



DIGITAL COMMUNITY WEEKEND 2021

SUMMARY OF Q&A SESSIONS

NHSE INHERITED WHITE MATTER DISORDERS REGISTRY & SERVICE

Can you confirm if I will have to give my consent for my doctor to add my details to the Registry?

Dr John Livingston – No, the legal position from NHSE is that because the Registry's primary aim is to improve clinical care, and medical records are part of clinical care, we don't need consent to add this data to the Registry. However, we do envisage that any Doctor adding data to the Registry will discuss it with the patient concerned. One issue we haven't finalised yet is how we will share Registry data for research purposes, but this will be resolved shortly. Patients are welcome to feedback on how they would like to consent to share data for research purposes – a one time consent when they are entered on the Registry or consent each time there is a request for research data.

When do you think clinicians will start to use the Registry data and will this be through NHS England or will Europe or wider countries have access?

Dr John Livingston – We are doing a pilot in early 2022 and within a month should be able to start collecting real patient data. The Service should be live in April and we hope the Registry will be collecting data a couple of months before this. We would hope that we will ultimately be able to share data globally, this is the only Registry of its kind in the world which is collecting data about all genetic leukodystrophies. Most registries that are currently running are disease specific and collecting more detail such as the Alexander's Disease or MLD registries and we definitely need to find a way of sharing information with these registries, which is work for the future.

Will data from past natural histories or Registries be included in the Registry?

Dr John Livingston – If there is a body of data already there, that is a very good point which I will raise at our next development meeting.

Will this registry overlap the national rare disease framework registry run by NCARDRS?

Dr John Livingston – In theory yes but NCARDRS will probably not have as much detail on patients as the new IWMD registry. We have had discussions with NCARDRS during the development stage of the white matter registry and we will collaborate with them in the future and share data

Will the IWMD centres lead to new treatments being offered/trialled for patients for whom there is currently no treatment or support available via the NHS (eg Pol related/ 4h leukodystrophy)?

Dr John Livingston – The short answer is yes. One of the aims of the IWMD service is to ensure a fast track for patients to be able to access new treatments and trials. However, this obviously depends on trial/treatments being underway and for many IWMDs there are currently no treatments available. This is changing quite quickly. and we envisage that there will be more and more treatments and trials available before long.

Are there going to be links with NHS Scotland?

Yes. The IWMD service has been developed by NHS England. However, there are arrangements in place for patients in the devolved nations (Wales, Northern Ireland, Scotland) to be referred to the new service. This already is the case for many Highly Specialised Services. The majority of patients referred to the IWMD service

will not need to travel anywhere but will be discussed at a virtual MDT. However, for some patients specialised outpatient clinics will be available at one of the designated centres (2 for adults and 3 for children). There will be a centre for the North of England which may ultimately cover Scotland as well. We will know where the centres have been designated soon (January 2022).

Will all the devolved nations (Wales, Scotland and Northern Ireland) have access to the IWMD Service and Registry?

Dr Rahul Singh – Yes, there is a provision for this within development of the Service and Registry which we will be able to confirm later on.

Will the IWMD Service provide input and support for patients who are adults and have a diagnosis for which there is no treatment or clinical trial eg POLR3A ie will the Service cover all leukodystrophies and age groups?

Dr Rahul Singh – The aim is to capture all genetic leukodystrophies in children and adults and involve in any appropriate studies.

Who will notify existing patients and cover referral to the IWMD Registry?

Dr Rahul Singh – Any clinician will be able to refer patients to the Registry and patients can refer themselves or if they are unable their approved patient representative can refer on their behalf.

How do the leukodystrophy specialists on the panel envisage the new IWMD Service helping you care for your patients?

Alasdair Parker – I will ensure the BPNA (British Paediatric Neurology Association) can assist in expediting a service where patients get very quick and easy access to expert opinion that both gives them the correct diagnosis and either, sends them on for a disease modification therapy early in their journey before the window for that might potentially close, but if that's not possible feeds them back into excellent primary and secondary level care and they get excellent multi-disciplinary support locally.

Robin Lachmann – This will be a Highly Specialised Service which is commissioned as a diagnostic service, so anyone can refer in. When new treatments come along they are commissioned by NHSE and will be very expensive. Therefore, NHSE will be looking for specific named services to run them and with the IWMD Service up and running they will be in a very good position to take that on. So, they may very well become therapeutic centres in the future. The other thing, that probably meshes in with this, is that one of the main four pillars of the UK Rare Disease Strategy is coordination of care, which the IWMD Service will be well positioned to take on.

