

My prog-MS ezine

For people with progressive MS and other interested people

Issue number 23, January/February2019

Hello and welcome to the latest edition of my 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 eight pages of important prog-MS news stories plus two features about issues that matter to prog-MSers. In the first feature (page 5) I tell you about a trip to Benidorm and how incredibly disability-friendly it was.

The second feature looks at the nine hole peg test that is used to measure hand function in MS. It's incredibly useful way of measuring progression in those who can't walk and it's available online for just £10. See page 10.

IN THIS ISSUE



Scooting off on holiday to Spain. See page 5 – hola!

Epstein-Barr virus treatment could help in prog-MS– page 2
Lipoic acid supplement may aid walking – page 3

Positive results for Epstein-Barr treatment in prog-MS

In the first study of its kind, Australian researchers have tested the feasibility and safety of a new cell-based therapy which targets The Epstein-Barr virus (EBV) in ten people with secondary and primary progressive MS.

Participants in the study had been diagnosed with MS for between 3 to 25 years and all had experienced disability progression for at least 2 years, with EDSS scores of 5.0 to 8.0. Blood from each participant was treated in the lab to recognise and kill EBV-infected cells. Blood was then given back to participants in four infusions over an eight week period. Participants were monitored for 27 weeks with a range of tests including changes in EDSS, fatigue, quality of life and thinking and memory skills.

Seven of the ten participants had improved symptoms starting 2 to 14 weeks after the first infusion. Three of these had an improvement in level of disability. Improvement occurred in people with both primary and secondary progressive MS. Fatigue improved significantly for the whole group over the 27 week period, particularly for five of the seven participants who showed other improvements. The treatment was well tolerated with no serious side effects.

Seven of the ten participants either reported or showed measureable improvements in symptoms starting 2 to 14 weeks after the first infusion, accompanied by a reduction in EDSS score in 3 participants. Improvement occurred in people with primary as well as secondary progressive MS.

Participants whose T cells showed a stronger ability to attack EBV-infected cells were more likely to improve with the treatment than those whose T cells showed a weaker response. The results confirm the feasibility and safety of the new treatment. The improvements seen in this small study are hugely encouraging to those who believe EBV has a role to play in MS or may even be its cause. However these results will need to be confirmed in larger studies which compare the cell-based therapy with a dummy, or control, group. Plans for further studies are being drawn up. ***For details of sources for all news stories go to page 14***

Lipoic Acid Supplements May Help to Delay Decline in Walking Speed in SPMS Patients, Study Says

Lipoic acid (LA), an over-the-counter antioxidant supplement, helps to mildly delay a decline in walking speed in secondary progressive MS (SPMS) patients, particularly those with lesser disability, a, two-year clinical study reports.

The study, "Effects of lipoic acid on walking performance, gait, and balance in secondary progressive multiple sclerosis," was published in the journal Complementary Therapies in Medicine, and the findings are of enough interest to justify further studies, researchers said.

A recently concluded clinical trial in 51 SPMS patients at the Veterans Affairs Portland Health Care System in Oregon suggested that 1200 mg of oral LA, taken daily, improved walking abilities and reduced the extent of brain volume loss compared to placebo, while being safe and well-tolerated.

The trial was a randomized, double-blind Phase 2/3 study, with participants randomly allocated to either a treatment group given 1200 mg pills of LA daily (28 patients) or to a placebo group (26 patients) for two years. Results showed that LA supplement use slightly delayed the decline in walking speed at six months and moderately at two years of treatment. No differences in balance were found between the groups. Researchers said their study's findings warrant further investigation of use of LA as a treatment for walking impairment.

NB: I take 600 mg of Lipoic Acid with my breakfast and a similar amount with my evening meal. I obtain these 600mg high strength Lipoic Acid pills from Piping Rock in the US. https://gb.pipingrock.com/alpha-lipoic-acid

For details of sources for all news stories go to page 14

Adult oligodendrocytes may boost myelin production in MS, study suggests

Mature, adult oligodendrocytes can reacquire their ability to produce myelin to replace ones lost in diseases like multiple sclerosis (MS) without undergoing a stem cell-like state, a new study shows.

