GBS ……..CIDP **Issue 85. January, 2014.**

INFORMATION

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SLOW BUT SURE

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)
26 Belmont Road, Glen Waverley, 3150. Victoria, Australia. www.ingroup.org.au email: info@ingroup.org.au.

NEXT MEETING – SUNDAY, 23RD FEBRUARY, 2014
AT THE BALWYN LIBRARY MEETING ROOM,
WHITEHORSE ROAD, BALWYN AT 2.00PM.

GUEST SPEAKER – DR. ROBBIE HUNT, CHIROPRACTOR
A small plate for afternoon tea would be appreciated.

Dates to remember – PLEASE NOTE NEW STARTING TIME.

18th May, 2014 at **2.00pm**	General Meeting - Guest speaker to be advised.
17th August, 2014 at **2.00pm**	Annual General Meeting
16th November, 2014 at 12.30pm	Annual Christmas Luncheon

Note from the Annual Christmas Luncheon.

We had a smaller than usual gathering with quite a few people apologising due to illness. As usual the atmosphere was friendly and a lot of fun and good fare was enjoyed by those attending. Thank you to all who donated time, effort, food, gifts and funds to this special day. A net profit of $604 was achieved. An amazing effort.

TALK BY ASSOC. PROF. RICHARD STARK AT AUGUST MEETING CONTINUED…

Treatment

Talking about the treatment of these conditions; the thing about **GBS** of course is it **is a disturbance of the immune system.** Basically we think the problem relates to **circulating proteins in the blood, maybe with anti-bodies and other immune conflicts of inflammatory proteins and usually these are triggered by infection**. An infection makes **the body's immune system active to try to fight off the infection and produce anti-bodies and the anti-bodies then deal with the bug but they may actually cross over to the nervous system and damage the nervous system as well. By the time the symptoms appear as Guillain-Barre` the bug is no longer there.** Giving antibiotics to deal with the bug is not going to solve the problem. There is one exception as occasionally there is **a bug called campylobacter juni** which can cause this, but the thing is to deal with the GBS. **It can cause life threatening acute complications and so our treatment for dealing with GBS is to keep the person alive, avoiding the life threatening complications and to deal with the immune process; get rid of the anti-bodies and what have you.** It is true that GBS gets substantially better by itself if you can keep the person alive, but it is pretty clear that treatment can speed up recovery and we like to **get treatment going as quickly as we can**. Once that is done it is a matter of rehab. to try and get things moving and to deal with particularly ongoing symptoms that might arise.

Most patients with Guillain-Barre` do well but there is certainly a sub group of patients who do have residual problems from an acute attack of Guillain-Barre` and very likely what has happened is that the **damage to the myelin has been severe enough that the underlying axon has been damaged as well**. There is a huge range as to how severe the problem can be and in some cases it is mild. In the olden days they wouldn't be called GBS but it is the same process.

There was a patient I was involved with recently who really was walking about but was aware of weakness in the legs and it was getting worse day by day. When treated, his legs were better within a week and they were really 100% back to normal within a couple of weeks. Now **probably if that had not been treated they wouldn't have been a very severe case, but they probably would have had on -going weakness for some time** – weeks or months – and they probably would have recovered gradually over that time and might have got back to 100% normal but it would have been a much longer process.

