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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)
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GBS……..CIDP

Issue 92. September, 2015.

INFORMATION

STICK WITH IT
SLOW BUT SURE

NEWSLETTER OF THE IN GROUP: THE INFLAMMATORY NEUROPATHY SUPPORT GROUP OF VICTORIA INC.

Supporting patients with acute Guillain-Barre Syndrome (GBS) & Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

ANNUAL CHRISTMAS LUNCHEON AND DUTCH AUCTION

at the Balwyn Library Meeting Room, Whitehorse Road, Balwyn 12.30pm.

SUNDAY, NOVEMBER 15TH, 2015. $20 PER HEAD

RSVP to Margaret 9802 5319 or Melva 9707 3278 by Wednesday 11th Nov.
If possible, please bring a wrapped gift with an indication of value for Auctioneer.

Annual General Meeting held on the 16th August, 2015.

President's Report – Margaret Lawrence

My report this year is a pleasure as always for me to delivery. The members of the group make it easy and enjoyable to be President. They are especially wonderful with their generous donations towards research.

The Christmas Luncheon was a great fund-raiser with delicious food finishing off a good 2014. This year we tried a different mid-year function with a happy small band of us at McDonald's Balwyn. We had a "Mac attack" which was all good.

Speakers are always a challenge for the committee to arrange but I feel we have had very interesting meetings. Our members always enjoy a discussion afternoon if we are not able to have a speaker.

I would like to thank the Committee for their assistance and generosity and Gwen for all the craft work she sells, bringing us a tidy little sum each year. So thank you Gwen.

The Balwyn Library is very reasonable with our requests and small hiring fee that they charge. As a support group I feel one of our main ways of assistance is arranging phone calls for new and other people who just need someone to chat to about their concerns. Good friendships have been formed amongst The IN Group and help is always available.

The blood products are being looked into by the Government so more reports will be produced in the Newsletter.

My thanks go to Melva and Joe who produce Newsletters four times a year, especially important to people unable to attend the meetings.

In closing now, many thanks from me go to all IN Group members and the nicest committee anyone could ask for. Thank you very much.

Treasurer's Report –Doug Lawrence

It is my pleasure to give the Financial Report from 1st July 2014 until the 30th June, 2015. It has varied from last year as overall our subscriptions and donations for the last year are lower by $1753, however, our fundraising throughout the year (which is fairly minimal) increased by $1066 which offset that downturn. Our two major fundraisers, the midyear one at McDonalds instead of at our home and the End of Year High Tea which included our Auction, were down $857 for the year.

The expenses were down by $8670 as a result of the timing of our donation to Dr Andrew Kornberg. We should be in a position to offer a sizeable donation by the end of the year. Overall we have had a good year financially.

I would like to say a very big **thank you** to our members and our Committee who work very hard, giving not only their time but the cost of foods and things at our meetings, which helps to keep our expenses low. **We also have a tremendous response from donations**. When we look at it, the **donations represent approximately 300% more than we get from subscriptions**. I think that is a **fabulous effort**. We don't have a huge membership (I think we are down to about 180 now) and we have been able to give $10,000 for the past 8-10 years. 100% of donations go into the research aspect.

I would remind people that our new financial year started on the 1st July so therefore subs for the year 2015-2016 are now due (for those who haven't paid them).

I would like to finish by saying **thank you for your generosity and the financial help given to allow us to run the group, produce our newsletters and still make a sizeable donation.** Thank you.

The Committee remained the same.

Meeting closed.

John Burke: There are a lot of new people here today. If anyone would like to be on our mailing list, please give me your email address before you go home or email me at **jburke@contracts.com.au** If you use *hotmail* or have junk mail filtering software running you will have to include the above email address in your "safe list" otherwise *hotmail* or your junk mail software is very likely to delete our emails.

Margaret: It is a great pleasure to welcome **Tim Day** who I am sure will be very interesting and thank you for joining us today.

Talk by Assoc. Professor Tim Day

Thank you very much for the invitation to speak to the Group. It is good to see some familiar faces but also good to meet some folk I haven't met before.

One of the things I will be talking about today is some of the clinical trial work that has gone on in CIDP and some previous research studies mainly to set some background.

There is some interest in a Research Study we are running at present as part of an International Study. I want to talk a little about that and I think there will be some other questions and interest in **the whole question of treatment for CIDP, Inflammatory Neuropathies,** in particular **those which revolve around blood products**. I'm sure there will be questions about that.

Let me see if I can get this projector up and running.

Tim: Shows International Group Logo. Are you affiliated with the International Foundation?
Answer: We are a liaison for it.

Tim: If you **go onto the Internet and type in CIDP** this can be a **source of useful information.** There are a lot of other CIDP associations around the world I discovered. This is the logo for the Pakistani group but there are a number of different groups in different countries.

I probably don't have to explain to you what **CIDP** is but for those of you who may be family members, or don't know, we are talking about **a relatively uncommon neurological disease where the nerves are affected by an auto-immune condition and which usually has an ongoing course.** Instead of being over and done with **like Guillain-Barre` Syndrome** within a period of time, it often comes with **either multiple relapses or a progressive course.** It reflects the fact that **this is an ongoing chronic long-term process for a number of people**.

There are **a number of treatments** which have been used over many years. If I use the words **Plasma Exchange** would people have heard that? (Most replied Yes.) **I will use the word either IVIg or 'Intragam' which is our local product which I'm sure you are all very familiar with**. I will be talking a little about **Prednisolone or steroids** and about **how those relate to each other.**

One of the big questions is: What eventually happens to the person with CIDP? What happens to people with these Inflammatory Neuropathies over time?

