Glisten

Glycogen Storage News

AGSD

March 2015

Volume 13 Issue 1

Memories from 2014 Conference

Research Update

AGSD Annual Conference 2015 Venue

Diet & Excercise tips

Expressions of Hope

Contents

Developement Update

Green Shoots?

I was a little disappointed that there has been virtually no snow in Hampshire this winter, especially as I'd bought a shiny new snow shovel last year. But it has given me the opportunity to spend a little more time in the garden to trim back a couple of trees, a hazel and a willow, that were getting dangerously out of hand. I'm sure that they'll soon start to grow into their new reduced stature and provide a secure environment for those little green shoots and, eventually, hazelnuts to grow.

And so it is with the AGSD-UK; having reduced the office staff to a minimum and cut back on our fundraising support, we are actually beginning to see some encouraging green shoots of our own. Fundraising has not abated over the winter months, as you'll see within these pages, providing a little more security for the Association. Equally as encouraging are the other aspects of our work that are improving too…

I am very pleased to welcome our new GSD 0 Coordinator, a first for the AGSD-UK. A youthful Abbie Maguire will introduce herself later in this newsletter. On paper at least we have a full complement of coordinators, although I am aware that one or two have work commitments that prevent them from becoming as active as they would like.

We were introduced to three new Trustees at our conference in October. Wendy Bascal, Shaun Griffin (Treasurer) and Stuart Alderson bring their varied experiences to help grow the Association further.

Research into new medical treatments is always painfully slow, as anyone who has been monitoring the progress of the Gene Therapy work in Florida will know. But there is now speculation that the therapy will be used in clinical trials for GSD I very soon.

I recently attended a conference in Florida where I had arranged to meet with a large number of companies, mostly interested in developing next-generation therapies for Pompe disease. But there was one company that has a small-molecule technology that could be applied to several of the GSDs. Hopefully they will retain their interest in GSDs and will join us at a future conference to report on their work. One compliment that I'm happy to pass on was that the company were attracted to the AGSD-UK because they were very impressed by the information contained in our website.

Given this growth in GSD research I have introduced a new section in this issue of Glisten that lists some of the clinical studies being undertaken around the world. For this issue I've restricted my search to the hepatic

GSDs, but in future issues I hope to give a more comprehensive round-up.

Our conference last October was certainly one of our best, with a good attendance in a very comfortable and well-equipped venue. There are workshop reports in the Hepatic and Pompe sections of this issue. We were fortunate that we received support to hold an art workshop on the Saturday, open to everybody, and with one piece of art being selected for submission into Genzyme's "Expression of Hope" competition; it may appear online shortly (http://expressionofhope.com). A few of the finished paintings are reproduced throughout this newsletter.

Our conference this year will return to Wyboston Lakes in Bedfordshire. So put the date in your diary (October 10/11) and I'm sure we'll have a very interesting programme for another rewarding weekend.

One last request – if you have a personal story that you'd like to tell, please contact me directly; I do like to have new case-studies for the newsletter, for grant applications and for presenting at our annual conference, so keep them coming – I enjoy reading them too!

Allan Muir
Development Director

National health screening: government response

Allan Muir

There is currently a pilot study underway to validate the screening technology for a small number of Lysosomal Storage Diseases, including Pompe Disease. Once that is completed there will be an application to commence a pilot newborn screening programme that will, we hope, ultimately lead to national screening for Pompe disease.

The AGSD-UK may, at sometime, like to support other GSDs being added to the newborn screening programme to overcome issues of late diagnosis. Given that dietary or exercise management has a very low cost to the

NHS, and the complications of late diagnosis can be so costly, it may well be a proposal that could seek favour if cheap and reliable screening tests become available.

The Department of Health has published a policy paper with 22 recommendations for the future of National Health Screening, affecting both newborn and population screening. The full document is available at the web address below, and I have also extracted a few paragraphs most relevant to the AGSD-UK: **www.gov.uk government/publications/national-health-screening-government-response**

Allan Muir

Introduction

Health screening is a vital public health tool that saves lives and improves the quality of life through early diagnosis of serious conditions, enabling early treatment and care. Screening programmes offer tests to assess risk or detect early disease and guide people through the whole process – from the initial invitation to attend for screening to the test itself; communicating and interpreting results; advising on options; and referring those who need it for further investigation and diagnosis.

Recommendation Responses

1. Health screening policy and practice provokes strong reactions among those who argue that the UK should screen for more conditions and in those who question the operation of, and evidence base for, current programmes. Since its establishment, the UK National Screening Committee has discouraged the haphazard growth of localised, unplanned programmes that are not grounded in high-quality evidence and has presented a barrier to entry. We agree that all screening programmes should be grounded in robust evidence and, given the difficulty of withdrawing a programme, support the idea that the evidential barrier to entry should remain high.

4. If it is to be effective and trusted, the UK National Screening Committee (UK NSC) must be open to a plurality of perspectives when reviewing the evidence base for its policies. We are satisfied that efforts continue to be made to consult with stakeholders and note that the UK NSC is currently producing updated guidance for stakeholders on "engaging with its policy review process". Engagement, however, should be a two-way process. In addition to being transparent and opening up its policy review process to external input and scrutiny, it is vital that the UK NSC proactively looks beyond traditional, large stakeholder groups and seeks to engage with those smaller – often condition-specific – groups especially where they offer scientific insight. We recommend that the UK National Screening Committee, in its response to this report, details how it will proactively engage with a broader range of stakeholders.

Reporting Evidence Reviews

8. Any evidence review process must be flexible enough to accommodate the wide range of screening programmes the UK National Screening Committee (UK NSC) examines and some subjective judgements will be made. However, it is currently unclear what procedures the UK NSC has

for reaching decisions about whether to recommend a programme. In line with the guidance outlined in the Code of Practice for Scientific Advisory Committees, we recommend that the UK National Screening Committee formally agree, and make public, the procedural mechanism by which it will reach decisions and recommendations.

Communicating the Risks and Benefits of Screening

12. We support the principle of enabling informed choices to be made about participation in a screening programme. However, we are struck by the lack of clarity over what is meant by "informed choice", how it should be measured and the corresponding dearth of information on whether it is being achieved in practice. We recommend that a definition of "informed choice" is agreed by the UK National Screening Committee, in conjunction with its stakeholders, as soon as possible. The definition should have regard to the legal rights set out in the NHS Constitution, particularly those rights that make reference to consent and informed choice. We also recommend that this definition is subsequently used as a starting point to evaluate, and compare across screening programmes, whether individuals are being supported to make an informed choice about participating.

14. We encourage the UK National Screening Committee and NHS to develop, pilot and evaluate approaches to providing screening information that can be accessed at the level of detail desired by individual patients and practitioners.

15. To avoid inconsistencies in the information provided across programmes, we recommend that the UK National Screening Committee devises and implements a standard process, underpinned by a publicly available set of criteria, for producing information that facilitates an informed choice to be made about participating in a screening programme. The production process should consult with a wide range of stakeholders and should subject information materials to extensive user testing, both before and after implementation. Information materials for all NHS screening programmes should subsequently be revised according to the process and be reviewed at regular intervals

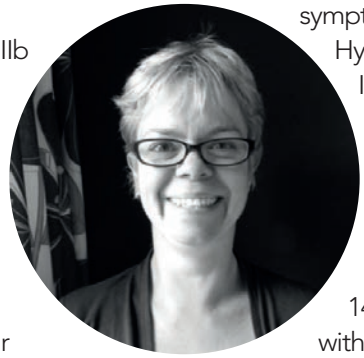
17. Under the NHS Constitution, patients have the right to be given information about the test and treatment options available to them, what they involve, and their risks and benefits. We are concerned that the rarity of some conditions may lead health professionals to downplay the possibility of participants in a screening programme receiving a positive result and that health professionals can struggle with screening terminology and concepts. We recommend that the Government supports the UK National Screening Committee to step up its education programme and ensure that

all front-line health care professionals delivering screening programmes receive regular training to refresh their communication skills, as well as their understanding of available screening programmes and their associated benefits and risks

Innovations in Screening

19. Throughout this inquiry we have heard about the potential benefits, and concerns about the possible harms, arising from participation in a screening programme. The Committee welcomes the current, on-going research that aims to improve the targeting of screening programmes towards those in higher risk groups. We have previously documented the NHS's resistance to change and therefore consider it imperative that the UK National Screening Committee (UK NSC) and the NHS set out how they will ensure proven developments in screening risk stratification are supported, and where recommended, implemented, as well as how best practice is to be disseminated. We also recommend that the UK NSC is supported by the Department of Health and the Government Office for Science to develop its capacity for "horizon scanning" and to embed it in its operations.

