte production.

The cocktail of drugs also reduced astrogliosis - an abnormal increase in the number of nerve cells called astrocytes brought about by the destruction of nearby neurons. The drugs cocktail also promoted axonal health and oligodendrocyte production.

By contrast neural stem cells transplanted with just one or two of these three proteins and produced only a limited improvements when injected. The scientists behind the research said it represents a novel and potentially effective therapy for the chronic stage of MS, for which there is currently no treatment.

Spinal steroid drug injections may help in prog-MS

Injecting steroid drugs into the spine of patients with progressive MS may help them by decreasing oxidative stress in their cerebrospinal fluid (CSF).

That is the finding of a study “One-time intrathecal triamcinolone acetonide application alters the redox potential in cerebrospinal fluid of progressive multiple sclerosis patients: a pilot study,” published in the journal *Therapeutic Advances in Neurological Disorders*.

In the study researchers looked at the effect of injecting the cortico-steroid drug

triamcinolone (TCA) into the CSF of 16 chronic progressive MS patients. Previous studies have shown that the composition of CSF changes in MS. These changes may be the result of a chronic neurodegenerative process taking place in the illness. The research team who carried out the study saw TCA decreased the generation of damaging reactive oxygen species, the outcome of oxidative stress. The results suggest that intrathecal TCA may help patients with progressive MS. **Sources for all news stories are on page 15**

Anti-psychotic drugs to be tested in SPMS

Researchers in New Zealand are to test two commonly used psychiatric drugs in a group of patients with secondary progressive MS (SPMS).

The two medications - clozapine and risperidone - have for years been used to treat schizophrenia, bipolar disorder (manic depression) and autism. The drugs trial will take place at Victoria University of Wellington, New Zealand.

Professor Anne La Flamme, an immunologist at Victoria University who is leading the trial says studies carried out at the university show clozapine and risperidone are able to tone down the immune system in the brain, and it is this anti-inflammatory action that may help in

secondary progressive MS.

The trial will run for six months, and its goals are to investigate both the “acceptability” of the drugs among participants as well as the drugs’ effect on secondary progressive MS, as measured by the MS Functional Composite and the Expanded Disability Status Score (EDSS).

Prof La Flamme added that re-purposing medicines is an approach often used in MS drug development. “Most agents used to treat relapsing remitting MS were originally used for something else,” she said. Both anti-psychotics are approved by the U.S. Food and Drug Administration (FDA), with risperidone one of the few such drugs allowed to be used in children.

Ocrelizumab is accepted for European and US drugs review

Swiss pharmaceutical company Roche has said that the European Medicines Agency (EMA) has validated the company’s Marketing Authorisation Application (MAA) for ocrelizumab to treat primary progressive MS and relapsing remitting MS in the European Union (EU).

Validation confirms that the submission is complete and signifies the MAA is under

review by the EMA’s Committee for Medicinal Products for Human Use (CHMP). The U.S. Food and Drug Administration (FDA) has also accepted for review Roche’s Biologics Licence Application for Ocrevus, as ocrelizumab will trade under, to treat both types of MS, and has granted the application a “Priority Review Designation” with a targeted action date of December 28, 2016.

Sources for all news stories on page 15



My fun day out with the disabled ramblers

Going on a long countryside ramble might sound like a mad idea if you have problems walking.

After all, the great outdoors with its muddy fields, gates and stiles is hardly disability friendly. Then I found out about the disabled ramblers.

This group of adventure seeking disabled people explore the countryside using tough outdoor scooters, power-chairs – even on occasions manually powered wheelchairs. As their website says –We are truly ramblers although very few of us can walk more than a few yards. So with their help I thought I would explore the great outdoors once again.

The group was set up more than ten years ago by disabled countryside enthusiasts and organises rambles each year between May and September in a variety of locations throughout England and Wales. After looking through their brochure I signed up for a year's membership and decided to join them in the picturesque Peak district national park for a six mile hike. We snaked our way through the Derbyshire moorlands. I must admit I was a little apprehensive to begin with but the Disabled Ramblers have a real “can-do” mentality and put my mind at rest. I was able to hire one of their all-terrain scooters - a Trampler - for the day and there was someone on hand to show me how to use it. There was also an able bodied marshal to keep an eye on me.