The study "The adult oligodendrocyte can participate in remyelination" was published in the journal PNAS.

Mature, myelin-producing oligodendrocytes develop from more immature, stem cell-like cells, called oligodendrocyte progenitor cells. So, when myelin is lost, the only way to recover it is to have a new oligodendrocyte from progenitor cells to produce it again.

This has been the dogma in MS research, and the reason why MS treatments aimed at remyelination have been focused on recruiting oligodendrocyte progenitor cells to the sites of myelin damage, in order to induce new myelin production.Now, researchers at the University of Wisconsin–Madison's School of Veterinary Medicine show evidence that mature oligodendrocytes can reactivate and produce myelin again.

Using cats and Old World monkeys, called rhesus macaques, that suffered a severe loss of myelin in their axons, the researchers showed that mature oligodendrocytes could begin re-myelinating the damaged axons.

Overall, the new findings "indicate that mature oligodendrocytes can participate in remyelination," the researchers wrote, and open new avenues for MS treatment that may help slow or even halt disease progression.

"Right now, the emphasis is on promoting the numbers of oligo progenitors and their differentiation, particularly into adult oligodendrocytes. What this work provides is a different target," said Duncan. "In fighting complex diseases, such as MS, the more tools you have on hand, the better. If these adult cells are recruitable in some fashion, we should be looking at ways to do it."

For details of all news stories go to page 14



Scooting off on a week's holiday to Benidorm

Benidorm! Sangria, sun, stag dos and cheap beer for Brits - a great basis for a soap opera on ITV, but surely not a practical proposition for a middle aged MSer like myself?

That's what I thought and perhaps was the reason I was unable to make a family celebration earlier last year. When my family, especially my elder sister Susan and my 93 year old Uncle Ron , who are fully aware of my needs reported back on what they saw in Spain, I did wonder if I'd made the right decision. Luckily a second family get together presented itself and I thought "now or never".

So, with the help of my elder sister, who as a mother, ex-teacher and army trained, is a wonder at organisation, we set off via Birmingham Airport and Jet2 to Alicante. Thanks to my sister's pre-planning, we sailed through security, pre-loaded via a sort of fork-lift onto the plane . Being first on the plane means you're last off - but we didn't have to go through the scrum at baggage collection as we had help there too.

And then straight to our pre-booked disabled taxi and 45 minutes later we arrived at the hotel in Benidorm. Things having pretty well worked out on our journey as promised on the various websites of the organisations we were relying on.

After the usual Spanish admin on arrival at the hotel, which I left to my sister, I was here. Family assembled - check. Mobility scooter - check. Fully charged - double checked. Sun out and 28 degrees - just the same as Birmingham, except centigrade not Fahrenheit.

So what of Benidorm - it was my first visit? Mile after mile of promenade, clean beaches and an endless sequence of bars, cafes and restaurants.

continued on page 6







(l-r) View from my room, Sister Sue with me and Uncle Ron, scooters outside cafe

Continued from page 5 The biggest surprise being how much a resort for Spanish people Benidorm actually is - complete with an Old Town, tapas bars and everyone of all generations out promenading until the late hours. And despite being early October, out-of-season in most resorts, this being Benidorm, a year round resort, everything was fully open. Most big hotels seem to run nightly entertainment and there were no end of bars with tribute acts, most being actually quite decent – that is if you like tribute acts.

And our hotel? On a main road one street back from the beach so no issues with noise etc. Rooms very clean and spacious and geared up for an older clientele. Facilities included a undercover parking area for the "grand prix" line-up of scooters all being recharged.

