New Book on Gaucher Disease

Edited by Professor Anthony Futerman from The Weizmann Institute of Science and Professor Ari Zimran of the Shaare Zedek Medical Centre in Jerusalem, this book is the first truly comprehensive and multifaceted reference on Gaucher disease. Further details can be found on page 12.

Conference Reminder
Gauchers Association Conference 20th and 21st January 2007

Please remember to return your conference registration and celebratory dinner forms by 31st December if you have not yet done so. If you are attending the celebratory dinner, please ensure that you return your green menu selection form.

Wishing You a Happy and Healthy New Year

Visit Gauchers News on line at www.gaucher.org.uk
**Chairman’s Foreword**


This edition reports in some detail the important presentations made at the EWGDD in July by Scientists clinicians industry and patient representatives from around the world. The meeting was challenging, providing a focus for a robust exchange of views and from a patient perspective this is both encouraging and exciting.

It is encouraging to witness the world leaders debate scientific discoveries and clinical practices to exchange ideas for the benefit of patients and it is exciting to hear of the development of potential new treatments. What is equally important is that such meetings also ensure that the spotlight remains shining on areas of unmet medical need which so badly need to be addressed.

The cessation of the Zavesca trial for type 3 patients is a bitter disappointment to patients and their families and I know that efforts will be redoubled to try to understand the mechanism of the neurological manifestations of Gauchers in an effort to find an effective treatment.

The newsletter again highlights the marvellous work going on up and down the country on behalf of the Association. Thank you to each and every one of you involved in such important work.

I wish all members and their families a happy and healthy new year and look forwards to seeing you in Wembley on the 20/21st January 2007.

With Good wishes

Jeremy”

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**Nadia’s Story: Outings for Type 3 Girls**

Nadia is 12 years old and has Type 3 Gaucher disease. She has just started her first year at secondary school and describes how she feels about having Gaucher’s disease:

‘I was diagnosed with Gaucher’s disease at the age of 13 months. I can’t run or jump or do anything physical because my bones are affected. I have broken my legs quite a few times, although I have been having Cerezyme infusions for about ten years.

‘In the summer I went on holiday with my family, I had lovely time. Unfortunately at the end of the holiday I had an incident and broke my leg again and ended up coming back to England in plaster.

‘Sometimes I feel lonely; I am the only one who has this kind of problem where I live and go to school. Elin Haf-Davies, my nurse at Great Ormond Street Hospital decided to give the girls who have Type 3 Gauchers disease the chance to meet together and talk about things that I cannot discuss with my friends in school.

‘When we meet up in London we also go to some exciting places, like the London Eye and on an open top bus. I always have a great time. In October I was so happy because all of the Type 3 girls together with Elin and Niamh another nurse at Great Ormond Street Hospital visited the Blue Peter studio and watched the show live. I was lucky enough to have my plaster cast signed by all Blue Peter presenters (see picture right).’

**The Girls Go to Blue Peter**

The last edition of Gauchers News described the project ‘Aunty Elin Days’ involving a group of girls who have Type 3 Gauchers disease. Following a successful day out in London in June on an open top bus, the group of girls wrote letters to Blue Peter and asked if they could come to see Blue Peter being filmed. The girls were invited to the BBC studios where they met the Blue Peter presenters and watched the live show being aired on Monday 2nd October.
European Working Group on Gaucher Disease – Seventh Workshop

Prof Timothy Cox welcomes the 250 guests.

250 delegates including physicians and other healthcare professionals, pharmaceutical companies and patient representatives from 18 European Gaucher Associations met at the seventh workshop of the European Working Group on Gaucher Disease at St John’s College, Cambridge on 16 to 22 July 2006. Tanya Collin-Histed provides a taste of some of the major presentations:

‘The seventh Workshop of the European Working Group on Gaucher Disease (EWG/GD) gave an opportunity for delegates to hear up-to-date reports on scientific discoveries, and to discuss their implications in relation to clinical practice. The meeting allowed international scientists and medical professionals to learn from each other and for patient representatives to participate fully. For the first time four pharmaceutical companies and a healthcare company made presentations to the audience about the latest pharmaceutical initiatives. The European Gaucher Alliance (EGA) addressed the audience during a half day session highlighting issues including: home treatment; collaboration amongst patient organisations; clinical trials; the human cost of having a long term condition; Eastern Europe and the management of neuropathic Gaucher disease.’

Welcome

Prof Hans Aerts from the University of Amsterdam and Chairman of the EWG/GD welcomed the delegates stressing the importance of both clinical research and initiatives. The European Gaucher Alliance (EGA) addressed the audience during a half day session highlighting issues including: home treatment; collaboration amongst patient organisations; clinical trials; the human cost of having a long term condition; Eastern Europe and the management of neuropathic Gaucher disease.’

