

Gauchers NEWS

December 2011

Gauchers ASSOCIATION



Members, Doctors, Friends and Industry Celebrating 20 Years of the Gauchers Association



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Chairman's Chat

Dear Friend,

Welcome to December 2011 edition of Gaucher News. As you will see, this edition includes a description and some photographs of our 20th anniversary celebrations held on 5th November. The Association was greatly honoured by the presence of members with their family and friends, doctors and their teams from the wonderful national treatment centres, distinguished overseas guests and representatives

from the pharmaceutical companies. It is very hard to believe that the Gaucher world has changed so much in that at the beginning of the year we were formed, there was no authorised treatment, no specialist treatment centres and patients experienced isolation, and often misdiagnosis.

Congratulations to Dan Brown, Emily Lew, Sarah Allard, who together with Tanya organised this terrific party, and to Sue Noe for taking charge of our fundraising advertising brochure. Thanks go to Jamie Brown for putting together such a great publication.

The pages that follow provide reports and information on the wide range of activities with which the Association is now involved. When we started, we never thought that we would be working with the authorities in the shaping of the delivery of health care in this country, in working with the scientists and doctors both here and overseas, and be consulted by pharmaceutical companies. As you will see from these pages, we have now moved into our own offices to accommodate additional people who will help us deliver our further responsibilities. The appointment of an advocacy researcher is an important new step and we aim to provide more administrative support to the European Gaucher Alliance.

Although in 2011 the Gaucher world looks entirely different to the way it looked in 1991, there are still significant challenges to address. You will see from this newsletter that we are seeking to encourage a research into neurological manifestation for Gaucher disease to facilitate scientists and specialist clinicians investigate novel ways to deliver therapy. You will see the report on the most extraordinary meeting held in Amsterdam where all drug companies involved in the Gaucher world participated with the EWGGD, EGA and NGF in looking at the provision of humanitarian aid. Access to treatment for patients remains our prime focus, whether those patients are in the United Kingdom, Ireland, or other parts of the world. The European economic crisis will bring new pressures and we remain committed to address these for the benefit of patients.

On behalf of the board I send you Season's Greetings and every good wish for healthy and happy 2012 and beyond.

With best wishes

Jeremy

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Front page photo (top to bottom): Raising Tower Bridge; Medical Teams from the specialist centres; Jeremy Manuel receives a certificate in recognition of his dedicated support and service to the Gaucher community and Tanya Collin-Histed as a representative of the Gauchers Association from David Meeker of Genzyme, a Sanofi Company

Second Gauchers Association Sponsored Cycle Ride raises over £60,000 for the Association

More than 100 Cyclists assembled for a second time at the playing fields of University College School in Hampstead London on the 4th September to take part in the London to Cambridge Gauchers Association sponsored Cycle ride.

Following the same route as the previous year, cyclists enjoyed a warm and dry early start to the day although the weather forecast of "Hail over Hertfordshire" did cause some worry for the organisers.

Lord Monroe Palmer of Childs Hill, local London Borough of Barnet Councillor and friend and supporter of the Association set the riders off on their way. He told a reporter from the local newspaper the Ham and High "I am not a medical expert. I just know the people who work very hard for the organisation. If I can give it a shot in the arm by starting it and cheering them on that is what I will do".



Riders from Medco (Mandy and Dominic) receive their medals from Prof. Timothy Cox

The ride was supported by sponsorship from Genzyme, Shire and Protalix. In addition Shire fielded a team of riders. A new rider this year was Professor Atul Mehta who had been previously spotted training in the streets of North West London. Clearly the training had paid off as he reached Cambridge in just under 5 hours.

The four refreshment stops on route were lead and supported by friends and family members of the riders. The Association is very grateful to all the volunteers and to the Sun Inn at Northaw, The Horns at Datchworth, The trustees of

the Village Hall in Westmill and the Coach House at Flint Cross who once again allowed the use of their premises without charge and let volunteers set up and provide the much needed sustenance for the riders.

Both the St Johns Ambulance medics and Marcus the mechanic were well employed this year. Fortunately the ambulance crew were only needed to clean and tend some cuts and scrapes of cyclists who had for some reason been parted from their cycles. Marcus the mechanic had some more challenging tasks to resolve than just the odd puncture. A minor collision just outside Northaw resulted in broken spokes which Marcus was able to resolve. The rider James said "The provision of the technician was a masterstroke: without him I would have been stranded with broken spokes in Barnet with only 10 miles on the clock"

Motor Cycle support rider Avi saved the day for Kirsty after her tyre split by racing off to a bike shop to find a new wheel that Marcus quickly fitted. Although the rider was by now the very last person on the ride she resisted all offers of a lift to the next stop and quickly mounted the bike and must have peddled like mad to catch up the others.

The first riders were over the finish line in just over 4 hours and Professor Cox awarded finisher medals to all riders. Sadly the weather did deteriorate as the day progressed and whilst approximately 75% of riders were in Cambridge before the downpour the rest were subjected to torrential rain described by one rider as "like cycling in the shower" No Hail in Hertfordshire but certainly "Cloudburst in Cambridgeshire".

Wet (and dry) riders were once again



First riders over the finishing line

especially cheered by the selection of home made cakes baked and provided at the last stop by Liz Morris' family and the medals awarded by Professor Cox who unflinching ran out in the rain to greet the sopping riders (getting his own drenching in the process).

Gaucher Chairman Jeremy Manuel said after the ride "Once again I must thank everybody involved in this great day. We have a fantastic team of volunteers who have manned the start, marshalled along the route, run the refreshment stops, driven the mobile support vehicles and of course run the finish line. Thanks go to them all. Thanks too go to the St Johns Ambulance Crew and Les and his team from Cycle Support Services who organised the route, the signage and provided the sweep vehicle. Special thanks again goes to the bike ride organising team of Lawrence Gould, Ian Bennett, Alan Rosen and Liz Manuel without whom the ride would simply not have taken place. I express great appreciation to our sponsors Genzyme, Shire and Protalix who have generously supported this event. Finally an extra special thank you to all our riders who made the day such huge fun and raised significant sums in sponsorship for the Association."

Once again there were plenty of farewells at the end of the day with the words "see you next year". The ride is certainly taking its place as a fixture in the Gaucher calendar. The organising committee are looking at holding the next ride on the weekend of the first May bank holiday in 2013 so there will be plenty of time for training!

"Congratulations to the Gauchers Association for putting on such a fantastic ride!"

Dr. Elin Haf Davies, PhD

Congratulations to Dr. Elin Haf Davies on completing her PhD. We first met Elin in 2002 when she became the clinical trial nurse for the Type III Zavesca trial and over the last nine years, Elin has been a huge support to many of the Type III patients and their families.

On receiving her PhD Elin said, “after working in the field of Gaucher disease for nine years it was an honour to graduate from UCL with a PhD thesis titled ‘Developing Markers of Neurological Manifestations in Neuronopathic Gaucher Disease’.

With clinical experience of recruiting children to participate in clinical trials and regulatory experience of evaluating paediatric investigation plans at the European Medicine Agency, I wanted to explore the possibility of developing markers that were –

- a) acceptable for children to comply with
- b) informative for doctors to make clinical decisions
- c) validated to evaluate emerging therapies in clinical trials

On these bases I selected three assessment tools to study. A Severity Scoring Tool (SST) that I developed specifically for nGD to quantify disease severity, gait analysis using a portable mat and brain imaging using diffusion tensor analysis.

Under the supervision of Dr. Ashok Vellodi and in collaboration with Dr. Eugen Mengel in Germany and Professor Anna Tytki-Symanska in Poland, the SST was modified (mSST) and validated – demonstrating its ability to capture disease progression. Gait analysis and diffusion tensor imaging (DTI) was used to compare children with nGD and children with Type I disease, along with comparing both data sets to that obtained from a normative, healthy cohort of children. Both assessments distinguished



Elin Haf Davies and Nadia Fattouki enjoying a day out in London

between the nGD and the Type I, statistically and with clinical relevance.

Unfortunately, the gait analysis was not sensitive enough to monitor change over time as there is a large amount of variability observed, limiting its value. Sequential assessment of DTI was not done, but the findings highlight the potential for its use and the need for this long-term monitoring.

The work provides a foundation for monitoring disease progression. On-going use of these assessments will hopefully provide a data-pool which can inform decision making and facilitate the designing of clinical trials in the future.”

Association funds research into novel pathways

The Association has awarded PhD candidate Andres Klein a grant of £7,900 which allows him to undertake an important research study at Professor Tony Futerman’s lab at the Weizmann Institute of Science in Israel. The fund has been made possible through the money donated to the Gauchers Association by the family of Ellie Carter who had Type II Gaucher disease and the study is titled ‘Identification of novel pathways that modify severity and neuronal degeneration of Gaucher disease’. Andrew writes –

“I have a strong interest in identifying genetic factors that modify Gaucher disease (GD) progression. GD is caused by the defective activity of lysosomal acid-glucosidase (glucocerebrosidase, GBA), resulting in accumulation of the glyco- sphingolipid, glucosylceramide (GlcCer). The disease can be divided into three major subtypes: type 1 present non-neuronopathic, types 2 and 3 result in severe neurological disorders in patients.