The rest of the holiday went smoothly with no issues for myself in family participation and I did become quite good at slaloming through the crowds and around the tandem scooters and never at anytime exceeding a responsible walking pace speed (honestly) The large number of cafes and bars meant that stopping for drinks was never a problem. Most places were accessible and if less so then the next door establishment would be fine. With me feeling the heat at times, I sometimes felt I was slowing down the group - especially in the early days, but then I bought a hat and a water spray, both of which I'd cleverly forgotten in my packing. Lessons learnt? Pre-planning is essential and it helps to have an enthusiastic "personal assistant" such as my sister, but it is worthwhile.

As I sat in our accessible taxi speeding down the motorway back to Alicante airport, I thought of the "A Team" on television in the 1980s and Hannibal Smith's' catchphrase, "I love it when a plan comes together".

(Thanks to my cousin Paul for his help with this article.) **For further details go to page 14**

Stem cell trial's mixed results for prog-MSers

A study of 35 MSers (15 with secondary progressive MS and 20 with relapsing-remitting MS) who received Haematopoietic stem cell therapy (HSCT) showed 21 experienced no disease activity for three years after treatment and 13 participants showed improvements in their EDSS disability scores.

However eight people in the trial had continued disability progression during the follow-up period. Of these eight people with disability progression six had progressive MS and two had relapsing remitting MS.

This means that nine of the progressive MSers in the trial showed improvement (60% of prog MSers) and six progressive MSers (40%) continued to progress. Among the 20 with relapsing remitting MS 18 (90%) showed improvement and only two (10%) got worse. The results suggest that while HSCT works for the majority of relapsing remitting MSers it sees improvement in just over half of those with progressive MS.

Haematopoietic stem cell therapy (HSCT) uses a combination of chemotherapy and reinfusion of blood stem cells to rebuild and reset the immune system. Immune cell analysis showed that after one year attacking immune cells are still wiped out by HSCT but cells that regulate the immune system are restored.

Participants in the study had levels of disability that ranged from low to moderately severe (EDSS scores between 2 and 7).

Participants experienced the expected side effects of high dose chemotherapy, including ulcers in the digestive tract, nausea and hair loss. One third required red blood cell transfusions and a half required platelet transfusions during their hospital stay. No-one died as a result of the treatment in this study.

The response results are similar to those seen in other international studies and confirm that people with relapsing-remitting MS respond better to HSCT than those with secondary progressive MS. **For details of all news stories go to page 14**

News

Trial of new stem cell therapy for prog-MS approved in US

The U.S. Food and Drug Administration (FDA) has approved a request by BrainStorm Cell Therapeutics to open a Phase 2 clinical trial testing the safety and effectiveness of its NurOwn mesenchymal stem cell (MSC) treatment in progressive MS. BrainStorm plans to launch the study in early 2019.

NurOwn cells are MSCs obtained from a patient's bone marrow — the spongy tissue inside bones — and grown in the lab under patented conditions in order to induce the cells to secrete high levels of neurotrophic factors (NTF), molecules that support the growth, survival, and differentiation of neurons. These MSC-NTF cells are then injected back into the patient intravenously or into the spinal canal.

Experiments with mice suggest that injected NurOwn stem cells do not themselves replace damaged cells. Instead, the lab treatment customizes MSCs, converting them into biological factories that secrete high levels of NTFs, which in turn encourage neural stem cells to replace damaged cells.

NTFs may also exert a therapeutic effect in progressive MS by other mechanisms. They can improve neuronal survival following injury, protecting cells from oxidative stress, and can modulate the immune response, shifting it from pro-inflammatory to anti-inflammatory, dampening the autoimmune damage done to myelin (the protective cover of neurons that is destroyed in MS).

NurOwn cell therapy is currently being evaluated for safety and efficacy in a Phase 3 clinical trial (NCT03280056) in up to 200 people with amyotrophic lateral sclerosis (motor neurone disease) at sites in the U.S.

For details of all news stories go to page 14

Antidepressant Clomipramine Shows Potential as Treatment for Progressive MS

Research that used a systematic screening of more than 1,000 generic drugs showed the anti-depressant drug clomipramine could be a promising therapy for progressive multiple sclerosis.