Trustee Profile - Wendy Bascal



Hi, I'm Wendy Bascal. I was diagnosed with GSD Type IIIb in 1973 when I was around 9mths old, following a lot of tests including a liver biopsy which in those days was a full scar.

My symptoms were challenging for my family when I was a child, cornflour wasn't a routine treatment and I had to be 'fed' every 2 hours day and night! I remember going to school with sandwiches for snack, having a cooked lunch and then more sandwiches for afternoon snack. Not surprisingly I'm not a great fan of bread these days ...

As I grew older apart from a large abdomen (which led to me being teased), limited stamina and a short stature, my symptoms were relatively mild. Hypos were not very frequent as I got older and I managed quite well with diet.

Family wise, I have an older brother and sister who do not have GSD. I am married and have 4 children – aged 14, 12, 9 & 5 yrs. I was involved with the AGSD a number of years ago as the Secretary when we had a Committee.

At the 2013 Annual Conference I expressed an interest in becoming a Trustee and was co-opted onto the Board of Trustees at their meeting on 22nd February 2014, and was formerly elected by the membership (in my absence) at the Annual Conference a few months ago in October 2014.

A little bit about my life outside of GSD – I have always had an interest in healthcare, perhaps unsurprisingly, and worked first as an Occupational Therapist in mental health and more recently I qualified as a midwife. Last year I started my own business providing midwifery advice and support and I continue to do 'bank' shifts at my local hospital.

I am lucky to have found Type IIIb quite 'mild', so much so I sometimes forget I have it, and with no real outward signs many of my friends don't know I have the condition until I tell them. The down side to that is that I find myself overdoing it perhaps in a bid to prove I am just the same as everyone else! In the last 2 years I have developed scars on the liver and it has made me stop and think about looking after myself a bit more and educating others.

I am passionate about making sure those with GSD get everything they need, be that getting an accurate diagnosis, advice on the correct diet and other treatments or, emotional support from others who have experienced what they are going through. The AGSD is going through a major transition and I am excited to be a part of that.

Last year I also agreed to help the Type III co-ordinator but due to changes in circumstances I have found myself taking on more of that role. It is unrealistic for me to do both justice and I would appreciate others with Type III coming forward to become part of a 'team'.

Introducing Abbie Maguire

Introducing Abbie Maguire
Coordinator for GSD 0 (Glycogen Synthase Deficiency)

My diagnosis began in 2001, when I was six years old, and it followed a childhood of severe hypoglycaemic and ketoacidosis episodes and seizures. As I grew older, my disease became harder to manage, and my hypo awareness began to suffer, so I started reaching out to other people with GSD, and have met some incredible, inspiring people.

I became a Type 0 Coordinator in January 2015, alongside reading for a degree in Phonological and Phonetic Linguistics. It's an honour to be involved in this fantastic support network full of very brave individuals - although we have yet to find a cure, we can all beat this disease in our own way.

AGSD-UK Annual Conference 2015

Wyboston Lakes Training Centre, Great North Road, Wyboston, Bedfordshire, MK44 3AL - Weekend of October 10th and 11th 2015

The conference this year is returning to Wyboston Lakes Training Centre. For those who attended the conference here in 2012 please note that we are not using the Executive centre this year, but the Training Centre which has more accessible overnight accommodation but has slightly smaller conference facilities.

We don't have a complete programme for any of the workshops as yet, but we do have confirmation from Dr. Ulrike Steuerwald from the Screening Laboratories in Hannover; she would like to share her experiences of working with 16 Faroese GSD IIIa Patients for the last 20 years.

Provisional Programme:

Saturday

Noon: Registration and buffet lunch
Welcome
GSD Type-specific workshops

8pm: Conference dinner

Sunday

9:30 AGSD-UK Annual General Meeting
AGSD-UK Development update
GSD Type-specific workshops

1:30 Buffet Lunch

Conference close

Provisional workshop programmes will available for download closer to the event: Hepatic Workshop
Late-Onset Pompe Workshop
McArdle Workshop

Please visit our website for updated information: www.agsd.org.uk/tabid/2502/Default.aspx

Registration and bookings:

You must register in advance and a booking form is included with this issue of Glisten. An online version will also be available in the near future.

For further guidance please contact the office on 0300 123 2790 or email allan.muir@agsd.org.uk

Research Update

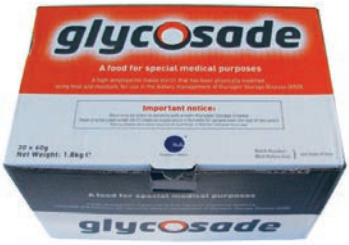
The US National Institutes of Health has a website that maintains a list of clinical trials being undertaken around the world. Below is a selection of studies of interest to the hepatic GSD community.

Anyone can visit clinicaltrials.gov for regular updates and use an appropriate search term to find studies that may be of interest, e.g. ("study number", "GSD", "McArdle", "Pompe").

NCT02318966: Glycosade vs. Uncooked Corn Starch in the Dietary Management of Hepatic GSD

Principal investigator: Helen MUNDY, Guys and St Thomas NHS Foundation Trust.
Sponsor: Vitaflo International, Ltd

This investigator initiated study aims to establish if Glycosade® improves the dietary management of GSD. The trial is a randomised double blind cross over study comparing the short term changes in blood glucose, insulin and ketone levels of patients with hepatic GSD (Types I, III, VI and IX) following equivalent intakes of carbohydrate provided by UCCS and Glycosade® supplied by Vitaflo International Ltd, with the aim of identifying a starch which provides the greatest duration of normal blood glucose levels for each patient.



Glycosade has been reported to increase the duration of euglycaemia.

NCT01961076: Overnight Feeding Study in Glycogen Storage Disease Type 1

Principal investigator: Giatgen Spinas, Prof MD, University Hospital Zurich.

We will compare the efficacy of different oral nutrition regimens for night-time glucose control in adult GSD 1 patients. Three different over-night nutrition regimens (=interventions) will be compared in each patient sequentially, (1) uncooked corn starch (UCSS, "Maizena"), (2) modified corn-starch, (3) other carbohydrate (starch) containing meal. During each intervention, glucose profiles will be continuously monitored by continuous glucose monitoring (CGMS). The duration of each intervention is 3d (minimum) to 6d (maximum), depending on the quality of night-time glucose control and the technical quality of glucose sensor readings. Between the interventions, the patients follow their normal prescribed diet.

NCT02176096: Comparison of the Effect of a Novel Starch (Glycosade) Versus Gastrostomy Tube-Dextrose Infusion on Overnight Euglycaemia Control in Children with Glycogen

Storage Disease Type I

Principal investigator: Dr. Aizeddin (Aziz) Mhanni, University of Manitoba, Canada.

The objective of this demonstration project is to compare a novel long-acting starch, Glycosade, a hydrothermally processed high amylopectin maize starch, versus gastrostomy tube-dextrose infusion in maintaining euglycaemia overnight in children with GSD-I.

Glycosade has been reported to increase the duration of euglycaemia. Its slow release and longer periods of normal blood sugar achieved would preclude the need for the overnight dextrose infusion and eliminate the need for the surgical insertion of a gastrostomy tube for this purpose. Glycosade also reportedly causes fewer gastrointestinal side effects, thus potentially improving compliance to therapy. The investigators intend to evaluate Glycosade in our patients and determine its efficacy on glucose control, on the length of normoglycemia achieved and to determine if there are reduced side effects in our patients with GSDI

NCT02054832: Sleep and Quality of Life in Patients With Glycogen Storage Disease on Standard Versus Modified Uncooked Cornstarch

Principal investigator: John J Mitchell, MD Montreal Children's Hospital, Canada.

The aim of the present study is to determine if there is a change in quality and quantity of sleep perceived by adults and children with GSD and their parents while starting a modified UCCS (Glycosade) to prevent nocturnal hypoglycaemia. The investigators also aim to evaluate if there is a change in quality of life perceived by adults and children and their parents with Glycosade.

NCT02338817: Clinical Evaluation of a Non-Invasive Hypoglycemia Detector in a Glycogen Storage Disease Population

Principal investigator: David A Weinstein, MD, MMSc, University of Florida.