For the majority of GD patients a defined correlation between genotype and phenotype does not exist. Indeed, the same mutation leads to completely different clinical manifestations, indicating that there are ‘modifiers of disease progression’. Little is known about the down-stream biochemical changes that occur upon GlcCer accumulation that result in cell and tissue dysfunction in different types of GD and I plan to



Andres Klein

identify the genetic and biochemical factors that regulate the severity of disease progression in order to design personalised therapies, customised for each patient.

“This is a big challenge but I am optimistic. With the technologies that we have available and by working hard, it is possible to reach this goal. Thanks again to the UK Gaucher Association for supporting me in this endeavour”.

Editor’s note: We will report on the progress of Andres’ research study in future editions of the Gauchers News.

Research into gene therapy for Type II Gaucher disease

In the October 2010 edition of Gauchers News, we reported on the £470,000 grant awarded from the Medical Research Council (MRC) to Simon Waddington and his team from the Department of Haematology at the Royal Free Hospital in London for their research into Gene therapy for type II Gaucher disease. We now provide an update on their work.

In 2009 the Association gave a small grant to the team to purchase some viral vectors for use in gene therapy research in type II Gaucher disease, it was based on the preliminary work carried out with these vectors that Simon and his team were awarded this major grant. Simon reports –

We are delighted to announce the publication of a paper in the Federation of

American Societies for Experimental Biology Journal in July 11, 2011 *'Intravenous administration of AAV2/9 to the fetal and neonatal mouse leads to differential targeting of CNS cell types and extensive transduction of the nervous system'*.

The paper describes the findings of the group when they injected fetal and neonatal mice with viral vectors. This produced global

delivery to the central (brain, spinal cord, and all layers of the retina) and peripheral (myenteric plexus and innervating nerves) nervous systems but with different expression profiles within the brain; fetal and neonatal administration resulted in expression in neurons and protoplasmic astrocytes, respectively. Neither single-stranded nor self-complementary AAV2/9 triggered a microglia-mediated immune response following either administration.

In summary, intravenous AAV2/9 targets gene expression to specific neural cell types dependent on developmental stage. This has implications for development of the brain, and for the progression of nGD. Furthermore, it may provide a therapeutic strategy for treatment of early lethal genetic diseases, such as Gaucher disease, and for disabling neuropathies, such as preterm brain injury.

Editor's note: We will continue to follow the work of this group and report in future editions of the Gauchers News on their progress.

Association appoints a new Advocacy Researcher

look at what is – or is not – happening currently and what services and information would support patients and their families, with an emphasis on newly diagnosed patients and those with Neuronopathic Gaucher disease (nGD). The researcher will spend time visiting families, doctors, nurses and other healthcare professionals to conduct interviews in relation to social care, health services and education. An update on progress with this project will follow in the next edition of the Gauchers News.

The Gauchers Association, in partnership with Great Ormond Street Hospital in London have secured funding to employ a researcher for one year to undertake a feasibility study to explore with patients, families and medical professionals the potential remit and benefits of a permanent advocacy post. The post will

PGD statement for Type III Gaucher disease

Together with Genetic Alliance UK, the Gauchers Association submitted a statement to the Human Fertilisation and Embryology Authority (HFEA) in July 2011 on Type III Gaucher disease to enable them to make an informed decision on whether to license Gaucher disease for preimplantation genetic diagnosis (PGD).

At the beginning of 2010 the licensing process for PGD changed. The licensing committee now make a single decision for each genetic condition based on the condition itself, not on any particular families' position. The law states that the

Human Fertilisation and Embryology Authority (HFEA) license committee must be "satisfied that there is a significant risk that a person with this abnormality will have or develop a serious physical or mental disability, a serious illness or any

other serious medical condition", (serious enough to warrant PGD).

Earlier this year, Genetic Alliance UK (of which the UK Gauchers Association is a member) contacted the Association and asked if we could work together to provide an accurate description of type III Gaucher disease and how it can affect the patient and the family.

The key focus therefore is on the impact of the condition on the patient and their family. The clinical aspects of the condition will be covered by the applying clinic.

We are delighted to report that the HFEA have now licensed PGD for type III Gaucher disease, thus giving families the choice if they have a known history of neuronopathic disease in their family.

Editor's note: Type II Gaucher disease was licensed for PGD a number of years ago.

Dr Philip Lee

Dr. Robin Lachmann pays tribute to his friend and colleague Dr. Philip Lee who sadly passed away peacefully at home on the 18th August 2011.

“It’s over three years since his cancer was diagnosed. He was determined to try everything available to keep it at bay and for most of that time he was remarkably well. Over the last months however, the disease relapsed and proved resistant to treatment. He and the family decided to stop active interventions a few weeks before he died”.

“Phil was a metabolic paediatrician by training, but he was a pioneer in recognising that children with inherited metabolic disease (IMD) were growing up and that, as adults, it was very difficult to get continuing specialist care. As well as developing the Charles Dent Metabolic Unit (CDMU) at the National Hospital for Neurology and Neurosurgery (NHNN), he was a tireless advocate for the needs of adults with IMD throughout the UK and beyond. He was

instrumental in developing a training programme in Metabolic Medicine for junior doctors and people who have come through this programme are now taking up consultant posts specialising in adult IMDs all over the country. This means that when children outgrow the excellent paediatric metabolic units in London, Manchester, Birmingham and elsewhere, there are now specialist adult units which can take over their long-term care. Without Phil’s contributions, metabolic services for adults in this country would be far less developed than they are”.

“Phil had a longstanding interest in lysosomal storage disorders. In particular, a large number of people with Fabry attend the CDMU, which led to Phil’s involvement in the successful clinical trials of Fabrazyme. After ERT for Fabry was licensed, Phil went



Dr Philip Lee

on to become a member of the European Board of the Fabry Disease Registry. When the national LSD service was commissioned, the CDMU became one of the national centres and now more than 200 patients with LSDs are cared for at the NHNN”.

“Phil was loved and respected by colleagues and patients, many of whom had known him for all of their lives. He will be sorely missed.”

Adult metabolic service at the ‘National’, London

In the UK, once a child reaches the ages of 16-18 they are transferred from a paediatric hospital to an adult service. Many Gaucher patients and children with other lysosomal storage disorders (LSDs) are being transferred from Great Ormond Street Hospital (GOSH) to the care of the adult service at the National Hospital for Neurology and Neurosurgery (NHNN). Here Dr. Elaine Murphy discusses the transition process –

Although historically these patients have moved from GOSH to the NHNN, they continued to see Dr. Vellodi, their paediatrician. Newly diagnosed adults with Gaucher disease would see Dr. Robin Lachmann or Dr. Elaine Murphy at The NHNN. Since the summer, the three doctors have begun the process of transferring adult patients being seen by Dr. Vellodi to either Dr. Lachmann or Dr. Murphy.

The process has been gradual with a doctor and a specialist nurse from the

adult metabolic services at the NHNN sitting in with Dr. Vellodi at his twice monthly LSD clinics at the NHNN in Queen Square since June 2010.

The long term care of adult patients will be undertaken by doctors trained in adult medicine, because the medical and social needs of older patients differ from those of children. In the past with rare diseases like Gaucher, it has not always been possible as suitably experienced physicians were not always available. Now, there is a specific training programme in

adult metabolic medicine and the Metabolic and Lysosomal Storage Disorders Service at the NHNN is run by Dr. Lachmann and Dr. Murphy, both of whom are experienced in the management of inherited metabolic disease in adult patients.

The team at the NHNN hopes that by meeting patients in clinic with Dr. Vellodi, they will make the transfer a smooth one. The arrangements for enzyme infusions and homecare will be similar. Alison Cousins and Ana Amado Fondo, the two specialist nurses for the adult metabolic services, are responsible for organising investigations and enzyme infusions. NHNN has prepared a leaflet ‘Adult Inherited Metabolic Disease Services at the Charles Dent Metabolic Unit’ which provides information about the adult services and contact details for all the staff.

If Gaucher patients that are in the process of transitioning from the paediatric services at Great Ormond Street Hospital are invited to find out more about the adult services at the NHNN, should contact Alison or Ana to arrange a visit to the outpatient department and day ward in the NHNN. Contact details for the service can be found on page two of this edition of Gauchers News.

Home treatment – Helping families, Helping the NHS

Steve Davis and Jill Stephenson from Healthcare at Home Ltd (www.hah.co.uk) explain what home treatment is and how it works –

Over the past two decades there has been a notable shift in what were once traditionally seen as hospital-based treatments towards treatment at a time and place which is more convenient to the patient and their family; at home, at work, at school, or even at a holiday location. In 2010, Healthcare at Home provided services to over 120,000 NHS patients. Not only has home treatment proved to be safe, effective and highly rated by patients and their families, it can also save money for patients, their families and the NHS.

Since 1995, the range of treatments that we can safely and effectively deliver has slowly but surely expanded. For some groups of patients, we request their prescriptions from the hospital and then dispense and deliver their medication at a time and place most convenient to them using our own in-house teams of pharmacists and delivery drivers.