There are **some people who have a single attack and things settle down**. Now that's **uncommon**. When it is **a single episode or maybe one or two short episodes**, about **one in 6 people may find that it settles down or goes away or doesn't come back for years and years.**

The majority on the other hand will **keep on going in one form or another**, **sometimes in a steady course or sometimes with little bumps along the way. The question is: What happens if we do nothing?** For a significant number of people **things seem to grumble on** like this. (Indicated on a graph.)

I am going to **talk about some of the research work that has been done overseas and introduce you to some very distinguished people.**

This is Peter Dyck, who was one of the people in the 1970 and 80's who was doing a lot of research on CIDP and looking at new treatments for it.

When I was a student **I learned about the subject of "An inflammatory neuropathy with steroid responsiveness".** They **didn't even use the term CIDP**, but people **recognised it responded to various treatments. Peter Dyck's contribution was the recognition that steroids worked well but also plasma exchange followed later, I think in the 80's, by the use of intravenous immunoglobulin (IVIg). A number of studies**, particularly like this one in the mid 90's, really **showed that in comparing the two treatments there was really no substantial difference between them. Plasma exchange or IVIg compared to steroids.**

Like any of these treatments some people respond better to one than to the other, but **the two treatments are considered virtually equivalent**. **Plasma exchange is much more awkward to arrange than putting up an IV bottle. Running fluid in is much easier**, but the **two treatments are basically much the same in effectiveness**.

In Peter Dyck's study in the late 80/90's they looked at disability. They looked at **muscle strength** and at **nerve conduction** and other measures of **how things were going.** They **showed that things were improving on a number of those measures. It was a small number of patients but patients tended to respond to an equal degree.**

This fellow is **Professor Richard Hughes from London** and he has been **involved with inflammatory neuropathy treatments for a long, long, time.**

This is **a study** reported just after the turn of the century showing a number of patients with CIDP, then **comparing response to immunoglobulin and response to Prednisolone**. Again this shows there is really **no major difference** between these two **in terms of effectiveness.** The same number of patients seemed to improve, but their influence was to **look not so much at blood test results or electrical test results, but whether the person could walk better**; could they **do things better** and **he introduced the concept of using disability as a means of working out whether things are making a difference.** The bottom line is as I said; the two treatments are fairly equivalent.

He went on to take a larger group of **patients (over 100)** in what was called the **"ICE Trial".**
This is what is called a **double blind, randomised control study, which is the **best** sort of **research study that you can do**. Some of these **patients had been on treatment with 'Intragam' or with steroids or other things for a period of time.**

Treatment was stopped for a period of three months while they were just observed to make sure they were dealing with patients who truly responded. Then they gave them treatment with either 'Intragam' or another intravenous treatment that looks like 'Intragam'. It is a blood product but it doesn't have the antibodies that seem to do the magic in CIDP. They used a disability scale; a muscle strength scale, among other things.

I mention this because this is starting to come into our clinical practice and one of the things that the blood authority is wanting us to do in terms of working out whether things improve or not.

The INCAT score is a measure based on a questionnaire or reporting as to whether you can do certain things with your hands; whether you can do them normally; whether you can do them with difficulty; whether you can do them not at all. These are some of the questions I ask my patients every time. I also ask "**What's your walking like? Can you walk normally? Can you walk with assistance? Do you need a walking stick or a frame or a wheelchair or can't get out of bed?" So there is a number of ways things are monitored.**

In their patients, a **couple of interesting things came out.** They obviously wanted to be **testing** people they called **"respondents" - patients who with continuing treatment did not deteriorate.**

About **half their patients who were treated with 'Intragam' were able to maintain their level of function,** whereas about **half of them deteriorated** in that period of time. Interestingly, **1 in 5 patients** who were not treated with the active drug but were **treated with the placebo, (about 20%) also remained pretty much unchanged. This is an interesting point as it begs the question of, when people are being treated, is there a stage where we need to back off and see whether treatment is still required.**

I'll put the numbers the other way around. **Half the patients failed their 'Intragam' treatment.** Only about **half responded well**, **whereas 80% on the placebo failed**. The point is **there were still a number of patients who maintained function even though they were not getting an active treatment.**

They then took the **patients and looked at them over a longer period of time** and looked at how they went. **Some were treated with 'Intragam**' and **some were treated with a placebo**. The **ones who were treated with placebo eventually deteriorated** and needed to go back onto more active treatment, whereas the **ones who remained on 'Intragam' (I don't know if you can see that graph) basically stayed much the same.**

This graph is telling us how soon people deteriorate. How quickly patients relapsed. One of the interesting things was, **when patients were treated actively with 'Intragam', the time to a relapse (getting worse) was much, much, more delayed than those who weren't**. Now that may seem pretty obvious as **if you are being treated with something that works, then you are not going to deteriorate.**

One of the reasons I mention this is because **there were about 20% of patients who were in a state where their condition was not getting worse. They may not have needed to be treated as actively as they had been before. Remember these patients were being taken off treatment. They had been treated prior to this. They were off treatment and in that period of time some of them did not need ongoing treatment.**

So people then ask you, "Well, **that's the situation for 'Intragam'**, **what about using Prednisolone** or **other steroid doses**? The reason for bringing this up is because **the practice around the world varies enormously. Even within Australia, neurologists in some States are more likely to use Prednisolone for treating CIDP and others are more likely to be using 'Intragam' alone, others will use a combination**. It is **important to know whether these drugs that work well and if they are any better or any worse than say other forms of treatment.**

This group looks at the **responsiveness in CIDP to corticosteroids** and they use two different forms. One was **where patients had a dose of Prednisolone every day. They were given the same dose on a daily basis which has been shown to work (Peter Dyck showed that ages ago). They gave a big dose and then tail it off.** Then they had **another group of patients who had a big dose once a month. At the beginning of the month they had two or three days of high dose and then nothing.** The two groups of **patients were very, very similar.**

After 6 months of treatment, about half of them went into remission ie thet **did not need any ongoing treatment**. **Both cases went into remission about 40% of the time** and then left to themselves**, after a period of time eventually things got worse**, but **after 4 or 5 years, about a quarter of patients still did not need ongoing treatment.**

Now the reason for saying that is **because you have CIDP does not mean that you are going to need treatment for ever?** That's the first message I want to get across.