When I attend the clinic will I be able to be seen by multiple professionals such as OT and physiotherapist, or would I have to be organised on separate occasions?

Dr Rahul Singh – It's a tiered service model and Tier1/2 is virtual, there will be limited patients seen in tier 3 (face to face) and there won't be any OT/PT in the face to face clinic. We (at ELCH) are using their existing therapy network, neurodisability network. We would encourage this pathway later as well, if we are successful in the bid. There will be a few who would need specialist PT/OT/SALT which we would be able to facilitate as an IWMD centre. Things might change in 5 years' time, depending on the feedback of patients and review of the outcome on registry etc that might instigate service reconfiguration.

There has been a distinction drawn between childhood and adult onset Leukodystrophies, and there is a plan for separate services for children and adults with the IWMD centres. I wonder where adults who have been diagnosed with a childhood onset Leukodystrophy and adults who are undiagnosed that have had symptoms since childhood fit into this system? It may be that the clinicians with specialised knowledge of the types of Leukodystrophy applicable to these adults would be placed within the children's hospital and childhood IWMD teams. My understanding is that the Queen Square adult leukodystrophy group is specialising in adult onset Leukodystrophies? So would it be more appropriate for these adults to be referred within the children's

services? Or will there be clinicians who have the expertise to diagnose and support adults with childhood onset Leukodystrophy?

Dr Rahul Singh – This is an all age IWMD service split between 2 adult centres and 3 paediatric centres with a common all age national IWMD registry. This is for all diagnosed and suspected IWMD. We are aiming to meet 3-4 times annually in our National IWMD clinical meetings to share these patients, discuss about diagnosed and undiagnosed patients. There will be IWMD registry steering/developmental committee meetings to discuss wider issues as well.

Dr David Lynch – We have significant expertise in seeing adults who developed symptoms as children, that's not a problem. The distinction between age of onset is somewhat artificial, and we work closely with our paediatric colleagues. Patients need to attend appropriate services for their age, and there is detailed planning involved in transitioning patients from paediatric to adult services when appropriate.

ALD & AMN RESEARCH

Why are women with AMN not included in clinical trials?

Dr Robin Lachmann – When you're conducting a clinical trial you really want a group of patients where you have good knowledge of the natural history and what the outcomes should be. With males there is more certainty around this, especially when informing regulators of what trial endpoints (outcomes) might be.

Marc Martinell, Minoryx Therapeutics – The most recent studies on women affected by AMN suggests that symptoms are similar to those on men with AMN, although the severity and rate of progression may differ between populations. Due to this, having both populations on the same trial increases the heterogeneity which makes clinical research more challenging, particularly on a rare disease where the sample size of the studies are already fairly small. Note that in 2017 when we were preparing the trial Advance there was no Natural History data on AMN and the differences between genders were poorly characterized, hence it was not possible to include both men and women. We are planning to complete our development with a trial on women with AMN, so the whole population can ultimately benefit from Leriglitazone.

David Moller, Poxel Pharmaceuticals – Due to the slower progression of symptoms, and that treatments are designed to slow or halt symptoms and not cure them, we would need to conduct longer studies to show efficacy in females. For males we can conduct two to three year studies, for women this would need to be at least five year studies. For small research companies this is a significant investment which is why we choose to study males first and then, if successful, we can confidently move on to study women.

Asif Paker, SwanBio – Added that any treatment that is developed for men with AMN should be able to be used for women once approved. There are still issues with the outcome measures for AMN which is being addressed through their Natural History Study. This will provide more certainty for regulators and improve research overall.

What is the difference between Minoryx and Poxel molecules/research?

David Moller, Poxel Pharmaceuticals – There are two different Poxel molecules in development, one of them is very distinct from Minoryx's Leriglitazone and has a different mechanism with the capacity to affect a variety of different components of the disease. The other molecule does have some similarities to Leriglitazone but has different mechanisms and has some potential to cause less weight gain and fluid retention which are issues with Leriglitazone.

Marc Martinell, Minoryx Therapeutics – Leriglitazone may have more effect against the mitochondrial component of AMN/ALD which is linked to the more chronic part of the disease.

Will ALD/AMN researchers be collaborating to learn from each other's experience?