There are certainly people who get **severely ill very quickly**. Again, there is a lot of variation. The things that can go wrong and can be life threatening complications of Guillain-Barre` are **mainly respiratory failure**. We are very tuned in when someone comes in with GBS to keep an eye on their respiratory function and we usually measure it by bed-side tests of lung function (how hard and fast you blow out), checking the oxygen saturation in the blood. That's a bit of a trap as it is very easy to do and probably any of you who have been in hospital recently will have had a little thing on your finger which produces a read out of what your oxygen levels are, so it gives you a nice number and your can follow the number and put it on a graph if you like. **The problem is that your respiratory function can actually go down quite significantly before the oxygen level does. In other words, the body adapts and acclimatizes and makes you breathe a bit faster and keeps the oxygen level up. One of the first things that actually happens is that the person feels that it is harder to breathe. They say "look I'm struggling to keep breathing" and often when we have junior doctors who have not seen a lot of such patients they are more inclined to look at what the oxygen level is rather than listen to what the patient says, but in fact the patient is right in this case and as soon as someone says that and they have Guillain-Barre` we should be tuned in. What we will often do is to get the intensive care people involved so they would likely move somebody into the intensive care unit and say "If things get any worse we can assist you to breathe". They can be put on a respirator or respiratory support.**

If you are **not breathing as deeply** as you should it is **easy to get pneumonia** which is one of the risks of course. If you are **not moving your legs** as you should then you can get a **DVT (deep vein thrombosis)** so you need to be tuned in to that. As I mentioned earlier the autonomic system can be affected in GBS and you can get **changes in your pulse and blood pressure**. Your blood pressure can shoot up or go down and that can be a problem as well.

The **first really effective treatment for GBS was plasma exchange** and it makes a lot of sense if the anti-bodies are causing the problem, just remove the anti-bodies. We take a persons blood, it goes through a machine and **their plasma is taken off and it is replaced by healthy plasma**. Their anti-bodies go down the sink. It became clear very early on that that was effective. There are technical problems with it; it is a big machine, it is an expensive machine, you have to have access to large veins to do it and it requires quite a lot of technician support standing next to the machine and doing it. **You have to start it early and some patients need a second course. Because you are removing quite a lot of blood and putting blood back in, the blood pressure can go up and down even more than it routinely does. It is not perfect, but it certainly was a revolution when it first occurred.**

I actually was going through some old papers awhile ago and came across this letter which was written on the 26th August, 1980 by a very eminent author. (Dr. Stark pointed to himself and there was laughter) You have to understand that I was a very young man at that time, barely out of nappies really, but the point about this paper is quite an interesting one. **We were using plasma exchange then to treat people with Guillain-Barre`** and the thing is that at that time (1980) plasma exchange had been used for about 3 or 4 years effectively for GBS and everyone who used it knew that it worked because we could see people and we could see how bad they were at the outset **and we would know how long we would expect them to be sick and you would treat them with plasma exchange and they would not actually be sick that long and they would get stronger quicker.** However, there was a very considerable difficulty proving this and the difficulty proving it really relates to the fact that everyone is a bit different. The way you would want to do it is to have a group of patients treated with plasma exchange and a group of patients who were exactly similar who were not treated with plasma exchange and you would want to be able to measure how long it was until they were up and about and doing all the things that they should do.

The problem is, if you take your next 10 patients here and you next 10 patients there, the odds are there are going to be significant differences between them and it is very difficult to prove that the two groups are equivalent and if one group got better a bit quicker, maybe it was just because they were going to get better a bit quicker. It actually took quite a bit of doing to set this up. **At that stage too I think people were not treating it early enough, so if you treated people too late, in fact it didn't do much good.** Of course to set up a trial like this was a bit of paper work and fiddling and that tended to delay things.

The point about this letter is: We had **a patient that we had done nerve conduction studies on**. We said **they have Guillain-Barre`**. We are going to **treat them with plasma exchange**. We treated them with **their first dose of plasma exchange and immediately after that we repeated the nerve conduction studies** and on one nerve **there was actually a substantial improvement** in the way that it functioned. It worked and you wouldn't expect that to happen if you hadn't done anything. We were just putting this on the record saying, "Look, this is **demonstrating that plasma exchange does do something and it is objective, rather than just our impressions**." It wasn't ground breaking research or anything of that sort, but it just reflects the fact that even at that time the treatment was available; it was being used in a number of centres, but there was scepticism about it. There was scepticism that it actually was doing any good because it was hard to prove. It wasn't until about **1984/85 that there was a large trial published that actually definitively proved that plasma exchange did work**, although **everyone who used it and had seen people before and after knew that it did so.**

It was quite an interesting time because **when I first started in neurology there was no recognized treatment for GBS or CIDP. During the time I was training these techniques became available** and we were quite excited about it. There were people with GBS sitting in the intensive care unit for months and months and this turned it around. **Plasma exchange was going to be something that would be really big**.