The Diabetes Sentry device, which is non-invasive and is worn on the wrist, will be used while an inpatient at the University of Florida Health & Shands Hospital. Participants will be monitored for the duration of the observational period on the unit; an expected average will be 24 hours. The device is designed to alarm during periods of perspiration and drops in body temperature. When this occurs, a blood draw will be taken to test for glucose, lactate, and ketone values at those times if there is not an already scheduled clinical care blood draw for normal clinical care.

NCT02057731: Study of Glycogen Storage Disease Expression in Carriers

Principal Investigator: David A Weinstein, MD, University of Florida.

The purpose of the study is to determine whether carrier status for any type of glycogen storage disease (GSD) predisposes the carrier to GSD markers, like high cholesterol, by testing blood, urine, and saliva samples.

Trusts and Foundations

Historically the AGSD-UK has found it quite difficult to attract donations from Charitable Trusts and Foundations, even with professional guidance, however we have had some significant success lately

Large donation from Local Trust

A charitable trust known to Allan and Barbara Muir has recently pledged £5,000 to the AGSD-UK after a selection process involving over 500 applicants. Allan was told by one of their trustees that they particularly like to support local causes.

Given that local interest seems to be so effective, it might be useful to make applications to charitable trusts and foundations in your local area. If you happen to know of one, please contact Allan and he may be able submit an application using your personal story to improve its chances of success.

Astor Foundation

The AGSD-UK was awarded £1000 by the Astor Foundation as a result of an application made by Naked Fundraising in 2014.

Fundraisers

Thanks to all of our hardworking fundraisers who strove to support the Association throughout the winter months.

If you would like to hold your own event please contact Allan who can help you by supplying sponsor forms, T-Shirts or letter templates to give to local stores and businesses for raffle prizes, for example.

Skydivers

On 6th December last year, at the Brackley skydiving centre, Robert McKenna, Scott Holden, Rocky McGee, Rossi Grinter and Shaun Bolster leapt from 10,000 feet in a Tandem Parachute Jump for AGSD-UK. They jumped in aid of young Harry McKenna who suffers Glycogen Storage Disease Type VI. Together they raised over £1,200 for the association.

Ollerton Fundraiser

The parents of Amanda Porter (Pompe) raised nearly £600 at a charity fundraising event at the end of November. Most of the funds were raised through a raffle that was well supported by Ollerton businesses that donated many valuable prizes.

Great North Run

Lisa Ash raised £500 by completing the Great North Run last year. Lisa works at a school in Darlington where one of her pupils, George Morrison, has GSD I. Lisa's time was 2hrs 45minutes, so congratulations to her on both counts

Lisa's Husband Stephen has accepted our place in the London Marathon this year, so good luck and many thanks to him also.

Painting Sale

Bronte Thomas Bush (13, McArdle) collected £510 for the AGSD-UK through the sale of a painting at a local art exhibition. Bronte is also planning to take part in a sponsored swim in April on behalf of the Association.

Motorbike Club Donation

Sonia Worthy's motorbike club raised an amazing £1500 for the AGSD-UK last December; Sonia made a short speech about the charity when the cheque was presented to her.

Naylor Car Club

Jane and Rob Bream presented their good friends Sylvia and Ed Wilson (Granddaughter Nora has GSD III) with a cheque for £350. Most was raised by a raffle during their car-club lunch at the Breams' house; an additional £70 was raised by Mrs Freda Taylor who sold knitted toys, hats, gloves and tea-cosies on the day.

Friendly Donations

Friends of Carla Woodford (son Joshua, GSD I) handed her cheques amounting to £40 in support of the AGSD-UK. Carla's friend Jenny Liquorice plans to run the Brighton Marathon on our behalf too.

AGSD-UK Events

You'll be aware that the AGSD-UK has been struggling lately to find the financial support it requires to continue its operations in its current form. Our professional fundraising consultants were unable to help us and so we are reverting to our tried and tested methods and we still have places available on our two overseas events – please encourage friends, family and colleagues to sign up; you my be surprised by how many people are looking for such an exciting challenge.

Trek Mount Toubkal

23–27 Sept 2015 - Climb North Africa's highest peak in Morocco

Explore the dramatic and breath-taking scenery of Morocco on this unique challenge. Journey from Marrakech to the Atlas Mountains to ascend Mount Toubkal - North Africa's highest mountain. Trek across spectacular rugged terrain carpeted with cedar and juniper trees. Discover traditional Berber villages clinging to the mountain sides. Camp out under the stars each night. Afterwards explore the imperial city of Marrakech with its bustling central square, fascinating souks and exotic traditions.

A truly unforgettable adventure.

Highlights

- Explore the spectacular Atlas Mountains
- Climb North Africa's highest peak
- Trek through remote Berber villages
- Camp out under the stars
- Discover the imperial city of Marrakech

Visit our website for more information and to sign up for a truly memorable experience.

London to Paris bike ride

22–26 Jul 2015 - See the Tour de France grande finale in Paris!

Cycling from London to Paris is one of the great European bike rides. This spectacular long weekend challenge covers 420km in 4 days. Ride through Kent with sweeping views of the North Downs to the white cliffs of Dover. Then set sail to France for three more action-packed days of cycling.

Encounter historic towns, sleepy villages and rolling countryside en-route. Experience the thrill of riding along wide boulevards and crossing the Seine to finish at the foot of the Eiffel Tower. Then explore Paris and see the grand finale of the Tour de France before taking the Eurostar back to London. Sign up today for this incredible London to Paris bike ride. Have a fantastic adventure whilst supporting AGSD-UK.

Highlights

- See the Tour de France grande finale
- Climb North Africa's highest peak
- Tree-lined route & historic towns
- Finish beneath the Eiffel Tower
- Time to explore Paris

Visit our website for more information and to sign up for this amazing challenge.

GSD Giant Sportive

Road cycling challenge
Sunday 6th September 2015

3 route options - 30, 62 or 100 miles (50,100 or 160km)

The event HQ for the GSD Giant has moved to The Petersfield School in Hampshire. This provides much better facilities as well as improved road and rail links.

New 30 miler for our 30th year

For 2015 the Demon course has been redesigned and shortened to 30 miles (50km).

The Spirit route has also been shortened and slightly flattened to provide a 100km (62 mile) course but retains much of the route and character of previous years.

The Giant century route (100 miles) has been changed radically towards the west to include a short climb onto Portsdown to enjoy fine views across Portsmouth and the Solent. Once it enters West Sussex it reverts to the familiar route running by Goodwood Racecourse and then returning through Fernhurst, Rogate and South Harting.

Visit the www.gsdgiant.org.uk for further details of this challenging sportive.

2016 Events

2016 will be our 30th Anniversary year, and I would love to hear from you, our members and supporters, to see if you have any interesting ideas to make 2016 go off with a bang! I know that I've concentrated on organising cycling events in the past, but the Association is very happy to consider anything that might engage with our supporters and with the public; events that require mental rather than physical effort may be more appropriate for many of us.

Jae's Story So Far – Diagnosing GSD IX

Dan Machin

Jae's first two years had not been the easiest. Like all parents experience, sleep was a rare and valuable commodity but when this continued past the first six months, we were not impressed. More so, the fact that Jae presented with a number of irregularities caused us some concerns. He would vomit on a daily basis (particularly early in the morning when he would also sometimes vomit small amounts of blood), he suffered horrendous nappy rash, eczema , sleep apnoea, had a distended stomach, repetitive viral and chest infections, enlarged tonsils, mood swings and very picky eating habits (especially avoiding milk and fruit products as these would make him vomit). Various medical routes, such as allergies, were pursued by our GPs to no avail. We realised that at his two year review he had stopped growing in height and dropped below the 1st percentile height line. Jae's mum had known that her dad had suffered with some kind of disorder during his childhood, but details were very unclear. He explained what he remembered from his childhood, but at that time knowledge on Glycogen Storage Disorders was very sketchy and he was never told much other than that there was a problem with his liver and that doctors believed it may have killed him as a child. Ungenerously he was described as 'a short fat child who never smiled'. Interestingly, the worst of his

symptoms lessened around puberty and he instinctively learned to regulate his diet to manage his symptoms.

It was around this point that we started trying to find out more. Like anyone who has started researching online, it was a worrying time! You dwell on the worst prognosis and flip from doom and gloom to optimism within a brief conversation. We put it to our GP who unwillingly agreed to refer us to a paediatrician and the genetics team at Sheffield Children's Hospital. After various consultations, we were eventually referred to the metabolic team for screening. Initial meetings in October 2013 were not very reassuring and some well-meant but pessimistic comments left us feeling depressed.

