Neuroscience Trials Newsletter

From the Birmingham Clinical Trials Unit

August 2014

August 2014 edition — Lauren Genders

Welcome to our first Newsletter of 2014. Also the very first newsletter from the Neurosciences new home of the Public Health Building. We are very excited about our new home and new school as it brings lots of opportunities for new trials.

Now you know where we are, lets move on and get up to date with all that is happening in our trial portfolio. Some of the eagle eyed amongst you will have noticed that it has been a while since our last newsletter. Sorry about that but it does mean we have lots to share with you.

We have a new article written by one of our participants. Maureen Wakeman writes of her journey from being diagnosed with Parkinson's disease and goes on to give her experiences of the PD SURG trial.
As many of you are aware we are in the final push for PD GEN samples from participants who joined the PD REHAB trial. PD REHAB has finished and the result is in the process of being written up, our funding for collection of blood samples from these participants also runs out at the end of this year. But have you ever wondered what happens after you have had your blood taken? Turn to page 3 to read Dr J Stockton & Prof KE Morrison's article on just that.

We have invited a number of people with Parkinson's and their carers to join our Patient and Public Involvement Group. The purpose of this group is to improve our research by ensuring we are asking the right questions and are communicating with trial participants and the broader community most effectively.

Now for my PD SURG experience — Maureen Wakeman

I was diagnosed with PD at the age of 38 in May 1983, following four days of tests at the National Hospital, Queen Square, London. The tests included a brain scan, lumbar puncture and blood tests and the registrar told my husband, not me, that I had most probably got PD, but they couldn't be sure as there was no test that could show that I had got it. They could only use the tests to eliminate other complaints.

I was given a date to return to the hospital and I arranged for a friend to accompany me to see the consultant, not expecting to be given any seriously bad news. Just before I left home my husband told me what the registrar had said and I didn't really take it on board, so when the consultant told me that I almost certainly had PD, I was quite taken aback and had not armed myself with any questions. Now I have had PD diagnosed for 30 years, I've had most of my questions answered. My main questions over the years have been: Has anyone found the cause of PD? Has anyone found the cure? The answer to both questions is still NO.

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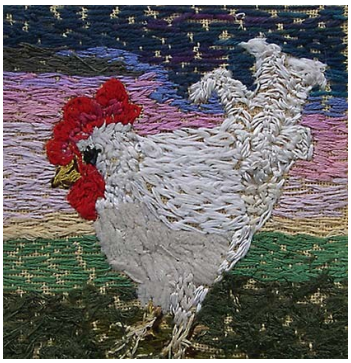
Now for my PD SURG experience cont'd…. — Maureen Wakeman

I won't take up space with the years of misery I had after about 8-10 years on Madopar, suffice to say it was a nightmare of being switched off, then getting switched on with awful dyskinesia, which persisted until my next dose of Madopar was due. I couldn't do anything : sleeping was difficult as I couldn't turn over in bed, eating was an exhausting business of trying to get food to my mouth without flinging it all over the place, even just walking was a trial as I high-stepped or shuffled along according to how the medication affected me.

I am quite a creative person, I trained and worked as a dress designer, then brought up my family of four children and when I started working again it was as a prop maker at Shepperton Studios. It was fun when I was well but too pressurised for me once PD got a grip.



By the time I was offered the chance to take part in the PD SURG trials, I was at my wit's end and after discussion with all the family, I put my name forward.

I was accepted as a suitable candidate and met the team who would take care of me before, during and after the operation for Deep Brain Stimulation.

The team was led by Professor Marwan Hariz. He was terrific as were the whole team and everything was explained to me in detail. I had masses of tests to be sure I would have every chance of benefitting from DBS and was given the date for the first operation to insert two electrodes into my brain, using a metal frame, screwed into place on my skull, to pinpoint accurately the correct position for the electrodes. I had to be awake for the whole procedure so that the team could see the effect of the electrical impulses on my symptoms. The worst part was when Prof. Hariz drilled the holes in my skull, but the anaesthetist said that she gave me an extra puff of tranquilliser before each drilling, so it wasn't as traumatic as I had feared. A short time later the stimulator and battery were inserted under general anaesthetic, just below my left collar bone. When it was turned on I really felt the improvement.

September 3rd 2013 marked the 10th anniversary of the start of my DBS treatment. It took several visits to the hospital and a small operation to pull one of the electrodes out a fraction to get the right setting for me, and I have had two batteries replaced. DBS has transformed my life, I still take Madopar but I don't suffer from debilitating dyskinesia or shaking anymore. I can go out in the evening for meals or even the odd party. I make collage/embroideries of which I have exhibited and sold quite a few. I can go shopping without attracting the stares and giggles of children and some of their parents, who should know better. These may seem like simple pleasures but believe me when you have had most of the enjoyment taken out of your life the restoration of the small pleasures is wonderful.

There have been a couple of drawbacks, which don't seem to have a solution and cause me quite a lot of difficulty. I find it almost impossible to get any volume to my voice in normal conversation and my speech is often slurred. This makes communication difficult, especially by phone. Also my handwriting is illegible and I have to type all my letters. I have put on over three stone in weight since I had DBS, which seems to be quite a common effect.

The improvements far outweigh the disadvantages and I am very glad that I was chosen to take part in the trial.