Ctd page 5



Continued from p4 So one early Summer morning armed with my packed lunch, water bottle, waterproof jacket and sunscreen I was with a group of disabled ramblers in the Peak District national Park at the start of a ramble sitting in my Trammer and listening to a briefing about the route we would be just south of Buxton.

The ramble took us along country tracks over fields snaking through some pretty Derbyshire moorlands with rolling limestone hills and dales typical of the white peak area. There were occasional climbs up some slopes but the Trammer seemed able to handle the climb. It wasn't all walking or tramping through the area, there were several stops on the route to admire the views. We also stopped to look at old lead mine workings and admire rare country flowers and birds. Two National park rangers who accompanied us became almost our tour guides. **Continued on page 6**



Ctd from page 5. At 1 pm we had lunch and a toilet break. Incredibly there was a wheelchair accessible toilet which had been shipped to the location loaded on the back of a trailer. After lunch with beautiful views of the National Park on all sides we started the return journey. Feeling more confident on the Trampler I felt able to chat to the other ramblers who included another rambler with progressive MS. We ended our ramble after a modest descent of 500 feet to the village of Monyash where we retired to a local café and then the pub.

As I left the ramble I reflected that it was great to join a group who were so welcoming to a novice such as me and who never left me feeling on my own. This was my first disabled ramble but it won't be my last.

For more information on disabled rambling go to page 15



New Russian drug for SPMS to enter Phase 3 trials

A new experimental drug for secondary progressive MS (SPMS) is showing positive results in clinical trials taking place in Russia and is soon to enter Phase 3 clinical testing.

The drug, called Xemys, treats SPMS by delivering three myelin basic protein (MBP) peptides to cells from the immune system, resulting in the development of an immune tolerance toward myelin proteins which are thought to be a primary target of auto-immune attacks that characterise MS.

A Phase 2a proof-of-concept trial showed Xemys to be effective in slowing or preventing MS disease progression in humans. Twenty weeks after study

enrolment, seven of the 20 patients (37%) treated had no evidence of disease activity. Xemys is said to be well tolerated, and has a very low probability of producing damaging side effects according to trial organisers. Tests have also been performed in rats with experimental autoimmune encephalomyelitis, (EAE) the animal model for human MS. The three MBP peptides were said to have had “positive effects” on immune cells in the EAE rats.

Scientists better understand effect of statins in SPMS

Danish scientists studying the cholesterol-lowering drug simvastatin believe they now have a better understanding of how the drug achieves its positive effects in reducing brain shrinkage and progression in secondary progressive MS (SPMS).

The scientists from Aarhus University believe that, when swallowed, simvastatin binds to an immune structure known as complement receptor (CR)3, and blocks immune cells from binding to it, effectively stopping the immune cells triggering auto-immune attacks.

Thomas Vorup-Jensen, a professor in the Department of Biomedicine at Aarhus, believes that since the discovery was made in lab studies the research team

now needs to prove the same is true in humans. “Of course, we now need to establish whether it works in the same way in vivo, but we think it’s likely,” Dr. Vorup-Jensen said.

Earlier studies have found that simvastatin also prevents the release of immune cytokines - substances, secreted by immune system cells such as T-cells, suggesting that the drug might prevent auto-immunity in various other ways.

Sources for all news stories is on page 15

Australian trial of new spasm and spasticity drug

A clinical trial testing a new treatment for MS -related spasms, spasticity and cramps is taking place in Australia.

Bio-tech company Flex Pharma Inc is to test a new drug called FLX-787 on 50 MS patients who suffer from spasms, spasticity or cramps as a result of the disease. The trial is being run in conjunction with Neuroscience Trials Australia.

On their website the company says that new research has shown that spasms do not originate in the muscle itself, but are caused instead by a neural mechanism: excessive firing of the motor neurons in the spinal cord that control muscle contraction.

“We believe that Chemical Neuro Stimulation, the process whereby small molecules activate TRP ion channels topically, leads to sensory stimulation that in turn reduces hyper-excitability in motor neurons,” said Dr. Rod MacKinnon, Flex Pharma’s scientific co-founder, and a Nobel laureate in Chemistry (2003) for his structural and mechanistic studies of ion channels.

“We hypothesize that this approach may be generally applicable as a treatment for cramps and spasms in a spectrum of neuromuscular conditions.”