David Moller, Poxel Pharmaceuticals – we are very open to collaboration with all companies exploring this area eg Minoryx, SwanBio, Autobahn, Viking and there is potential that we will need to combine different molecules, also with gene therapy for effective treatments. It is important to be able to demonstrate efficacy of one molecule/treatment before you look to combine efforts.

Marc Martinell, Minoryx Therapeutics – agreed absolutely, we must have as much knowledge as possible to envisage successful collaborations and we are working together to fill the many knowledge gaps we have of this difficult condition. It is clear there will be no single treatment and there will need to be different treatments or combinations of treatments for different condition stages.

Asif Paker, SwanBio – We have committed to share data from our Natural History Study with researchers and it will be available throughout the study and beyond.

Will the SwanBio gene therapy help with bowel and bladder issues?

Asif Paker, SwanBio – We will be measuring this closely and we hope this may be the case. However, bowel and bladder issues can be complex and this should be born in mind.

Following on from the challenges experienced by the bluebird bio gene therapy, are these same risks applicable to SwanBio gene therapy?

Asif Paker, SwanBio – There were challenges with the type of gene therapy used by bluebird bio (Lenti) and our gene therapy (AAV) is different and should have less challenges.

With BMT available for adults in other countries, why is it not available in the UK?

Dr Robin Lachmann – It is currently only funded in paediatrics up to 18 years old and not in adults. This is a ridiculous situation considering nothing remarkable happens biologically at the age of 18 to make you ineligible for the treatment, or to make transplants significantly more dangerous. It is purely a funding issue. We have tried to get NHS England to change their policy, however the commissioners felt there was not enough evidence at that point. There is now more evidence from Europe and Japan, and we are in the process of asking them to look at it again, emphasising the point that there is an equity issue here in the hope they will change their minds. Undoubtedly transplants are expensive, but they are nowhere near as expensive as looking after someone with cerebral ALD.

Are there any studies/links for AMN patients suffering from seizures?

Dr Robin Lachmann – AMN is rare and epilepsy is relatively common so it's highly likely that someone with AMN may also have epilepsy and so there may not be a causal link. AMN is not classically associated with seizures unless there is cerebral involvement. The first place to start would be to investigate the cause of the seizures and these can be relatively easily treated.

NEWBORN SCREENING FOR ALD

Do you think we will ever get newborn screening for ALD passed in the UK?

Professor Colin Steward – If other factors come in, such as Whole Genome Sequencing (WGS) this could circumvent the current approach to newborn screening.

Dr Robin Lachmann – We must remember that WGS is just the tool and the conditions sequenced for would still need to be agreed by the National Screening Committee and the existing criteria is unlikely to change. Additionally doing WGS on all babies will create huge ethical issues.

Why is there so little published evidence about ALD from the UK?

Professor Colin Steward – with regard to incidence I feel there may be some variations to US data due to regional variations that confuse the issue, and we may see a lower incidence rate in the UK. The whole area of

incidence is really complicated, for example cumulative US data following their extensive screening history is demonstrating incidence rates that are nearly twice what we previously thought.

ALEXANDER'S DISEASE RESEARCH (ION373 STUDY)

When will the trial start in the UK?

Dr Amy Waldman – There is no confirmed date as yet, and the trial is currently in a pre-planned monitoring phase which means that no new patients are being enrolled at the moment. There are various deliberate pauses built into the trial and these are not anything to be concerned about, these have been planned in order to observe patients at each trial phase. This also does not mean that the trial will not come to the UK, we just don't have a confirmed date as yet.

If the trial is something that you're interested in, first meet with your regular neurologist or consultant. You must be in a very stable condition before you can join the trial. Therefore, it is prudent to meet with your doctor now and ensure the patient is in the optimal state ready to begin the trial when it starts.

You should also have full documentation ready, including dates when symptoms started, a full history of medication – when started, any changes. The more information that is available, the easier enrolment and screening will be.

Why are patients who are actively declining not used in the trial, wouldn't this give more significant results?

You don't know how a non-declining patient would progress with or without the drug.

Dr Amy Waldman – The statisticians felt it would be more difficult to interpret the data if all trial participants were not at a stable point at the start of the trial. This is a very early trial, and in Phase 1 we would usually use volunteers that were not affected by the condition in order to test safety. This is not appropriate here and why we are using patients who are stable. If a patient is declining, it is very difficult to say if that is because of the drug, and this is why stability is such an important factor.

If a patient uses seizure medication before a trial will they be allowed to participate?

