

My prog-MS ezine

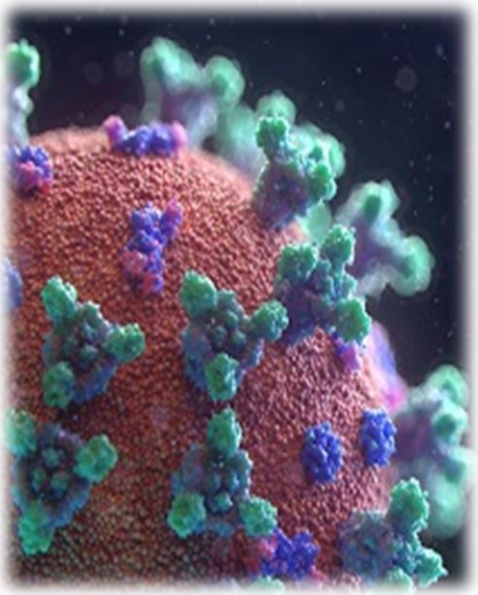
For people with progressive MS and other interested people

Issue number 31, May/June 2020

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 (sorry it's a bit late) are seven pages of important prog-MS news stories including one on MS and Covid-19 (page 2) There are also two features one on page 5 about getting older with MS – I will be 62 in the Summer – and another looking at all the indoor hobbies I have taken up in the lockdown, including learning the ukelele. See page 10.

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Research on Covid-19 in MS is reassuring for MSers

People with MS who contracted Covid-19 did no worse than the general population according to preliminary results from Italy.

Researchers in Italy have been collecting data to understand the relationship between MS and Covid-19. They're trying to understand whether having MS increases the risk of a more severe Covid-19 infection.

The Italian Multiple Sclerosis Society (AISM), the Italian Multiple Sclerosis Foundation (FISM), and the Multiple Sclerosis Study Group of the Italian Neurological Society set up an online platform to record and collect data about people with MS in Italy who have been diagnosed with Covid-19 or have developed symptoms (suspected Covid-19). MS neurologists across Italy were asked to input data and share patient outcomes.

Early results from the data they've collected so far have now been published. Their preliminary data includes 232 people with MS who have tested positive for Covid-19 (57 people) or have suspected Covid-19 (175 people

The data recorded the severity of Covid-19 in these 232 people: 223 (96%) had a mild infection , 4 (2%) had a severe infection and 6 (3%) had a critical infection Of those who were critical, one person recovered and five people died. The people who died tended to be older (50+) and have other health conditions.

Although this research is preliminary and the numbers are fairly small, these results are reassuring for people with MS. They suggest that having MS doesn't increase your likelihood of a more severe Covid-19 infection and that the majority of people with MS are likely to have a mild infection, the same as the general population.

Picture on page 1 is courtesy of Fusion Medical Animation and Unsplash

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Starting Mayzent (siponimod) early is better

People with secondary progressive MS (SPMS) who begin treatment with siponimod (Mayzent) early and continue its use for five years are less likely to experience disability progression than those starting the medication later in their disease course, five-year data from a study suggests.

Five year data from the Phase 3 clinical trial called EXPAND further suggests that Mayzent can help preserve important tissues in the brain, delaying physical disability and slowing cognitive decline. These findings were published in a supplementary issue of the journal Neurology.

Mayzent (siponimod), developed by Novartis, is approved to treat active SPMS in both the United States and Europe. The oral therapy belongs to a class of medications called S1P receptor modulators. These work by 'trapping' immune cells in lymph nodes (immunological structures), which can limit the inflammation that causes nervous system damage in MS. The Phase 3 EXPAND clinical trial (NCT01665144) was set up to evaluate the safety and efficacy of Mayzent in people with SPMS. In the first part of this Novartis-sponsored study, participants were given either Mayzent or a placebo tablet for about three years. Results from this core part of the study, released in 2017, showed that Mayzent significantly slowed disability progression and cognitive decline compared to the placebo.

Those first given Mayzent rather than placebo were significantly less likely to experience disability progression, and they were 23% less likely to show worsening on the Symbol Digit Modalities Test (a measurement of cognitive impairment). Importantly, previous data from EXPAND suggested that treatment with Mayzent can reduce the risk of people with SPMS becoming dependent on a wheelchair. In the second (2 years) part of the study, 1,224 people entered an open-label extension phase, in which all were given the active treatment. New data cover this part of the trial. The EXPAND trial is to continue to the end of March 2024 when further results will be published The European Commission has granted marketing authorization for siponimod (Mayzent) for the treatment of active secondary progressive MS. This follows a recommendation from the European Medicines Agency that a licence should be granted. NICE has begun an appraisal of siponimod for SPMS to decide whether it should be prescribed by the NHS in England and Wales. The decision was due to be published in May. The Scottish Medicines Consortium has also scheduled an appraisal to be published in July but Covid-19 may cause delays in the UK.