US bio-tech firm’s new mitochondrial MS treatment

Mitochon Pharmaceuticals, a US biotech firm, is developing a drug that acts on mitochondria – the energy producing parts of a cell - to treat MS.

Mitochondria are parts of cells including nerve cells that generate the energy responsible for cells’ maintenance and transmission of nerve signals. Changes in mitochondrial function or structure can lead to nerve cell damage. It is believed improving mitochondrial function would decrease the severity of a variety of symptoms in diseases characterized by nerve damage such as progressive MS.

Mitochon’s treatment -MP101- is a mitochondrial targeted neuro-protective agent taken as a daily pill which aims to protect cells from neurodegenerative processes caused by auto-immune responses, injuries, or genetic factors. The company expects to take MP101 into Phase 1 studies in healthy volunteers as the first stage of their research this year. Other mitochondrial treatments for progressive MS are being developed elsewhere by drugs companies

For sources of all news stories go to page 15



Here comes the sun

It is now high Summer and many of us progressive MSers will be off with our families to get some sun while, of course, avoiding the heat.

We all know that the sun is good for us because lack of sunlight is linked to MS and the illness is more common in cloudy climates than sunny ones.

And most MSers like me have been told it is vitamin D in sunlight which offers protection against MS or even some relief from its symptoms because the vitamin is believed to work on the immune system as an “immune-modulator”. But is this true, or is this the whole truth?

A study carried out in 2013 titled “Interdependence and contributions of sun exposure and vitamin D to MRI measures in multiple sclerosis” raised some serious questions. It found high levels of vitamin D which you get from the sun didn’t always translate into high whole brain volumes - an indicator of less MS damage.

So, the researchers concluded there must be something else in sunshine combatting MS as there is, of course, less MS in sunny climes. The researchers put it like this: “Sun exposure may have direct effects on MRI measures of neurodegeneration in MS, independently of vitamin D.” Sadly, the researchers didn’t say what else in sunlight might be slowing down neurodegeneration.

Most people with MS probably know that sunshine gives you vitamin D, but fewer MSers probably know that human skin when exposed to sunlight can “photosynthesise” nitric oxide (NO) as well. **Continued on page 10**

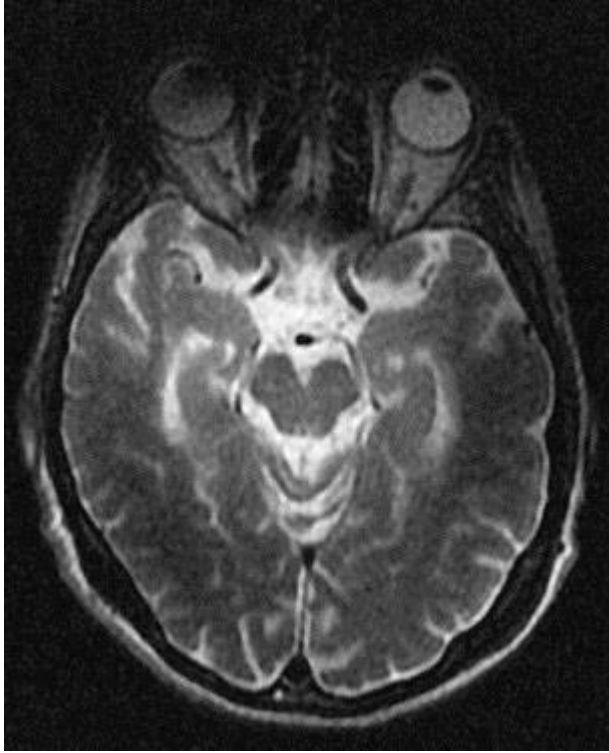


Ctd from page 9 Nitric oxide is a powerful vasodilator – a substance that opens up blood vessels. It improves blood flow and lowers blood pressure. This may explain why we feel positive and relaxed outside on a sunny day or spending a day on the beach. It may also account for the fact that cases of hypertension and cardiovascular disease increase in cloudy places like northern Europe.

So, could nitric oxide play a role in the human brain and control MS too? In a paper “The role of the nitric oxide pathway in brain injury and its treatment — From bench to bedside”, published in the journal *Experimental Neurology* in 2015, a group of scientists said that nitric oxide acts as a neurotransmitter and is a component of the signalling pathways that operate between cerebral blood vessels, neurons and other brain cells called glial cells. Nitric oxide is also associated with nervous system blood flow, and neurotransmitter release.