Prof Konrad Sandhoff of the University of Bonn in Germany delivered the keynote lecture, describing the breakdown of glycosphingolipid or glycolipid as it passes through lysosomal membranes. He explained the role of lysosomes in the breakdown and digestion of cellular and intracellular membranes. He said: ‘All cells have membranes. However, it is often forgotten that intracellular structures such as lysosomes and endosomes themselves have membranes. Glycolipids are important components of these membranes and contribute to membrane stability. Clearly it is important that these membranes remain intact and are broken down only when the time is right. But the glycolipids in these membranes are in close proximity to acid lysosomal enzymes. So how do the membranes of the lysosomes themselves remain protected from the enzymes?’

The answer lies in the fact that there are two “pools” of glycolipid-containing membrane; one that is accessible to lysosomal enzymes and one that is not. The second set of membranes is part of the limiting membrane of lysosomes. This is coated by a thick protective layer called the glycolipid, which protects it from attack by lysosomal enzymes.

And how do these membrane glycolipids get degraded? This is achieved by a set of enzymes called saposins or activator proteins. There are four of these, named saposins A-D. They insert themselves into the membrane, attach themselves to the glycolipid and ‘lit’ it out of the membrane. The glycolipid is then easily reached by the respective lysosomal enzyme and degraded.

‘However, this is not the only prerequisite for the breakdown of the lipids. Critical levels of cholesterol and another lipid called BMP are also required. Clearly, membrane breakdown is a complicated, finely tuned process, in which lysosomes play a critical role.’

Therapeutic Goals

Dr Neil Weinreb of the Gaucher Disease-Fabry Disease Treatment Center, Florida spoke on behalf of the International Gaucher Disease Management Board. He described a benchmark for the achievement of therapeutic goals for patients with Type 1 Gaucher disease. Of the 337 patients were chosen from Type 1 Gaucher disease patients enrolled in the International Collaborative Gaucher Group (ICGG) Registry who had been on enzyme replacement therapy for four or more years.

Six clinical parameters were used for analysis: haemoglobin, platelets, liver volume, spleen volume, bone pain, bone crisis. The six parameters varied in the proportion of patients achieving each goal: the bone crisis goal was achieved by 98.8% of patients, haemoglobin by 90.8%, liver volume by 89.9%, bone pain by 74.8%, platelets by 72.7% and spleen volume by 69.4%.

Deficits in Auditory Brainstem

Pauline Campbell of the University of Plymouth (UK) spoke about the emerging concern of auditory perceptual deficits reported in children with Type 3 Gaucher disease.

She explained that the Auditory-Brainstem Response (ABR) when recorded using simple stimuli (clicks or tones) has been shown to be a sensitive measure of neural deterioration in neurometabolic Gaucher disease (MGD). In light of this, the ABRs of Type 3 GD patients were recorded with simple and complex auditory stimuli and examined by her.

Should Society Fund Orphan Treatments?

Ms Hanna Hyry from the University of Cambridge gave an eloquent presentation at the EWG/GD workshop on the debate of efficacy versus equity in dealing with the question: Should society fund orphan treatments?

‘In many public health care systems, spending is prioritised with a view to efficiency - the goal being to maximise the units of health improvement for a given budget,’ Ms Hyry explained. ‘However, professionals agree that efficiency does not always equate to justice and it is impossible not to treat those with a rare disease simply because their disease is rare. Rare diseases fare poorly on measures of efficiency because of the high cost of treatment and relatively poor gains in length and quality of life. Equity then, represents an alternative strategy to efficiency.

‘Rather than a utilitarian approach - the greatest good for the greatest number (J.S Mill) – 20th Century philosopher John Rawls provided the theory of equity within society. This means equality of opportunity, equity provides an individual the opportunity to gain health.

Ms Hyry applied John Rawls’ theory of social justice to the orphan disease setting with particular reference to Gaucher disease. Using this theory she said: ‘Cost effectiveness has no role to play when the choice is between an expensive treatment and no treatment at all. Rawls’ theory is a challenging alternative to understanding the meaning of societal obligations to the individual, and applying this model poses a particular challenge to the issue of pricing orphan drugs in the UK.’

Ms Hyry will present the thesis at the Gauchers Association’s Conference on 21 January 2007.

Patient Presentations to Professionals

For the first time at a European Working Group on Gaucher Disease workshop, patient representatives of the European Gaucher Alliance were allocated an entire morning at a central time of proceedings to make presentations on a number of important issues.

Overview

Jeremy Manuel OBE, co-founder of the European Gaucher Alliance (EGA) and Chairman of the UK Gauchers Association, opened the session by quoting a Lennon/McCartney song entitled The Long and Winding Road: ‘Many times I have been alone, many times I cried’.