Secondly, **the treatment that is used can sometimes determine or influence whether or not you are more likely for things to settle down, or if you like "burn out".**

Patients that have high dose treatment tend to take longer to relapse, so it seemed to be better to take a bigger dose with pulses of treatment, rather than to take a small dose all the time.

These **patients had a variety of different side-effects and that influenced** to some degree **whether they wanted to continue on with their treatment**. The point is **these patients not being treated with IVIg were able to maintain their condition and not deteriorate in a significant proportion of patients**.

Thirdly, a European study, **"The Immunoglobulin and Prednisolone in CIDP Trial"**, was run by an Italian group Dr. Nobile-Orazio from Milan, (I think he is) and they are now **comparing Prednisolone and IVIg looking at a direct comparison between the two.** The sort of dose a lot of you would have been given when starting off with **IVIg; and also a group treated over 4 days with high dose intravenous cortisone**.

They **looked at how long the patients stayed on the drug and how effective it was** and **these are the results**:-

The **patients who were given the cortisone based treatment.**
About half had to stop. In about a third it was because it didn't work. They didn't get a response within a couple of months. Only a **few had to stop because of side-effects**. A couple of patients decided they didn't want to stay on for various reasons.

In the **patients who were getting the IVIg**
13% had to stop and all of those because of an inadequate response.

Both of the drugs seemed to work to varying degrees, **perhaps more effective in 'Intragam' and seemed to work more quickly**, but the **side-effect profile was fairly low** and if anything a **bit more in the steroid dose**.

Interestingly they had two deaths in the 'Intragam' group, but none in the steroid group. Now these were thought to be unrelated to the treatment. One patient had a heart attack and the other patient had respiratory failure and these were several months after taking part in the treatment, so we don't think that was caused by the treatment, but keep in mind when you are dealing with a large number of people, sometimes bad things can happen as well. The side-effects profile is very similar between the two.

Then their question was, "Do these patients need further treatment?" What they found was, **after the treatment they were left alone and watched. Later, about a third of patients who were given 'Intragam', needed to go back on treatment.**

Remember **these patients, some of them treated with cortisone, some of them treated with 'Intragam' . After Intragam treatment**, about **a third of them needed to go back onto 'Intragam'** but **none of the patients given the cortisone needed to go back on treatment**.

They are **small numbers, but interesting data**. It seems that **using the cortisone may be better at switching off the disease and may be inducing remission or stopping the disease becoming more active.**

Then when the patients treated with cortisone were watched **over a period time**, these patients, **some of them eventually got worse**, about **2/3 or ¾ got worse**, but **the average was more than a year until things got worse**.

The patients who had been treated with 'Intragam', about 5 out of 6 got worse over an average of 4 or 5 months. Interesting information about **how the different treatment may affect the activity of the disease.**

It raises a couple of interesting questions. Are there ways we can predict who is going to be a responder? **Who will respond better to cortisone? Who will respond better to 'Intragam'? Which one should we choose?**

Some treatments seem more effective first up. I think most people would agree that the intravenous blood product 'Intragam' (IVIg) seems to work better and more quickly in most patients, but a significant proportion of patients on the steroid will also respond.

Then there is the question of the long term benefit. This is the other side of the coin. Those treated with the steroids often seem to have a longer term benefit and be more likely to go into an inactive phase. It is a bit of a swings and roundabouts type of question.

If you have **a severe problem and you want to get on top of it straight away**, then **'Intragam' is probably the best drug to use first up**. If you are **more interested in length of treatment, am I going to be needing some sort of treatment longer term,** then there are some arguments for **using the steroid-based material because that may help to "turn off" the disease more quickly.**

These are **interesting results which have come out of a number of different trials**. This is **not definitive proof**, but it raises the question as to **whether the 'Intragam' is just treating the symptoms and not treating the disease** or **whether there are other forms of treatment that may be better able to switch off the disease**.

This may be a good time to take a question.

Question: How many people were in the trial? Answer: 44.

They are **not enormous numbers, but we are not dealing with a very common disease**. It is relatively **uncommon so getting these numbers together and getting patients that don't have a lot of other conditions can be a bit tricky.**

Question: How do you measure improvement? Is it by **definitive blood test or** is it just **how they feel**?

Answer: It is **a very good point**. In the recent trials the improvement has been judged **according to disability scales**. These are measures of **how well somebody can do certain functions, certain tasks.** It is **not judged on a blood test**. It is **not judged on nerve conduction** studies, **it is judged on functional ability**. I think we

are realizing more and more that the **more important thing is** not what your blood test shows but **what you can do**. **Can you do up your buttons? Can you hold a knife and fork? Can you walk without a stick? Going from one level of function to a better level of function** was the way these **were assessed**.

Richard Hughes has introduced that so called INCAT scale which we use quite extensively and it has started to become **the "Gold Standard" in research studies**. It is dependent on **getting accurate information** from you guys, the patients, because we can only judge the way you are travelling by what you tell us ,so **it depends on you telling me what you can do.**

Question: How long have these people been affected and on cortisone before they have undertaken these tests?