Of course this is far from scientific proof that nitric oxide from sunshine on your skin will increase your whole brain volume and help your MS. However, another drug which also works on the nitric oxide pathway has been shown to act on the brain and even preserve myelin and axons. The drug is Viagra. Although best known as an erection aid, the drug was originally used as a vasodilator in angina – a disease where the blood supply to the muscles of the heart is restricted by poor blood flow. In 2012 a group of Spanish scientists using a mouse model of MS wrote a paper in which they claimed Viagra could be considered as an MS treatment.

I am still taking 4,000 IU of vitamin D a day but I have started to sunbathe safely to get some other things like nitric oxide from the sun too. What I’m also hoping to do is open up a debate about sunshine, vitamin D MS, oh and nitric oxide too. **For more information on any of this go to page 15**



Brain blood vessel leaks linked to MS disability

Leaky blood vessels in the brain called cerebral microbleeds are linked with increased physical and mental disability in MS.

That is according to a new study by researchers in the University of Buffalo's Jacobs School of Medicine and Biomedical Sciences and

published in the journal *Radiology*. "Our hypothesis was that there is increased prevalence of cerebral microbleeds in MS because progression of that disease is associated with increased likelihood of cardiovascular comorbidities, including hypertension, altered lipid metabolism, overweight/obesity, smoking and diabetes and migraine - all risk factors for cerebral microbleeds, said Robert Zivadinov, first author of the study and professor of neurology at Buffalo University, USA.

In the Buffalo study 20 percent of MS patients over the age of 50 were found to have cerebral microbleeds compared to 7 percent of healthy people. Among subjects under the age of 50, 14 percent of patients with a clinically isolated syndrome of MS had microbleeds versus just 3 percent of healthy people. The Buffalo researchers also found that the more cerebral microbleeds a patient had, the more severe were their physical and cognitive outcomes. In particular MS patients with more cerebral microbleeds had more physical disability after adjusting for age, hypertension and whole-brain volume.

"This is significant because it suggests that cerebral microbleeds are associated with increased physical disability in MS patients, independent from these additional risk factors for cerebral microbleeds," prof. Zivadinov added.

In terms of cognitive disability, the researchers found that in the subgroup of MS patients who underwent neuropsychological testing, those with more cerebral microbleeds had higher disability on verbal and other cognitive function tests.

For sources of all news stories go to page 15

For some time I have been thinking that it would be good if there was some way you could send in letters about things they read in the ezine and things you want to share with other readers. So if there is something you have to say which you want to see in the ezine then send it by email to me at iancookjournalist@yahoo.co.uk



Pleased to see Kool Max Zipper Vest was top cooling product

Dear Ian,

I just wanted to say how thrilled I was to see the Kool Max Zipper Vest (left) rated as your No.1 cooling product in your “beat the heat” feature (June/ July 2016)

The Kool Max Zipper Vest is just one of many items we sell on our website www.peakpersonalcooling.uk (my wife suffers migraines and her favourite is the Soft Ice Head and Neck Wrap.)

It really eases her pain while the Kool Max Zipper vest is definitely my favourite too).Originally the company was set up to help people who suffer heat intolerance like I do but many people are coming to the site for various reasons including hot flushes, lupus or simply comfort without any ailments.

We even had a gentleman who visits children but once a year make a purchase because he gets too hot in his big red suit! (our first celebrity customer, and what a guy!)

In all seriousness Peak Personal Cooling is still a young company and I hope it continues for years to come bringing relief and comfort to many. We sell Items we truly believe in and running a small business that can help so many is among our greatest achievements!

Paul D. Edwards www.peakpersonalcooling.uk

Being pro-active helps my PPMS

Dear Ian

As a PPMS sufferer I am always pleased to read your ezine.

In your last issue I was surprised to read a news story that said many sufferers received little or no support once they had 'advanced' to secondary progressive and primary progressive stages of the condition.

Since I was diagnosed with primary progressive in 2010 I have received invaluable support from the MS nurse at the Walton Centre in Liverpool and yearly visits to the consultant. In fact we have arranged appointments on a 6 monthly basis ie I see the consultant and MS nurse alternately during the year.

I am also a member of the local MS Society and branch member of the committee.

