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INFORMATION

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NEWSLETTER OF THE 'IN' GROUP: THE INFLAMMATORY NEUROPATHY SUPPORT GROUP OF VICTORIA INC., supporting sufferers from acute Guillain-Barre` Syndrome (GBS) & Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and other Inflammatory neuropathies.

OUR NEXT MEETING WILL BE ON

SUNDAY, 23RD JUNE, 2019, 2PM TO 4PM
****AT THE ASHBURTON LIBRARY,**
High Street, Ashburton.

Guest Speaker: Scott Earle
"Where I am on my journey."

A small plate to share would be appreciated.

Dates to Remember **Please note venue.

Sunday, August 18th	Annual General Meeting- Ashburton Library	2pm to 4pm
Sunday, December 8th	Annual Christmas Luncheon " "	12 noon to 4pm

Notes from Meeting Held Sunday, 17th March, 2019.

President Margaret Lawrence:

Apologies: I have one apology from Melva. Melva is in hospital and not at all well. She has Salmonella which is terrible so we wish her a quick recovery.

Correspondence: We have just received a donation of $1000, which is tremendous to put towards the research. Having said that, I will read you the letter we received from the Children's Hospital.

"Thank you for supporting the Royal Children's Hospital Foundation. Your funds will be directed to our Neurology Department. Thank you so much for supporting the RCH to help patients like my daughter Brooke. Your donation helps her lead a better life. Thank You.
Your generation means that the RCH can continue to provide the world leading care that so many patients like Brooke rely on.

I look forward to keeping in touch and sharing how your support is creating a brighter future for sick children. On behalf of the patients and their families, thank you for supporting the hospital. (This is a general letter from the hospital to thank people for donations.)

Then we got an email. The IN Group. "Dear Margaret and Doug, Thank you for the most recent donation of $12,000 received for the Department of Neurology at the RCH – greatly appreciated. I wanted to reach out to you personally and introduce myself as I have been working closely with Andrew Kornberg here at the RCH assisting both Andrew and the Department with their ongoing philanthropic needs for some time now.

I cannot overstate the impact that your support has made over so many years, thank you, thank you, thank you!!! It's been an incredible level of generosity and trust and to that end, I would like to offer my assistance. I steward many of the major philanthropic Neurology relationships and in this way, ensure that our donors are feeling engaged and connected with the RCH and the Department.

I wondered if you or any members of your group might enjoy a tour or visit to the RCH. I do these regularly and they are always a highlight, especially for the grown-up patients or families who as yet have not been to the new RCH. I would be very happy to arrange one of these for your group if of interest.

I also wanted to share with you a very **special event** we are planning for our most generous donors being held on Monday, 1st April, **"Neurology Then and Now – The Impact of Philanthropy". Andrew Kornberg will be speaking** at this invite only event along with colleagues from the department of Neurology."

Finally, I really want to express my thanks to you and for your kind and generous support. **Please feel free to contact me directly if you would ever like to come and visit with us or if you have any questions re the invaluable impact of your support."**

Our reply: "Thank you very much for your email. **The IN Group has only a small membership and I am always amazed at how generous they are. Their assistance to the "Research Programme" in the hope of finding more answers to their "conditions" is their inspiration.**

Thank you for the offer to tour the hospital. I will put it to the members and reply to you with the outcome.

Also thank you for the invitation to attend "Neurology Then and Now – The Impact of Philanthropy". Doug and I are happy to accept your kind invitation. We look forward to meeting you on the 1st April.

Sincerely,
Margaret Lawrence,
President.

Dear Members,

Doug and I attended this special function at The Royal Children's Hospital on April 1st.

It was a privilege and inspiration to meet and hear from dedicated doctors speaking on their field of work and research at the hospital.

The IN Group was announced on the power presentation as a special donor towards the work they are doing with Neurology, Epilepsy, Complex Movement Disorders and Stroke.

It was inspiring to see what can be achieved with research donations.

Thank you to all our members for the donations we receive. It is all of you who have made the difference.

Margaret Lawrence.