Answer: Most of these patients have been on treatment for **6 – 12 months at least**. There were a few where they were newly diagnosed patients. One of the other things that came out of some of these studies were that **patients who were treated early**, in other words the **diagnosis was made and effective treatment was put into place more quickly, certainly did much better**. It makes sense that **if you have an active disease and if you get on top of it early**; you are going to have a **much better chance of things settling down in the long term** rather than something that has been going on for 5 or 10 years.

Question: When you say early **is that within the first year**?

Answer: Within the **6 -12 month period**.

<u>DRUG TRIAL</u>.

I would like to talk about the trial we are doing with another drug which is **being trialled in CIDP.** This is part of a **multi centre study being run by a drug company named Novartis** and we are using a **drug called Fingolimod or 'Gilenya'** which is **currently used for treating Multiple Sclerosis.**

Now **MS is a chronic demyelinating disease of the brain and spinal cord** and in some ways **CIDP is a chronic demyelinating disease of the peripheral nerves**. There are obviously differences between the two, but **there is some experimental evidence, certainly in animals with an inflammatory condition** called experimental allergic neuritis, which is **a bit like CIDP.** They found the drug was quite **useful in preventing the weakness developing and helping to improve the degree of disability or degree of involvement** in laboratory animals. It has been **used safely in MS so we want to trynthis in CIDP** patients.

Obviously the way **to test that properly is to make sure we have patients who are truly responding. We take patients who have active CIDP and try the drug or the placebo**. These **patients are matched so nobody knows who is getting what** and we follow them over a period of time. The **measures** here again are being based **primarily on muscle strength** measurements **and the INCAT score**.

The trial **drug works on the immune system** and helps **to reduce the degree of inflammation** and it seems to be quite **an effective drug in MS** and it **may turn out to be quite a useful drug in CIDP**. I can't say that for sure at present because we don't have any of the long term results. **I don't know if any of the patients who have been involved in Australia, in our study, are on the real drug or the placebo.** The whole **reason for doing a trial** like that **is to really sort out the question without having any inbuilt biases.**

This is **how we are doing the study**. We are **finding patients with CIDP**. We have to make sure **patients have got basically CIDP by itself without other conditions**. Now if you have **diabetic neuropathy or other forms of neuropathy or you have had a stroke, or there are other things that affect your level of disability, then it makes it hard to measure improvement,** so there are a lot of reasons why **we try to find patients who have CIDP and not much else.** We **need CIDP patients where it is not too severe, not too mild and willing to be part of a research study.**

What we do with these patients is **stop the treatment they are on, replace it with the drug or a placebo and then watch those patients over a period of time**. We **do a lot of checks every month**. **Patients have to see respiratory people. They see a dermatologist. They have blood taken.** They have a whole lot of **checks to make sure there are no side effects developing with the drug** and we see **how things go over a couple of years until things get to a worse stage;** and **if they drop below a certain level then that patient goes back on their original treatment.**

We have had a couple of patients we have been following. We **don't know whether they are getting one or the other treatment**. **Over a period of time** we have **been following their INCAT scores**, doing **muscle testing and blood tests**. After they are selected for the study they either get the active drug or a placebo and **at a certain stage, if their deterioration goes beyond 1 INCAT point, they go back on their original treatment.**

At the end of the day we are going to be **comparing the patients who have been getting the active drug and those getting the placebo and it seems to be fairly safe. W**e are **getting the same sort of side-effects** you expect in the patients, **where we treated MS patients** with it. **I can't give you any results on this so far**. We have **only had a handful of patients involved with the trial. They are trying to get 180 patients worldwide and I think they are up to about half that number.**

There are a number of inclusion and exclusion Criteria. I won't go through that except to say, **patients are expected to have fairly typical CIDP, have a certain level of disability and be on active treatment.**

One of the reasons for going over some of that data before was we want to be sure that **if we have a patient who is on a particular treatment, they are really needing that treatment. If we take that patient and put them on any sort of drug, we want this drug to be replacing their current treatment.** If their **condition was not going to get worse** anyway, then **that is not going to be a useful comparison**.

There are **a number of other diseases you mustn't have**. You mustn't have **other sorts of neuropathy, hepatitis, lots of other things. There are lots of reasons not to be involved**. This is to rule **out other diseases so we can get a clear picture**.

I wanted to outline that particular trial just to say that, if there are any of you who are interested in being involved in this trial, we can certainly talk about whether you would be suitable for it. We are still looking for patients to be involved in that particular study.

Results are still being gathered so **we still can't give you a definite answer** yet. **It is looking encouraging I would say**. We have a couple of **patients we have been following for over 12 months** now. **One has only just needed to go back on her old treatment**. It **may be the drug is workin**g and this will provide some means of giving us another **alternative**, apart from medication that needs to be injected on a regular basis. Having **an oral treatment would be quite useful**.

Question: What do they think the **mechanism of action is of Fingolimod and what does it actually do?**

Answer: **Fingolimod is a drug** that **works on some of the white blood cells** called the **lymphocytes**. Normally they are **floating around the blood stream** and they are part of the immune system that **trigger the attack on the myelin**, the lining on the nerves. What **this drug** does is **keeps the white blood cells bound up inside the lymph glands and stops them circulating** throughout the rest of the body. They can **still have an effect on the immune system** while they are inside the lymph glands, but they don't circulate around so **they are not spreading around or eating away at other tissues.**

Certainly **in the MS situation it is a very, very effective treatment for controlling the immune system.** The way it works is really just by locking them up in certain parts of the body so they are not spreading more widely throughout the system.

Question: How difficult would it be to go back on 'Intragam'?

Answer: We would just put in the request for 'Intragam' back to the blood bank and it is usually processed within a day or so.