I feel that having the condition I should be pro-active in ensuring that I seek advice when necessary, and be as positive as I can in coping with MS.

For information 19 years ago I had a major brain operation for a condition called Arnold Chiari malformation and often wonder if there is any connection with my current condition.

Keep up the good work.

Mike

Reading the ezine in different formats

Dear Ian,

Re: Margaret Clarke's letter in the last edition regarding her problems reading the ezine in the Adobe Acrobat format in which it is delivered,

I don't use Adobe Acrobat but prefer a program called Foxit PDF reader which is freely available online. Accessibility of increasing and reducing page size is shown on each page in the middle of the screen just below the menu bar.

Regards

Chris Janovitz

Warrington



Help me develop this ezine

I am a journalist who loves writing news and features. And having had progressive MS for ten years I have lots to write about.

However, the aim of this site is also to provide news and information for all people with progressive MS and that includes you.

So, please send me your stories, air other views, and give me hints and suggestions.. Finally, please send this ezine to all other progressive MSers in your address book so we can raise our profile and lobby for a better life.

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 (Oct-Nov 2016)

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



PLUS MY EXPERIENCES TAKING STATINS FOR SPMS

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Stem cells “cocktail” story

Sources: 1. A triple-effect cocktail produced by neural stem cells as a novel neurorepair therapy for chronic stage CNS autoimmunity.

Li X, Zhang Y, Yan Y, Ciric B, Ma CG, Gran B, Curtis M, Rostami AM, Zhang GX. Mol Ther. 2016. doi: 10.1038/mt.2016.104. [Epub ahead of print]

2. : <http://multiple-sclerosis-research.blogspot.com/11/6/16>

Intrathecal steroids story

Source: http://multiplesclerosisnewstoday.com/2016/07/13/steroid-lowers-oxidative-stress-in-cerebrospinal-fluid-of-progressive-ms-patients/?utm_source=Multiple+Sclerosis&utm_campaign=d63d85d812-RSS_THURSDAY_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_b5fb7a3dae-d63d85d812-71290133

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Anti-psychotic drugs story

<http://www.victoria.ac.nz/news/2016/06/multiple-sclerosis-trial-begins-at-wellington-hospital>

ocrelizumab story

Source:

Pharmabiz.com <http://www.pharmabiz.com/NewsDetails.aspx?aid=95982&sid=2>

pages 4-6 Feature on disabled rambling

<http://disabledramblers.co.uk/>

page 7 Xemys story

The paper involving human subjects can be viewed free online at

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4864531/>

See also [http://multiplesclerosisnewstoday.com/2016/06/30/new-MS-vaccine-soon-to-enter-phase-3-](http://multiplesclerosisnewstoday.com/2016/06/30/new-MS-vaccine-soon-to-enter-phase-3-testing/?utm_source=Multiple+Sclerosis&utm_campaign=699485ae8a-RSS_MONDAY_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_b5fb7a3dae-699485ae8a-71290133)

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Page 7 simvastatin story

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P8 spasticity story

<http://www.flex-pharma.com/company.php>

<http://multiplesclerosisnewstoday.com/2016/06/20/2016061520160615flex-pharma-starts-phase-2-efficacy-study-in-multiple-sclerosis-patients-with-spasticity/>

p8 mitochondria story

Source: <http://multiplesclerosisnewstoday.com/2016/05/25/mitochondria-pharmaceuticals-raised-1-6-million-to-develop-new-neuroprotective-agent-mp101/>

page 9 -10 sunshine

<http://sunlightinstitute.org/exceptionally-important-findings-on-sunlight-exposure-multiple-sclerosis-ms-and-brain-volume-independent-of-vitamin-d/>

<https://rosemarycottageclinic.wordpress.com/2014/11/02/human-photosynthesis-beyond-vitamin-d/>

Cytokine 2012 Nov;60(2):540-51. doi: 10.1016/j.cyto.2012.06.011. Epub 2012 Jun 30. Sildenafil (Viagra®) down regulates cytokines and prevents demyelination in a cuprizone-induced MS mouse model. Nunes AK

The role of the nitric oxide pathway in brain injury and its treatment — From bench to bedside P.S. Garrya, Experimental Neurology Volume 263, January 2015, Pages 235–243

Page 11 Brain micro-bleeds and prog-MS

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

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