Lysosomal storage disorders such as Gaucher disease can require a lifetime of treatment. Due to the limited number of clinical specialists within this area, patients and their families often have to travel long distances for review by their clinical team, but in many cases this is no longer necessary for the routine aspects of their treatment such as the administration of enzyme replacement therapy (ERT). Healthcare at Home now has almost 15 years' experience of home administration of ERT and currently provides home treatment programmes for both adult and paediatric patients with Fabry disease, Gaucher disease, Hunter disease, Pompe disease, Maroteaux-Lamy syndrome and Hurler/Hurler-Scheie/Scheie patients.

Wherever home administration of ERT is deemed appropriate by the clinical team at the hospital, it offers a wide range of benefits to patients and their families. Perhaps most importantly, home treatment ensures minimal disruption to daily life by reducing the need to travel to the hospital for treatment, which involves the direct costs of travel and parking, but also the indirect costs of time off school or work, arranging child care, etc. Patients

regularly tell us that they feel far more comfortable having treatment in familiar surroundings, and find this less stressful than a trip to hospital.

Wherever and whenever treatment takes place, our patients get the undivided attention of one of our friendly, experienced nurses throughout their treatment. Our nurses are extensively trained and equipped for dealing with any medical problems or emergencies that may arise, and as treatment progresses, more than half of our patients and carers have sought approval from their hospital team for our home treatment nurses to train them to administer their own treatment.

To enable safe infusion administration by a patient or carer, a personalised training plan is agreed between the nurse, patient and carer ensuring that adequate time is allocated to each element of the training plan to ensure patient/carer competence is achieved, regardless of the length of time taken to achieve this. 'Competence' is defined as the knowledge and ability to perform the action and also the confidence with which to perform it. At all times, our patients and their families continue to be supported by the Healthcare at Home team, allowing complete flexibility of access to all service elements, should their needs change at all.

With around 400 nurses operating from offices throughout the UK, we are able to provide treatment anywhere in the UK, which can make going on holiday, visiting relatives etc. much easier to do. Our customer care team contact our patients or their families each time that we are due to provide treatment, in order to ensure that treatment is still progressing as planned and to arrange a suitable time and location for the next treatment to be provided. We then make all the necessary arrangements with the hospital regarding prescriptions for medication etc. as part of the service. For patients/families who are trained to self-infuse and who wish to take holidays overseas, we can provide assistance with refrigerated transportation of medication and provision of associated customs documentation.

From the regular feedback that we get it is clear that where possible, patients prefer home treatment. For the clinical teams at the hospital there are also a number of benefits of working with a clinical homecare provider, such as the ability to reduce waiting times or capacity pressures in their department or in the hospital pharmacy, and the ability to offer greater choice to patients and carers as to how and when treatment is received. Additionally, it actually costs the NHS less money to provide ERT at home than it does to provide treatment at the hospital, so maybe clinical homecare can help the NHS just like it helps the families that receive it!

Home treatment – the benefits

- Minimal disruption to daily life
- Comfort and convenience of treatment in familiar surroundings
- Less time taken to receive treatment versus travelling to hospital
- Less dependence on others for transport, child care, etc.
- Reduction in costs associated with travelling to and parking at hospital
- Healthcare at Home call you to arrange your treatment and make all the arrangement with the hospital regarding prescriptions etc. on your behalf
- Undivided attention of a friendly experienced nurse throughout treatment, who is extensively trained and equipped for dealing with medical emergencies, e.g. anaphylaxis
- Reassurance of 24 hour access to advice and assessment from an experienced, local Healthcare at Home nurse by phone and/or in person, which can reduce unnecessary/inappropriate hospital admissions
- Daytime access to our customer care and pharmacy teams

*Shire information website on Gaucher disease
at www.vpriv.co.uk*

5th Neuronopathic Gaucher Disease Family Conference

On the weekend of 29 April to 1 May 2011, the fifth European Family Neuronopathic Gaucher Disease conference took place at the Hilton hotel, Reading. 75 people, including parents, carers, patients, siblings, speakers, doctors, nurses and representatives from pharmaceutical/homecare companies attended the three day conference. Summaries of each of the presentations are below:



The first speaker was **Professor Fran Platt** from the University of Oxford who spoke about understanding and treating lysosomal disorders. She pointed out that lysosomes are more complex, both in structure and function, than was originally thought so there are many places where things could go wrong. However, this also means that treatment can be directed at more than one area. She emphasised the importance of secondary events resulting from the primary one of storage, and referred to this as a pathogenic cascade, offering opportunities for multiple biomarkers as well as interventions. An example of this is Niemann-Pick disease type C. She talked about inflammation and its role in LSDs, giving as an example the 'multi-pronged' approach used in the Sandhoff mouse model. Professor Platt then talked about treatment, and the challenges facing clinicians and researchers in bringing it to the bedside. Often many years can elapse between the 'proof of concept' and actual clinical trials. Clinical trials are difficult to conduct; there are many reasons for this. Patients have established/advanced disease; there is considerable variation in clinical presentation, age of onset and genotype. The numbers were small as these are rare conditions and statistically underpowered trials are inevitable. Often the endpoints chosen are not useful ones so the trial does not predict outcome of what can be improved/stabilised in a symptomatic patient. Professor Platt suggested some ways of addressing these difficulties such as having a run-in period for trials. A run-in period is a period during which the therapy is not given; this will provide an idea of the 'natural history' of the disease so that we get an idea of how much change one might expect over a period of time. If therapy then decreases the rate of deterioration, one might interpret this as a positive effect.

Professor Tony Futerman from the Weizman Institute in Israel talked about recent

advances in our understanding of nGD. He summarised earlier work that his group had done, identifying the role of intracellular calcium, and elucidating the 3-D structure of the glucocerebrosidase molecule. He briefly discussed the relationship of Gaucher disease with Parkinsonism, and pointed out that there were at least five other LSDs where an association had been reported. He then told us about the recent work that his group had been doing with the Karlsson mouse model of nGD. First they identified three clinical stages; pre-symptomatic, early symptomatic and late symptomatic. They then systematically defined which areas were affected at different times. They have shown that brain inflammation, for example, is not present at birth but appears after birth, and then progresses in some areas but not in others. It is associated with neuronal loss in a number of areas, some of which may be linked to signs and symptoms. Examples are the reticular tegmentum (eye movements) and the cochlear nucleus and inferior colliculus (abnormal brainstem response).

Lauren McPartlan, from the Child and Adolescent Mental Health Services at Great Ormond Street Hospital, presented the results of her study of the behavioural phenotypes in type III GD. The study group consisted of affected children over age 12, parents of children aged 4-18, and teachers. The tools used were the Development and Well-Being Assessment (DAWBA), Profile of Neuro-psychiatric Symptoms (PONS) questionnaire, Social Communication Questionnaire (SCQ), and Parental Stress Index (PSI) questionnaire. The children were administered the DAWBA and PONS, the parents the DAWBA, PONS, SCQ and PSI and general information, and the teachers the DAWBA, PONS and SCQ. The PONS data revealed that 71.4% of the patients had difficulties with learning and clumsiness,

42.9% had difficulties arising from sensory symptoms, low mood, manic episodes and oppositional and defiant behaviour, and 28.6% had difficulties due to hyperactivity, impulsivity, social communication, aggression, poor language, circumscribed interests, self-injury, poor empathy, obsessions & compulsions, depressive thoughts, worries, fears and poor memory. According to the rating scales the PSI indicated that 50% of GD type III parents show levels of distress that warrant professional attention. The Strength and Difficulties Questionnaire showed that 42% reported abnormal stress and burden as a result of the difficulties that the child had. These results show that type III GD is associated with a significantly higher risk of behavioral problems. Furthermore, this risk is higher than in the wider population with chronic disease (1:2 vs. 1:10).

Elin Haf Davies talked about ways of measuring disease severity, using her work with type III GD as an example. She pointed out that a primary endpoint should be a reliable and validated variable measuring some clinically relevant and important treatment benefit in the patient population. She discussed the importance of content validity, inter- and intra-rater reliability and responsiveness for detecting changes in the severity of disease. She told us how the currently used tool (the Severity Scoring Tool, SST) was developed, and how it was later modified and renamed the Modified Severity Scoring Tool (mSST). A total of 39 patients in three countries had been studied to develop this scoring tool. She also presented data on gait analysis using the GAITRite™ Gait Analysis System. It was easy to use and tolerated well by all ambulatory children. It appeared to be able to distinguish between Type I, normative and nGD cohort. However, it appears to have a high variability, and was therefore unlikely to offer a sensitive measure of disease over time. Lastly she

presented a small amount of data that had been gathered using Diffusion Tensor Imaging. This is a method for probing the microstructure of materials and is being increasingly used nowadays to image the white matter tracts in the brain. Using this, some differences had been demonstrated between type I and III children. However the numbers were small and needs further study.

Victoria Crook, one of the Clinical Nurse Specialists at GOSH, presented the experience of the Aunty Days. They are a fun way of bringing the girls (and their parents) together to discuss common issues. Events so far had included outings to Blue Peter, the London Eye, Careology, and a PGL weekend. The latest excursion was a trip on the London Underground to see how well the girls adapted to its challenges.