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Fruit peel compound may reverse damage in prog-MS

A compound found in some herbs and fruit peels may help protect against and reverse some of the damage caused in progressive multiple sclerosis, according to a new study carried out of Thomas Jefferson University in the US.

The researchers focused on mice suffering chronically from the disease, meaning that the central nervous system in these mice had already suffered damage as a consequence of the condition.

Treating the mice with the herbs and fruit peels compound -purified, lab-grade ursolic acid - was started at day 60 of the disease in the mice, which is described as an advanced stage involving damage to the spinal cord and brain. After 20 days of treatment, which was day 80 of the disease in the mice, the researchers found that paralyzed mice, though still experiencing muscle weakness, could once again walk.

This indicated a reversal of the damage that had been caused by the disease at such a late stage. In addition, the researchers found that ursolic acid may activate precursor cells that lead to the formation of cells that make the myelin sheath damaged by the immune system in MS sufferers, which may explain the positive changes observed in the mice.

Ursolic acid is present in many plants, fruits and herbs - including many ordinary foods consumed every day. Ursolic acid can be found among others in apples, basil, cranberry, peppermint, rosemary, lavender, oregano, thyme and dried plums

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Getting on with MS

When it comes to public discussions of life, death and MS there is often talk in the media of euthanasia. Sadly, you see little discussion of the decades of life the vast majority of us, like me, live with MS into our sixties and beyond.

Looking forward to my 62nd birthday in three months' time it's reassuring, therefore, to read research published recently by the US National Multiple Sclerosis Society (NMSS), that the majority of us MSers can look forward to an almost normal lifespan, well a lifespan just a few years shorter than the general population.

The exact figure is seven years shorter but this figure isn't so bad when you consider people with type 2 diabetes, on average, have a shorter life expectancy of about 10 years and people with type 1 diabetes, on average, a shorter life expectancy of about 20 years.

As well as longevity, the research publicised by the NMSS challenges other preconceptions. MSers not only have roughly the same lifespan as others, but mortality studies show MSers tend to die from many of the same conditions like cancer and heart disease as people who don't have MS. Apart from cases of severe MS, which are relatively rare, the prognosis is generally good.

That is not to say MS doesn't bring additional problems as we grow older. Those of us getting on with MS are realists. We know we may also have to contend with issues like self-catheterisation and health problems others don't, and our MS related health problems can decrease our quality of life. Although most of us will never become severely disabled, many of us will experience problems that cause pain, discomfort and inconvenience, and we will suffer more problems than those without MS. According to the US National MS Society , a third of us will need to use a wheelchair two decades after diagnosis. Others, like me, will need crutches or a cane to remain on our legs. Well that's the general picture.

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Continued from page 5. One of the problems of making more precise predictions about individual cases of MS is its unpredictability. Everyone is different when it comes to the so called "snowflake disease", and it's hard to predict with accuracy how MS will progress in individual cases. Most of us will have witnessed how the severity of the disease varies widely from person to person.

What you can say with greater certainty is that most MSers will undergo a certain amount of disease progression during the course of the illness. To help determine our personal risk of progression, it helps to understand the risk factors at work here.

According to the US Mayo Clinic certain factors indicate a higher risk of more severe symptoms, including the following: being over 40 at the initial onset of symptoms; initial symptoms affecting many parts of your body or initial symptoms affecting mental functioning, urinary control, or motor control. Looking at my own case my first symptoms included motor control and urinary function (a bad sign) but as I was under 40 (a good sign) you could say it's a mixed picture for me.

And when it comes to looking forward (prognosis) and complications that may arise it is interesting that these are affected by the type of MS you have. Primary progressive MS (PPMS) is characterized by a steady decline in function without relapses or remissions. Life expectancy here is the lowest of all the types of MS. For relapsing remitting MS and secondary progressive MS (my type), there are several guidelines that help predict prognosis.

People with RR and SP MS tend to do better if they have experienced few attacks in the initial few years post-diagnosis and a longer amount of time between attacks as well as a complete recovery from attacks. They also do better if symptoms relate to sensory problems, such as tingling, vision loss, or numbness and have neurological examinations that are almost normal five years after diagnosis.