I am sending you a few photos of my work so that you can see what I can do.

(The views and opinions of the articles included are those of the authors.)

Ever wonder what happens to the blood sample?

Dr J Stockton & Prof KE Morrison

An update for PD nurses, clinicians, and patients who have donated a blood sample for PDGEN.

You, as a patient or carer, have rolled up your sleeve and given a blood sample for PD GEN. You, as a PD nurse, have labelled the tubes, checked the completed questionnaires, parcelled them up securely and popped them in the post… Then what?

The samples arrive at the Institute of Biomedical Research at the University of Birmingham, usually within a day or two, and are collected by dedicated technicians. Once the details of the patient or carer have been recorded and encoded, and the completed consent forms checked and filed, the blood samples are processed for DNA extraction. DNA, our genetic material, is contained within the nucleus of nearly all cells in the body. Most of the cells in a typical blood sample are red blood cells. These cells contain the main protein that allows oxygen to be carried to the body's tissues but, interestingly, mature red blood cells do not contain a nucleus and thus do not contain any DNA. Instead the main cells in a blood sample that contain DNA are the white blood cells which have many functions, a key one being to help the body fight infections. Thus the first step in DNA extraction from the blood samples is to separate off the white blood cells from the majority red blood cells and the liquid components of the blood. The white blood cells are then treated with a concentrated solution so that they burst open, releasing their cellular contents. In the next step the cell's protein is removed, and then finally the DNA is precipitated out of solution by adding excess alcohol. The white, thread-like DNA molecules are literally hooked out of the solution using a sterile glass rod and then redissolved in a buffer solution which allows the DNA to be stored, undegraded, for many years. (Remember Jurassic Park? – While it is still in the realms of fantasy to imagine recreating a dinosaur from a DNA sample preserved in amber, it is certainly true that DNA can survive for a very long time).

It takes around 2 hours to process 6 samples through the initial phase of gathering the DNA. It then takes a further 24 hours to redissolve the DNA into the buffer, ready for long-term storage or use. The amount of DNA in each sample varies and this is calculated, along with the purity of the DNA. Each sample is then again finally labelled with its own unique coded number and placed in long term storage at -80°C. If sufficient blood has been collected from each donor then there is enough to make two aliquots of DNA to be stored in the PD GEN DNA bank. Duplicate aliquots are stored in a separate -80°C freezers, for extra security in case there are freezer failures, power cuts and such like.

A really important feature of the bank is that the coded sample identifiers are then linked to all the collected clinical and epidemiological data from the donor in a separate computer. This makes the DNA collection particularly important as it allows any genetic data identified on an individual sample to be linked to specific clinical features of the disease, such as age at onset of symptoms, presence of dyskinesias, or response to particular therapies.

Ever wonder what happens to the blood sample? - Continued

The Parkinson's disease DNA bank collected via PD GEN is now well established, and contains about 1500 high quality DNA patient samples and over 740 carer samples. The carer samples collected are really important in addition to the patient samples as they provide a very good comparison group so that our genetic studies can be appropriately controlled. This collection is an incredibly valuable resource for research. Not only is it a long standing collection (over 12 years old now), but the fact that the epidemiological information collected can be combined with any genetic results allows much more detailed analysis. PD GEN is one of the largest PD DNA banks in the world.

Back in the laboratory we participate in many global research projects to try and determine genetic factors involved in Parkinson's disease. We aim to increase understanding of the underlying disease mechanisms and ultimately develop effective therapies, with minimal side-effects. Aliquots from the main stock samples are taken and diluted ready for sending around the world, with several gene candidates already reported. Further to this we also undertake research work in our own laboratory to try and answer specific questions relating to Parkinson's disease genetics. The latest research has looked at a newly discovered region of DNA which is a major contributor to disease burden in other neurological diseases such as motor neurone disease and a form of dementia known as frontotemporal lobar dementia.

So a big thank you to all of you who have participated in the PD GEN study to date.

Recruitment and Study Updates

PD COMM Pilot has now finished its recruitment and ended up with 89 participants, that's well above our target of 60. We are still collecting the last pieces of data so if you do have any information please send it back. You are able to keep yourselves up to date with all that is happening on our website. (www.birmingham.ac.uk/pdcomm)

PD MED results have now been published in The Lancet (see here for the abstract (http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)60683-8/abstract) or type 'PD MED Lancet' into a search engine). This is giving the official publication of the results that we gave you back in the 2012 newsletter. PD MED is still collecting information from participants, their carers, and their clinicians. This long term follow up is crucial for the accuracy of future results and establishing best medical practice in patients with Parkinson's, so please be sure to continue sending us your questionnaires. (www.birmingham.ac.uk/pdmed)

PD REHAB has finished recruiting and all participants should have completed their last follow up. We are currently in the process of analysing the data and then writing up our results. Due to the commitments of our professors this will take a little longer than we thought but we will keep you posted. (www.birmingham.ac.uk/pdrehab)

PD SURG is currently in its last stages of data cleaning, please do not be surprised if you get a request for some information regarding the trial. As soon as we are finished we will be onto the write up of the results, don't worry we will keep you posted. (www.birmingham.ac.uk/pdsurg).

I still need articles!!! Please help

Contact Details

If you're interested in sharing with our community of Doctors, Nurses, Therapists and Patients, please supply your articles, stories or experiences to:

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