Now **these days we don't use plasma exchange all that much and it really is because IVIG works just as well or probably even a little bit better. It's now reliably available. It's easier to do. You don't need as much technical support. You don't need a big machine to do it. It doesn't make your blood pressure go up and down so it works very nicely.**

You might think that high dose cortisone would work well for Guillain-Barre` but it probably doesn't or if it does it's not much. That's a contrast between GBS and **CIDP where high dose cortisone definitely does work**. It is one of the differences.

Treating **CIDP and Multi Focal Motor Neuropathy (MFMN), again we rely mainly on IVIG** these days. Now of course when you are treating **GBS**, because it is a **"one off"** thing you have an infection that produces anti-bodies. **When the infection goes the anti-body production stops**. It is a matter of getting on top of it and **usually one course of treatment will do**. With **CIDP the difference is that the anti-bodies that are causing the damage are not necessarily caused in response to a bout of infection, but may occur as an auto-immune disorder.** In other words, **they occur because for some reason your body has started to produce anti-bodies** to cause this degree of damage. That seems to be **an ongoing phenomenon**. If you treat it once, that's fine, but in the end you will probably have to come back. So **most people who are treated for CIDP will get an initial course of treatment but then can go on to have treatment maybe on a monthly basis, some people 6 weeks, some people 2 weeks.**

Plasma exchange does work for CIDP, but it is a major undertaking and we really don't use it all that much. Oral steroids probably do work and for some patients who have resistant CIDP we fall back on immunosuppressants like Cyclosporine, Cyclophosphamide and Mycophenalate which will work.

There is a new group of medications now that are coming through which are specifically designed anti-bodies to prevent the development of certain cells within the body. **Now the anti-body producing cells are called B cells and there is a drug that will basically stop these cells from forming in the body called Rituximab.** Rituximab drops your anti-body levels beautifully, but of course there are problems with that in that anti-bodies are useful for some things. **It is a very powerful drug**. It is a drug that we use from time to time in certain anti-body related conditions and I think it is **probably something that we would think about using for someone with an acute disastrous neuropathy that wasn't responding to anything else.** It is probably not something we would use much in CIDP.

There are these groups of new medications that may be relevant in treating CIDP and again I think people are going to be looking at the most difficult patients first and then they may well flow on to be more widely used.

One of the things that tends to happen **with CIDP is that as time goes by there will be some axonal damage**. There will be some damage to the underlying nerve cells and **that tends not to be easily repaired**. When you see someone early in the course of CIDP, most of the problem is anti-body related and we would be hoping we could deal with that with IVIG**. As time goes by, probably the anti-body related damage is less but maybe the chronic axonal damage just from prolonged exposure to injury is more.** It may be that people become

less IVIG responsive as time goes by. It is the case that **sometimes people who initially needed IVIG every 3 or 4 weeks may later on find they don't need it as often and they go 6 or 8 weeks or whatever.**

(At this point Dr. Stark showed pictures and a graph and stated that it was borrowed from Prof. John Pollard in Sydney some time ago.)

John had a patient whose husband was an engineer and he was irritated that the way we measured power seemed to be so slack and wasn't terribly quantitated so he devised this device for measuring power. He plotted his wife's progress, sometimes several times a day and if ever you needed proof that 'Intragam' works, here is the strength. It wears off a bit and she gets a bit weaker, next 'Intragam' infusion, the strength comes back, wears off a bit, next infusion, getting better, getting better and as time went by different baselines, getting better and better. So he was able to produce this graph for John and John has been showing it at lectures ever since. 'Intragam' does work and this graph is beautifully plotted and a great demonstration.