Dr Amy Waldman – To be absolutely clear, there cannot be any changes to medication, including supplements such as vitamins, 3 months prior to a trial. A period of stability is absolutely essential. To address the specific question, a physician may weight adjust seizure medication annually, so make sure that any adjustments are done early enough so they do not interfere with the pre-trial stability period. However, this does not mean that a seizure or any other event, would not be treated appropriately if one should occur during the trial. In terms of adjusting medications during the trial, this is something that will need to be discussed and followed up on.

Similarly, if someone had planned surgery prior to the trial, would this affect participation?

Dr Amy Waldman – Yes, even if there is something like a dental procedure, this cannot happen three months prior to the trial. If you have planned surgery such as scoliosis surgery, you should make sure this will not happen during the trial or try and ensure any planned surgery is completed early enough. Of course, if there is an unexpected surgical need such as a fracture, treatment should not be delayed.

Once a child has been accepted into the recruitment process, how long will it take once all the screening tests have been done will you know if they have been accepted?

Dr Amy Waldman – It should be between one and six weeks. Get the official copy of your genetic report to get an answer sooner. Once accepted treatment will start within six weeks.

During the trial screening process, are aids and assistance allowed during the 10 metre walk eg splints, hand holding, walkers?

Dr Amy Waldman – Yes, except assistance that provides upper body support, for example holding someone under the arms, a walker that supports the trunk. Additionally, the walk must be completed in under 5 minutes, and the patient must be able to follow the direction to walk from one place to the other. This test is only for patients over the age of 5. For patients between 2 and 5, they must be able to sit independently.

If the trial shows the drug is effective, will compassionate use be available?

Dr Amy Waldman – Ionis does have a commitment statement regarding compassionate use and it will be considered, but only if the trial shows it is effective and safe.

What can we do, if we're not eligible for the trial to slow deterioration?

Dr Amy Waldman – There are no other disease modifying treatments available to slow deterioration. I would recommend optimising seizure medications, in particular weight adjusting medications even where there are no seizures for a lengthy period. For symptoms such as vomiting and anxiety consider Valproic acid or Fluoxetine or a combination of both but these require very careful monitoring and you need to talk to your physician first. Maximising physical therapy, occupational therapy and speech therapy is incredibly important for maintaining function, alongside careful monitoring of swallow function to avoid the risk of choking.

Can you comment on the various forms of ascertainment bias vs genetic variation?

Dr Amy Waldman – The genetics is complicated with many different mutations and sometimes it's hard to compare the disease course and we try to address this by measuring three different things: the earliest symptom, the earliest neurological symptom, and the indications for an MRI or genetic testing.

Have AxD children in the US been vaccinated against Covid, which age group and which vaccination was used?

Dr Amy Waldman – In the US AxD children over 12 have been successfully vaccinated and most recently under 12s. The majority receive the Pfizer vaccine as this is the one that has been approved for under 18s and now under 12s. We have seen the vaccine tolerated very well and would strongly recommend vaccination. This is not just for AxD patients, but for all genetic leukodystrophy paediatric patients.

METACHROMATIC LEUKODYSTROPHY RESEARCH

Is enzyme replacement therapy available in the UK, and is it available for symptomatic patients for compassionate use?

Professor Nicole Wolfe – It is only available within a study protocol. For late infantile patients, Manchester is the study site so there are UK patients included, but the recruitment period has now closed and the treatment cannot be prescribed for patients not on the study. The phase 1/2 study results showed there was sadly no real effect on symptomatic patients.

How can UK patients access stem cell transplant or gene therapy for MLD if eligible?

Professor Nicole Wolfe – Stem cell transplants are available in the UK. Gene therapy has been approved by the European Medicines Agency but is not available in the UK. Currently price negotiations are ongoing in the EU, specifically the Netherlands, Ireland, Benelux countries and Austria. The treatment is only registered for late infantile and juvenile patients in these countries, there is no access for patients outside these age groups. NICE unfortunately turned down Orchard Therapeutics' Gene Therapy in the UK (Dr Robin Lachmann).

Are there any ideas about why the juvenile form of MLD seems to be the commonest in the Netherlands, and is this a striking contrast with other countries?

Professor Nicole Wolfe – The question is whether older patients are escaping diagnosis... but in The Netherlands, the genetic variants associated with later onset are more common than the ones associated with the earliest onset.

