Dr Anu Jacob – Introduction to the Walton Centre and its work regarding TM, NMO, ADEM and ON & Clinical and research developments in TM, ADEM and NMO

At the Walton centre there are 30 Neurologists and they complete the team along with Neuro surgeons, radiologists, anaesthesia, Pain Control and Rehabilitation.
The field of TM has changed so drastically in the past 5 years. They are more optimistic about the research they are undertaking.

Section 1 - Research at the Walton centre

Between 2012 and 2014 there has been 20 publications regarding the research into TM, NMO and ADEM. If you Google research into TM, NMO and ADEM some of the research papers will come up. Dr. Anu Jacob said that although his examples primarily focus on NMO, they are applicable to certain aspects of TM. He focussed on certain aspects of research at the Walton centre

1. Azathioprine in NMO
   - NMO is a relapsing condition
     Because there is no cure for NMO relapse prevention is the goal of treatment
     Over the period of study, Azathioprine used daily in 100 people – 89 people will have reduced number of relapses and of these 61 did not have another attack. But about 50 stopped treatment because of side effects
2. IVIG used as a medication for treating acute attacks of TM
   - IVIG may benefit acute attacks of TM or NMO, if Plasma exchange cant be done
   - A £1.5 million trial has been approved to test this. In the trial some people will get IVIG and steroids some people will get only steroids and outcomes compared
3. Preventing relapses in NMO trial
   - SA237 (anti IL-6) trial– they are hoping this will prevent the replication of B cells that create the antibody that causes NMO
   - Eculizumab – Is one of the most expensive drugs in the world. In order for a relapse to occur there has to be 2 factors - the antibody and the complement. They are hoping that the Eculizumab will block the complement therefore stopping the two things working together.
4. Fampridine in NMO – This drug will be tested to see if it improves walking speed in people with NMO. There are currently 6 people enrolled in this and they are looking to test 20 people at the Walton Centre.
   - When you lose Myelin from spinal cord in MS the Potassium that helps send messages up and down your spinal cord leaks out. Fampridine can help to stop the leakage of Potassium and the nerves to send signals faster. It has been proven to make walking better in MS.
     They are hoping that because with TM and NMO there is only 1 lesion to overcome that this will work effectively. There is currently a study of this with NMO Patients at the John Hopkins – it is a double blinded test so neither you nor the doctor know who has the drug and who has the placebo version.

5. Pain in NMO
    a. There has been research conducted into the pain people suffer when living with the condition NMO.
    b. 62% of people with spinal cord inflammation TM in NMO reported a neuropathic kind pain.
    c. The research showed that women suffered more pain than men and that age had no effect on results
    d. Tonic spasms in NMO can be painful and last usually less than 1 minute.
    e. Around 25% of people mention the itch as a prominent symptom in NMO leading up to their TM attack.

Section 2 - Understanding Spinal Cord Restoration

Stem Cell Research

- It has been traditionally believed that only some parts of the human body can regrow (hair, nails, skin, lining of gut, blood cells, liver)), but the rest cannot. Perhaps humans during evolution may have have lost the ability to regrow their internal organs as they are so well protected that we do not need to learn how to replicate these. This has made it hard for our internal organs to repair themselves.
    - In TM there are many reasons why spinal cord repair is difficult
        - Scarring caused by inflammation in the spinal cord is difficult to traverse for any sprouting neurons.
        - There can be areas in the damaged cord devoid of any useful scaffolding for the neurons to grown on .
        - Also the cord produces many substances that promote scarring and reduce new cell sprouting
    - So we may first we need to put stem cells in there and some 'scaffolding'. This will hopefully stimulate the spinal cord to regrow.
    - They will also need to remove factors in the body that prevent growth.
    - Also, the cell growth has to be closely controlled – other wise uncontrolled cell multiplication will lead to tumours!!
    - They will need to get foetal cells from storage – as these are already designed to grow into any tissue hopefully in the presence of the correct environment and substances they will grow into nerve cells traversing the scar.
    - In 2006 two scientists Takahashi and Yamanaka (who won the nobel prize) discovered they could make an adult cell regress back to being an embryonic cell, which is then capable of maturing into another kind of cell They said "Any cell can reset and do the job of another by adding pluripotency transcription factors" (Pluripotency refers to a stem cell that has the potential to differentiate into any three germ layers.) This has creaeted a new ear in stem cell research
    - Stem cell research is taking place in the UK in many places. To name a few:

  - UCL in London the information can be found here http://www.ucl.ac.uk/stemcells Nottinghamhttps://www.nottingham.ac.uk/Pharmacy/Research/DDTE/StemCellResearch.aspx
  - Edinburgh http://www.crm.ed.ac.uk/research and
  - Bristol

- 2. Exercise stimulates the spinal cord even in paralysed limbs.
- 3. Remyelination is working in the labs in mice.

In comparison to 5 years ago, the TM field has changed. Specialists are more optimistic regarding stem cell treatment.

Section 3 - Understanding the approach to new drugs and treatment

- Often when you are diagnosed with TM the doctor will treat you in a way he believes is best (based on his knowledge and experience which can be limited) unless you are part of a trial.
- Many medications may seem to work because people believe they should be working! (placebo effect). Doctors and patients are vulnerable to such beliefs. This is human nature.
- 30% of drugs prescribed in medicine apparently have only marginal effects and the apparent benefit is a placebo response. So it's crucial that trials are done to ensure that there is no bias or placebo effect.
- In research cases there are 2 types of blinded studies – Double blind and single blinded.
  - In a double blind study neither the doctor nor the patient will know who has got the Placebo drug and who has the drug being tested one until this is revealed at a later date
  - In a single blind study the doctor knows which patient has which drug but the patient does not.
- Before you take a new drug – If you want to research it,, look at where the study was done, who did the research, who were the subjects, how many people undertook the study and what elements were controlled. Be sceptical.
- Dr Jacob's rule of thumb for unproven complimentary treatments: If a treatment does not risk harming your body (i.e., don't eat, inject or insert it anywhere!!) or hurt your wallet, then try it! But remember it can be a mere placebo effect.

Section 4 - Questions from Audience

1. *Do you always expect to see a lesion with TM? What happens if you only have a Myelin Inflammation?*

   Inflammation is seen on MRI Scan as damage – almost every person with TM would have had a lesion (lesion is just a nonspecific word for an abnormal 'thing') visible if the scan was done at the right time, using the right strength MRI scanner. The inflammation is responsible for the 'lesion'

2. *Why do some people get recurrent TM and some get only 1 attack?*

   Transverse 'Myelitis' is a descriptive term literally meaning "inflammation of the spinal cord (myelos= spinal cord, 'itis'= inflammation"). One off episodes are a mistake by the body when trying to get rid of bug from the system. The body's immune system mistakes some of the proteins in the spinal cord as being similar to the bug. So it's a case of 'friendly fire' due to mistaken identity. Once the bug gets removed. It doesn't happen again. This is the usual kind of TM- post infection TM

   In recurrent TM the body's immune system has some how been led to believe that those proteins in the spinal cord are an ongoing problem and keep repeatedly damaging it. There are many causes of recurrent TM. e.g MS, NMO. Some times we can't give it a disease name.

   The article here will help understand more about the many causes of TM:
   https://www.orpha.net/data/patho/Pro/en/AcuteTransverseMyelitis-FRenPro16890v01.pdf

   We should be careful not to mistake the mild worsening of existing symptoms (due to a cold or UTI, or constipation or menstruation or warm weather) as a true relapse.

3. *How can an epidemiology study on TM be done?*

   An epidemiology study would look at how frequently new cases of TM happen (incidence) and comparing that against the population prevalence in a definite geographic area. Islands are the best places to do an epidemiology study!! And the type and nature of the TM Participants would also be asked many other questions relating to various facets of their lives. Such a study can also look at other factors such as when the TM started. TM Society could help support such a study, i.e. survey TM Society members may be the starting point. An epidemiology study focusing on newly diagnosed CNS inflammation in children (PUDDLS study) is ongoing in UK .