Jae's life expectancy was in question and the screening that had taken place would take months to complete. As parents, we were both in an emotional state and wanted the quickest genetic diagnosis possible. We contacted our local church for prayer and unsuccessfully contacted other hospitals and clinics for possible private screenings.

Jae's mum then found the AGSD-UK website which listed their Annual Conference that weekend in Bristol. As we were in Yorkshire, it would have been unlikely that we would have gone but fortuitously, we were due to go down to Weymouth that weekend for an October half term holiday. The decision was made, short notice reservations were kindly booked for the Saturday conference meetings and a change of holiday plans were designed to incorporate our new hope. We didn't know what to expect but needed to hear some positive news and wanted to gain some more information about obtaining a quicker diagnosis for Jae.

The conference was fantastic. We met so many lovely people in similar situations who were further down the line and flourishing, gained a lot of interesting information and even got to speak to Dr David Weinstein from the University of Florida. It transpired that thanks to Allan Muir (and the AGSD -UK) we were able to stay overnight at the conference and in the morning Dr Weinstein recorded Jae's glucose and Ketone levels, using a monitor belonging to one of the delegates from the Faroe Islands. This, along with a brief family history, and Jae's 'cherub like' presentation gave him a good indication that Jae might have Glycogen Storage Disease type IXa. We felt delighted that our prayers had been answered and left with a greater insight and reassurance that no matter which form Jae had, it would not be as bad as we once thought. Amongst other things, we had made links with other families going through similar experiences, learnt about blood glucose monitoring, learnt about healthy eating plans for GSD patients and also had a kind offer of continued support for Jae from Dr Weinstein.

Just before Christmas we finally got a diagnosis from Sheffield Children's Hospital and it turned out that Dr Weinstein's suspicions of GSD type IXa had been well founded. We have now been able to tackle his hypos, diet and night time regime. As a result, Jae has started to grow in height slightly, his liver has decreased in size and Jae no longer suffers with vomiting, nappy rash or eczema. Jae has also had his tonsils removed and now sleeps through the night with the exception of his medication slot. Finally, Jae is a happier boy!

Due to the autosomal recessive manner of Type IXa, we have had to start testing procedures for other close relatives. Recently we had the good news that Jae's younger brother does not have GSD but big sister Lauren is still considering her options and has not had carrier testing yet. We look forward to

returning to the conference in 2014 where we can reunite with other families and learn more about current research, advice and the future for people with GSD . We are very grateful to Allan and others at AGSD as they were a tremendous source of reassurance, advice and support in a desperately confusing time. I hope that eventually our experiences might be of some help or comfort to others going through the early stages of diagnosis.

Conference Report from the Hepatic Workshop at Wychwood Park.

The following three reports illustrate a range of experiences from delegates attending the hepatic workshop. This year all Hepatic GSDs joined together to share experience and hear from the medical experts.

A personal View

Caroline Calder, GSD VI Coordinator

A Personal Experience of GSD 1 - Martin Grinnell

Martin Grinnell shared his personal experience of having GSD Type 1. This session was one that added great depth to the participants. Martin talked of his experience as a child and through into adulthood. He told his story in a very engaging manor and gave a great insight into his approach to the condition.

His talked prompted discussion on the management of disease that everyone in the room took something from. Martins talk highlighted the challenges of diagnosing GSD and the differences and similarities between 30 years ago, when little was known about GSD, and today where there is more knowledge on the disease but initial diagnosis remains an issue.

Sharing Experiences

Without making the session feel like group therapy we went around the room and introduced our reason for being there! As we went round questions were posed and discussion prompted. With this session being on the second day people were becoming more familiar and the conversation was light and informal. It was fantastic to see both the breadth of experiences but more so the areas in common and connection between all the hepatic GSD participants. The importance of dietary control, the use of cornstarch and patient experiences and practical tips of what helps them was very useful. Throughout it was great to have the participation of Dr David Weinstein from the USA.

Hepatic GSD Publications

We talked briefly about the current publications. There was general consensus that the website needed updating! We were informed that this was in the pipeline and are already starting to see some changes.

We also talked about the development of leaflets. Type III, which is complete, and Type I and VI that are under development.

Hepatic GSD Fundraising

Early in the day we had been presented the finances for the charity. It was apparent to all that more money needs to be generated to ensure the charity survives. The group discussed various ideas – from stamps for cash to cornflour challenges.

One idea that is easy to implement is to ask members where they can to contribute more than the £10 annual fee, and ideally contribute monthly. There is a link on setting up a standing order now on the website.

We all took away the challenge to consider how we can personally contribute. In order to help this we aim to share more detail on ideas, successful fundraising and how the money raised is being used.

Hepatic Workshop Synopsis

Sue Del Mar

Dr Weinstein from the University of Florida attended the conference again. Dr. Weinstein's career has been devoted to the glycogen storage disease since 1998. Initially, his work was performed at Harvard Medical School, but he moved to the University of Florida in Gainesville, FL in 2005 in order to work on gene therapy for the naturally occurring dog with GSD Ia.

Prognosis

Doctor Weinstein presently follows approximately 500 patients with GSD from 42 countries. When he took over care of the GSD patients in 1998, complications were common in the GSD I and GSD III populations, but the prognosis has dramatically changed.

There is increasing evidence that all complications are preventable in GSD 0, I, III, VI, and IX. It is critical to strive for normal laboratory results, and people should continue to work with their medical teams if these are not being obtained.

Pregnancy Update

In 1998, pregnancies in GSD patients were extremely rare worldwide, and none of Dr. Weinstein's patients had given birth. Now 43 babies have been born to mothers with GSD in his

born to mothers with GSD in his program including a mother with GSD Ia with 6 children, a mother with GSD Ib with 6 children, and a mother with GSD III with 3 children. Many more children have been born to fathers in the program.

None of the babies has been born with GSD, and only 2% of the babies have been born prematurely.

All of the babies have been healthy.
An article with recommendations regarding pregnancy management was recently published by Iris Ferrecchia, nurse at the University of Florida who also has 3 children with GSD Ia.

Glycogen Storage Diseases GSD VI & IX

Many more children with GSD VI and IX are now being discussed. Since protein and fat can be used to maintain blood glucose concentrations in GSD VI and IX, they clinically appear milder, and it is easy for the diagnosis to be missed. Recent work demonstrated that they are much more common than previously appreciated, and the diagnoses must be considered in any child that has 2 or more episodes of hypoglycaemia. GSD IX alpha is one of the most common causes of hypoglycaemia in boys. GSD VI must be considered in the UK since all type VI patients in the United States have been found with Scottish heritage. While milder typically than GSD I and III, GSD VI and IX must be treated with intense treatment. Most Dr. Weinstein's group and Dr. Mundy's team from London have demonstrated that treatment improves growth, stamina, and helps prevent future problems. Some patients without treatment have developed cirrhosis, but treatment with high protein and cornstarch appears to prevent those complications.

Future of GSD – New Starches

A recent study of long-term use of Glycosade in patients with GSD treated in Florida demonstrated very good success. In the United States, Glycosade is only used for treatment of GSD at night and in patients over 5 years of age. A new international study for daytime use of Glycosade will commence soon with doctors from the UK, USA, and the Netherlands. In addition to studying Glycosade, a new cassava root starch has been identified by the GSD team in Porto Alegre, Brazil. Recent testing by the teams in Brazil, the Netherlands (Groningen), and Florida revealed that cassava root product may last longer than any product presently available. Formal studies in humans will be beginning soon.

Future of GSD – Gene Therapy

While people with GSD are doing well, the ultimate goal is to treat or even cure it. Gene therapy work continues to progress around the world and success has been demonstrated in the United States and France in animal models of GSD Ia and GSD Ib. Based upon the success in treating the dogs with GSD, the team is Florida is pursuing FDA approval for a human gene therapy trial for people with GSD Ia. GSD Ib gene therapy work continues to be performed in the United States in mice. GSD III mice were recently created in Taiwan and Italy, and curly hair retrievers with GSD III are being studied at Duke University. Mice with GSD VI also are being created by Laurie Brown in Florida.