Derek Burke and **Simon Heales** gave a joint presentation on the relationship between Gaucher disease and Parkinson's. They summarised the known relationship between the two, which is that the incidence of Parkinson's is higher in both Gaucher patients as well as carriers. They then pointed out that there were in fact two enzymes in the body. The first is the well-known glucocerebrosidase type 1, GBA1. The other is virtually unknown as GBA2. Derek has measured the concentration of both enzymes in white blood cells (leukocytes) as well as brain (of mice). Surprisingly, although GBA1 is the predominant enzyme in the leukocytes, the reverse was found in the brain i.e. GBA2 levels were higher. Further work is in progress in a Gaucher mouse model to determine the distribution of GBA1 and

GBA2 in different areas of the brain as well as different cell types, and their relationship to each other.

Ahad Rahim and **Simon Waddington** presented their work on intrauterine gene transfer in mice. They outlined that several inherited neurological diseases are characterised by neurodegenerative changes at or around birth. Sadly prognosis remains dismal and for several of these diseases, including acute neuronopathic Gaucher disease, there is no treatment and palliative care remains the only option. They explained that their group is studying very early gene therapy, either in neonates or before birth that may provide a means of preventing the rapid onset of neurological damage in these diseases. They went on to say that recently, a gene therapy vector known as 'AAV9' has been shown by others to transduce the brain and spinal cord of mice, cats and macaques following intravenous injection in the neonatal period. They have investigated this further by comparing gene expression after intravenous injection into fetal and neonatal mice. They then injected this vector into the fetal mouse circulation via the vitelline vessel at 16 days post-conception and saw expression of the green marker protein 'GFP' in neurons throughout the central nervous system. However after neonatal administration they only saw the marker protein in cells called 'protoplasmic astrocytes'. They also saw green marker protein in the liver, heart, lungs muscle, bone, eye, and skin and

the peripheral nervous system. 'AAV9' may be useful for learning more about the early damage caused in neuronopathic Gaucher disease but more importantly, may provide a pathway towards treatment.

Dr Aiden Gill from Shire talked about the challenges of bringing a drug from the laboratory, through clinical trials, to the clinic.

Throughout the weekend, volunteers supervised the young children taking them to a local farm and then engaging them in arts and craft activities. We would like to thank Lucy and Rosie Claire, Sarah Allard and India Cully for giving up their time to help the Association.

On the Sunday the families had a closed group session facilitated by Dr. Ashok Vellodi from GOSH. He summarised the presentations from the day before, providing the families with the opportunity to ask questions and discuss other issues including the transition from paediatric to adult care services.



Expert Neuronopathic Gaucher Disease Meeting – A need to progress

The UK Gauchers Association together with Professor Tony Futerman of the Weitzman Institute in Israel and Dr Ashok Vellodi at Great Ormond Street Hospital in London brought together scientists and clinicians with a specialist interest in nGD and representatives of pharmaceutical companies to a meeting on the 4th November 2011 at the Institute of Child Health in London to discuss nGD. The aim of the meeting was to facilitate discussions on –

1. Advancing the understanding of basic pathological mechanisms
2. Identifying realistic potential therapeutic options and strategies for nGD for the next 1-3 years
3. Establishing realistic End Points – gaps for further development
4. Specific target dates for review and named person responsible

A report on the outcome of this meeting will be detailed in the next edition of the Gauchers News, with specific targets, set dates for review and a named person responsible.

The Gauchers Association celebrate their 20th Anniversary on the Thames

It was a crisp, cold 5th November evening with the crack of fireworks in the air. A large crowd of approximately 200 people started to gather on Millenium Pier in front of the Tower of London and as they looked east down the Thames they could see the glistening lights of the Dixie Queen, a large Mississippi steam boat, slowly sailing towards them...that's right a Mississippi steam boat. The centre of Tower Bridge opened and the Dixie Queen passed through, turned around and moored at the pier. The venue for the Gauchers Association 20th Anniversary celebration had arrived.



Alan, Linda and Jane – Gaucher Specialist Centre teams



Members enjoying the evening

The Association Directors were delighted to welcome on board friends and colleagues, old and new, including Lord Palmer, members, clinicians, scientists and industry representatives, a number of whom had travelled long distances from abroad to attend.

As the boat pulled away from Millenium Pier to head east towards the City and Canary Wharf, the evening started with a champagne and canapé reception. Guests mingled and caught up with old friends whilst in the background a four

piece jazz band filled the air with music. The captain welcomed everyone on board and ran through a few safety announcements and the evening was well and truly underway.

The drinks were soon flowing and before long everyone was asked to make their way to the upper deck of the boat to take their seats for dinner. The upper deck was beautifully set out with green and white balloons adorning the room and copies of a Souvenir Brochure at everyone's place. Once all of the guests were seated Association Director, Daniel Brown, officially welcomed everyone and made special presentations for Sarah Allard and Tanya Collin-Histed in recognition of their continuing dedication to the Association.

Dinner was then served and the room buzzed with conversation as guests reminisced and told stories of the past 20 years. As fireworks lit the air and echoed in the distance entertainment was provided by a magician going from table to table and



Everyone having fun



In full swing

wowing guests with his close up magic. His best trick was turning a £5 note in to a ten and then a twenty...sadly he then turned it back in to a five!

After the main course Jeremy Manuel took the microphone and provided a whistle stop tour of the key events in the Association's 20 year history. He also spoke of the challenges which still lie ahead with the unmet needs of Gaucher



Jeremy Manuel presents Prof Timothy Cox with a special award for his friendship and support JM and DM – Jeremy Manuel and David Meeker of Genzyme Sanofi

“Uplifting, so beautiful, I was totally overcome.”

patients and the on-going efforts of the humanitarian aid programme. Certificates were presented to the four original specialist Gaucher centres, the Royal Free, Addenbrooke's, Great Ormond Street and Manchester Children's Hospital, in recognition of their work with the Association and then a special presentation of a commemorative decanter was made to

Professor Timothy Cox for his unwavering friendship and guidance since the initial inception of the Association.

The final awards of the evening were made by David Meeker, the recently announced Chief Executive of Genzyme – Sanofi, who presented commemorative certificates to both the Association and Jeremy for his personal achievements in leading the Association over the past 20 years.

With the speeches and presentations for the evening completed, and the boat moored back at Millenium Pier, desserts and coffee were served and the jazz band started up again to play the evening out until disembarkation at midnight.

It was a fantastic event and the Board would like to thank

the sponsors for the evening – Genzyme, Shire and Protalix – all of the souvenir brochure sponsors, Jamie Brown and the Creative Clinic for designing the brochure, the Garden Pharmacy for providing the wonderful table gifts, all of the staff at Thames Luxury Charters and of course everyone who was able to attend for making it such a wonderful and memorable occasion.



Old friends Sandy and Maxine say hello



Ruth Wallrock, Julie Kelly and Emily Lew



Jeremy Manuel and Dan Brown

“THANKS SO MUCH. I had a ball.”

“The achievements that have been made by you all have been truly incredible and I am sure that the next twenty years will be just as successful. Thank you all for your very hard work.”



Dr Uma Ramaswami, Christine Lavery, Dr Aiden Gill, Tanya Collin-Histed and Skye Histed - Patient Organisations, Industry and family members get together

The 3rd Gaucher Leadership Forum

The 3rd Gaucher Leadership Forum (GLF) was held on the 23/24 September 2011 in Budapest, Hungary. Sponsored by Genzyme, the aim of GLF meetings is to promote networking and the exchange of experience amongst the Gaucher community. Around 200 delegates attended this year's event, including nine patient group representatives from the European Gaucher Alliance (EGA), including Tanya Collin-Histed and Jeremy Manuel from the UK Gauchers Association. Here we provide a report on the presentations –



Members of the EGA Board and representatives of Genzyme at the GLF in Budapest

The meeting, entitled 'Living with Gaucher Disease, Today and Tomorrow', was hosted by Professor György Kasztolányi from Hungary and chaired by Professor Stephan vom Dahl from Germany. Objectives were to highlight unmet needs in the management of Gaucher disease, outline research questions of clinical relevance and to contribute to the development and integration of the next generation of opinion leaders and treating physicians in Gaucher disease.

Past experience has been instrumental in increasing the understanding of the natural course of Gaucher disease and its response to treatment. Long-term follow-up of patients in expert centres and internationally pooled data from the International Collaborative Gaucher Group Registry (ICGG) shows that imiglucerase (Cerezyme) enzyme replacement therapy (ERT) is able to bring immense benefit to many patients, however there are still unmet needs for some patients receiving treatment – a prime focus of the meeting.

What are unmet needs?