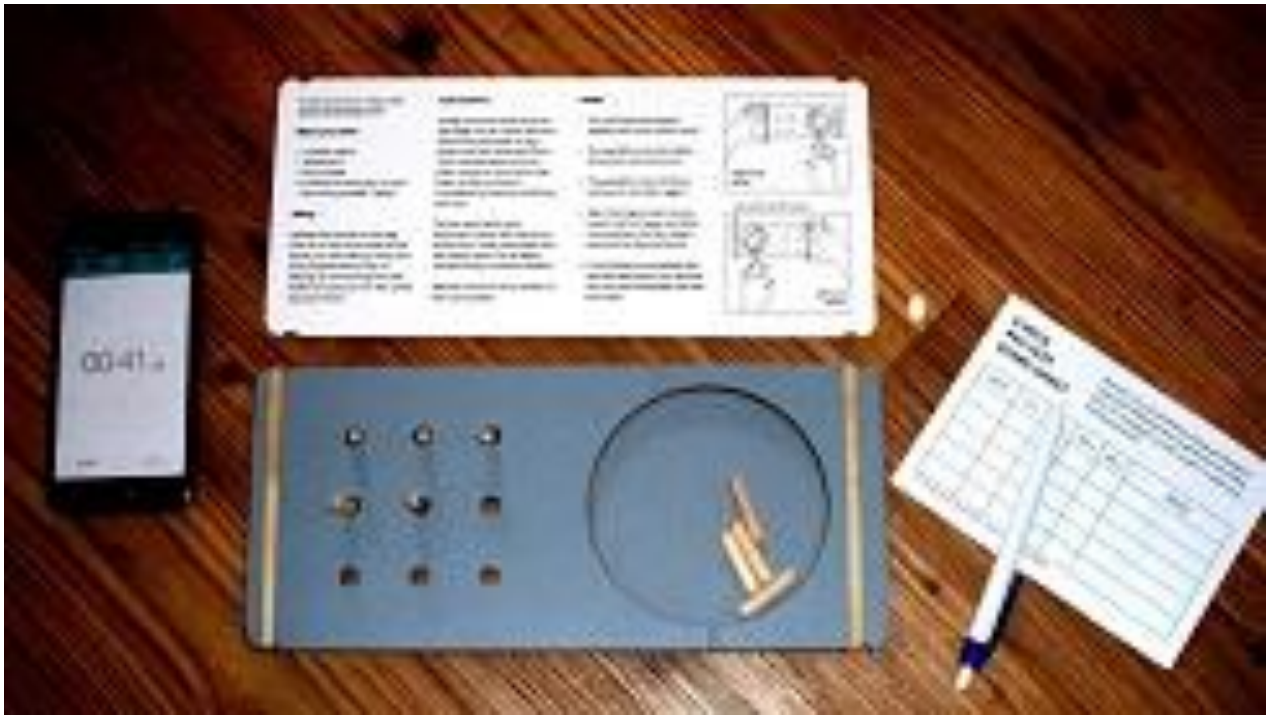
The research looked at generic, orally available medicines that cross the blood brain barrier and target three drivers of progressive MS- iron-mediated neurotoxicity, lymphocyte activity, and oxidative stress.

One drug that stood out above all the others was the antidepressant drug clomipramine. Discovered in 1964, clomipramine has been used to treat obsessive-compulsive disorder, panic disorder, major depressive disorder, and chronic pain.

The study also looked at clomipramine in mice, specifically those with autoimmune encephalomyelitis, which is considered a model for MS.In mice, clomipramine significantly improved the clinical signs of acute and chronic phases of MS.

“This is an interesting approach of ‘repurposing’ old drugs for new uses,” explained Dr. Barbara Giesser, professor of clinical neurology at the David Geffen School of Medicine at UCLA and clinical director of the UCLA MS programme. “The animal results are very intriguing, and if they are shown to translate into efficacy in human trials, [that] would represent significant advances in treating progressive MS,” she added.