If these patients have been followed in a trial and then they deteriorate, we have the data to say that this patient is worse than before. **We have all this information**. I think the **blood bank is quite happy to say, "Look these patients can definitely be shown to be in need of additional treatment".**

One of the concerns from the National Blood Authority or from the Blood Bank has been (and this might lead on to a discussion later on) that sometimes **patients are put onto a treatment which is continued for years and years and is not reviewed, not reconsidered** and **some of those patients,** maybe a **quarter to a**

third, <u>may not need the same level of treatment</u> or **may be able to come off** it. **We have certainly been able to reduce the dose in a number of our patients and some patients come off their treatment all together**. **It does happen**. **Just because you have been given the diagnosis of CIDP, it doesn't mean that this is something that is going to need life-long treatment.**

I think what has come out of those previous trials I mentioned is that **perhaps half of patients will actually go through phases where they settle right down or don't need to be treated with as high a dose** as they have been before.

Question: Then you could take yourself off and see what happens?

Answer: Yes, **we can take you off and see what happens**. **That's right. A number of patients are quite happy to say "Look I don't want to have to come into hospital each month, have a drip put in, my veins are getting bad, it takes several hours, I get a headache afterwards"** and **they are happy to take a tablet**. **If it works, then that's a major plus.**

The other question I wanted to bring up before, **it seems in Victoria we don't use Prednisolone, or other steroids as often as in other States** and **maybe we are not giving people the opportunity for things to be settle down into remission phase** as maybe they do in other States. So far **that is still a bit speculative**.

This research trial is still ongoing, so we are **still looking for patients who might be suitable** for that. The **other advantage** is **anyone who has been involved with it will get a lot of medical attention.** They get **seen on a very regular basis**. They have **a whole bunch of other tests done**. For **some people that will be good and for other people that will be bad**, but it does mean that **you are getting closely watched**.

Question: Where do you have to go?

Answer: We are involved with this at the **Royal Melbourne Hospital**. **I think Les Roberts at St. Vincent's is recruiting patients as well.** I don't think it is being run anywhere else in Melbourne. Is anyone involved elsewhere with the Fingolimod study anywhere else? No.

Question: Tim, if you are having no treatment you can't go on the trial?

Answer: Correct. **If your condition is well controlled on no treatment, then you don't need treatment.**

Question: What if it is not well controlled and it comes back?

Answer: There are going to be **some people whose condition doesn't settle down with the standard treatments and we often pull out other stops and use a lot more powerful immune suppression drugs**, as you well know.

Question: I don't know if you can answer this but **what's the risk to someone who comes off 'Intragam' to go onto a trial drug, they're tested and after more months their condition is worse, what's the risk of them going back on 'Intragam' that they will stay worse, they won't regain what they've lost?**

Answer: This **has been looked at in studies where people's treatment has been taken off –it has shown that on average they deteriorate by about 14-15% in that particular group and then when they went back on treatment they regained that function. I don't think it is true that you lose it permanently**. If you are **one of those patients where you are responding to treatment, you should go back to where you were before**. It **may be a matter of dosage**, of course, but **unless it is left for a long time**, then **you should regain that strength.**

Question: If you are an IVIg patient, how long would you have had to be on that before you could go on the trial?

Answer: You will be eligible straight away.

The **basic Criterion** is really saying "If **you have CIDP and you are still in need of treatment"**. The **only way to see if you need treatment is to stop it for a while and see if things deteriorate or show there have been ups and downs with the treatments.**

If you get a single treatment and you stay exactly the same, then it is arguable that the treatment is doing anything. Certainly if any of my patients says at the end of the four weeks or six weeks they feel exactly the same, I am really suspicious that they may be in remission or being over treated and we can quite reasonably back off.

Question: **What do you do if you are on IVIg and you feel you are declining?**

Answer: You need to **speak to your neurologist** about it, but **it would suggest a bigger dose of treatment or a different form of treatment.**

When they look at the bigger trials, the ICE or INCAT trials, **50% of patients will respond to IVIg but the other side of the coin is that not everybody responds** so you may need to **try something different or have other treatments** set up. Just **because one thing isn't getting you back to where you were, doesn't mean you shouldn't try something else.**

Question: What are the main side effects of this trial?

Answer: There are two or three main ones. **One is a slowing of the heart beat with the first dose, so we supervise people carefully with their first dose, because if the heart beat slows too much they will feel dizzy and faint.** If they get through that, then there are no heart problems beyond that.

Occasionally people can get high blood pressure.

There is a **slight risk of increased infections such as shingles and people need to be vaccinated against shingles** and **like any of these drugs there can be trouble with, liver function tests** (**blood tests)** and **we monitor them on an occasional basis.**

An unusual one with Fingolimod is swelling that can happen **at the back of the eye casuing blurred vision. If it happens it happens within the first 3 – 6 months** and so **we have careful eye checks before and afterwards**. This is **called Macular Oedema** and **anyone getting this drug** for MS for instance they **have their first dose monitored and they have their eyes carefully watched for the first three or four months.** If things are clear after that we don't need to do the heart of eye checks all the time.

So, the **Macular Oedema**, the **slow heart beat** and the **shingles risk** are the **three main ones** and there are a few nuisance ones down the track.

Question: You mentioned a **Dermatologist**.

Answer: With **anything to do with the immune system we often find there is an increase risk of things like skin cancers and so patients are routinely watched for skin cancers and other sun spots on the skin.**

Question: How does moderate alcohol react?
Answer: Moderate alcohol doesn't react directly. No.