At our next meeting we have Scott Earle speaking. Some of you might have heard Scott before, also seen him on TV because when Alistair Clarkson had all his trouble, Scott was on TV being interviewed. **Scott suffered with GBS and he is going to talk about how he is getting on in life. He is a very good speaker so that will be very interesting.**

Treasurer's Report: My report covers the quarter ending 31st December, 2018.
Income: $2000. Being $120 Subscriptions, $926 Donations and $954 Christmas Luncheon.

The Christmas Luncheon was not only enjoyable but financially well worthwhile and we thank the Committee members for their input and food and to everyone for turning up and bringing their items along. You can always bring them along next year if you don't want them. (Laughter).

Expenses: $12,000 donation to the RCH, Neurology Department. $123 Newsletter costs.

That gave us a cash deficit for the quarter of $-10,123. Balance 31/12/18 stands at $8,723.

Quite a good quarter, but for the record, I would also remind those members who have not paid their subscriptions that they are well past the due date as **our subs become due on the 1st July each year. Thank you.**

Talk by Dr. Nicholas Crump, Clinical Neurologist.

Thanks everyone. I know a couple of people here and I guess they may, or may not, be happy to say they are my patients. (Laughter) Most of you I don't know, but I am a Neurologist and I've worked with patients with CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) since **I was in the Neuromuscular Clinic at St. Vincent's about 12 years ago**. Now with my work at the Austin where I do the Neurology Clinic, is where I see my patients with CIDP.

I am also a Neurophysiologist and do Nerve Conduction Studies and that, combined with my work clinically, has led **me to have a real interest in CIDP for a long time**. As it currently stands, **I am now taking that further doing some research** looking at patients with CIDP, particularly **in the area of investigating the use of ultra-sound with patients with CIDP.**

I don't know if you are across any of the literature about the use of ultrasound in nerve diseases or ultrasound in CIDP at all? There has been a real push in recent times in trying to **improve the way we monitor and diagnose people with inflammatory nerve conditions**, in particular **CIDP,** which is the most common of the peripheral nerve conditions. Those of you, or all of you, who are **patients who have been through the process, may have had problems with delays in diagnosis for a number of reasons.**

For people who have got clear-cut CIDP it is pretty simple to recognise clinically to us as specialist neurologists. We don't really need tests often to know that patients have CIDP. They come in with **weakness and no reflexes** over a relatively short period of time and therefore we **know what the tests are probably going to show**. We do the **nerve conduction** studies and they look pretty typical. We might get **your spinal fluid tested** and it all fits together. For some patients it can be a bit more challenging, as they can present later on. **If you have more damage to the nerves the electric tests don't show the typical features always and people can have a misdiagnosis, or a late diagnosis.**

Some people present in different ways, with patchy presentations, or more numbness and pain than weakness, things that weren't felt to be part of the CIDP picture and that's probably not true. What we do is, we get **ways to try to improve how we pick these up**, particularly looking at **blood tests and special other tests**, but **nothing thus far has given us a good handle on it.**

There has been some thought **that maybe ultrasound might be helpful**. Most of you have probably had an ultrasound or know about ultrasound from looking for conditions inside the abdomen or looking at babies grow and the other areas where ultrasound is used, particularly things like shoulders and other areas with joints.

When we look with an ultrasound at the nerves, the nerves get big and swollen in people with CIDP. The pattern of those changes is pretty characteristic in CIDP. Nearly between 80 – 90% would have a pattern that changes an ultrasound that you won't see in any other sort of patient. That's much better than any blood tests we have; better than lumber punctures looking at the protein and better than nerve conductions probably looking across the range of the disease. Ultrasound may actually be the most useful diagnostic test, although it is just not widely used.

I started **doing this at the Austin. The Royal Melbourne has started doing it** recently. There are **a couple of hospitals in Sydney that do it**, otherwise really no-one in Australia is doing it, whereas **it is quite widely used in the United States, in Europe** in particular and it is growing.