Some patients receiving ERT do not respond optimally in one or more aspects of disease. These include patients with chronic progressive neuronopathic (type 3) Gaucher disease (nGD), but may also include patients who continue to suffer other persistent symptoms or 'atypical' complications of the disease. Professor Pram Mistry (USA) explained that patients vary in their response to Cerezyme and understanding why this happens will allow the full potential of ERT to be realised. The timing of therapy initiation appears to be important. Research shows that patients starting ERT within 1-2 years of diagnosis have a reduced incidence of osteonecrosis (death of bone cells) compared with patients with greater intervals between diagnosis and therapy. Similarly, timing of treatment initiation is critical in the management of osteopenia

(reduced bone mass or 'bone thinning') as treatment has the greatest impact during adolescence when bone formation is active. Established disease in any organ is more difficult to treat, and may have an impact on other disease manifestations. Increasing splenomegaly, for example, is associated with an increasing incidence of localised splenic damage (splenic lesions), and this is associated with a higher incidence of osteonecrosis and with a reduced platelet response. Every patient is different and personalised management is needed with individual genome analysis, genome-wide association studies to find out if and how, particular gene profiles affect disease patterns, and better serum and cellular markers to establish and monitor disease status.

Atypical Gaucher disease manifestations may be difficult to define, as they depend on context and the changing understanding of the multiple manifestations of Gaucher disease. As Professor Tim Cox (UK) explained, 'typical' type 1 Gaucher disease (seen in 90-95% of cases) is considered a blood disease where glucocerebrosidase laden macrophages (Gaucher cells) infiltrate organs to result in an enlarged liver and spleen; increased destruction of blood cells by the spleen and bone marrow failure with a resulting deficiency in the production of blood cells and bone disease. Manifestations outside these signs and symptoms could be considered atypical. Neurological symptoms within the traditional non-neuronopathic classification of type 1 would be considered atypical, but this classification has been 'exploded' by the association between glucocerebrosidase gene (GBA) mutations and an increased risk of developing Parkinsonism. There is also evidence, outlined by José Luis Capablo (Spain), that incidences of nerve damage outside the brain and spinal cord (peripheral neuropathy) may be increased in people with GBA mutations. 'Atypical' manifestations may

be better described by particularly severe disease, rare manifestations, non-macrophage-mediated signs and symptoms, or otherwise unexplained disease. Professor Cox described several manifestations representing unmet need, such as severe bone and liver complications, neuronopathic manifestations, cancers in long-standing Gaucher disease, rare conditions such as 'collodion' baby in type 2, kidney involvement, pulmonary hypertension, the presence of large benign masses of lymphocytes and macrophages in young patients, and cardiovascular disease in some type 3 patients. 'The pathogenesis of many atypical manifestations is poorly unexplained and their occurrence emphasises the need for persistent investigation until we thoroughly understand the molecular pathogenesis of this disorder – for this alone provides the most secure basis for its definitive and long-term cure.'

Neuronopathic disease (types 2 and 3 Gaucher disease)

Neurological manifestations are concerning, not only for patients but for those who try to classify and treat them. Professor Anna Tylki-Samanska (Poland) explained that approximately 6% of Gaucher patients are estimated to have neuronopathic disease (5% with type 3 and 1% with type 2). Type 2 neuronopathic disease is characterised by brainstem abnormalities and is usually fatal during the first three years of life. The neurological symptoms of type 3, which may include lack of coordination, loss of eye movement control, mental deterioration and seizures, are slowly progressive and appear later in childhood. Patients with nGD require regular and comprehensive examinations by a neurologist experienced in Gaucher disease to enable a better understanding of the dynamics of neuronopathic manifestations. While Cerezyme improves spleen, liver and blood profiles in children with type 3, enzyme cannot cross the blood brain barrier

and there is no evidence to indicate that enzyme therapy has an impact on neurological disease.

Cancer

Long standing Gaucher disease is associated with an increased risk of some forms of cancer, especially multiple myeloma (a blood cancer originating in the bone marrow). The pathophysiology of cancer in Gaucher disease is not well understood, but is thought to be related to long-term stimulation of the immune system as a result of glucocerebroside accumulation. Professor Maria Domenica Cappellini (Italy) explained that Gaucher disease is associated with a high prevalence of immune system abnormalities including a condition known as monoclonal gammopathy of unknown significance (MGUS), which is linked with progression to malignant myeloma. It is unknown whether the initiation of enzyme therapy after the detection of MGUS helps to decrease the likelihood of transformation to malignant disease in Gaucher patients. There are no published guidelines on how to treat multiple myeloma in the presence of Gaucher disease, although it is believed that Cerezyme may help patients tolerate chemotherapy used to treat multiple myeloma by reducing the number of Gaucher cells in the bone marrow and by improving macrophage and immune system function.

Parkinson's disease

There is an association between mutations in the gene encoding glucocerebrosidase (GBA) and an increased risk of developing Parkinson's disease and Parkinsonism and Lewy body dementia (characterised by abnormal aggregates of the protein alpha-synuclein inside nerve cells). Dr Ozlem Goker-Alpan (US) explained that patients with Parkinson's are five times more likely to have GBA mutations than people without it and that Parkinson's patients with GBA mutations develop disease earlier than patients without GBA mutations. Early symptoms of GBA-associated Parkinsonism include fatigue, changes in the sense of smell, depression,

anxiety, joint pain, muscle cramps/stiffness and internal tremor. Parkinson's disease in Gaucher patients does not warrant the initiation, or alteration, of Gaucher disease therapy, although Gaucher disease should be adequately followed and managed. Similarly, the symptoms of Parkinson's disease should also be managed and this might involve treating non-motor signs such as depression, pain, and quality of life issues in the early stages of disease; and pain, bone disease, mobility, and cognitive issues in later stages. Parkinson's disease is not a complication of Gaucher disease, but is associated and the majority of Gaucher patients do not develop Parkinsonism.

The way forward

A key unmet need in Gaucher disease is to find better treatments and/or better delivery methods that will impact on neuronopathic symptoms. This relies on a better understanding of brain pathology and biochemical changes in nGD so treatments can be better targeted. Current research into neuronopathic disease was described by Professor Tony Futerman. Using mouse models of nGD, his group have shown that only certain areas of the brain are affected, and these areas may correlate with disease manifestations such as eye movement abnormalities or abnormal brain stem functions. Pathology seems to be related to neuro inflammation.

Other research involving mouse models that show features of Parkinson's disease and dementia with Lewy bodies, is investigating the pathogenesis of GBA-related Parkinson's disease. One theory is that lack of glucocerebrosidase activity may compromise protein degradation to result in increased alpha-synuclein levels. Glucocerebroside is thought to stabilise alpha-synuclein aggregates and these, in turn, further impair glucocerebrosidase activity to create a pathogenic cycle.

Dr. Seng Cheng (US) acknowledged the need for improved therapies to address nGD manifestations not met by enzyme infusions. He described new treatment

strategies developed in Genzyme's research programme involving haematopoietic stem cell transplantation with gene modified stem cells, gene therapy, small molecule-based therapies, enzyme delivery directly into the brain (intracerebroventricular (ICV) delivery) and adjuvant therapy (e.g. anti-inflammatory drugs). Use of mouse models of nGD has shown that direct ICV delivery of enzyme leads to a reduction of substrate storage in the brain and a dose dependent increase in mouse survival. This delivery approach is invasive and requires repeated administration. Small molecule therapies offer non-invasive oral delivery and are able to pass across the blood brain barrier. Preliminary investigations in a mouse model using small molecule strategies have shown delayed disease progression. Research is also active for GBA-related Parkinsonism. Studies in mice have shown that gene delivery of glucocerebrosidase into the CNS reduced synuclein pathology. Current research efforts are aimed at discovering whether these results can be repeated in larger animals.

Awards

The meeting ended with award announcements:

The Senior Investigator Award of the Gaucher Generation Grant (a Genzyme programme supporting research in Gaucher disease) was awarded to Dr. Derralyn Hughes from UCL for her proposal: 'Characterisation of pathogenic pathways within the bone microenvironment of Gaucher Disease which contribute to bone pathology and haematological malignancy'.

One of the winning posters was by Drs. Derek Burke, Ashok Vellodi and Simon Heales for 'Glucocerebrosidase activities; Factors to consider in the Pathogenesis of Parkinson's disease?' One of the winning posters was by Dr. Derek Burke, Dr. Ashok Vellodi and Dr. Simon Heales (all UK) for 'Glucocerebrosidase activities; Factors to consider in the Pathogenesis of Parkinson's disease?'

Genzyme launches new website – GaucherLife

A new interactive website for people affected by Gaucher disease has been launched by Genzyme UK. The new site provides information on Gaucher disease, videos from patients and doctors, news to help keep up to date with what's going on in the Gaucher community and a chat area (GaucherZone) where visitors can share their own news and views, and take part in web based activities and competitions. Genzyme welcomes comments and suggestions for content to ensure that the website meets users' on-going needs and interests. To visit the site go to www.gaucherlife.co.uk

Shire launches patient organisation charter

Organisations established to support people living with rare medical conditions, such as the Gauchers Association, have long been invaluable to many patients and their families. At Shire, a specialist pharmaceutical company working in the area of rare diseases, we are developing a new charter in collaboration with Patient Organisations to highlight the value of such organisations beyond the patient community. Within the Charter, we formally commit to helping patient organisations in supporting people with life altering conditions to lead better lives. Ken O'Reilly, Director of Patient Advocacy, writes –

Organisations like the Gauchers Association make a real difference to the lives of people who are living with rare conditions. For patients to have access to supportive, knowledgeable and motivated people, beyond their healthcare team, to help them cope with managing their condition is really important. That is why we have developed a Shire Patient Organisation Charter and want to make formal our long standing commitment to supporting these teams of people who provide such a valuable and needed service. The communities of people living with or

working to combat rare diseases are so small, it is therefore imperative we all work together to achieve the best possible care for patients.