While most people with MS have a close-to-normal life expectancy, it can be difficult to predict whether the condition will worsen and by how much. In most cases, however, MS isn't a fatal condition. So although MS may mean living a life a little shorter than we would like, it's certainly is not a death sentence nor a reason to be preoccupied with euthanasia, despite what you might believe if you read certain sections of the tabloid press.

Bile Acid Supplements May Ease Prog-MS Symptoms

Treatment with a bile acid called tauroursodeoxycholic acid (TUDCA) which is now in a clinical trial for progressive MS reduced the number of immune cells infiltrating the brain as well as reducing demyelination in an animal model of MS, lessening disease severity, researchers reported.

The research "Bile acid metabolism is altered in multiple sclerosis and supplementation ameliorates neuroinflammation," was published in the Journal of Clinical Investigation.

Bile acids, the products of cholesterol metabolism, mainly work in the gut to help absorb lipids (fats). But they may also exert a neuroprotective role by preventing inflammation. Studies have shown that receptors for these molecules exist on many cells, including those in the brain and the immune system, and that activating these receptors lessens disease severity in animal models of MS.

A team led by researchers at Johns Hopkins University in the US investigated blood levels of bile acids in progressive MS patients. Results showed lower levels of several primary bile acids compared to controls, and multiple secondary bile acids were lower compared to healthy individuals.

"Overall, the data from both metabolomics [the study of metabolites] approaches in the adult cohorts revealed alterations in bile acid metabolism with greater abnormality noted in the PMS [progressive MS] group," the researchers wrote.

The team then treated astrocytes and brain immune cells (microglia) in the lab with TUDCA,. Results confirmed the protective role of bile acids in MS, as TUDCA prevented astrocytes and microglia from doing damage, without affecting their viability as cells.

This team in now leading a Phase 1/2 clinical trial (NCT03423121) testing the safety and early efficacy of a daily oral TUDCA supplement versus placebo in progressive MS patients with low blood levels of bile acids. Funded by the US National MS Society, the study is enrolling up to 60 adults with progressive disease at Johns Hopkins University.

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Ocrevus Lowers Progression Risk in More Disabled MSers

Ocrevus (ocrelizumab) lowers the risk of continued progression among Primary Progressive MS patients with considerable disability, according to data from an exploratory and post-hoc analysis of three Phase 3 trials.

This is according to the study, "An exploratory analysis of the efficacy of ocrelizumab in patients with multiple sclerosis with increased disability," which was published in the Multiple Sclerosis Journal – Experimental, Translational and Clinical.

Ocrevus is a monoclonal antibody that targets CD20, a protein found on the surface of immune B-cells. It works to lower the activity of the immune system to prevent immune cells from attacking nerve cells, triggering MS progression.

The exploratory study results show that "in patients with increased disability, Ocrevus reduced the risk of confirmed disability progression versus placebo in patients with progression-onset MS," the researchers wrote.

But, they continued, "due to the exploratory nature of this analysis, additional prospective studies are warranted to assess treatment benefit in patients with MS with advanced disease using qualified, sensitive, and meaningful assessments of disability."

MedDay Trial into biotin drug from prog-MS disappoints

French pharma MedDay has just announced the second Phase III trial, SPI2, of high-dose biotin (MD1003) for progressive MS is negative as the biotin drug did not meet its primary and secondary endpoints.

"We are clearly disappointed that SPI2 did not meet its primary and secondary endpoints. Going forward, we will continue to evaluate the trial data and confer with regulators," commented Catherine Moukheibir, Chief Executive Officer of MedDay Pharmaceuticals.

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FDA Approves Zeposia (Ozanimod) capsules for SPMS

The U.S. Food and Drug Administration (FDA) has approved Zeposia (ozanimod) oral capsules to treat adults with active secondary progressive MS (SPMS).

Due to the COVID-19 pandemic, however, when it will arrive in clinics for patient use is not yet known, Bristol Myers Squibb (BMS), which will market Zeposia, said in a press release announcing the approval.

“The Company made the decision based on what’s in the best health interest of our patients, customers and employees,” it said. “Bristol Myers Squibb will continue to monitor the environment and will partner with the neurology community to inform launch timing.

An sphingosine-1-phosphate (S1P) receptor modulator and a small molecule, Zeposia selectively blocks S1P receptor subtypes S1PR1 and S1PR5 present at the surface of lymphocytes — white blood cells involved in the inflammatory attacks against nerve cell fibres (a hallmark of MS).

By blocking the activity of these receptors, it prevents lymphocytes from exiting the lymph nodes, entering the circulation, and reaching the brain and spinal cord, where they promote inflammation and nerve cell damage.