I am very happy to answer any questions you might have.

Question: There is one symptom missing that I find. **I feel like I've got a virus, like flu. It lasts an hour or two or a day and the next day I'm fairly fit and better.** Why is that? Is it the immune system?

Richard: It may be an immune based thing. It is certainly true that people with inflammatory neuropathies often will get a lot of fatigue related symptoms too. I think that is because a lot of the things we normally do day by day that should be effortless become effortful and so require more energy and more input. I think that probably is a significant part of fluctuating symptoms of vague and malaise is often related to this fatigue component. Certainly people with Guillain-Barre` in the acute inflammatory phase often do get this feeling of illness and chills, being unwell and so on. Probably a bit less with CIDP but again I think it can happen.

Question: **With the discomfort of feelings of burning feet are there medications?**

Richard: I really haven't talked much about symptomatic medication but **there are a number of medications** we can use particularly for neuropathic pain and there is a list of those. Probably some of you know of the drug '**Lyrica**'. It has been around a little while now. There was a problem because it has not been on the PBS. It is designed for damping down neuropathic pain. **The government has finally put this on the PBS** which is **going to make a difference to many people**. There are some **older drugs** we use for neuropathic pain. They are mostly in two groups; the **anti-epilepsy drugs** which are designed to stop the brain from firing off and a number of them **stop the peripheral nerve fibres firing off when they shouldn't be so stopping neuropathic pain**. The oldest of them we use is 'Tegretol' and a couple of newer ones, 'Lyrica' is one and 'Neurontin' or 'Gavapentin' is the other.

The other group we use for neuropathic pain started life as anti-depressants. One of them is amitriptyline or 'Endep' and their pain relieving is quite separate from their anti-depressant aspect. For amitriptyline the dose we used for depression was 150mg per day. Particularly the dose we use in pain management is 10mg, 20mg maybe up to 75mg per day. It is not going to have any anti-depressant effect at those doses but it does dampen down the pain.

Question: Exercise – is Neuro Physiotherapy a better option?

Richard: Physiotherapy is very helpful for a lot of reasons. What tends to happen, particularly if you have weakness, is that the way people adapt to weakness is to use trick movements. **If you can't move something the way you should, you tend to use a trick movement. That can be good in the short term, but it may not be good in the long term. A Physio will tend to work on you to try to improve the pattern of movement. Obviously if there are muscles that can be strengthened by specific exercises they will be able to show you how to do that as well. I think that is helpful. Seeing someone who is familiar with the sort of condition you have is always a bonus. How much extra value a Neuro Physio is going to be over a standard Physio will depend a bit on the detail of what needs to be done and if it is simply a matter of strengthening muscle, most Physios are going to be able to identify which muscles are weak and give you an appropriate exercise to try to strengthen them. If it is really a matter of looking at patterns of movement and saying, "That's an inefficient pattern of movement. I know why you are doing it. It's a trick movement you have worked out as the best way to get around the problem, but it is not the most efficient way of doing it in the long run," I think a Neuro Physio would obviously be better in that situation.**

If you have someone who is not aware of where their feet are in space therefore they have balance problems, probably someone like a Neuro Physio is going to be better at dealing with that.

Question: Is a nerve conduction test a good indication of the treatment you have had?