I went away for six **months in 2017 where I spent some time with one of the leading centres doing the ultrasound and building up my skills.** I also **worked with some colleagues in Europe** and brought back and started **now to do some research with patients in Melbourne, starting at the Austin.** Hopefully, by expanding out with others of my colleagues around Melbourne**, seeing more patients, trying to see if we see**

the same pattern here in Australia with the way <u>we</u> do thing, particularly going ahead, if we can do more than just **recognise someone has CIDP because something about these tests helped.**

At the moment **we are doing some work trying to build up a similar pattern. Can we see that the same rate of 80 – 90% of people have the changes we expect to see and prove that we can do what other people around the world said we can do? Is there more you can get out of ultrasound to help look after people with CIDP? Can we predict people who might need treatments apart from IVIg? People who might need steroids? People who need more treatment? People who need less treatment? All these things at the moment are in flux.**

I'm not sure **how many of you have had problems with the ongoing supply of IVIg. Has anyone had to cut their IVIg recently because of the new rules?** (Comments and laughter from the audience.)

I am happy to talk about the Blood Authority Rules at length or in brevity with people. I am sure the room has a vested interest in that, but there has been **a lot of moves towards optimizing the use of IVIg and blood products in general, specifically IVIg and specifically with CIDP and there are a big number of reasons for that.**

The theory that the reason **why they are looking at the IVIg rules is, in the main study that showed that IVIg works for CIDP, (which was only done about 10 years ago, the "ICE" trial, which was done in UK and Europe), it showed that when people who responded to IVIg came off and either went on placebo or IVIg to see what happened, they established that <u>of the half that came off</u>, <u>half of them</u> didn't have any flair up in their disease over 6 months.**

That suggests that after a period of response to IVIg, there are some people (that was a very high rate but from my experience I don't think 50% can come off and all be fine), who don't need ongoing treatment. That's what is driving a lot of what is going on. There are a lot of people who started treatment a long time ago who maybe aren't getting any benefit out of it now and are exposing themselves to risk.

The flip side to that **from my perspective** and isn't played up in the new rules, **is there are a lot of people who aren't getting enough treatment as well**. I am not sure of people who are getting IVIg in the room and what their doses are, **but in that same trial, the "ICE" trial, the dose used was 1 gram per kilogram, every 3 weeks. That's the dose that has been shown to work.** I am not sure if I have got one patient who would be on that dose**. I have patients with more and patients with less.**

Traditionally, most people get .4 grams per kilogram every 4 weeks, sometimes less, sometimes more. I don't know if anyone here knows why that is the dose? Does anyone know why it is .4? It seems like a strange number.

Member: It goes by your weight doesn't it?

Dr. Crump: **Yes, but why .4?** It seems like a funny number to pick out of your head. It is close to half. Why isn't it half? Why would they pick .4?

Member: Maybe that's what your body needs?

Dr. Crump: Well you would say that they give me this dose because someone once worked out that's the right dose to give. No. As I said, the control showed it was 1. The base dose you should start with for CIDP should be 1g per kg. Then you should increase or decrease the dose depending how people go, either in the amount they get and/or how regularly they get it. Some people need more, some people need less.

We were doing a study where we were part of an international study looking at whether .5, 1 or 2 worked better, but unfortunately, due to the **very restrictive nature** of that study, **we couldn't get anyone in it**. That study is going on around the World and **we may have some more information actually saying <u>is more or less better</u>. We will soon know,** because even the big studies have actually not done a lot with dose findings.

The reason it is .4 is simple. That is 2 divided by 5. Why 2? Essentially 2 grams per kilogram is the weight number and the reason it is .4 is because it's given over 5 days a week and if you divide 2 by 5 you get .4.

Why 2 grams per kilograms? 2 grams per kilogram is the amount of IVIg you need to give to a baby with no immune system to replace their immunoglobulins. Everything that has happened ever since in IVIg is based on a dose that was worked out to replace immunoglobulin in babies without immunoglobulin, who can't make it themselves.

You have all got doses based on what a baby was given in the 1970's for something completely unrelated to CIDP.

The reason they worked out that IVIg works in CIDP is because it worked in Guillian-Barre` Syndrome and they knew that because they had some little kids who had an immune deficiency and they gave them IVIg and their GBS got better. They then thought maybe this works, so they started giving it to people and it showed that it works and they give you the 2 grams. You know hospitals don't function much on weekends so from Monday to Friday you split the 2 into 5 and there you go. That's it .4.