Zeposia belongs to the same class of compounds as Gilenya (fingolimod) and Mayzent (siponimod), two oral S1PR modulators by Novartis. But, due to its higher selectivity to S1P receptors, Zeposia is thought to have a better safety profile than Gilenya.

The FDA’s decision was based on positive data from two global Phase 3 clinical trials — SUNBEAM (NCT02294058) and RADIANCE part B (NCT02047734) — showing that ozanimod was superior to Avonex (an injectable formulation of interferon beta-1a by Biogen).The trials compared the safety and effectiveness of two doses of ozanimod capsules (0.5 mg and 1 mg), given daily, to that of weekly intramuscular injections of Avonex for up to two years in people with RRMS or active SPMS.

Results from each trial showed that Zeposia’s use also led to significantly lesser brain atrophy (shrinkage), and to clinically meaningful improvements in patients’ cognitive processing speed.

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Surviving lockdown with MS –playing a ukulele!

Lockdown can be tough if you've got prog-MS. With nowhere to go and nobody to see, I have found myself indoors more than usual. So, keeping busy has been a necessity for me to stay healthy and happy. But what to do?

Well, trying to be positive, I have decided lockdown should be a time for learning a new skill or taking up a new hobby. And my challenge has been to find one to choose from.

Among the hundreds of hobbies, music can be a good, creative and accessible pastime. But what if, like me, you aren't very musical? Last year I found a musical instrument that's both creative and accessible, the ukulele, and it's sat in the cupboard not doing very much since I bought it – that was 'til lockdown.

At its heart the ukulele is a four string instrument -great for simple tunes played by those with little or no knowledge of music who want to play an instrument and even teach themselves. Originally from Hawaii, but now with worldwide following, the ukulele or "uke" is small, easy to carry and store. It's ideal for people like me who have trouble carrying things around. It's also robust and easy to play . Although there are loads of ukulele groups around I clearly can't join one at the present time. But there are plenty of online

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Continued from page 10 ukulele clases including watching the Ukulele Orchestra of Great Britain. I bought my second-hand ukulele for just £5 at a local charity shop just after Christmas last year and in lockdown I have made great progress. Alright I am not exactly a virtuoso but I have a lot of fun. Yes, that is what the ukulele is all about –fun. What you play is pretty much up to you but I like everything – folk, contemporary even, the Morecambe and Wise seventies classic "Bring me Sunshine". You might say that the humble ukelele brings me a little bit of sunshine at the end of the tunnel .

Clearly I don't spend my whole day strumming my "uke" but I have found a few other things to fill the days. I am learning a new language (Greek) using an online resource called Duolingo - https://www.duolingo.com/learn I have discovered the lockdown is the perfect time for learning a new language And when we are finally allowed out I can use my newfound Greek language skills on a Summer holiday.

Learning a new language is a leisure activity/ hobby that is keeping my mind stimulated and, if I keep it up, it might come in useful on my future holidays. That is just two ideas, I am sure there are lots more but whatever you do activity keeps the mind busy and the morale high, and that, in my opinion is how to survive lockdown –things like dreaming of playing ukulele on a yacht moored up at a Greek island. - dream on!



Picture credit: Daria Nepriakhina on Unsplash

US Patent for MedRhythms' "Audio Engine" to aid walking

The United States Patent and Trademark Office has issued a patent covering the intellectual rights to MedRhythms' proprietary audio engine, a core component of the company's rhythmic sound products designed to improve the walking ability of adults with MS.

The new patent (US20190022351A1), "Enhancing Music for Repetitive Motion Activities," covers the audio engine's ability to both screen and augment songs, which is a crucial aspect of MedRhythms' products designed to stimulate a patient's motor system using auditory stimuli delivered through music.

This is the second patent protecting the intellectual property rights of the company's digital therapeutics platform. The first (US20170296116A1), "Systems and Methods for Neurologic Rehabilitation," was issued in December 2019.

Related to this intellectual property, the company is currently looking for opportunities for internal development and partnerships to further advance its product pipeline.

The issuance of the new patent follows the announcement of the launch of a pivotal trial assessing the efficacy of one of the company's digital products at improving the walking abilities of stroke survivors who developed chronic walking impairments.

It also follows the creation of scientific advisory boards to help steer the company's clinical and research activities in the areas of MS, stroke, and Parkinson's disease.

More recently, MedRhythms announced it is planning to launch another pivotal trial to evaluate the safety and efficacy of MR-004, a product based on rhythmic auditory stimulation that is currently being developed as a form of walking therapy for those with MS. The trial, which is being supported by a grant from the Consortium of Multiple Sclerosis Centers, will be conducted at the Cleveland Clinic in the US.

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