Richard: Nerve conduction tests show you a few different things. The speed of conduction over the nerve will tell you how much damage there has been to the myelin. When the myelin repairs you tend to improve your conduction velocity a bit but not back to normal. **The thing that really goes along with nerve conduction studies with people with GBS is nerve conduction block. Basically if you can imagine that I have an axon that goes from my neck all the way to my fingers and it is coated with myelin all the way down. If you actually get an area of local damage to that myelin (say on your forearm) it can be severe damage so as that impulse travels down and gets to that area of myelin damage then it can't get across. That's what we call conduction block.**

It is important clinically **because if the impulse can't get across in the conduction study, it can't get across to say please flex this muscle. Demonstrating conduction block usually correlates to how weak you are and if you are able to demonstrate that the conduction block is no longer there, that will often correlate to getting clinically better. If fact, when we showed that paper that was exactly what we were showing - before the plasma exchange to after the reduction block got better. Obviously there was an area of dodgy myelin that was under pressure from immune damage and removing a bit of the immune damage allowed the myelin to function to a degree. That's what we were able to show.**

The answer is: **It gives you an idea of how things are going**. It certainly is very good at telling you what sort of problem is going on **with the nerve whether it is primarily a demyelinating problem or an axonal problem**. Sometimes, improvement in nerve conduction will parallel an improvement in clinical function as well.

How often should we do nerve conduction tests if they help us to follow things? If you go from being able to lift 2kg to being able to lift 10kg, that's fine, your nerve conduction tests are not going to tell you much more than that. I guess sometimes if we are not quite sure whether things are going in the right direction or not we might repeat nerve conduction studies to see how they are looking as well. **Mostly they are better for diagnosis than for monitoring progress is what I'm saying.**

Question: I notice that when I wake up in the morning I feel "ordinary" then once I get moving around, I seem to come better. Is that just because you have been sleeping and your nerves have relaxed?
Richard: There is probably a bit of secondary stiffening up. Your muscles and your joints get stiffer as you are immobile and so that general loosening up (again**, most of us are not 10 years old anymore** and our joints all suffer and it does take a little while to get going) **if the nerve fibres are not functioning 100% it can take a bit longer as well.**

Question: (Unfortunately this question could not be heard but ended in "**support for IVIG in CIDP?**)

Richard: There is a good level of evidence. Again the same technical evidence of demonstrating compared with placebo. There have been big placebo controlled trials done.

Question: What type of test sizes?

Richard: I think they were looking at **200 patients** in these groups or something of that order. They are quite a technical thing to set up. You have to **multi-sample and it has to be organized and coordinated**. One of the problems is it is such **a major undertaking to do a randomised trial** like that but what tends to happen is you get **one or two done and they show what you think they are going to show** and then no-one is going to do it again, because **it costs hundreds of thousands of dollars to do** and so we end up **basing our practise on trials** which probably now for IVIG were **done late 80's early 90's**. If we were designing the trials these days, we would do it a different way but no-one is going to set it up again.

Question: Does CIDP ever get confused with Post Polio Syndrome?

Richard: Look it might get confused with Post Polio Syndrome. Post Polio Syndrome is an interesting topic in itself which we could talk about for a long time. Have people heard about this condition? Polio was around in

Australia probably in the 50's and early 60's so most of the people who have had significant problems with polio are now getting on a bit. The way Polio causes damage is (if you remember that early picture of the neuron with the myelin around it), to the anterior horn cell, so it is the actual cell body of that neuron within the spinal cord. What typically happens is there would be a group of cells close to each other that would be damaged directly as a result of the virus. Typically Polio causes areas of weakness caused by adjacent horn cell damage. You might end up with weakness of one arm or of one leg or you might end up with a foot drop on one leg and weakness around the hip on the other leg. You end up with areas of patchy weakness.

The way the body tries to adapt to that is if you have lost three quarters of your anterior horn cells supplying that area, the quarter that are left try to take up the load, so instead of one ante rial horn cell supplying 20 muscle fibres, they will actually try and send out branches and try and pick up some of the muscle fibres that have lost their innovation. You end up with a very small number of anterior horn cells, each of which is doing a huge amount of work.