We are in this bizarre world where we have a lot of pressure with the costs and the uses of IVIg to bring things down, but then also they don't talk about the fact that so many people are probably not getting enough both in the short, medium and long term.

In terms of the IVIg, the reason that it is a big deal for CIDP patients is that **CIDP patients are the biggest single users of IVIg in the country. In 2015 – 2016 there were about 18,000 people who received IVIg in Australia and about 2,250 were CIDP patients.** That's about 17% or a bit less than that, whereas it was about **5 million grams of IVIg over that year and1 million of those grams went to CIDP patients.** A little bit over 20% of the IVIg used. So, it is **the biggest single patient group with the biggest single use**. IVIg costs if it is local IVIg about $60 per gram and if it is imported it is about $45 per gram.

It is not as much as some of these cancer drugs and things but it is a lot of money.

Member: How do they ensure when they refine the IVIg and that it is constant and has the right density? Is it when they extract it and refine it?

Dr. Crump: I think both **the local and imported products have pretty good quality control and dosages. There probably is inter-product difference and I certainly know patients who have had problems with both tolerability change and with efficacy change, with change in formulation.**

With the upcoming arrival of the subcutaneous IVIg, which I'm not sure if anyone has heard about and I was not going to talk about that at length, but **that may change things completely as well, as the doses with that will be potentially different again.**
You assume that a dose is a dose, but **like all things if you change products there may be some variation.**

It is a lot of IVIg product that is used and that's what is driving people to look at whether you need more or whether you need less**. Now you are all going to be subjected to doctors talking numbers and pushing a bit harder on you and writing things down a bit more than they did. We have to write everything down in great documented detail about how you were going before, during and after your treatments.**

It is interesting for us at the moment. **All the guidelines are still guidelines**, but guidelines **can change to strict criteria quickly** and **the next iteration of the change is likely to be if you don't meet the numbers you are going to struggle to get the treatment.**

Member: If you don't get the treatment, what happens then?

Dr. Crump: If you stop the treatment and you worsen, then that says you needed it and you go back on it. It is not like it is out and you are done. Essentially **if people are stable, what you have to do is justify its ongoing use** by some ill determined period of time. You have to **either have a trial off or a reduction to the dose and if things get worse again then you can say you have justification to go back on. That period you are allowed to be stable on a dose is probably about 12 to 18 months before you will be expected to see if you need less.**

It has got basis in that some of the studies have shown around a third of people will do well with cutting their IVIg doses, or potentially stopping it.

Member: I asked my neurologist what would happen if I went off the IVIg. She said if you went off and you got worse it will be too hard to get you back again. That was her explanation.

Dr. Crump: And that's part of, I guess, what we are trying to do and look at. The way the rules are is, that yes**, we do very detailed examinations and scores of how you are going and at the first sign of deterioration you can go back on. Now that may be not quick enough to pick up a deterioration and so that's quite understandable that you say "I don't see my doctor for 3 months and if I have been off for 3 months and I've got worse, what have I lost in those months?"**

Are there better ways of seeing how people are going?

That may be more based on you as the patients checking in more regularly with technology, or with self - assessments, so that at the first sign of deterioration you can get back onto IVIg, whether that be through how you feel, or some other way. There has been talk about whether we can give people grip strength things they can do themselves and if they see it is stable, then drops off, they can get back on IVIg. No-one knows. These are all things we are looking at.

Are there ways we can check you are stable and not getting worse while you are off treatment or reducing treatment? I guess **that's what we are looking for with ultrasound**.
Ultrasound is another way of monitoring people. The electric tests don't help and the nerve conduction tests don't help for monitoring generally as they usually get better well after patients have got better and they get worse after people have got worse. There is a bit of delay. They are not very sensitive to the change, particularly if you have more damage. These are the things we are looking at.

Are there better ways of keeping a check on people?