BONE MARROW TRANSPLANT & GENE THERAPY

How long does it take from collection of cells from the patient for the cells to be corrected (in gene therapy)?

Katie Snell, Orchard Therapeutics – This is different for different conditions, but overall is between four and six weeks.

Is it the same chemotherapy for gene therapy as with a bone marrow transplant, or is it less severe because the patient's own cells are used?

Katie Snell, Orchard Therapeutics – This differs slightly dependent on the underlying disease but it is very similar to bone marrow transplant. Due to the fact that in leukodystrophy, the bone marrow transplant function is fine, a decent amount of chemotherapy is needed to effectively.

Why is someone having gene therapy not at risk of Graft versus Host Disease?

Katie Snell, Orchard Therapeutics – GvHD is a condition where the donor cells fight with the patient's own cells. This is not unusual as it is the job of the immune system to fight off cells it doesn't recognise. In bone marrow transplants, medications are used to suppress that fight. In gene therapy, you are putting back the patient's own cells, which the body recognises and therefore does not try and fight them.

After a bone marrow transplant, you often have to have lots of blood and platelet transfusions. Is it the same with gene therapy?

Katie Snell, Orchard Therapeutics – Yes, because it is due to the chemotherapy that you need these treatments. The chemo kills off the red and white blood cells and as part of the recovery from transplant or gene therapy, these will need topping up.

There have been some concerns with patients contracting cancer following Lenti viral vector gene therapy such as bluebird bio's Starbeam Study. Are these worrying setbacks for gene therapy?

Katie Snell, Orchard Therapeutics – Every side effect needs to be looked at carefully. It is a risk that needs careful exploration with all bone marrow transplants, stem cell transplants and all gene therapy treatments, Lenti viral or AAV viral vectors. Patients and their families should discuss the risks and benefits with their treatment teams carefully to ensure they are fully informed and understand the various issues on an individual basis.

Gene therapy is hugely expensive in comparison to bone marrow transplant. Do you envisage gene therapy becoming more widely available and will this drive down the cost?

Katie Snell, Orchard Therapeutics – To develop a gene therapy from conception, through trials to a stage of being a viable treatment takes extensive investment, research and thorough studies. The goal would be to make this an accessible and affordable treatment for more patients for the future.

Do you envisage a time where gene therapy will be safe enough to use with any appropriate pre-symptomatic leukodystrophy patient and therefore avoid any risk of symptom development?

Katie Snell, Orchard Therapeutics – The risks of putting patients through chemotherapy and the long term side effects would need to be considered very carefully for those that may not go on to develop symptoms. There is a lot of research going on right now in the bone marrow transplant world to find alternatives to chemotherapy. A lot of elements would have to come together first, for example the ability to predict phenotype, improved risks from transplant or gene therapy treatments before this could be considered.

Is Orchard's gene therapy for Metachromatic Leukodystrophy currently available in the UK? We know NICE turned it down but is there a way to access it.

Katie Snell, Orchard Therapeutics – We are still exploring this with NICE but I don't have any further news I can share at this point. If a patient is eligible they should discuss with their consultant who can explore access to gene therapy within other areas of Europe.

Do you think that gene therapy will ever replace bone marrow transplant?

Katie Snell, Orchard Therapeutics – No, it is more likely they may work together where appropriate.

We know that fertility is affected for boys having bone marrow transplants, is it the same with gene therapy?

Katie Snell, Orchard Therapeutics – It is a side effect of the chemotherapy so most likely yes. However, this is a new therapy so we don't really know yet.

LATE EFFECTS OF BONE MARROW TRANSPLANT

How many late effects clinics are there in the UK and how can those in remoter areas get access to help?

Claire Turner, Bristol Late Effects Clinic – There are 8 centres right across the UK and all centres provide a different level of service dependent on location. Bristol is the only clinic providing a special service for ALD patients which started this year. There are ongoing efforts to contact other centres and share experiences. Any patient wishing to enquire about more specialist support can contact Alex TLC who will liaise with us.

How has Covid-19 affected mental health services supporting young men experiencing survivor guilt or fertility worries?

Claire Turner, Bristol Late Effects Clinic – There is a huge burden on mental health due to Covid-19 and currently they are prioritising those patients at risk of self-harm. There are likely to be increased waiting times, and these issues are across the Board. Charitable resources such as MIND and the Samaritans have some excellent services and are worth exploring, although there is increased demand for these also.