Discussion Regarding Diet

The glycogen storage diseases are still primarily treated with diet. There still lacks full consensus regarding diets, but some advice is as follows:

- All types of the liver forms of GSD should avoid sugar
- While carbohydrates such as pasta, brown rice, lentils, porridge, sweet potatoes, yams, plantains are good, too much leads to excessive weight gain and glycogen storage.
  In Florida, recent work with restricting carbohydrate meals to 30 grams in all types of GSD has resulted in significant weight loss without sacrificing metabolic control
- Avoid fruit and fruit juices in GSD Ia and Ib as fruit sugars go directly to the liver. In GSD III, excessive fruit intake can lead to excessive storage of glycogen in the heart.
  Vegetables are much better as they have less sugar and also a fibrous content.
- Dairy intake should also be restricted in GSD Ia and Ib, but hard cheeses are allowed since they have minimal dairy sugar
- Use vitamin supplements
- Belvita breakfast biscuit are good
- Most heptatic GSD patients like spicy, sour, salty, food
- Never drink Lucozade, Coca-Cola etc
- Glycosade during the day must be used with careful monitoring since the experience has been mixed. Daytime use is not recommended at this time in the US.

Exercise

It is very important to take exercise. Dr Weinstein showed photographs of his patients before and after they had kept to the diet and also taken exercise. The difference in body shape was amazing.

Final Recommendations

- Try to keep blood sugar levels above glycogen breakdown i.e. over 4.2 mmol/L
- Avoid Lactic Acid production, ideally keep it below 2.2mmol/L in GSD Ia and Ib
- High protein (over 3 g/kg) is usually required in GSD III
- Aim to normalize prealbumin* in

GSD 0, III, VI, and IX

- Do not eat excessive pasta say 30 grams per meal
- Keep triglycerides below 3.5 mmol/L (without medications)
- Keep cholesterol below 5mmolL
- Strive for normal laboratory studies
- Citrate supplementation prevents kidney stones in GSD Ia

*A prealbumin screen is a blood test to see whether you are getting proper nourishment from your diet. Specifically, the test finds out if you have been getting enough protein. Prealbumin is a protein that is made mainly by your liver. Your body uses prealbumin as a building block to make other proteins.

Hepatic Workshop Report

Kastur Pindolia - Dr David Weinstein – Research developments

Dr Weinstein opened his talk by saying that despite improvements in therapy for hepatic GSD, hypoglycemia and long-term complications remained common. However he believes that with the correct metabolic control (especially diet) that many complications can be avoided. In particular he cited the following:

- Hepatic adenomas (Ia/Ib)
- Osteoporosis (Ia, Ib, III)
- Anemia (Ia, Ib)
- Splenic Complications (Ib)
- Myopathy (GSD III)
- Cardiomyopathy (III)
- Cirrhosis (IX)
- Growth (0, Ia, Ib, III, IX)
- Obesity (0, Ia, Ib, III, VI, IX)

All types of hepatic GSD can do well with fewer complications (such as adenomas, kidney stones, and renal failure) if treated properly with a good diet and medication control.

By controlling triglyceride levels and carbohydrates consumed body weight can be kept within normal range, similar to someone who does not have GSD.

During pregnancy in GSD 1a & 1b treatment needs to altered and monitored closely. Many patients have gone on to have healthy babies.

Dr Weinstein spoke about GSD III saying that the goal is to provide energy for the muscles without over storing glucose as glycogen.

He also mentioned the Chocolate Bar Book written by the close friend of a young boy with GSD. In December 2014 sales of the book hit $1 Million; funds that will help in the fight to find treatments for GSD. The story was published in Glisten last year.

New research projects 2014/15

Finally Dr Weinstein gave a round-up of projects due to start or complete in the year ahead.

General GSD research

- Testing of new non-invasive continuous glucose meter
- Testing Glycosade therapy for daytime use
- Testing of new non-invasive continuous glucose meter
- Testing new starches

GSD Ia

- Application to the FDA seeking permission to perform gene therapy in humans will be submitted. The future of GSD I gene therapy looks promising and it is hoped to start human trials by 2015
- Studies on inflammatory bowel disease

GSD Ib

- Attempting a trial of an oral medication aimed at treating neutropenia (low white blood cell count – cells that fight bacterial infection in the blood).
- Created new inflammatory bowel disease team aimed at preventing gastrointestinal complications

GSD III

- Expanding studies on the Faroe Islands
- Gene therapy using new animal models- mouse and canine models are being investigated
- Working with the Netherlands on trials aimed at preventing damage during exercise

The role of the Laboratory in GSDs

Dr Ralph Wigley, Senior Clinical Scientist - Enzyme laboratory, Great Ormond Street Hospital

Dr Wigley discussed the variable presentation of glycogen storage disorders and the difficulty of diagnosis. He showed how an initial biochemical investigation can provide diagnostic clues but added that enzymatic diagnosis is not always definitive, particularly when measured in the blood.

There is sometimes high residual activity and there may be tissue-specific

forms (liver, muscle) of some enzymes that can be difficult to measure. Specimen deterioration is also a common problem and so sometimes biopsy and genetic tests are required to confirm diagnosis.

Genetic testing on the increase but enzymology is still required to confirm that a genetic mutation is having an effect.

Characterizing expression of GSD in heterozygous carriers

Tayoot (Todd) Chengsupanimit
GSD Program, University of Florida College of Medicine, Gainesville, FL

Todd spoke about how GSD carriers can potentially have symptoms without actually suffering from the condition. Reviewing oral records of 111 GSD1a Carriers he reported that

- 16% suffered from hypoglycaemic episodes (sweating, shaking, irritability)
- 27% had high cholesterol and triglycerides
- 13% suffered from kidney stones
- 7% had joint pain (gout)

A study of 21 Maltese-Beagles (15 carriers, 6 unaffected) showed significant growth retardation associated with an increase in liver glycogen (2.9 times normal). Other biochemical measurements supported the findings that carriers may exhibit some of the symptoms of GSD.

Todd described results from other studies of GSD Ia, Ib, II, 0, VI and IX that also supported this finding. He concluded that GSD Genetics may not be as simple as current science suggests, and that further understanding of GSD genetics may be critical in the future, when determining treatment strategies or the risk of side effects of treatments.

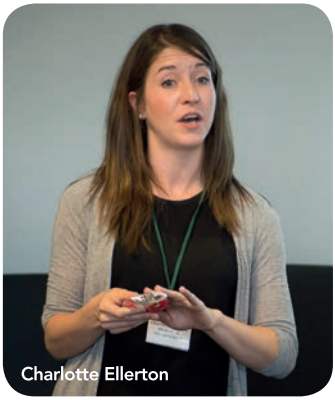
Are all carbs equal?

Charlotte Ellerton and Rachel Carruthers, Metabolic Dietitians

Charlotte and Rachel ran an Interactive and highly entertaining workshop on identifying amount of sugar in various foods we may eat daily.

They began by showing a video illustrating how added sugar to processed foods is bad for you, especially for someone with GSD. They encouraged eating only the naturally occurring sugars in fruits and vegetables. **The video is available on YouTube here: www.youtube.com/watch?v=aCUbvOwwfWM**

After playing a Sugar-Cube game (guessing the amount of sugar in common foods) we discussed different types of sugars and carbohydrates, particularly in regard to their Glycaemic Index (GI). The tables below show foods and their GI and suggestions for improving a typical diet


Charlotte Ellerton

Are all carbs equal? *continued*

Low GI (<55)	Medium GI (56-69)	High GI (>70)
All Bran, Oat porridge, Fruit & Fibre	Shreddies, Weetabix, Ready Brek	Cheerios, Cornflakes, Coco Pops
Granary bread, rye bread, pumpernickel	Pitta bread, wholemeal, crumpets	Bagel, French stick, white bread
Brown rice	Basmati, wild, long grain	Bagel, French stick, white bread
Most pasta	Macaroni	
Apples, grapes, pear, orange, mango	Banana, kiwi, melon, pineapple, raisins, figs	Watermelon
Sweet potatoes, yam, plantain	Crisps, new potatoes	Baked, french fries, mashed, boiled, instant

	Current Diet	Suggested Improvements
Breakfast	Rice Crispies and large glass of fruit juice	All bran /Porridge with whole or dried fruit
Lunch	White baguette with tuna and mayonnaise	Granary bap/pitta bread with tuna, sweetcorn and salad
Evening Meal	Grilled chicken with mashed potato, small portion of veg	Grilled chicken with new potatoes/pasta/noodles/rice + large portion of veg/beans
Snacks	Rice cakes Sweets Puffed crispbreads	Oatcakes, Fruit/veg, Yogurt Glass of milk

It was also stressed that it is important to combine a balanced diet with regular exercise.