The Charter outlines our approach to working with patient organisations, where we strive for our relationships to demonstrate the highest standards of integrity, trust and transparency – things we believe are imperative to forming strong and effective partnerships. We are pleased to be working with the Gauchers Association to find ways to provide additional benefit to the needs of the patient community.

Shire Patient Organisations Charter

At Shire we believe that patient organisations are fundamental to the support and care of patients and their families affected by rare and orphan diseases. We value and respect the experience of patient organisations and their deep understanding of the conditions they represent, and we are committed to helping them to achieve their mission for patients.

Our vision

To support patient organisations to enable people with life altering conditions to lead better lives.

Our values

We recognise the challenge that patients with rare diseases face every day and we strive to relentlessly keep the needs of these patients at the centre of everything we do.

Our commitment

Shire is committed to supporting and working with patient organisations in the rare and orphan disease areas. We undertake this work in the spirit of transparent partnership while ensuring the independence and integrity of the patient organisations are always maintained.

Our guide

We aim to be a beacon of best practice across the pharmaceutical industry in our relationships with patient organisations. At all times we respect the international and national codes of practice and the laws which govern our relationships with patient organisations. Through our policies and working practices, we ensure that our relationships demonstrate the highest standards of integrity, trust and transparency.

Global Humanitarian Aid Meeting

The European Working Group on Gaucher Disease (EWGGD), European Gaucher Alliance (EGA) and the US National Gaucher Foundation (NGF) invited representatives from five pharmaceutical companies involved in the development, manufacturing and marketing of treatments for Gaucher disease to a meeting in Amsterdam (see photo) on the 5th October 2011 to discuss the on-going need for humanitarian aid.

The meeting agenda was to discuss the development of a global co-ordinated structure for humanitarian aid for Gaucher patients who are unable to access treatment in their own countries due to the cost of the treatment. The Genzyme Corporation have been involved in providing humanitarian aid globally for Gaucher patients for many years and the patient groups work closely with them to get treatment to patients. The meeting was co-chaired by Professor Carla Hollak from the Amsterdam Medical Centre and

Professor Timothy Cox from Addenbrooke's Hospital in Cambridge.

The meeting concluded with the establishment of a working party, led by the patient advocates Tanya Collin-Histed (EGA) and Rhonda Buyers (NGF) to develop a pilot framework for the distribution of humanitarian aid in India and Pakistan where there are a large number of children with Gaucher disease who do not have access to treatment.

UK Gauchers Association Chief Executive Tanya Collin-Histed and Chairman



Jeremy Manuel attended the meeting as the lead EGA representative. Project updates will be reported in future editions of the Gauchers News.

National Collaborative Study for Lysosomal Storage Disorders (NCS-LSD)

Enzyme replacement therapies are now available and licensed in the UK for the treatment of six lysosomal storage disorders (LSDs), including Gaucher disease. In addition, substrate reduction is licensed for Type I mild to moderate Gaucher patients for whom ERT is inappropriate. In 2005, the Peninsula Medical School, in collaboration with the National Commissioning Group (NCG), designated treatment centres and the UK LSD patient support groups, were funded by the National Institute for Health Research's Health Technology Assessment (NIHR-HTA) Programme to examine the effectiveness and cost-effectiveness of these therapies. Lindsey Anderson, Research Fellow at the National Collaborative Study of Lysosomal Storage Disorders (NCS-LSD) reports on this study –

We sought to carry out a long term cohort study by collecting data at each treatment centre from consenting adults and children with these conditions. By following people with these conditions over time, the NCS-LSD aimed to gain a better understanding of treatment effectiveness, when the best time to start giving these treatments is, and which symptoms led to the diagnosis.

Current and historical clinical data were collected from participating patients' hospital records. We asked participants to complete a series of questionnaires about how they were feeling each time they attended their clinic. Finally, we asked participants to tell us how frequently they use the NHS, treatment costs and the related costs to them and their family. Our aim was to compare the quality of life and treatment costs for people who are receiving treatment with those people who are not, or for whom no treatment is available.

When the study started in 2006, there

were 272 patients diagnosed with Gaucher disease in the UK. Forty-nine were deemed ineligible by their clinicians who believed they would be distressed by participation. 185 were asked to participate and of these 175 (78% of all eligible patients) agreed; a fantastic response, and we are grateful to every patient who participated. Clinical data has now been extracted, and historical data has been taken from the medical notes of over 80% of these patients.

In addition, over 50% of the participating Gaucher patients have completed at least two sets of quality of life and service-use questionnaires. This will help us to understand how Gaucher patients' general well-being is affected by being on treatment, as well as calculating the financial burden faced by families affected by this disease.

We finished collecting data in earlier this year and statisticians are analysing the data. For Gaucher patients, we are focussing the analysis on haematology, spleen and liver size, bone involvement

and neurological involvement. We are creating models or graphs, which will:

- Show the relationship between length of time on treatment and severity of disease in Gaucher patients
- Predict how treatment will affect the progression of Gaucher disease in patients

We also hope to create a severity score using the key clinical markers associated with the condition which might help us to understand disease progression.

The researchers will be completing their report to funders by January 2012. Each participant will receive a summary of the results, and further copies of the report will be available through the Association. The full report will also be available on the HTA website (www.hta.ac.uk).

The NCS-LSD researchers wish to thank the Association for their on-going support of this study, and all patients and their families who agreed to participate.

Medco Homecare Solutions

Homecare services for Gaucher disease patients in the UK are provided by two companies Healthcare at Home based in Burton-on-Trent and Medco Homecare Solutions who recently merged with Careology, based in Northampton.

Medco Homecare Solutions are a pharmacy homecare provider which provides medicines and nursing services across the UK through regional logistics and a network of vehicles.

Gaucher patients and their families

who previously had their treatment and ancillaries delivered by Careology will receive their treatment and nursing services in the same manner but may have noticed small changes, including in the staff who now call or e-mail to make delivery

arrangements. Kate Wilson and Will Walker from Medco will be responsible for Gaucher patients and deliveries will be scheduled on an agreed date within a two hour window.

Delivery drivers are dressed discreetly and carry photo ID. The Medco driver will require a nominated contact to sign for the treatment and this information will be asked for by Kate or Will when they contact you regarding delivery arrangements.

The Association works with Healthcare at Home and Medco on a regular basis and the Association seeks to ensure that the needs of our members are being met at all times. Contact Tanya or Sarah at the Gauchers Association on 01453 549231 if you have any feedback, comments or concerns.

Global Patient Group Leader Summit

In May 2011, Tanya Collin-Histed, Chief Executive of the Gauchers Association and 18 other patient leaders representing rare diseases from around the world travelled at the invitation of the Genzyme patient advocacy team to meet in Boston, USA. The purpose of the meeting was to discuss current events, emerging trends and other topics of interest in the rare disease community.

The two-day programme provided the opportunity to tour Genzyme's manufacturing plant at Allston where Genzyme manufacture Cerezyme, view the Hope Art Gallery which displays artwork by rare disease patients from all over the world and listened to a number of presentations on manufacturing, research and development. This was followed by a bus ride to visit Genzyme's new manufacturing plant at Framingham which is expected to receive final approval for the manufacturing of Fabrazyme from early 2012, leaving the Allston plant to manufacture Cerezyme only in the future.

Day two of the programme enabled the patient organisations to listen to

presentations on Genzyme's LSD Registries with a demonstration of the new registry; Genzyme's Humanitarian Aid programmes and a Q&A session with member of Genzyme's Senior Management team.

During the lunch break, patient organisations were broken into disease specific groups and had the opportunity to meet with members of Genzyme involved in the disease areas. In the Gaucher camp was Tanya, Rhonda Buyers from the National Gaucher Foundation in the US and Myriam Estivill Flores from Chile who has a daughter with Gaucher disease. During the session the group discussed recruitment for the Genzyme oral therapy Eliglustat and the unmet needs of



Patient representatives from all over the world gather together

neurological Gaucher (nGD) patients.

The day ended with a session led by Jamie Manganello, head of the Patient Advocacy team. During these discussions, members of the patient organisations highlighted areas for future working partnerships with Genzyme, including a Q&A booklet on humanitarian aid; the translation of materials into other languages; access to visual information such as a video clip of small molecules; a patient organisation page on Genzyme's website for information and patient awareness of research and development initiatives.

Editor's note: since the meeting in May, Tanya has been invited by Genzyme to comment and contribute on their 'questions and answers' booklet for Genzyme's humanitarian aid programmes.

EGA Visit to Shire's New Lexington Facility

On 3rd June 2011, members of the EGA board travelled to Boston, USA at the invitation of Shire Human Genetics to meet members of the senior management team and have a tour of their new manufacturing plant in Lexington. Tanya Collin-Histed reports on the trip –

The purpose of the meeting was threefold; to meet with members of Shire to learn more about the company and their commitment to the Gaucher community and to update them on the work of the EGA; to visit the new manufacturing plant at Lexington and to have a full face to face board meeting of the EGA.