We have had **a couple of patients involved in the trial over the age of 60**. We obviously **try to have patients who don't have other diseases because they might interfere with the ability to measure whether the CIDP is getting better or worse.** We are not being ageist. We are not trying to discriminate, it is more when we are checking things out we want to be sure that things are getting worse or better because of the CIDP and not because someone has a broken leg or some other health problem.

For anyone who is really interested there is data coming. (See final page of Newsletter.)

Question: CIDP versus peripheral neuropathy. I have **just been diagnosed with peripheral neuropathy. Is it the same, is it nothing similar?**

Answer: It is a bit **like saying "I've got the flu or I have any sort of pneumonia"**.

CIDP is a particular sort of peripheral neuropathy. **Peripheral neuropathies are** conditions **affecting the nerves that run through the arms and the legs** and they can be affected by a whole bunch of things. The commonest things worldwide are **diabetes, alcohol abuse, drug reactions, some inherited conditions and a small group which are affected by the immune system.** This is **Guillain-Barre` Syndrome** which is the **acute, rapid onset form** and also the more **chronic form which we call CIDP**. A lot of people in this room know a lot about this from personal experience.

CIDP occurs in a small group of patients who have a neuropathy where their immune system affects the nerves and the **treatment** for that, by and large, **is to modify the immune system** to try and both **settle the condition down and help improve function**. **One of the important things we are trying to do is** not to make the nerve conduction look better, not to make the blood tests look better, but **make you work better so you can do things more easily.**

It has really **got to be about function**. It means the **ways we measure how things are working or not have to be about function**, **not about some obscure test you have to send off to the laboratory.**

Question: I had GBS two years and two months ago and I had two lots of IVIg. I eventually got to walk again. I am two years on and wonder if I can ever get rid of it out of my legs and fingers.

Answer: 90% of people who have Guillain-Barre` will be back to **almost normal within 6 to 9 months**. Now there are a few people who take much, much longer to recover and there are **a small proportion, maybe less than 5%, where it doesn't settle down 100%.** There are a few **people who, usually if they have been much more severely affected to begin with, where the condition will just leave you with some scarring.** It is probably the best way to think about it. Usually the **improvement will be in the first several months**. Even then, **improvement can continue on** for some period of time.

Question: If you have arthritis in your back will it attack nerves in that area?

Answer: It can attack the nerves everywhere, but I think if you have arthritis in your back that is another problem you have to deal with as well. If you have got **problems with walking,** the **neuropathy** can cause problems, but the **arthritis** can cause problems and **strokes** can cause problems and it is **a case of multiple problems coming together**. It could be **your immune system is not 100%.**

Question: Do you give steroids?

Answer: Not for Guillain-Barre`. People tried using steroids for GBS earlier on and found the **patients were no better but probably a bit worse** and certainly later on **it makes no difference.** With **GBS it is over and done with in that first couple of weeks** and after that it is a matter of recovery. It is coming back from that. Again **the person who is much more severely affected to begin with has a much lower chance of getting back to 100% normal.**

Question: Does the treatment work better on sensory or motor nerves?

Answer: I think it **works equally well**. The disability has more to do with the motor involvement. People can do a lot more with a numb hand but if you have **weakness on top of that is much more limiting than just having numbness**. There are very rare forms of CIDP which are purely sensory but most patients will have **significant amounts of muscle weakness and that is the thing that causes most problems.**

Question: Fatigue. What can you do about that?

Answer: A big question which is **not measured easily. Fatigue is very common in GBS, CIDP, very common in MS and probably telling us that there is something happening in the immune system that is not right but it is a very difficult thing to measure.** There is **no blood test for fatigue.** It is **very difficult to get any scale to measure it**. It is **something that affects quality of life and quality of life** is something we need to keep a very close eye on in any of these studies.

Question: These **tests** you are showing us here are **mainly between IVIg and Prednisolone**. Have there been **tests between with IVIg and Plasma Pheresis?**

Answer: That was the **first one I showed you. The Peter Dyck study** which compared Plasma Exchange and IVIg and **showed that they were basically equivalent in effectiveness** and **other studies have shown that steroids and IVIg were pretty well equivalent.**

Of the **three main treatments** they are fairly **equivalent** in the proportions of people that get better or show improvement and on the average you would say that **about 60 to 70% respond with one of these single forms of treatment. Others may need a different treatment to get benefit.** Beyond that there are **people who need a combination treatment** and often we **use much more powerful combinations of effectively chemotherapy**. We try and **hit the immune system a bit harder and although Steroids do that,** often they need to be **combined with 'Imuran' or other drugs**. The stronger treatment you use, the **more side-effects you may run into**. We have to balance that all the time.

Question: A combination of IVIg and Steroids? Some people do that?
Answer: Yes

No research has done that systematically, but certainly **looking at those recent studies, people have suggested maybe this needs to be tested.** What we could do is- **if you need a rapid effect, hit someone with 'Intragam'** but if we really **want them to go into remission, you might want the Steroid. Maybe we use a combination to begin with** and then taper off the 'Intragam' and see if the remission will kick in after that after the first few months.

A number of **studies are starting to hint that remission is more likely for patients on steroid**, if it is effective. Not everybody responds to that particular combination, but maybe combinations are the way to go.

Question: And also with a combination you don't know if they overlap or underlap.

Question: Complications or side effects?

Answer: The **complications with Prednisolone** include **things like fluid retention, weight gain and of course because we are modifying the immune system there are risks of infection, increased blood pressure,** things like that, there are **a lot of things that can happen.** We **don't want people to be on high doses long term**. In studies where they use the treatment **patients are often on a big dose (60mg)** and then it was tailed **down until the lowest dose that worked.** Some patients are on **5 or 10mg a day**. Any of these have side effects. The question is **if we are able to modify the disease and it goes away, then patients can come off treatment all together.** We may use **short term exposure for long term gain.**

Question: If you go off 'Intragam' and you go down hill would it be pretty hard to get you back up again?