Psychological support for rare genetic conditions

Jatin Pattni

Jatin spoke about the common themes of how families cope, how individuals react and cope with living with a rare disease. This prompted much discussion and food for thought.


Jatin Pattni

Personal experience of living with GSD 1A

Trushal Pindolia

Trushal described how following the USA metabolic diet guidelines for GSD type 1A has bought his bloods back within normal range. He has also increased his exercise through cycling – he took part in the GSD Giant (50 mile course) last September, beating all of his friends and family to the finish line.

Essentially the dietary modifications involved switching to lactose-free products (milk, butter and cheese) and eating no fruit but more fresh vegetables.

His metabolic control has improved measurably as shown in the results he presented here:

Before following the US guidelines

- Triglycerides: 14 mmol/L
- Cholesterol of 8
- High Insulin levels
- HbA1c* level nearing diabetic diagnosis range.

After 6 weeks of the new diet

- Triglycerides: 3.4 mmol/L
- Cholesterol of 4.8
- Insulin levels came down
- HbA1c level decreased considerably.

* The term HbA1c refers to glycated haemoglobin. By measuring HbA1c, clinicians are able to get an overall picture of what your average blood sugar levels have been over a period of weeks or months.

Euromac Registry opens to applicants

After several years of lead up, grant applications, planning and software development, the Euromac Registry is finally now open for the first applicants. As well as McArdle Disease (GSD V) it also covers the other very rare muscle glycogenoses such as GSD VII (Tarui), but excluding GSD II (Pompe) which has its own registry. Initially it is open to patients from the Euromac member countries, which include the UK where registration will be made via the McArdle Disease Service in London. It is hoped that it will be expanded to other European countries and eventually become a worldwide registry.

Bringing together patients from across Europe into one registry will enable analysis and research on that data. It will also be a resource for the selection of suitable participants in future multi-centre trials. As an ultra-rare disease, it is necessary to have multi-centre trials in order to increase participant numbers to a statistically valid level. There are a number potential trials in the pipeline, so having the registry populated with patients is an important step towards hoped for future treatments or even a cure.

Another objective of Euromac is to establish standards of care (covering diagnosis, management and emergencies) and to promote those across Europe. AGSD-UK is a partner in the Euromac project and Andrew Wakelin is in charge of the "Dissemination" work package. Euromac leaflets and exhibit displays have been produced. Our "101 Tips" book and "Reference for GPs" booklet are being produced in eight other languages.

Most McArdle people in the UK now have genetic (DNA) confirmation of their diagnosis. If you have not got that yet, it will need to be done before you can join the registry. It only requires a blood sample and can be organised via the McArdle service.

In the coming weeks everyone will receive a Patient Information Leaflet and a Consent Form. If you wish to be entered into the Registry, please read the leaflet. If in agreement, please complete, sign and return the consent form in the reply paid envelope provided.

For a video about Euromac search YouTube for "Euromac registry introduction", or for further information visit the web site: www.euromacregistry.eu

McArdle's news

- The Patient Liaison Panel for the McArdle's Service met in February and also listened in on the annual report of the service to the NHS commissioners. This was useful to gain a fuller understanding of the whole service rather than just the clinic.
- I attended a Euromac meeting in Madrid in February and reported on my Dissemination role. The registry is now open.
- I shall be speaking at a scientific meeting of the French GSD association in Paris on 28 February, which is addressing GSD Types V and III.
- I have been invited to present at the German Association's AGM on 28/29 March.
- The Sodium Valproate trial is now assessing the recruited participants in London and Copenhagen.
- A small trial of a protein supplement is currently underway in Denmark.
- In April we have a three-day workshop in Amsterdam, sponsored by the European Neuromuscular Centre and Euromac. This will be the start of the international standards of care for diagnosis and management. I shall be presenting on the patient perspective.
- This year we will run a walking course again, from 23-30 July, see details elsewhere in this newsletter.
- In Italy Dr Andrea Martinuzzi has now run three of his own courses, on a slightly modified basis, and plans to do more.
- The French and German associations are looking into putting on courses.
- Our '101 Tips' book is now available in German and French editions, with Spanish and Italian on their way.
- We have had 6 children in the UK under the age of 17 diagnosed in the last 12 months, a huge increase on the usual levels (normally one every few years).
- We have started a private Facebook Group for the parents of children diagnosed with McArdle's, to focus on the issues that affect them. 35 members from around the world to date.
- In August we are holding a get- together for the

Andrew with Dan Chambers, backpacking to the Minarets, Sierras, California, September 2014

people who were involved in "Walk over Wales" in 2010, as this is the fifth anniversary. Those who have attended the walking courses are also invited. That week a group of us plan to take up the sponsored challenge of climbing the "Welsh 3000s" – the 15 peaks over 3,000 feet.

- There are currently 242 of us diagnosed with McArdle's in the UK. That is an increase of around 40 in the last year. Some of those have been diagnosed for a long time but never been in touch before.

Andrew Wakelin - GSD Type V (McArdle's) Co-ordinator

McArdle's walking course

For the fifth year running we are offering a one-week residential course of level and downhill walking for McArdle people. Course members have previously attended from 12 countries

Dates are 23 to 30 July 2015, cost is £320 with concessions available.Full details and a booking form are on the AGSD-UK web site, McArdle's section.

This is an opportunity to meet other people with McArdle's, swap experiences and walk together to compare notes. Walks are set each day to suit the abilities of the group, and there is a support car to pick you up if you find you have done enough for the day. We can help guide you in a supportive and encouraging atmosphere, with no worries about embarrassment or competition.

We stay in a comfortable converted farmhouse with single en-suite rooms near Capel Curig, in the heart of the Snowdonia National Park.

Film of "Walking with McArdle's"

Last summer we made a 16 minute film of what it is like to attend one of our courses for people with McArdle's. The hope is that it will help to overcome the natural fears and worries that people have prior to attending. As well as giving an idea of what is involved; capturing the encouraging atmosphere; providing some useful tips; and putting over the support and understanding received from other participants; the film also captures some wonderful scenery.

The film has been viewed on YouTube over 350 times so far. It was shown at the UK and US conferences, and is due to be shown at French and German meetings. Euromac is commissioning subtitled versions in eight languages.

In addition to encouraging attendance, we hope that it will inspire other countries to offer similar courses. Already courses have run in Italy and the USA. Courses are in development for France and Germany.

Thanks to Charlotte Knowles of Shoots & Leaves films who made such an excellent job of the production. And thanks to all the course participants who put up with the camera and microphone being relentlessly pointed at them!

To view the film on YouTube search for "Walking with McArdle's", or look for the AGSDUK channel.

Pompe Workshop Report

Allan Muir, Pompe Coordinator, AGSD-UK

The conference in October was a great success for the Pompe community, we had some excellent speakers bringing fresh insights into understanding and management of Pompe disease, and we also had time to discuss many aspects of living with the condition.

IPA/Erasmus MC Pompe Survey

Deniz Gungor, Erasmus MC, Rotterdam

The Erasmus/IPA survey was initiated in 2004, two years before Myozyme was approved in Europe and was initially sponsored by countries represented on the IPA Board, including the UK. Every few years, participants are invited to repeat the survey so that the natural history of Pompe disease, with and without ERT, can be recorded. Deniz ran through the study design and many of the features that affect mobility and quality of life.

Deniz Gungor

One significant problem she reported was that of fatigue, two thirds of the Pompe population report that fatigue is the most disabling symptom of the condition.

Another issue that has significant implications for the reimbursement of drug costs in countries around the world was that of survival. The study was able to show that survival is significantly improved over the 8 years since treatment became available.

The Survey has also been useful in highlighting the beneficial effects of Newborn Screening and for calculating the overall burden of disease, something that is of interest to the health economists.

If you would like to sign up to the Erasmus/IPA Survey you can do so via Allan Muir or by writing directly to Chris van der Meijden (c.vandermeijden.1@erasmusmc.nl) at the Erasmus Medical Centre in Rotterdam.

Pompe Disease and Pain

Dr. Mark Roberts, Royal Salford NHS Foundation Trust

Dr Roberts noted that an Erasmus MC Pain Survey had highlighted pain as a significant feature in Pompe. The survey showed that of 124 patients, 45% had experienced pain in the previos 24 hours, as opposed to 27% in 11 control subjects. He described the various mechanisms that cause pain, including Biomechanical compensation

(predominantly spinal misalignment) and Myalgia. Dr Roberts presented data that illustrated how scoliosis was associated with increased muscle weakness (upper and lower extremities and trunk), scapular winging, wheelchair use and joint contractures, when compared with patients without scoliosis. The biomechanical back pain is believed to be caused by some muscle groups over-compensating for weakness in others.