We know that BMT causes infertility, so if a male was too young at the point of transplant for sperm collection, what are their chances of having children?

Claire Turner, Bristol Late Effects Clinic – Levels of fertility depend on the chemotherapy received so it is important to have that knowledge. Unless radiation has been used, testosterone levels should be normal and therefore puberty would not be affected, but this is different to fertility. The first step for confirming fertility would be to ask your GP for a referral to the Assisted Conception Unit. This will allow for a semen analysis to confirm sperm numbers and activity levels. It is also important to discuss inheritance risks if you are in a position to have children, or alternatives for having children if fertility levels are low.

I no longer have access to my child's medical records at the time of transplant, so how do I know if he's at risk from any late effects?

Claire Turner, Bristol Late Effects Clinic – Patients (dependent on age), parents and carers are able to apply for a copy of their records from the hospital who provided the treatment.

How can we encourage young men to access these services once they're post 18?

Claire Turner, Bristol Late Effects Clinic – It's a difficulty across the board and we often find that young men don't access services during teenage and early twenties, but return once they begin thinking about settling down and having their own families. It's important to note that patients can refer back into the service at any age and that it is more an information sharing service than an active treatment service. The service is optional with some patients finding that one appointment provides all the information they need, and others find a yearly check in more reassuring.

TRANSITION TO ADULT SERVICES

Who is responsible for getting the transition process started?

Rick Thompson, Findacure – This can vary dependent on location, condition, many factors. It's important to be proactive yourself. You shouldn't be driving the process, but do ask questions in good time and include all involved professionals.

Do patients have any say in what age they transition?

Rick Thompson, Findacure – There are individual examples of different ages across different conditions, but be involved and make sure you get the transition you want.

Should we expect paediatric doctors to provide a summary for the new adult professionals?

Dr Alasdair Parker – There are very good NICE guidelines for transition and the Neurological Alliance is looking at transitions this year. It's important for paediatricians to provide a comprehensive summary of notes, especially regarding medication ie why was it prescribed, what were the results, how is it prescribed, rather than lengthy copies of medical notes.

Dr Rahul Singh – The IWMD Registry will also provide valuable information and processes to expedite efficient transitions.

Dr Robin Lachmann – As an adult provider we must remember that patients will spend more time in our service than paediatrics. At NHNN we do joint transition appointments with GOSH which are very successful. With virtual appointments now more usual the technology should ensure that transitions can be managed more effectively and easily.

MANAGING CONTINENCE ISSUES

How can you tell if your bladder problems are leukodystrophy related or age/child bearing related?

Dr Sarah Wright – That would depend on what the symptoms you have are. Stress incontinence, for example when sneezing, coughing, laughing, is more likely to be related to stress on the pelvic floor caused by events such as bearing a child as opposed to urgency, a rush to pass urine. Important to discuss any issues with your consultant.

I take Solifenacin for bladder issues which is causing a really dry mouth, is this usual or am I taking too high a dose?

Dr Sarah Wright – This is a really common side effect, others can be dry eyes and constipation. It is not dose related.

Males use Botox to assist with bladder urgency, can this work for females?

Dr Sarah Wright – Yes absolutely, bladder treatments are not restrictive in terms of gender or age.

GENERAL QUESTIONS

During Covid virtual appointments were utilised for many patients although there has been a return to face to face. Do you see a return to this during the winter and, moving forward, will you continue to use virtual appointments for improved access to patients who do not have easy access for face to face appointments?

Dr Robin Lachmann – Yes, due to Covid measures we are limited to how many patients we can see in clinics as opposed to before. However, we do want to see patients face to face, especially those who we haven't seen since before Covid. We are also utilising virtual clinics more which is very effective for those who do not have easy access.

My wife has started showing symptoms in her early 40s with no previous indication – I don't understand how this can be possible?

Dr David Lynch – There are many different conditions with varying stages of symptom onset which can sometimes relate to the gene mutation and sometimes not. In some cases, we have different members of the same family displaying different symptoms, starting at different times. Unfortunately, we don't yet know why this is and it is impossible to predict in many cases. It's an area people are conducting research into but something we don't have an answer for right now.

How can patients get a referral to the adult leukodystrophy unit at NHNN from the mitochondrial service?

Dr David Lynch – At NHNN we don't tend to look after mitochondrial leukodystrophy patients as the mitochondrial service takes very good care of them. However, we do work very closely with the service and would be happy to liaise on individual patients' care at their request.