Today 24 European countries have thriving patient associations dedicated to helping those with Gaucher disease,’ he said. He reminded the audience of this voyage, stressing the importance of the meetings of the European Working Group on Gaucher Disease held every other year since 1994. He also reported the growing strength of the European associations including the two German patient organisations with more experienced groups with fl edgling ones. ‘Not least was the part played by the European Gaucher Alliance in encouraging Genzyme to develop its humanitarian aid programme European Cerzeza Access Programme (ECAP) in Eastern Europe.’

Nordic Alliance

Anita Grethe Lauridsen, President of the Danish Gaucher Association talked about collaboration between Norway, Finland and Sweden and the development of a Nordic Alliance to support patients with Gaucher disease. She said: ‘In the Nordic countries there is a long tradition of working together across borders. Even though we speak different languages, we can still understand each other. This is a remarkable achievement when you remember the history of all the people in these countries. We are all at war with our Gaucher disease. She said: ‘In the Nordic countries there is a long tradition of working together across borders. Even though we speak different languages, we can still understand each other. This is a remarkable achievement when you remember the history of all the people in these countries. We are all at war with our Gaucher disease.’

Home Treatment around Europe

Dagmar Bartosikova from The Czech Republic and Marianna Popovici from Romania shared their personal experiences of receiving enzyme replacement therapy at home in their countries and the impact on patients when there is no provision for home treatment. Marianna described her 12 hour journey to Cluj every two weeks when she first received therapy.

Linda Richfield, Clinical Nurse Specialist, Lysosomal Storage Disorders Unit, Royal Free Hospital, London talked about homecare services in the UK. She described a survey of UK patients receiving home treatment. The results showed that patients felt their receiving their treatment at home was more convenient, less stressful, allowed treatment to be integrated into normal daily living and reduced the impact of treatment on work, education and family life.

As a result of their presentation the EWG/GD have agreed to establish a European Working party to develop guidelines on Home Infusions.

Neuropathic Gaucher Disease

Dr Ashok Vellodi, Metabolic Consultant at Great Ormond Street Hospital for Children was invited by the EGA to present an update on the Taskforce Guidelines for the Management of Neuropathic Gaucher Disease which were published in 2001. A report of his presentation is given on page 15.

Continued on page 6

Hanna Hyry

Gauchers Association Newsletter

Gaugers Association Newsletter
The Cost of Gaucher Disease

Susan Lewis, co-founder of the EGA and Honourary Life President of the UK Gauchers Association, was unfortunately unable to give her presentation at the EWGDD meeting in Cambridge, on the financial and human cost of Gaucher disease. Jeremy Manuel gave her presentation:

‘A group of scientists at St. George’s Hospital in London have been working with the Royal Free Hospital to investigate the flexibility and membrane properties of red blood cells in patients with Gaucher’s disease. Dr Alph Mehta, Haematologist Consultant at the Royal Free Hospital, London writes:

‘Red cells carry oxygen around the body and they have to negotiate small blood vessels, some of which are smaller in diameter than the red cell itself. The cells therefore have to be able to squeeze through small capillaries and release oxygen into the tissues. Red cells expend energy in maintaining their membranes in a flexible condition such that they are able to squeeze through the capillary circulation. We do not fully understand the functions of the spleen, but one important spleen function is to maintain the flexibility of the red cell membrane. The lipid composition of the membrane is also important in maintaining its flexibility. Gaucher’s disease is due to a deficiency of an enzyme involved in breaking down lipids. Some of these lipids derive from red cell membranes; furthermore, the lipid composition of red cell membranes in Gaucher’s patients is abnormal.

Study Details
Dr Bridget Bax of St. George’s Hospital London and her colleagues chose to study four subject groups; patients with Gaucher’s disease with an intact spleen who were receiving enzyme replacement therapy, Gaucher’s patients with an intact spleen not receiving enzyme replacement therapy, patients with Gaucher’s disease who had undergone splenectomy (all of these patients with Type 1 Gaucher’s disease do not know the cost of their treatment) and thus creates stress of a different type caused by worry about cutbacks and adverse public and media opinion.’

The Findings
‘The capacity of red blood cells to clump together (erythrocyte aggregation) was increased in all patients who had undergone splenectomy. This feature was common to Gaucher’s and non Gaucher’s patients. In addition, however, the deformability of red cells was reduced in Gaucher’s patients lacking spleen, but not in the non Gaucher’s patients who had undergone a splenectomy. The lipid composition of the red cell membrane of Gaucher’s patients is known to differ from non Gaucher’s patients and these differences may well contribute to the reduced deformability of the red blood cells.

‘These changes might lead to significant alterations in the flow properties of the red blood cells of Gaucher’s patients. It is known that patients with Gaucher’s disease are more likely to develop blockages in the very small capillaries. This could contribute to the bone changes and also to changes observed in the lungs.