Patients who had Polio end up with a few cells doing a huge amount of work; they end up with areas of weakness which are patchy and asymmetrical and most were affected as young people so they tended to adopt a lot of trick movement to try to enable them to function. That's terrific when you are 10, 15, and 20. All of these people are now 60 or close enough and what tends to happen as you get older

a) your joints become less supple so some of the trick movements you used when you were young Won't work anymore;

b) you drop out anterior horn cells. We are all dropping out anterior horn cells as time goes by, but if you have a few huge anterior horn cells that are basically keeping you going, losing one or two of them is not good – it makes a noticeable difference – so they drop out anterior horn cells as they get older as well and what that means is they really don't have any functional reserve so things they used to be able to do they no longer can do.

For the vast majority of people who have got this late Post Polio Syndrome it is simply a matter of loss of capacity to make these adaptations which explains most of it. It is a highly controversial area. There is a Post Polio support network that have put together the concept that a lot of this is a reactivation of an inflammatory process and I guess it is possible, it happens sometimes, but certainly the vast majority of patients that I've seen, the situation is easily explained just by this failure of adaptations as people get older and the loss of these really important large surviving motor units.

That's enough to explain the problems they have and they are real problems no doubt. It means that people who have been able to get about with certain devices no longer can and end up requiring more support.

Question: What would happen if they had nerve conductivity tests?

Richard: They would have a very specific pattern because what they will actually have is evidence of loss of innovation of the muscles in particular; they will have reserved sensory fuzz because the sensory nerves are normal and they typically don't get slowing of conduction because the myelin is perfectly healthy. You actually get a very characteristic appearance you would see.

Question: What of the Pathology?

Richard: The pathology, **because the actual trouble is in the spinal cord, if you cut up the spinal cord you see the degenerative changes where the anterior horn cells in the spinal cord are** and **if you look at their peripheral nerves you will see that there are degenerate axons which these anterior horn cells used to supply, but no changes in the myelin.**

Question: You mentioned before about CIDP and neuralgic neuropathy. How common is that and how common is it for CIDP to begin in the arms and hands?

Richard: It is a separate condition. It is not rare. I think we would probably see three or four patients a year coming through the hospital. It is not something every GP is going to see every second week, but it is something **we see reasonably often**. In fact the **biggest diagnostic mistake** that people make is they get pain in the arm and weakness and **they think they must have a disc out in their neck**. They often have scans of their neck and some even get sent off to neurosurgeons because of it. Most of us have slightly dodgy looking necks

and so **they have a scan** and are told "Oh it's not quite right but it **doesn't look bad enough to cause this trouble"** They go off for the neurosurgeon's opinion and the **neurosurgeon says "I don't think that's the cause of it" and so they end up being sent to the neurologist down the track.**

CIDP staying in the arms? It can happen, but it **more often starts in the feet and then the hands**. **Typical standard neuropathy starts distal (feet first) then the hands, but again every one is different and there are patients where it starts near the hips but most people it is feet and hands.**

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ANNUAL SUBSCRIPTION
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

Subscriptions due on the 1st July of each year.
1st July 2012 – 30th June, 2014.

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Other Items		
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- **Boy, Is This Guy Sick**	$2	$
- **CIDP**	$2	$
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REHABILITION SUPPORT

Many of our Victorian members have benefited from being placed at the Austin Health's Royal Talbot Rehabilitation Centre (RTRC) after being discharged from hospitals following GBS and CIDP. **They have a team of specialists dedicated to providing the best chance to learn to walk again. The team includes physiotherapists, occupational therapists and creative therapists who design a program of therapy specific to each patient for their physical and emotional wellbeing. Their aim is to raise $72,000 so more patients have access to the most up-to-date physiotherapy equipment for their motor skills and Creative Therapies.**

One of our members agreed that every member of the team at Royal Talbot was focused on one thing, to re-teach her legs to move when her brain said move. She is very grateful and wished to draw our attention to the RTRC appeal. If you would care to help this very worthy cause,

Donations can be sent to Austin Health (ABN 96 237 388 063)
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