Answer: I guess that's the reason why people are often left on treatment, because of that fear of things deteriorating. We would expect them to come back but it may take some time.

Member: CIDP is like a roller coaster ride. Some times you are up and sometimes you go down. **You may feel fatigued one day and the next you feel like you can do some work**.

Answer: The important thing to realise is that **'Intragam' is not treating your fatigue**. It **may make your fatigue better** but the **reason for using 'Intragam' is to get strength and function back**.

What the other data is telling us is there are a substantial proportion of patients who do not need to stay on it long term. **Maybe 20 to 30% may be able to have some degree of reduction or come off it.**

This is the form I have to fill out if I want to renew someone's 'Intragam' or to put information on.

Your name:
Where the product is being infused:
How are you going to measure this person's response?
It is not "I feel a bit better afterwards or I feel I have more energy".
It has to be "I can function. I can do more. I can walk better".

Question: If you come off and you go down 10% and you don't regain that then who is benefiting? No-one? (Others answered The Government.) **The risk is all on the patient. If they get worse well then they deserve to have the product. The logic doesn't seem right. If you are stable, then the aim of the doctor should be to keep the patient stable. If a new patient goes on it, that's fair enough that you see well have they benefited and do they feel better.**

Answer: Then **do you leave them on that dose?**

If **a patient is benefiting from it they will tell me they feel better after they get the drug and usually they say they feel a deterioration coming up to their next treatment. If they don't report that to me, then I would think that they don't need as high a dose as they are getting. I would like to see a little bit of fluctuation to reassure me that we are at a level where things are still responsive. It is all about – Is the condition still in an active phase or not?** Otherwise (and this is what came out of the trials before) **perhaps 20 or 30% of patients could come off their treatment and not get any worse for a period of 3 months. That was situation in the INCAT study; significant numbers of over treatment and it is because people have that anxiety about things deteriorating**. I think **if you monitor that closely and things do deteriorate and it is in an objective manner, then go back onto 'Intragam' or increase the dose.**

I have had some **patients where I have had to scale the dose up quite high and have had to go to the Blood Bank because they say "This is outside guidelines".** I say **"So what? The patient is not benefiting so we have escalated the dose where it has been necessary."**

Equally I have been able to get the dose down without patients' deteriorating. It has to be a dynamic thing. We don't lock it in and leave it there and don't think about it ever again. **I think it has to be monitored**.

Member: We do have **two members who have come off IVIg and neither of them has deteriorated**. In fact, over the years my husband feels his myelin is growing back slowly and he is able to do more. **When you come off you still may have a disability because over 20 odd years or 5 years whatever, there has been residual damage.** My husband still **has foot drop but the muscles have come back in his arms and his legs** and he **can do more.**

Answer: The scarring may limit how much things get better.
We know **this condition does go through phases of activity and remission**. Sometimes there are **patients who** seem to settle right down off treatment and **don't need ongoing treatment.**

We could put the question the other way around. **Why be on treatment if you don't need it?** Secondly **if things do deteriorate, then you get back on treatment straight away.**

Member: Getting back on treatment straight away is what the anxiety is about.

Answer: I understand what the anxiety is about but I can **also understand where the Blood Bank is coming from. They have a limited resource, they are trying to make supplies available to people and the requests seem to be going up and sometimes it is because things are not being monitored critically.**

Question: How often do you have to monitor it?

Answer: Probably at least about every 6 months. In **different patients** it may be over a **shorter time period**.

Question: Is this in effect now?

Answer: It has been in effect for about 12 months.

This is **a brochure put out by the Blood Authority**. The other thing that your **neurologist** or **whoever is giving you your treatment is going to be asking you is "Do you realize that by having 'Intragam' the Blood Bank is collecting information on your condition? Whether you are responding or not?** At some stage, I suspect they may be **tightening up on people who are just signing a form once a year. They will want stronger evidence that there is improvement.**

In the **last 12 months** and because I have been involved in the trials I am **thinking more about INCAT scales and the sort of muscle testing we do and measure that in a certain standardised way.** I am **using the hand grip strength** which is as good **a measure of overall function in CIDP** and **measuring them all the time**. **Every time I see a patient I get those done**. Then you can **track whether things are worse or the same**. **I have the information to go back to the Blood Authority and say "This person is worse".**

Question: What if the person doesn't have a drop in strength?

Answer: It makes it harder **but if it is purely sensory it would also affect walking times and balance tests and the neurologist and physiotherapist will be able to monitor that aspect**.

Question: Is there no other test you can use?

Answer: Most of the disability is strongly weighted towards strength measures.

Question: What is the prospect of medical science coming up with a definitive antibody measurement designed to predict how bad you are or what is wrong with you?

Answer: There are heaps of anti-bodies. I'm involved with **another group in Melbourne and Sydney where we are looking at a number of patients with CIDP and we are measuring a whole lot of things in the blood. We are looking at blood before and after 'Intragam'** and we are **trying to see are there markers in the blood stream that tell us that someone is going to respond well or not going to respond**. There are **one or two markers there that have shown promise. This is work that Wayne Dyer has done in Sydney.** He is **working for the Blood Bank** and **we have been co-operating** with him in that trial and the **hope is that we can identify a marker in the blood that says "This person is a responder**. This **person is not going to respond and they are going to need a different sort of treatment." That sort of work is ongoing.**

What you have got to **expect from your neurologist is that there is going to be more detailed measurement and monitoring of what you are like, what your strength is like and what your function is like** and those **measurements need to be done in a standardised way on a regular basis.**

Last time I spoke to this group which was a long time ago, we were **talking about different ways of measuring response, measuring overall assessment of function**. That's where it is going to head. **We need to have good measures, not just you telling us you feel better, but ways we can track that in some other way. Blood is not going to hack it and nerve conduction is not going to be the way forward**. It is not pleasant having that done anyway.