‘Enzyme replacement therapy did not appear to make any difference to the intrinsic properties of the red blood cells. Further studies are planned.

‘It would be interesting to see what Miglustat (Zavesca), the oral treatment for Type 1 Gaucher’s disease, has on the red cell deformability. One would predict that Miglustat would normalise the red cells since its action is to alter the synthesis of the membrane lipids.

Future Study
‘An ambitious long term aim of the St. George’s group is to use the patient’s own red cells as a means of delivering enzyme replacement therapy. This technique is already being used to deliver other enzymes to patients with immune deficiency. The rationale is that the patient’s own red cells would be removed from the body, incubated and injected with enzyme, and then returned to the body. The red cells would then release enzyme treatment into the patient’s circulation gradually over a period of time.

How Flexible are the Red Cells from Patients with Gaucher’s Disease?

Dr Alph Mehta

European Working Group on Gaucher Disease – continued from page 4

The ABRs were recorded in five children with Type 3 Gaucher disease (five females, 7 – 22 years). An equal number of age- and gender matched children with no known predisposing factors for hearing loss were used as controls. The study was approved by the Ethical Committee of the Academic Medical Centre in Amsterdam, who agreed to the monitoring of the study. The study was open to all members of the family. However for families with Type 3 and even more so Type 2, the future remains unknown and the personal costs are far greater.

Dr Mario Maas of the Academic Medical Centre in Amsterdam, spoke about the importance of monitoring the skeleton in Gaucher’s disease. He explained that radiological imaging is used in patients with Gaucher’s disease to estimate the disease burden, to evaluate the presence of specific skeletal complications and to track response to therapy. He explained: ‘My view is that MRI is currently the best technique for assessing bone marrow involvement in Gaucher disease. Conventional MRI also detects other skeletal complications in Gaucher disease, including oedema (excess fluid) resulting from acute bone infarction, infection and trauma, avascular necrosis, pathological fractures and vertebral compression.’

Between 2004 and 2006, members of the UK Gauchers Association received treatment by the EGA, with co-founder of the EGA Marina Terekhova from Ukraine spoke about the situation in their countries and how through working in partnership with Government, the EGA and Genzyme Corporation, patients had gone from no treatment, to receiving humanitarian treatment through Genzyme’s ECAP, with some patients receiving treatment paid for by their own Governments.

Personal Experience of Clinical Trial
Tanya Collin-Histed of the UK Gaucher Association gave a personal account of being a parent of a child on a clinical trial. She outlined the importance of clinical trials being patient centred and highlighted the anxieties and challenges that patients and their family may cross.

She said that in any clinical trial, three parties are involved: the pharmaceutical company; the investigators (usually doctors and nurses) and the patients. These parties have the same ultimate goal to gain information or to achieve an effective therapy but each also has its own priorities. The impact upon, and the potential benefit to, patients both as a group and as individuals taking part in the trial, must however remain paramount.

‘It is essential to consider how invasive, intrusive or disturbing different aspects of the trial will be and to avoid these elements if at all possible. The expectations of the individual patients involved and their families should be considered at all times and every possible outcome should be addressed before a trial starts. The need to push back the boundaries of human knowledge need to be balanced against the impact on individuals.’

ECAP
As Chairman of the ECAP (European Gaucher Access Programme) Medical Advisory Board, Dr Carlo Incerti of the Genzyme Corporation outlined the development of the programme since its inception in 2004. 101 patients from 13 countries are now receiving treatment by humanitarian aid.

Earlier Jeremy Manuel had quoted Henri termeur, (Chief Executive of Genzyme Corporation) commitment to ECAP patients: ‘Once a patient is on treatment, it is a lifetime commitment’. The ECAP Medical Advisory Board had established guidelines ensuring appropriate management and treatment for patients with life-threatening and severe disease.

European Working Group on Gaucher Disease – in January 2007. The UK Gauchers Association has awarded Ms Campbell a small travel grant to support this project.

Monitoring the Skeleton
Dr Mario Maas of the Academic Medical Centre in Amsterdam, spoke about monitoring the skeleton in Gaucher disease. He explained that radiological imaging is used in patients with Gaucher’s disease to estimate the disease burden, to evaluate the presence of specific skeletal complications and to track response to therapy. He explained: ‘My view is that MRI is currently the best technique for assessing bone marrow involvement in Gaucher disease. Conventional MRI also detects other skeletal complications in Gaucher disease, including oedema (excess fluid) resulting from acute bone infarction, infection and trauma, avascular necrosis, pathological fractures and vertebral compression.’
Third Annual Gauchers Association Golf Day Brings in £15,000

The third Gauchers Association Charity Golf Day was held on 13th September 2006 at Dytham Park Country Club, writes Alan Rosen.