On the Friday morning the EGA board met with Shire staff Bill Ciambro, Head of Technical Operations; Martha Fournier, Medical Director; Ken O'Reilly, Director of Patient Advocacy; Mark Forshaw, Senior

Director LSD Products and Mike Heartlein, Vice President, Research, who gave a number of informative presentations on their Research and Development pipeline, an insight into their manufacturing process and an update on their investment into technology and manufacturing facilities. Members of the EGA board gave an update on their work programme for 2011/12 including the new EGA website and the proposed global Humanitarian aid programme for Gaucher disease.

Later on that day the board made a



The EGA Board and representatives of Shire

tour of the new manufacturing facility which was given by Chuck Hart (Director of Cell Culture Operations) and Albert Shkuti (Upstream Operations Manufacturing). The new facility will provide significantly greater capacity for the production of medicines for rare disease patients, using a 'single use' bioreactor process which is a first within the industry at this scale. Subject to regulatory approvals manufacturing is expected to begin at the beginning of 2012.

On the Saturday the EGA had the opportunity to meet for a formal board meeting to progress the work programme of the EGA.

Elaine Benton's Book of Poems

Elaine writes – My name is Elaine Benton, I am 48 years old and have Gaucher disease. I was born in England but I have lived in Israel for the last 28 years. I am married with one daughter. I worked as an English secretary, but had to retire 15 years ago due to my health deteriorating. My husband and I were part of the initial committee who helped set up the Gaucher Association in Israel 20 years ago, and I started to receive the enzyme replacement therapy administered through infusions in 1991 when it was very new and not yet on the Ministry of Health's list of drugs in Israel.



I had an AVN (Avascular Necrosis) of the hip joint four years ago and had surgery, which thankfully was a success. About three months after the surgery I began to feel tremors in my left thigh and left hand. Soon after was diagnosed with Parkinson's and immediately put on PD medication. Naturally this was a great shock to my husband and daughter, family and friends. To be honest, although I was devastated at the news, when the tremors began, I instinctively knew it was Parkinson's due to my family's medical history. My father was a carrier of Gaucher and had PD, and a brother who suffered from Gaucher also developed PD.

As hard as it is having Gaucher, the addition of Parkinson's makes my daily life extremely debilitating. It's almost as if these two diseases are battling inside my body. My life has changed drastically over the last four years and there are so many things I can no longer do that I used to take for granted. Parkinson's is a degenerative disease, and in my family appears quite aggressive. There is much research going on as there may be a link between Gaucher and Parkinson's.

I have always loved writing stories and poetry but some months ago, my creativity suddenly became much enhanced. Lines of poetry would come to me, sometimes in the middle of the night, and I found myself scribbling down thoughts and lines in the dark in our bedroom, not wanting to wake up my husband by turning on the light. I had to be careful to leave large gaps between my writing, so that in the morning I could decipher what I had written blindly in the middle of the night. I couldn't stop writing, and poems were pouring forth from me, as if a creative fountain of thoughts had suddenly been released.

I have met a number of PD patients, all of whom seem to be quite depressed, which I understand is due partially to the disease itself and to the medication. Thankfully I do not suffer from depression, but realised that I may have something to

offer Gaucher/PD sufferers – words of support, hope, and to let them know they are not alone and that I am going through what they are experiencing.

I have written a book which is a collection of poems about Gaucher/Parkinson's disease but it's not exclusively for Gaucher/PD sufferers, I hope that anyone suffering from a chronic disease can relate to them.

I felt I had something to offer with a sense of humour, looking at life from the bright side with a smile on my face and regardless of how difficult life can be when afflicted by chronic disease. I have always been a positive person, and as I was born with Gaucher disease, I think this gave me the tools to deal with PD when I was diagnosed. I believe that staying cheerful and looking at things with a sense of humour not only helps me, but also helps my family cope better. I have a fierce desire to live life to the full and a strong fighting spirit. I refuse to let anything get me down, and make the best out of what I have.

Some of my poems are on a serious note, others are light hearted and funny, but all come straight from my heart and my personal experiences. The book is

available on Kindle through Amazon, and for those who don't have a Kindle, you can download the book to a your PC, iPad or mobile phone using a 'kindle application' which you can find online for free by Googling 'Kindle app for PC' and following the instructions given. There is also a paperback copy available by contacting me through my website www.elainebenton.net where I also have a blog. The book is called "Parkinson's: Shaken not Stirred!"

This project, as I'm sure you can understand, is very important to my husband and I. It has given me reason and purpose by making me feel I have something of value to contribute. The interest that has been shown in this book is quite remarkable and heartwarming. People seem to be identifying with the poems and know they are not alone, which was the message I wanted to impart. Fellow sufferers, care givers, doctors and even some of my family and friends who have known me for years had no idea what I go through daily. I put my heart on the table with this book and opened up. I held nothing back. The poems are raw and written with stark honesty and sincerity – I tell it how it is.

Gauchers Association moves office

We are pleased to announce that we have now completed our office move to:

Evesham House Business Centre
48/52 Silver Street
Dursley
Gloucestershire GL11 4ND

Our email address (ga@gaucher.org.uk), phone number (00(44) 1453 549231) and website (www.gaucher.org.uk) stay exactly the same.

London Marathon

Runners raise £ 11,500

Over 35,000 runners were accepted for this year's Virgin London Marathon on Sunday 17th April. David Hershman, Jenny Hurst, Janine Simon, Dan Lerner and Elan Hirshler all completed the 26.2 mile course to benefit the Gauchers Association. Five intrepid athletes describe their experiences –

David Hershman: "In April I ran the marathon after a 12 year break from marathon running. Training went well until about four weeks before when I developed tendonitis in my leg. It was incredibly painful and my physio-therapist advised me to take a two week break along with intense treatment. Ten days later after an agonising break from exercise I ran 22 miles with my leg heavily strapped. With the tendonitis easing I felt confident I would be able to cover the distance just a fortnight later.

The big day came around very quickly and I couldn't sleep the night before. Even at 7am on a Sunday and as we approached London Bridge, the buzz was amazing. Greenwich Park was heaving and despite having arrived with ample time to spare, it was soon time to get into our starting areas.

There was a huge number of spectators along the entire route, cheering us on and providing that lift we needed when near to exhaustion.

What an amazing day. It was a memory for life that will stay with me forever. It was only after crossing the finishing line that I realised how exhausted I was. The rest of the day was spent drinking hot tea and enjoying the huge sense of achievement that running a marathon gives you.

The next day I cycled to work as I always do, somewhat more wobbly than usual!"



Jenny Hurst and Janine Simon: "If you 'hit the wall', there's no cure. It hurts and progress will be slow. Think of your charity

and keep running. The crowd will be there to cheer you on.

These words are so true. I left Portugal two days before the marathon with Algarvian flu. There was nothing I could do and it was impossible to keep pace with my running buddy Janine. Her run was amazing. She had never really run before and was across the line in five hours!

It took me at least another hour but it's not about the time, although there were times I thought I was never going to make it!

Highlights of the day include meeting Janine's nine year old niece Verity the night before the marathon. She has Gaucher disease and was so tiny for her age yet so mature. She kept me going that's for sure. And to my kids who had a change of clothing around mile 19 and for all their help fundraising, we all had a lot of fun, especially the Full Monty night...!

Thank you to Janine and to the Gauchers Association for letting me take part. It was a day that will never be forgotten."

Dan Lerner who ran with Elan Hirshler: "Having never run more than a mile, signing up to do the marathon for the Gauchers Association was a big decision, but I am glad I did and what an incredible experience it was.

Training started six months beforehand. It was a tough task through the cold winter but I persevered and worked as hard as possible. The incredible support from my friends and family really helped and training with my friend Elan helped a lot too.

Before I knew it the day had arrived. It was the most nerve-racking morning I had ever experienced, but once it started I could see why it's such a special day.

From the beginning the streets were packed with cheering supporters, and it continued for the whole 26.2 miles. Bands were entertaining everyone and volunteers were positioned all along the course to provide water and energy drinks.

The first 13 miles were fairly comfortable, but after a few more miles the reality of the task set in, however adrenaline and the chance of seeing my friends and

family along the route kept my spirits up. Crossing the finish line was one of the best feelings I have had. I finished in 5h 2min which wasn't bad for a first time runner! I hope to get a better time in next year's marathon, which I have already signed up for!

The most rewarding aspect was the chance to do something good. The Gauchers Association does an incredible job in their support of sufferers and their families and the vital research they do should not be overlooked either. Being able to raise over £2,000 to help them is a great feeling and one which I cannot recommend enough to anyone able to do so."



Looking forward to 2012

Once again we have five Golden Bond places for the 2012 London Marathon on Sunday 22 April and we are pleased to announce we have five runners who will be training hard over the next few months. Please read the stories from three of them and support them as much as you can.

Tanya Collin-Histed, Chief Executive of the Gauchers Association and Director of the European Gaucher Alliance (EGA): "Over 15 years ago my daughter Maddie was diagnosed with type III Gaucher disease, she is now 17 and studying Children and Young People's Development at college. Maddie has been on ERT for over 15 years and whilst she is doing physically very well there is still no treatment for the neurological aspects of the disease. Sadly, many patients with type III are not doing as well as Maddie and each year many lose their brave battles.