It is unclear what causes myalgia in Pompe; it may be due to differential shearing of muscle fibres, Myotonia (delayed relaxation, or prolonged contraction of the skeletal muscles after voluntary contraction or electrical stimulation), inflammation or mitochondrial dysfunction. Myalgia may also originate in the central nervous system and Dr Roberts quoted the gene-therapy work by Dr Barry Byrne (University of Florida) that seems to show how nerve stimulation is improved by clearing glycogen within nerve fibres and neuromuscular junctions.

In conclusion Dr Roberts suggested that all forms of pain should be considered when studying Pompe disease, including itching, and discussed on-going reviews and studies to investigate this symptom more closely.

Newborn Screening

Prof Simon Heales, Great Ormond Street Hospital

In an enthusiastic, entertaining and dynamic style, more associated with Michael McIntyre than a professor of chemical pathology, Prof Heales ran through the rationale for Newborn Screening and highlighted some of the issues ahead and work to be undertaken in preparation. His key points were:

- It is well documented that early implementation of treatment is associated with better outcome, particularly with infants
- Methods are becoming established that may enable high throughput screening for many Lysosomal Storage Diseases (LSDs) including Pompe
- Incorporation into existing screening programmes needs careful planning
- Access to an enzyme laboratory may be necessary for second tier testing to reduce the number of false-positive results
- Identification of specific and predictive biomarkers may improve ease of adoption into a newborn screening programme. This may be necessary to distinguish between infantile- and late-onset Pompe diseases
- There will be other factors to consider following a positive diagnosis, for example CRIM (Cross Reactive Immunologic Material) status will help to determine the best treatment protocol to follow for infantile-onset diagnoses
- Pilot studies will be required for proof of principle of any methods proposed before Pompe can be added to the list of conditions screened

Mindfulness

Annabel Rajgor

Annabel uses Cognitive Behavioural Therapy in her professional work, and whilst confessing to be no expert on the subject of "Mindfulness" she gave an extremely interesting and relaxing workshop on how to fully appreciate the smell, taste and texture of a single sultana!

Whilst I expect that everyone in the room felt the benefit of such a brief introduction to the subject, it may be that further development of the techniques could be of considerable benefit to anyone living with Pompe disease, given the oft-reported feelings of anxiety, depression and fatigue associated with the condition.

A Wearable Device to Monitor Diet and Exercise in Pompe Disease

Manuela Corti, University of Florida

Manuela gave an overview of the work she is involved with at the University of Florida's Rare Disease Research Laboratory. She concentrated on the importance for Pompe patients to consume appropriate nutrition and to balance their intake with regular exercise.

People with Pompe will experience rapid falls in plasma amino-acid and glucose during fasting periods; both are involved in processes related to energy, recovery, mood, brain function and muscle strength gains.

Examples of what lack of exercise might lead to include muscle weakness, fatigue, muscle atrophy, contractures, reduced bone density, diminished respiratory capacity and back pain.

To help their patients comply with their prescribed Nutrition and Exercise Therapy (NET) programmes, the "Plus" team at UF have developed a medical fitness application for smartphones that integrates with an activity tracking device (e.g. FitBit, Apple Watch, etc) with three objectives in mind: 1) Weight-gain, 2) Build strength and 3) Increase endurance.

The phone App tracks progress with the patient's exercise and food intake and provides feedback to the healthcare provider via a web application, the PLUS Web Portal.

The team are currently using this technology in a study, but for the time being Manuela concluded that:

- A program of daily exercise and diet might be useful to reduce symptoms in Pompe disease
- A medical fitness application with an activity tracker might be a useful tool to improve monitoring and enhance compliance
- A G-tube might be needed to improve nutritional requirements in severe cases of patients with very low body mass index (BMI) and respiratory symptoms

Nutrition and Exercise Therapy (NET) phone app and web portal

Exercise in Pompe Disease

Steve Dando and Nicola Condon, National, London and UHB

Steve and Nicola gave a double act summarising the principles of exercising and stretching for Pompe disease. Below is a summary of their general advice:

Exercises should be:

- **Planned:**
  - Set aside designated time to exercise
  - Find time during your day to exercise
- **Structured:**
  - Taking into account your limitations
  - Allocated rest periods to enable recovery
- **Repetitive:**
  - Leads to improvement which enables progression
  - Allows you to improve technique
- **Goal orientated:**
  - Goals should be personal and realistic
  - Should provide a source of motivation

Benefits of exercise

- Prevent muscle shortening which can lead to tightness and contracture
- Increase/maintain functional independence
- Inhibit the use of compensatory movements
- Improved balance and confidence when mobile
- Improve respiratory function

Principles of exercise

- Do not exercise to fatigue, avoid intense levels of exercise – remain within 70% of your capacity
- Use the 20 point Borg Scale – no higher than point 13, "somewhat hard"

- Allow sufficient rest periods between sets during your exercises
- Perform two sets of each exercise
- Exercise little and often – 3 x a week with full "rest" day in-between
- Incorporate stretches into your routine to improve recovery and maintain muscle length

Examples of suitable exercises

- Low-intensity resistance training
- Swiss Ball
- Thera-band (large elastic band)
- Cycling
- Cross-trainer
- Vibration therapy
- Pilates/Yoga
- Hydrotherapy
- Swimming

Principles of hydrotherapy

- Upright posture with full body awareness – reduces compensatory movement
- Being deeper in the water will be more supportive to the body when exercising
- Moving the limb slowly through the water will be easier than if its done faster
- Floatation aids can be used to create buoyancy on the surface and provide resistance when submerged
- The support of the water may make some exercises feel "easy" – be cautious when leaving the water

Principles of stretching

- Focus on the muscles / joints that cause most problems with mobility in activities of daily living
- Easier and safer to stretch when your muscle or joints are warm
- Stretch the muscle slowly to the point of stretching sensation not pain – repeat 2-4 times
- Hold each stretch for 30-60seconds; don't 'bounce'!
- Try to incorporate in daily routine

Emerging Therapies: Diaphragmatic Pacing and Gene Therapy

Barbara Smith, University of Florida

Barbara Smith gave a comprehensive overview of progress being made at the University of Florida in research that she presented at our conference in 2013. Much of their research was inspired by the poor performance of Pompe infants who did not respond well to Enzyme Replacement Therapy (ERT), the team have been trying to find ways to improve the respiratory response of these children. She began by discussing what the body requires to breathe independently:

Breathing is a little complicated, but we can think about three general areas:

- **Neural Drive:**
  - When breathing is going right, we don't think about it. Stimuli come from nuclei in our brainstem to the phrenic motor nucleus in our spinal cord, then down the phrenic nerve to activate the diaphragm, which is the primary muscle for resting breathing
  - This is called the "bulbospinal pathway"
- **Adequate Muscular Capacity:**
  - Pump muscles – Diaphragm and inter-costal
  - Expiratory
  - Airway dilators
- **Manageable Breathing Loads:**
  - Resistive airflow through the airways
  - Elastic from chest wall stiffness

In Pompe mice it has been shown that there is disrupted communication in the bulbospinal pathway as well as weakness in the respiratory muscles. The situation is further complicated when mechanical ventilators are used in patients because they can reduce the natural drive to breathe.

The rational for Diaphragm Pacing is that it bypasses the neural "traffic jam" from the brain to the diaphragm. Electrodes are implanted in the diaphragm and breathing is controlled by an external pulse generator. Rather than applying positive pressure through a tracheostomy, direct stimulation triggers airflow in through nose and mouth.

At the time of her presentation patients had benefitted from pacing to the extent that they could spend much more time breathing independently, up to 14 hours in one case. Studies continue to assess the benefits of pacing and to see if the benefit continues.

Moving on to Gene Therapy, Barbara explained that it is designed to introduce genetic material into cells to compensate for abnormal genes or to make a beneficial protein. If a mutated gene causes a necessary protein to be faulty or missing, gene therapy may be able to introduce a normal copy of the gene to restore the function of the protein.

A gene therapy product is manufactured with three main components: a vector, a promoter, and the target DNA. A gene that is inserted directly into a cell usually does not function. Instead, a carrier called a vector is genetically engineered to deliver the gene.