‘The Tournament was organized by Golf Committee members: Sharon and Alan Rosen, Lola, Lane and Clive Bednash. The Committee arrived early to ensure everything was ready for when the golfers arrived. The players registered and then set out in their teams in the glorious sunshine to the course at 1.30pm to commence play. At the half way house, players were served drinks and “Krispy Kreme” doughnuts which were donated by the company.’

‘The day was generously sponsored by Hummingbird Motors who had offered a Mitsubishi car, as a prize for any golfer who scored a hole-in-one – unfortunately no one achieved this, maybe next year!’

‘At around 6pm players gradually returned to the clubhouse with their scorecards completed. They changed for the reception and other dinner guests began arriving. ‘As in the previous two years Martin Chivers (ex Tottenham Hotspur and England centre forward) acted as Master of Ceremony at the dinner. He also helped Sharon and Carl Rosen present golf, raffle prizes and ran the auction of a framed Golf Shirt signed by Chris De Marco.

‘Dinner was followed by speeches from Gauchers Chairman Jeremy Manuel, Alan Rosen and Capt Alan Milligan from the Royal Free Hospital. The day was a great success and raised £15,000 for the Association.’

Fund Raising Events

The Association has been fortunate to receive generous donations from many members and friends over the past six months. The Association is always touched by the way its members, friends and families support patients through organising events, making donations, filling collection boxes and supporting the fundraising on birthdays and wedding Anniversaries and is grateful for all support, writes Treasurer Don Tendell.

Marathon and 101athon raise £1,128

On the 21 May, Anne Ormond and three friends ran the Woman’s B.A. 10K marathon in Glasgow. They kindly agreed to donate the money raised to the Gauchers Association and the Friends Foundation at the Sick Children’s Hospital in Edinburgh. £786 was raised for both charities. £393 was donated by Mr Daniel Long in Memory.

In Memory

Donations have been received in memory of-

Mr Christopher Wood; his sister Pauline had Gaucher disease.
Mr Clive Harries who would have celebrated his 40th Birthday this year.
Mr Daniel Long; Daniel had Gaucher disease.

The Association sends condolences to the bereaved families at this sad time.

Aiden who had Type 2 Gaucher disease, sadly Aiden died in January this year. Aiden was cared for by staff at the Sick Children’s Hospital in Edinburgh.

Nick Rowe who was inspired by his friend Pauline Diaper whose daughter Jade has Gaucher disease raised £735 by completing a triathlon. This sport involves a continuous race comprising of swimming, followed by a cycle, and then a run. Competitors race against the clock, which starts as they enter the swim and stops as they cross the finish line after the run.

Donors

Thanks go to donors: St James Church Cheshunt, Chance Law LLP, St Peter’s First School on Romas Tremain’s retirement, Schon Family Charitable Trust, Gableholt Ltd, Mischon De Reya Solicitors from their dress down day, Stephen Alder, Mr and Mrs Adam Winston, Beareham Charitable Trust. Radlett Horticultural Society, Southgate WIZO, Kenneth Steel, David & Joyce Lithner, S P Charitable Trust.

Wedding Gift of £700

To celebrate the marriage of Maxine to Jeremy Brent guests were invited to donate to the Gauchers Association instead of buying presents. £700 was received.

Educational Seminars donate £200

Alan Rosen and Sueie Noe addressed doctors from around Europe on the role of the Gauchers Association at a lecture at the Royal Free Hospital in July. The organisers donated £200 to the Association to thank Alan and Susie for their time.

Wedding Anniversaries: £320

In celebration of their Ruby Wedding Anniversaries, Mr & Mrs William Sloan donated £200 and friends of Pam and Tony Wray donated £80. To celebrate the Silver Wedding Anniversary of Melanie and Ebardt Lison, Mr and Mrs S Lison donated £50, K Alexander donated £30 and J Supree donated £100.

London Marathon 22 April 2007

In its June 2006 edition, Gauchers News asked for a volunteer to run the London Marathon on behalf of the Gauchers Association on Sunday 22 April 2007. Elin Haf-Davies, a clinical trial research nurse at Great Ormond Street Hospital, has kindly agreed to take up this challenge.

‘I have been aware of the Gauchers Association’s work since I became the clinical trial research nurse for the OGT 918 study in Type 3 Gaucher disease at Great Ormond Street Children’s Hospital (GOSH) four years ago,’ writes Elin Haf-Davies.

‘During this time I have seen how much families benefit from the support offered by the Association.

‘I have worked at GOSH on and off for 12 years now and feel a great sense of pride and loyalty to be part of the hospital, and this has not diminished since I became a member of the metabolic team.