For further information on news stories go to page 14

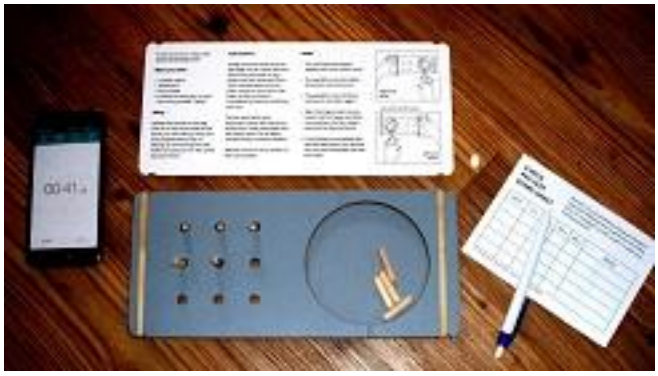


A £10 test to measure your MS progression – and it's available online

Everyone with progressive MS probably knows about the timed 25 foot walk test - the gold standard used by neurologists to see how fast MS is progressing. The test is also used by pharma companies trialling new drugs. The great thing about the test is its simplicity. All is needed is a stop watch and the MSer is timed walking 25 yards.

Of course the 25 yard walk test is only useful if you can walk, and is therefore useless for wheelchair users and those with limited walking. This means those with less mobility are less likely to be given a test to see how fast their MS is progressing and are often excluded from clinical trials because it's more difficult to measure any change in their condition.

Continued on page 11



Continued from page 10

For this reason in 2016 neurologists at London's Barts Hospital launched a campaign called "Think Hand". This aimed to convince those organising trials that hand function is very important to measure. They were also trying to emphasise the importance of preserving upper body use in progressive MS.

Hand function can be measured by something called the nine hole peg test (9HPT) where you take nine wooden pegs from a bowl and place these in a board which has nine holes. The trial is done twice with both hands and the time taken to perform the test is measured. Until last year there was just one problem. The equipment, although simple, was not available outside specialist settings like clinics and hospitals. Unlike the 25 yard timed walk you couldn't really test yourself at home.

Then in 2017 Barts MS Trust in London came up with a brilliant innovation, a cheap, environmentally friendly, cardboard 9HPT was launched for home use at a very reasonable price of £9.99. See https://www.youtube.com/watch?v=U1lzIXWByTI

Right away I sent off for one and for the past year I have been testing myself monthly. From an initial time of 2 minutes I can now perform the test in I minute 48 seconds which means that I am about 10% faster than a year ago.

In a medical world dominated by high technology the nine hole peg test is cheap, accessible and reliable. Being able to measure my hand movement has made me feel involved in monitoring my MS and measuring any change. In my opinion the home- use nine hole peg test is the sort of thing that every progressive MSer should have at home. It's a tenner well spent.

To obtain the £9.99 9HPT go to the website http://www.clinicspeak.com/9-hole-peg-test

Walking is better with mental rehearsal, music and prompts

Mentally rehearsing walking improves actual walking and this effect is enhanced when you imagine walking while listening to rhythmic music with additional verbal prompts.

That is the finding of a study which assessed walking in people with mild to moderate disability (up to EDSS 4.5) before and after practising MI (Motor Imaging)for four weeks

Motor imagery (MI) is a technique where you visualise yourself doing an activity without actually moving. This technique is used by athletes to improve their performance and also by physiotherapists to help people regain movements.

This study assessed walking in 60 people with mild to moderate disability (EDSS up to EDSS 4.5) before and after practising MI for four weeks. Participants were divided into three groups to test the effect of adding additional cues or prompts: MI alone, MI combined with rhythmic music, and MI with music plus additional simple instructions.

All of the groups had improvements in walking speed and walking distance, with the biggest improvements seen in the group which practised MI combined with music and instructions. Fatigue and quality of life improved significantly using cued MI, with the greatest changes seen after MI plus music and instructions. Both types of cued MI also resulted in better synchronization of walking to fast and slow music.