For the past 14 years I have been working with the Association to support patients and their families with Type II and III Gaucher disease. I have witnessed the struggles and heartache that families experience and the despair at having no new treatment has caused. Gene therapy was ten years away when Maddie was diagnosed, 15 years later we are still years away. We will keep pushing together!

I have decided to run the marathon to

raise money for the Association to continue to support our sufferers and their families in whatever way we can, but this needs money. Please sponsor me online at: <http://uk.virginmoneygiving.com/TanyaCollin-Histed>."

Jamie Rosen: "I'm running my first marathon this April. I am a Gaucher sufferer and was diagnosed when I was 19. I was using Cerezyme and now Velagluarase treatment since then and two months ago I started infusing myself and now do it every two weeks from home. The support I've had from my family and the team at the Royal Free Hospital has been immense and

considering I am a sufferer, I am fitter than I have ever been. I am already running around 8-10 miles four times a week so by April it will be a breeze...!

I run an online marketing company in Cape Town, South Africa. I came out here to watch the 2010 World Cup and haven't left!

Other than the fitness we have to achieve to run the marathon, it will be wonderful to raise money for this incredible association that work tirelessly. As I don't have time for the committee, this is the least I can do. Here's to a sub-five hour finish!"

Simon Azouelos: "I'm 24 & I live in north-west London. When I'm not busy running

my business I enjoy watching films, listening to music and playing with my dog, Tofu.

Running the marathon to help promote awareness of the Gauchers Association will be a massive honour & something I will undertake with pride. I love a challenge and will do all I can to rise to it."

Our fifth runner will be **Charlie Gould**.

If you are inspired and would like to support us by taking part in the 2013 London Marathon, please contact Tanya or Sarah on 01453 549231 or email the office ga@gauchers.org.uk.

A 'blooming' good day for charity at Highgrove!

All eyes were on the Royal family this April and not only for the wedding. Just a few days before the big day, a group of 26 north London gardening enthusiasts headed off to the gardens at Highgrove House, the Prince of Wales' country home. The visit, organised by Susan Morris-Manuel raised £680 split between two charities, Gauchers Association and Cruse Bereavement Care.

The tour offered up a two and a half hour visual feast, revealing the personal passions of the Prince, not least his commitment to sustainable, organic gardening. A series of linked areas, each with a distinct character, including the patch where Prince Charles first tried the organic approach, a wildflower meadow, the elegant topiary of the Thyme Walk and the Stumpery, a darkly magical Victorian-inspired enclave dedicated to ferns with an outstanding sculpture by Isabel and Julian Bannerman.

The thatched tree house in which William and Harry used to play offers a touching insight into the gardens' use while the busts of significant others – the explorer Laurens Van Der Post, Lord Mountbatten, the naturalist Dame Miriam Rothschild, the composer John Tavener, the Queen Mother – in pearls and gardening hat – provide a further glimpse into how very cherished this space is in the Prince's life. As we walked, the gardeners at work were happy to share their tips with us, including how tulips from the formal

garden are re-planted the following year in the wildflower meadow.

After the tour, the group headed off for tea and cakes in the Highgrove tea-room, and for a scout around the gift shop to bring back treats for those who didn't make the lucky 26. The Prince may not have been at Highgrove to meet and greet that day, but the gardens, in their own way, present their own multi-faceted, eclectic portrait of him that very few are privileged to experience.

Gauchers Association Golf Day

On May 18th 2011 we held our 4th Golf Day at Dyrham Park Country Club.

The day was brilliant even if the weather wasn't! The organising team of Lola, Clive and Lane Bednash, Sharon and Alan Rosen and new recruits Carly and Ben Doltis did a great job.



The winning team with Sharon Rosen and Lola Bednash

It was our most successful event to date, with 68 players across a variety of abilities with handicaps ranging from six to 28 and we held the price of previous tournaments at £100 per player including snack lunch, halfway house and dinner. Everyone who took part commented on what a wonderful day it was, and we raised £10,000 from the golf, raffles, table collections and sponsorship in the brochure. Humming Bird Motors were one of the day's sponsors providing a car for a hole in one on the 5th hole. Alas the car went unclaimed, albeit by a mere two inches! The winning team of Mark Meltzer, Rob Lerner, Michael Lerner and Ben Doltis were thrilled to receive their trophies and Ben said "my team thoroughly enjoyed the day, the organisers did a fantastic job and we are looking forward to retaining our crown in 2012!"



Mark Meltzer, Rob Lerner, Michael Lerner and Ben Doltis

Royal Garden Party

On Wednesday 29th June 2011, Liz Morris and Linda Richfield, Specialist nurses at two of our designated centres for Gaucher disease, were honoured to attend the Queen's Garden Party at Buckingham Palace. They were both nominated by the Association in recognition for their care and commitment to Gaucher patients. They write –

“We met at the Hyde Park entrance to the Palace and joined the queues of people, beautifully dressed complete with hats and the precautionary umbrellas. After our identity and invitations had been checked by policeman who looked like they should still be at school we entered in through the immaculate gardens. The weather was warm and sunny and we strolled around the grounds and the lake. On arriving at the lawn we were entertained by two military bands playing at opposite corners of the lawn. The tea tents stretched welcomingly before us and we enjoyed drinks, cakes and of course, cucumber sandwiches.

The National Anthem heralded the arrival of the Royal party. The Queen and Prince Phillip walked through the gardens looking extremely well and greeting some of the guests. The pageantry was in evidence everywhere with Yeoman of the Guard, Gentlemen-at-Arms and Gentlemen Ushers managing the event with precision and style. We took the opportunity to peruse the outfits worn by other guests, enjoying the array of national dresses, military and religious uniforms and of course checking to make sure no one else was wearing the same outfits as us!

We met up with Dr. Fiona Steward and



Liz Morris (left) and Linda Richfield (right)

her husband and were served with tubs of strawberry ice cream. After the Royal party had left and the military bands played the National Anthem for the final time, we headed into Buckingham Palace itself for a quick look round. Finally somewhat foot-sore in our new shoes, we headed for home after a truly memorable day.

We would like to take this opportunity to say a very big thank you to all at the Gauchers Association for nominating us to attend this very special event. It was a fantastic experience and a day that neither of us will ever forget.”

Members' Fundraising

Fundraising brings in over £8,000 for the Association

We would like to thank all of our members who generously donated additional funds to the Association with payment of their annual subscription totalling £964.

In memory

The Haberdashers' Benevolent Foundation donated £100 in memory of Mr Leonard Wood. Two of his children are affected by Gauchers disease.

Mr Ralph Wood very kindly asked for donations instead of flowers at the funeral of his father Mr Leonard Wood. £20 was generously donated.

Joy Burrowes and her family kindly donated £30 in memory of Clive Harries who passed away 22 years ago.

Donations received totalling £5,940

Generous donations have been received from the following: Dr R M Altmann, Mr & Mrs Eric Beecham, Mr John Quint, Ronger Props, The Manuel Charitable Foundation, Pauline Gusack, Michael Heller, The Parish Church of St Mary, Heworth, Gateshead, HOD Lodge, Debra Hale, Bridging & Commercial Ltd, Merched yr Undeb,

William Brake Charitable Trust, Mr & Mrs Cyril Metliss, English Martyrs School, Stephanie & David Reitman, Gerald Cohen, Joan & Brian Graham, L Green, Dursley Tangent Club (Mrs C Jenkins), K Moore, Galley Family Trust, Dr C Bush, P Gusack, Jane Mortimore, Linda Hurren, E Lipson, S Lipson and A Supree, as well as Payroll giving donations through Charities Trust.

Sharon Stokes kindly donated £405 following on from a coffee cake morning. Sharon says “we had a lovely time chatting, drinking coffee and eating cake so it was such a fantastic added bonus to raise this amount the Gauchers Association.”

Jeff Hammerschlag generously donated £50 on behalf of **Mr Allan Swiel** who celebrated his 60th birthday.

Robert Sloan kindly donated £69 from a collection box along with his great aunt Ingrid, Janette Graham and William Sloan.

Rona Troman donated £10 to support our runners in the London Marathon.

Lisa Robson and best friend **Jacqueline Smith** took part in the Middlesbrough Tees Pride 10k Run. They completed the

course in just under one and a half hours and through the generosity of friends and family, they raised around £500 in memory of Lisa's baby sister Emma



Hall. Emma had Type 2 Gauchers and died in April 1996 when she was just over two and a half years old. Emma would have been celebrating her 18th birthday this September, so to commemorate her short but happy life, they decided to raise funds for the Gaucher Association by taking part in their first ever 10k run.

For more information on fundraising ideas and organisation please call us on 01453 549231 or email ga@gaucher.org.uk

Gauchers Association Raffle Licence – We are pleased to report that the Association now holds a Small Society Lottery Registration. If you're thinking of running a fundraising event for the Association and would like to get raffle tickets printed to be sold before the event, please contact either Tanya or Sarah on 01453 549231 or email ga@gaucher.org.uk.