‘I have learned how patients can benefit from money raised to help with research projects, such as the collaborative bone study funded by the Gauchers Association. I am also a member of the European Working Group on Gaucher Disease Neuropsychopath Gaucher Disease Task Force. Through a grant from the Gauchers Association, the Task Force has made tremendous leaps forward in our current knowledge base of Type 3 management. This will ultimately help in the improvement of care and support offered to patients and their families.

‘Over the past four years I have built up a strong relationship with all of the children and young people on the Type 3 OGT 918 trial. Together, Tanya Collin-Histed and I have developed a project called ‘Auntie Elin Days’ which allowed a group of girls with Type 3 Gaucher disease to come together for various activities, and an opportunity to discuss problems and concerns that may be important to them at that time. These days have been tremendously valuable for us as professionals in planning suitable support for the children in the future.

‘Through Tanya’s and the Association’s hard work, it was possible to secure funding from a charity called Wednesday’s Child, the proceeds of the Auntie Elin Days. I would like to take this opportunity to thank the fund raisers at Wednesday’s Child for their hard work and generosity in thinking of children with Gaucher disease.

‘None of all this work would have been possible without the support of the Association. When the opportunity came to run the London Marathon for the benefit of the Gauchers Association, I jumped at the chance! Having recently turned 30, I regularly seek challenges to keep me busy and fit. With Welsh international rugby caps to my name, medals for a few Great South and Great North runs and the experience of cycling from Paris to London, the opportunity to run the London Marathon while supporting the great work of the Association was one I did not want to miss.’

Together with Ward Sister Herdip Sidhu also from Great Ormond Street Hospital we will be taking on our biggest challenge yet when we row across the Atlantic in November 2007 to raise money for metabolic medicine at Great Ormond Street Hospital.

Sponsor Elin

The Gauchers Association is delighted that Elin has agreed to run in the London Marathon and use this opportunity to raise funds for the Association’s work. A sponsorship form has been included with this newsletter. Please encourage your friends and family to sponsor Elin. If you need more than one form, photocopy the sheet or contact Tanya Collin-Histed at the Gauchers office for more copies.

New Offices for Careology Ltd

On 14 October Careology Ltd moved premises to Unit 2-3, Fenchurch Court, Bobby Fryer Close, Oxford OX4 6ZN writes Mandy Wakefield, Director of Careology Ltd.

‘We have been looking for a new base for Careology since July 2005. The site needed to meet all the needs of a specialist clinical service provider and we decided to stay in Oxford so that we could retain our experienced team of coordinators, pharmacy technicians and homecare drivers. We have commissioned extensive work to create a bespoke pharmacy and patient support unit that enables us to safeguard the complex pharmaceutical products that we handle on a day to day basis.

‘The office is open plan with all the directors working alongside the office and pharmacy based teams.

‘We are currently recruiting new team members to ensure that the specialist service that we offer continues to grow and develop. Our single aim remains to provide exceptional standards of medical care to people receiving therapy for complex disorders in their own homes.

‘Our telephone numbers, email addresses and fax numbers have not changed, only the postal address.’
Shire Human Genetic Therapies - Emerging New Enzyme Treatment

In the last edition of Gauchers News, Prof Ari Zimran, Director of the Gaucher Clinic at Shaare Zedek Medical Center in Israel reported that the 9-month Phase I/II results for a new enzyme preparation for patients with Type 1 Gaucher disease, produced by Shire Human Genetic Therapies. Prof Zimran provides a further update on the preliminary results at 24 months:

"Shire Human Genetic Therapies Inc’s enzyme preparation known as GA-GCB is a human glucocerebrosidase which is produced in a continuous human cell line using proprietary Gene-Activated technology. GA-GCB has an identical amino acid sequence to the naturally occurring human enzyme. The preliminary results show significant increases in hemoglobin from baseline (mean increase of 2.44g/dL from baseline; mean percent increase of 21.3% from baseline) and in platelet and liver volume (by 70.9% and 26.9% from baseline, respectively). Similarly, there were significant decreases in the biomarker Chitotriosidase (by 79.7% from baseline) and CCL18 (by 51.2% from baseline).

"Improvements in some parameters were apparent as early as three months after the start of the therapy and patients continue to improve over time." In terms of safety, as of 24 months on treatment, there have been no drug related serious adverse events nor the need for pre-infusion medication. In addition, no patient has developed antibodies to GA-GCB to date.

"Following the results of the Phase I/II trial in adult patients, two global, multi-center Phase III clinical trials will be conducted to determine the safety and efficacy of GA-GCB in children and adults will take place. One study will be for untreated patients and the other study will be for those patients who are currently on enzyme replacement therapy. These Phase III studies will start in the UK and the rest of Europe in the early Spring of 2007. In the UK, Dr. Cox at Addenbrooke’s Hospital, Cambridge and Dr. Mehta of the Royal Free, Hospital, London have expressed an interest in these studies."