The study shows that, if your walking is mildly impaired, mentally rehearsing walking could improve actual walking and this effect can be enhanced if you imagine walking while listening to rhythmic music with additional verbal cues.

For further details of all news stories go to page 14

Ocrevus Helps upper limb Function in PPMS Trial Shows

Treating primary progressive multiple sclerosis (PPMS) patients with Ocrevus (ocrelizumab) can preserve strength and function in their hands and the arms, analysis of data from a Phase 3 trial has found.

The research, "Ocrelizumab reduces progression of upper extremity impairment in patients with primary progressive multiple sclerosis: Findings from the phase III randomized ORATORIO trial," was published in the Multiple Sclerosis Journal.

A randomized, double-blind, and placebo-controlled Phase 3 trial, ORATORIO (NCT01194570; study funded by Roche, which owns Genentech) enrolled 732 PPMS patients, ages 18–55. Treatment with Ocrevus led to lower rates of disease progression, as assessed at 12 and 24 weeks based on EDSS, the timed 25-foot walk, brain lesion volume, and total brain volume loss.

Now, in an exploratory analysis, researchers looked specifically at the effects of Ocrevus on UE (Upper extremity – hand) dysfunction in these patient as measured by the nine hole peg test (9HPT)

Treatment with Ocrevus reduced the risk of confirmed progression of 20% or greater in 9HPT time for both hands at 12 and 24 weeks, both in the overall patient population and in patients with abnormal 9HPT times at baseline. Similar differences were found at higher confirmed progression thresholds (25%, 30%, and 35%, meaning higher UE disability).

Data further revealed a "significantly improved" change in 9HPT time from baseline to week 120 in patients treated with Ocrevus compared to those given placebo. This benefit was consistent in 9HPT and EDSS subgroup analyses. Overall, "findings from this analysis showed that ocrelizumab [Ocrevus] mitigated progression of UE impairment in patients with PPMS using the 9HPT," the researchers wrote.

For details of all news stories go to page 14

References contact details etc

Page 2

Source: Epstein-Barr virus-specific T cell therapy for progressive multiple sclerosis. Pender MP, et al. Journal of Clinical Investigation Insight 2018;3(22). Pii: 124714.

https://insight.jci.org/articles/view/124714

Page 3

Alpha Lipoic acid story

Source: https://multiplesclerosisnewstoday.com/2018/12/13/lipoic-acid-supplements-may-help-delay-gait-worsening-in-spms-study-reports/

Page 4 Adult oligodendrocytes story

Source: https://multiplesclerosisnewstoday.com/2018/11/29/adult-oligodendrocytes-may-replenish-myelin-production-in-ms-study/??utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

page 7 Australian stem cells story

https://msra.org.au/news/australian-ahsct-trial/

page 8 US stem cells story

https://multiplesclerosisnewstoday.com/2018/12/19/fda-approves-phase-2-trial-of-nurown-stem-cell-therapy-in-progressive-ms-patents-brainstorm-says/?utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

Page 9 Clomipramine story

https://www.healthline.com/health-news/antidepressant-potential-progressive-ms-treatment

page 12 walking story

Seebacher B, et al.

Effects and mechanisms of differently cued and non-cued motor imagery in people with multiple sclerosis: A randomised controlled trial.Mult Scler. 2018 Aug 14. [Epub ahead of print]

2. https://www.mstrust.org.uk/research/research-updates/181108-walking-improves-mental-rehearsal?utm_source=Researchupdate&utm_medium=Email&utm_campaign=October2018

Page 13 Ocrevus story

Source: https://multiplesclerosisnewstoday.com/2018/10/29/blocking-overproduced-molecule-in-ms-eases-spms-like-disease-in-mouse-model-study-reports/?utm_medium=desktop-push-notification&utm_source=Notifications&utm_campaign=OneSignal

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

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