This is what we need to do if we go with this IVIg as there is not enough of it. We are importing about half of our IVIg in Australia and **most of you as CIDP patients will be on imported product, because that's the National Blood Authorities rules. Unless you have a good reason, high frequency, high regularity users use imported product because it is cheaper, so we are importing more and more.** If we need more and more, that's fine. **We should be using it if it works.**

It is the best thing for people, but how are we going to implement this plan of making sure that everyone gets exactly enough, no more, no less. With any system built on being exactly right, you are always going to risk people being on not enough and that's the problem.

Member: I have been having 'Intragam' for sixteen years but the last few years I have been on 'Intragam 10" and they reduced the dosage and I have been going down very gradually. They tell me it can't be because of the 'Intragam' being reduced in quantity. At the same time Medibank advised that if I went back to hospital within 28 days the hospital would have to pay, so I was extending it to 30 – 34 days.

Dr. Crump: The issue with all this is that the way people are treated is based on a bunch of arbitrary stuff. You can't go back to the day ward for 28 days because it will trigger something, so all these factors come in to play as opposed to **what is the right dose for any given person, because there is no "<u>this dose for everyone</u>".** It's not a tablet. Everyone doesn't take the same thing. Different **people need different amounts and over different periods of time.**

Similarly**, after a prolonged period of time you may well still be an IVIg responder**. **If you worsened, but you are partly responding,** then the question is **<u>do you need more IVIg?</u>** The flip side is**, after a longer time, is some of the worsening more related to other factors or wearing out and less responsive.** There are lots of unknown factors. **It may also be you are not getting enough IVIg**. They are very opposite problems and need to be treated in a very different way. That's our problem. **The focus you will be facing is this push to reduce use.** The flip side is that, **we, also as the Doctors and your advocates to the system, need to be saying, "Some of our patients need more" and how do we do that, as we have to be able to justify that it is not just because you feel better. It has to be more than that.**

You have to be better in a way that we can show and you can show. This is what **everything in medicine is now becoming, where you have to "show things" not just "say things".** We need to work out better ways of showing, be that better patient recorded measures where there are things we can do that are simple, that you can

do, or we can do for you that show differences, or whether there is **some sort of test that is not reliant on my opinion, or your opinion, or anyone else's opinion.**
This is what we are hoping with the ultrasound. Maybe that's one way of showing if you have this sort of pattern then you need this sort of treatment, or if you have this sort of change on our tests it suggests you are doing well, or you are doing badly. We don't know if it will work like that.

It may be that ultrasound is not sensitive enough to these changes from month to month either, or even over a six-month period. That is what we are hoping to do. That and other **ways of looking at how people are going over the length of their illness so that everyone is getting as much as they need for as long as possible.** It is a balance. It shouldn't be about a reduced use, **it should be about optimal use**. **Optimising involves giving everyone enough, not too much and not less than enough.**

Member: Is 'Intragam 10' more concentrated than 'Intragam P'?

Dr. Crump: Yes 'Intragam P' was 6% and 'Intragam 10' is the same Australian product made by CSL in Broadmeadows like it always was, but it is just a higher percentage. Higher percentage is better for infusion centres as the amount of fluid is lower, so when you get up to rate, it runs quicker. IVIg producers have all moved towards higher percentage because essentially it allows for quicker infusion and shorter times in chairs.

Member: **Doctor you mentioned that ultrasound has certain diagnostic advantages for CIDP. I was just wondering if it is the same for GBS?**

Dr. Crump: There certainly has been a lot of work done and a lot of the ultrasound work was originally looking at GBS. Certainly, there are some changes in GBS patients as well**. One of the interesting things about the ultrasound and one of its potential uses is that, for those of you who had a more dramatic onset CIDP as opposed to GBS and sometimes with people it is hard to know early on whether they are going to have acute onset CIDP or GBS, ultrasound seems to look different between the two groups.**

The ultrasound is more abnormal in people who will have CIDP rather than GBS. In GBS you do see changes, but often it is not as dramatic as CIDP and sometimes it is in more specific nerves. We seem to see it more in the nerves up near the neck than the nerves in the arms and the legs, so we can check in CIDP, but even in people who look like they might be GBS, **if their nerves look larger then we can probably tell they have CIDP earlier with ultrasound, than by other factors.**

There have been other ways we have tried to separate the two. If you keep an eye on people it can make a big difference to what you do. For some people (and I know some in the room that have had acute onset CIDP) it can be a challenge as if no-one is really sure if it is GBS and then you get a bit worse because the treatment has worn off, or because the disease is a taking a little bit longer than what you were expecting, we treat people differently if that is the case.