In the last edition of Gauchers News, Dr Einat Almon, Vice President Product Development, Protalix Biotherapeutics reported on a new enzyme replacement therapy product in plant cells for patients with Type 1 Gaucher disease. Dr Almon provides a further update:

"Protalix Biotherapeutics has developed a novel plant-cell culture system for the production of active biopharmaceutical proteins. Glucocerebrosidase for enzyme replacement therapy (prGCD) in plant cells culture may offer an interest in these studies."

"A world wide Phase III clinical trial to assess the safety and efficacy of prGCD will be conducted according to FDA guidelines and will be initiated at the beginning of 2007. Leading medical experts of the Gaucher field from EU, UK, USA and other countries will participate in this study coordinated by Prof Ari Zimran from Shaare Zedek Medical Center, Jerusalem, Israel. Dr Raul Chertkoff, former chairman of the Israel Gaucher Association and now Medical Director of Protalix will play an active role in the trial. Protalix advances in production of active glucocerebrosidase enzyme (prGCD) in plant cells culture may offer several advantages in safety, efficacy and cost."

Phase III trial on new Enzyme Replacement Therapy from Plant Cells begins 2007

Dr Raul Chertkoff (left) and Dr Einat Almon at the EWGGD meeting in Cambridge 2006

Results showed that prGCD was well tolerated; no significant adverse reactions were observed showing safety together with a promising pharmacokinetic profile. Prof Anthony Futterman of the Weizmann Institute of Science, presented data demonstrating that the three dimensional structures of prGCD and Cerzyme were practically identical, as were other biochemical parameters.

"A world wide Phase III clinical trial to assess the safety and efficacy of prGCD will be conducted according to FDA guidelines and will be initiated at the beginning of 2007. Leading medical experts of the Gaucher field from EU, UK, USA and other countries will participate in this study coordinated by Prof Ari Zimran from Shaare Zedek Medical Center, Jerusalem, Israel. Dr Raul Chertkoff, former chairman of the Israel Gaucher Association and now Medical Director of Protalix will play an active role in the trial. Protalix advances in production of active glucocerebrosidase enzyme (prGCD) in plant cells culture may offer several advantages in safety, efficacy and cost."
Gaucher disease has proven to be a paradigm for many lysosomal storage disorders. The scientific research and clinical management of the disease has been ground breaking not only for Gaucher patients but also for patients with other such disorders.

The Gauchers Association congratulate Jill and Ian Carter on the birth of their second child Zacharia who was born on 17 July 2006. Shevi has Gaucher disease.

In 2004, Actelion took over responsibility for the miglustat study in type 3 Gaucher disease (GD3). This was an international effort involving two expert centres led by Dr Ashok Vellodi, London, UK and Dr Raphael Schiffmann, Bethesda, USA. The Haemophilia Centre in Addenbrooke’s Hospital, Cambridge: Dr Penny Stein has been appointed to a senior research position within the University of Cambridge but very much allied to the Lysosomal Disorders Unit as a practising clinician. Dr Penny Stein will bring to the group a wealth of scientific research experience in addition to her excellent clinical and personal skills.

In October 31st, the investigators and the Actelion’s team met to review the 24-month results. The final consensus was to end the study as it could not demonstrate effects on the primary end-point of eye movements abnormalities.

The Gauchers Association would like to announce two new appointments to the group, writes Dr Patrick Deegan, Consultant at Addenbrooke’s Hospital, Cambridge:

‘Sister Jane Tindall, familiar to many of the readers of the newsletter for her involvement with the Bone Research Project, has taken up a position within the Addenbrooke’s NHS Trust as a Clinical Nurse Specialist. We are very fortunate to have Jane as a valued member of the clinical team.

Dr Penny Stein has been appointed to a senior research position within the University of Cambridge but very much allied to the Lysosomal Disorders Unit as a practising clinician. Doctor Stein will bring to the group a wealth of scientific research experience in addition to her excellent clinical and personal skills.

‘Six months have passed since the opening of the new Lysosomal Disorders Unit in Addenbrooke’s Hospital. We hope that our patients are as pleased with the facility as we are. We are now able to provide nursing, medical and secretarial services in a single, compact suite of rooms. Most of the essential materials for running a clinic are close to hand, like patients’ notes, fax machine and tea.

‘A particular advantage is the ability to give infusions during the outpatient clinic. The facility gives us more flexibility to see patients outside of normal clinic times for particular specialist investigations and treatments. We look forward to seeing you there.’

Update from Addenbrooke’s Hospital

In its May 2005 edition, Gaucers News reported on the Dept of Health Update from Addenbrooke’s Hospital telephone: 00 44 (0) 1453 549231.