In manufacturing a product, the target DNA is implanted inside of the vector. Think of the vector as a bus, driving the target gene into a cell. A vector has to be able to get into the cell, so a non-toxic virus is an ideal candidate:

The vector binds to the cell membrane and enters cell, then the nucleus of cells

- The vector binds to the cell membrane and enters cell, then the nucleus of cells
- The vector then injects the new gene into the nucleus
- The cell can then make the required protein (enzyme) using the new gene

The first human studies of these therapies must be extremely cautious and so doses are smaller than the optimal

therapeutic dose. Small numbers of participants are enrolled and, in this case, participants will be full-time ventilator users.

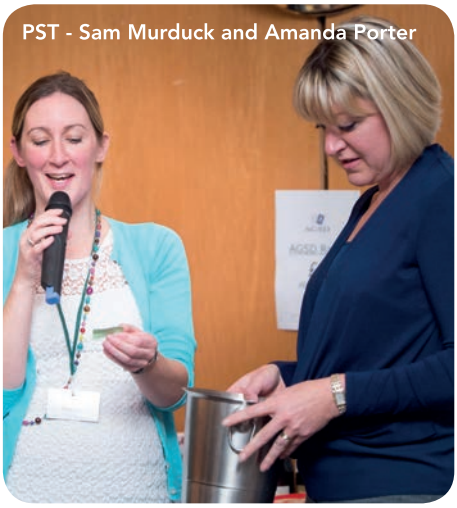
Recapping on earlier studies where GT was administered to the diaphragm of 7 Pompe infants, small improvements in unassisted breathing have been noted in most cases and a very impressive improvement in one child after one year.

For future studies a new study agent has been selected that has a higher neuromuscular affinity. The study will be restricted to one muscle in the lower leg – the tibialis anterior, and will investigate the feasibility of re-dosing with the same agent. The long-tem goal of this work is to develop a systemic gene therapy that will reach all muscles in the body with a single treatment.

Pompe Publications: 101 Top Tips

Pompe Support Team

The Pompe support team led an interactive workshop to develop ideas for a new book we are currently planning. The book will be based on the same format as the AGSD-UK publication **"101 Tips for a good life with McArdle Disease" by Andrew Wakelin. This can be viewed online here: www.agsd.org.uk/tabid/2679/default.aspx**


PST - Sam Murduck and Amanda Porter

Many ideas for the book were collected and it is hoped to publish the book before the conference this year.

Next Generation ERT

Nita Patel, Amicus Therapeutics

Nita Patel presented a company overview and their product pipeline; their Pompe programme took a step back to pre-clinical work after acquiring a Proprietary ERT (AT-B200) from Callidus that they are investigating as a co-formulation with their own CHART (Chaperone-Advanced Replacement Therapy) technology.

Nita introduced the Amicus patient and professional advocacy team who reach out the Pompe community to, for example:

- Gather perspectives on Pompe disease
- Develop patient information and address educational needs
- Support Patient associations
- Promote increased access to healthcare for rare diseases

Amicus have created a Patient Advisory Board made up of international patients and representatives; this complements their Medical and Scientific Advisory Boards.

Nita Patel and the Patient & Professional Advocacy Team

Nita presented a summary of the results from their earlier proof of concept study using CHART AT2220 co-administered with Myozyme concluding that:

- All 25 patients (100%) had increased plasma rhGAA* activity suggesting AT2220 stabilizes active rhGAA enzyme in the blood, thereby facilitating greater uptake into tissues.
- Approximately 70% (16 out of 23) patients had increased muscle rhGAA activity from Days 3 or 7 biopsy samples suggesting more active rhGAA is taken up into muscle.
- Dose-related increases were observed for muscle AT2220 concentrations, however cleared to near unmeasurable levels suggesting low risk for accumulation and consequent inhibition.
- 50, 100, 250, and 600 mg AT2220 were well tolerated; no changes in key safety variables were observed.

*rhGAA is Myozyme, the recombinant human acid alpha-glucosidase enzyme.

Nita briefly introduced AT-B200; the next generation ERT for Pompe. Amicus are confident that AT-B200 has demonstrated significant advantages in preclinical studies that may be further improved by co-formulating with a chaperone. Further preclinical studies are on-going to inform future clinical studies.

Revealing the Pathway to Diagnosis for Late-Onset Pompe Disease

Vivienne Beckett, Genzyme (UK)

Vivienne reported on an online survey of 84 LOPD participants from the US and Brazil in early 2014. The objective of the survey was to "better understand how the Pompe community may be able to positively impact the long diagnostic journey for people living with late-onset Pompe". A great deal of data was presented and below are few key points:

- People with Pompe often minimize early signs
- Symptom variability complicates diagnosis
- Lack of symptom recognition prolongs timeline
- If all Neurologists considered Pompe as part of their differential diagnosis, time to diagnosis could be greatly reduced
- People living with Pompe explain away early symptoms and most do not seek out an doctor
- Globally the presence of new symptoms or increase in severity prompts a visit a doctor
- People with Pompe could see up to 7 different types of specialists before arriving at one who gives a Pompe diagnosis
- The increase in respiratory distress plays a role in receiving a Pompe diagnosis

Key Takeaways

- Most people living with late-onset Pompe disease experience symptoms at an early age but often explain them away for several years until there is a change or worsening of symptoms
- People with Pompe could see up to 7 different types of specialists before arriving at one who gives a Pompe diagnosis
- The increase in respiratory distress plays a role in receiving a Pompe diagnosis
- There is a role for the Pompe community to support individuals and caregivers through increasing recognition of Pompe symptoms and encouraging earlier discussion with their doctor
- As several specialists are involved during the diagnostic journey, it is important to continue global Pompe disease awareness efforts among the medical community

International Pompe Day

Ben Parker, Pompe Support Team

Ben led a discussion that led to the decision to hold a small Pompe meeting at the Coventry Hilton on the afternoon of **April 11th 2015**.

Many people have since decided to remain overnight and have dinner in the hotel that evening. Ben has negotiated the following rates for couples:

Bed & breakfast @ £89.00 per couple per night - Quote AGSDB

Dinner, bed & breakfast @ £97.00 per couple per night - Quote AGSDD

Hilton Coventry
Paradise Way, Walsgrave Triangle
Coventry CV2 2ST
Tel: 02476-603-000

Directions: http://www3.hilton.com/en/hotels/united-kingdom/hilton-coventry-CVTHNHN/index.html

Together We Are Strong
International Pompe Day

BioMarin Programme update

BioMarin Clinical Programme for BMN-701

BioMArin have provided the update below for public release. In it they mention three studies included in their programme, these can be found on the Internet on the clinicaltrials.gov website. You can find the studies by putting "biomarin pompe" into the search box on www.clinicaltrials.gov.

From that website you will notice that there is a study (NCT02191917) at the Royal Brompton Hospital, London investigating "Respiratory muscle strength measurements by different techniques". The Principal Investigator for that study is Dr Michael Polkey.

BioMarin Update to Pompe Disease Clinical Programme January 2015

BioMarin is pleased to update the Pompe patient community on the progress made in our programme to develop a treatment for people living with Pompe disease.

Over the past year, BioMarin has initiated a global clinical development program of BMN-701 treatment in Pompe patients this is currently on-going in over 20 countries. The program includes three studies: a switchover study in patients currently treated with commercially available enzyme replacement therapy (ERT), an observational study in Pompe patients treated or untreated with commercially available ERT, and a study to better understand efficacy endpoints used in clinical trials.

We have decided to move to an updated manufacturing process. This has no reflection on the safety or efficacy of the drug but we believe it will provide better

long-term availability. In order to avoid having to repeat the switchover study to generate the necessary data for regulatory filings, we are pausing enrolment of the switchover study so that the revised material can be introduced.

Enrolment to the study will recommence when new material is ready in the second half of 2015.

Patients currently enrolled and receiving BMN 701 study drug will not be affected by this change and will continue to receive existing study drug. They will have the opportunity to continue treatment in the study with the revised drug once it is available. There are no changes planned to the observational or the endpoint studies and enrolment will continue throughout this period.

If you have queries or concerns about your enrolment or participation in this study please contact your treating clinician or medical team.

BioMarin is committed to the Pompe community and to developing a therapy for late onset Pompe disease. We thank you for your on-going commitment and involvement in this study.

The AGSD-UK Ltd is managed by a Board of Trustees elected by its members at the AGM held each year during our Annual Conference.

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If you have anything interesting for the newsletter we'd be very pleased to hear from you.

A look back at 2014 Conference

AGSD

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