Member: With the ultrasound, does that require newer technology, or does the hospital have the ultrasound, or what would be the next steps to seeing more wider use in Australia?

Dr. Crump: The ultrasound we are using at the Austin is a spare machine that we have been allowed to use, but essentially it needs to be a good reasonable machine rather than a fancy one. It tends to **need a specific type of ultrasound probe one which is a high frequency probe with very, very, good detail of nerves in the arms, legs and neck. It is better in the arms than the legs but certainly good in the arms and neck and that is usually enough information.**

We have to get what are called "high frequency probes". Essentially a lot of places can actually get an ultrasound and if you get a good probe with a machine that otherwise would be used to look at shoulders, elbows and things like that, it would be completely adequate.

How we build that in a neurology sense, where we maybe have not done it as much, involves some different technology and access. Certainly, the radiology colleagues are not particularly interested in it as they are more interested in MRI.

People say why aren't MRI's better than ultrasounds? **Actually, for nerves in the arms and legs right now in 2019, ultrasound is better than MRI. We can get better definition of things within a couple of centimetres of the skin than MRI.** In five years that probably won't be the case. MRI might be better, but MRI is always

going to be limited by expense, access, people who can't have MRI because of the metal or claustrophobia. Ultrasound can be done quickly anywhere; in an infusion centre, in a hospital bed, in 10 to 15 minutes and it's cheap. MRI's will not be cheap anytime soon.

It will involve a difference in thinking because **it is not easily Medicare billable for neurologists, or accessible,** but a lot of people are interested, particularly as we know the limits of nerve conduction studies, where people don't like having them done over and over again, quite reasonably.

There are a lot of people interested in ultrasound and in seeing how it takes off. There is **the cost of the technology and then there is the expertise to build up**, **as although in parts of the world it is becoming widespread, here it is very much in its infancy.**

Member: No-body has ever been able to sus out what actually causes CIDP have they?
They don't know if it could be stress, something else, or the auto immune system.

Dr. Crump: That's right. There is no specific pattern of change on blood tests on antibodies. We know there has been some anti-bodies in CIDP found over recent years. Some of the groups in Sydney have found them. These antibodies seem to cover about 1-2% of CIDP patients and often very specific types of CIDP, not your typical type of CIDP patients. It is often people with more pain, lots of problems with balance, problems with hands and feet rather than the more weakness pattern of CIDP. We know there is a difference.

If we had some easy blood test which said you have CIDP and the treatment is going well or better than everything else, that would be great. Things would be very clear cut if we could get a pattern on testing, but we don't have that yet.

Currently we are undertaking a single test study that involves a clinical and ultrasound assessment for any patient with CIDP. A parking voucher will be provided to attend the visit at the Austin.

The other study will be a 12 month follow up for CIDP patients either currently on, or about to commence treatment for their CIDP. That will involve 3 visits to the Austin (again for clinical and ultrasound assessment, no nerve conduction studies). The ethics approval is likely over the next month or so, with a plan to start in July.

I can be contacted via my Austin (nicholas.crump@austin.org.au) or Melbourne Uni (ncrump@student.unimelb.edu.au) emails, or via the Austin phone number 03 9496 2845.

INFORMATION
Newsletter of THE 'IN' GROUP: THE INFLAMMATORY NEUROPATHY SUPPORT GROUP OF VICTORIA INC. Supporting sufferers from acute Guillain-Barre` Syndrome(GBS), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and other inflammatory neuropathies.
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Intensive Care	$3	
A Road to Recovery – A - Z	$6	
Boy, Is this Guy Sick Booklet	$2	
Recipe Book	$16	
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Thank you. Please forward this form along with your payment to:
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