Question: What about **some sort of machine like a walking machine that would show your heartbeat or blood pressure going up if you over exert yourself or some other mechanical way of testing** you?

Answer: That's a good thought.

Question: Why isn't nerve conduction tests a reasonably accurate way of defining things?

Answer: Nerve conduction is very useful in helping make the diagnosis but **nerve conduction doesn't change from one treatment to the next**. **If it recovers**, **it will take ages and ages** because **a lot of damage is done in areas where you can't test** with electrical tests. You **can't wait for that to recover before you get a functional improvement** whereas you often get better strength and better co-ordination within a few days and the nerve conduction isn't going to change that quickly. **We need an answer a lot sooner**. It may take **several months-years to get a measurable improvement** and then we are really **only testing** some nerves which are in the **hands and the feet** and the **muscles** that are **more important may be in the shoulders and hips. We just can't get at them.**

John Burke: Alright I think we're done. **Tim:** Do you want me to stop talking?
John: No. Have you got anything else to say? **Tim:** No.

John: I have a particular interest in saying **"THANK YOU" to Tim** because **I am one of his success stories. After 15 years he managed to actually wean me off 'Intragam' altogether with no loss of dexterity or no increase in disability.** So personally I would like to say "**Thank you" but on behalf of the Group a very interesting talk** and we look forward to **further advances in the future**. Applause.

Oral replacement for IVIg (i.e. Intragam / Octagam / Kiovig)

Patients need to be otherwise healthy, have CIDP which is still clearly responding to IVIg and are prepared to trial stopping the IVIg and replacing it with an oral drug (Fingolomod) to see if that can fully replace the benefit of the IVIg. This would clearly have greater convenience, but the responsiveness and effectiveness over time needs to be tested. If the CIDP breaks through the oral drug treatment, previous IVIg treatment would be resumed. More detailed instructions could be discussed with any interested subjects.

Any patients interested in the trial should contact A/Professor Tim Day at the Royal Melbourne Hospital on Timothy.Day@mh.org.au. If you are interstate or overseas contact your Neurologist to see if there is a trial near you.

Study purpose and conduct

Patients are invited to participate in a clinical research study to evaluate how effective and safe the drug FTY720/Fingolimod is when used to treat people who have chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Fingolimod is an oral once-a-day medication that has been approved in over 40 countries for the treatment of relapsing multiple sclerosis (MS) but has not been approved for the treatment of patients with CIDP. (In Australia Fingolimod (Gilenya ®) is approved by the Therapeutic Goods Administration for the treatment of MS). Fingolimod is not available for doctors to prescribe for CIDP therefore it is considered an “investigational” drug.

Fingolimod acts on certain types of white blood cells (lymphocytes) responsible for immune reactions. It makes some of these cells move away from areas of inflammation (tissue injury) and redirects them towards lymph nodes and other places in the body where they rest. These cells are believed to play an important role in the inflammation process associated with MS and CIDP. It has been shown in CIDP animal studies that Fingolimod completely suppresses paraparesis (partial paralysis of the legs) and reduces the severity and duration of the disease. Fingolimod has not yet been studied in humans with CIDP. Most of the information on Fingolimod has been obtained in patients with MS, which may or may not apply to patients with CIDP.

This is a clinical research study sponsored by the pharmaceutical company named Novartis. The main purpose of this study is to determine if Fingolimod is effective in treating CIDP and if it is safe for patients with CIDP. Information from this study may be used to support the registration of Fingolimod as a treatment for CIDP if it proves to be effective.

Subjects who participate in this study will be randomly assigned (like flipping a coin) to receive 1 of 2 treatments:

- Fingolimod 0.5 mg (1 capsule a day)
- Placebo (1 capsule a day that is identical in appearance to the Fingolimod capsule but contains no active drug).

The treatment assignments will be equally distributed among all participants, so that half of the patients will be assigned to receive Fingolimod and half to receive placebo. You have an “equal” or 50% chance of being treated with either Fingolimod or placebo. Neither you nor your study doctor will know which treatment you are receiving (that is, your treatment assignment will be masked or blinded). However, your study doctor can find out what you are taking if there is an emergency. Otherwise, you will not be able to know which treatment you were receiving until the study is completed and the data have been analyzed.

THE 'IN' GROUP

The Inflammatory Neuropathy Support Group of Victoria Inc.
Supporting sufferers from acute Guillain-Barre` Syndrome (GBS and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
Registered No: A0025170R

Annual Subscription 1/7/15 to 30/6/16.

Annual Subscription		$ 15.00
Other Items		
Booklets- GBS	$3	$
CIDP	$3	$
After GBS	$3	$
The Road to Recovery A-Z	$6	$
- Boy, Is This Guy Sick	$2	$
Recipe Book -$12 plus postage & handling	$16	$
Donation to support medical research		$
(Donations of $2 or more are tax deductible)		_____
(Tick if receipt required ……..)		
Total Payable:		**$_____**

Enclosed is a cheque/money order (payable to The IN Group)

Membership Details

Name: _____
Address: _____
_____
_____Postcode _____

Telephone: (Home) _____ (Work) _____
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Signed: _____Date: _____
Thank you. Please forward this form along with your payment to:
The Treasurer, The 'IN' Group, 26 Belmont Rd., GLEN WAVERLEY 3150