NSCAG Designation for LSD to be extended

In its May 2005 edition, Gaucers News reported on the Dept of Health announcement that for two years, from April 2005 to March 2007, Cerezyme and Zavesca prescribed for patients with Gaucher disease was to be centrally funded by the Dept of Health under the auspices of the National Specialised Commissioning Advisory Group (NSCAG). In September NSCAG agreed to continue to commission services for the treatment of patients with Lysosomal Storage Disorders until March 2008.

The Chairman of the Gauchers Association attends regular meetings of the Expert Advisory group for NSCAG’s lysosomal storage disorder service.

The Lysosomal Disorders Team is pleased to announce two new appointments to the group, writes Dr Patrick Deegan, Consultant at Addenbrooke’s Hospital, Cambridge:

‘Sister Jane Tindall, familiar to many of the readers of the newsletter for her involvement with the Bone Research Project, has taken up a position within the Addenbrooke’s NHS Trust as a Clinical Nurse Specialist. We are very fortunate to have Jane as a valued member of the clinical team.

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‘We are also pleased to announce that Sister Liz Morris has taken on an expanded role in the service, with increased managerial responsibility in the running of the unit in addition to her clinical nursing role.

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In October 31st, the investigators and the Actelion’s team met to review the 24-month results. The final consensus was to end the study as it could not demonstrate effects on the primary end-point of eye movements abnormalities.

Investigator’s Statement

Dr Ashok Vellodi, principle investigator for the study at Great Ormond Street said “We were very disappointed that the results did not show an effect as we had all hoped. Paediatric trials involve parents just as much as they do their children, and we fully appreciate how difficult this has been for the parents. It was particularly frustrating that the recruitment took so long and that this resulted in the trial taking nearly twice as long to complete as was originally planned. We would like to express our gratitude to all the families who participated in the study, and we hope that the results will help us, both in our understanding of this disease as well as in developing future therapies.”

The Families

A parent of a child on the trial told the Gauchers Association: “The cessation of the trial is a bitter disappointment. Of course we understand that the purpose of the trial was to evaluate the effectiveness of a drug and as such there is always the risk it might not actually give sufficient evidence that it works. However my child has had to go through so much in the last three years. It has been very hard; the problems of persuading her to swallow the pill, the impact of the diarrhoea and the real challenge of having to complete all the tests.

We must now look to the future and hope that other options will soon become available.”
Lysosomal Diseases and the Brain

During the European Working Group on Lysosomal Diseases Workshop held at the Park Plaza Riverbank Hotel, Cambridge on 18 – 22 July 2006, Dr Askoh Vellodi, Metabolic Consultant from Great Ormond Street Hospital presented on behalf of the EWG Task Force guidelines for the management of GD that were published in 2000. Dr Vellodi reports:

'It was felt that the NAL guidelines needed revision. Accordingly, the Task Force met initially in London in July 2005 and reviewed long term follow up data on patients from four centres based in Sweden, Poland, Germany and the UK. However, there were difficulties with the analysis, largely related to inter-centre differences in practice. It was felt that data quality could be considerably enhanced by a systematic collection of data. Only a small proportion of patients had been treated at this dose for more than 3 years and for whom good follow up data were available. Some of these patients seemed to be quite stable neither on 

European Task Force for Neuronalopathic Gaucher Diseases

Institute, California) spoke about “Therapeutic strategies against gain and loss of function misfolding diseases”. This included the exciting new area of chaperone therapy. Dr Kelly explained that chaperone therapy, while certainly offering promise, seemed to be more effective against certain genetic mutations than others. However, the reasons for these differences were becoming clearer and hopefully one day it would be possible to overcome them.

Further Talks

This report highlights only a handful of the presentations at the Conference. Various presentations at the meeting were in Sacramento and were videoed by GOLD (Global Organisation Lysosomal Diseases). If you would like to access the video to see and hear the presentations to more of the talks please visit www.gold.org and select the ‘Education and Information’ which will lead to many of the talks.

Lysosomal Diseases and the Brain: continued from page 14

The term “Parkinsonism” refers to neurologic disorders that have many different causes, but share the classic manifestations of Parkinson’s disease, such as tremor, stiffness and a shuffle walk.

To further explore this association, the GBA gene was sequenced in 75 autopsy brain samples. Postmortem diagnosis identified 35 cases with diffuse Lewy body dementia (DLB), 29 with Parkinson’s disease (PD), 8 with Parkinson-plus syndromes (PPS) and 3 with atypical parkinsonism (ataxia). Of the 75 subjects, the majority of adult patients (most with obvious Gaucher cells in the spleen). The majority were homozygous with decreased glucocerebrosidase activity in the brain and contribute to the changes seen in Parkinsonism. Researchers hope that understanding how defects in glucocerebrosidase might affect the symptoms of Parkinson disease will lead to the development of more effective treatments or both disorders.

Advances in Treatment

Dr Beverley Davidson (University of Iowa) spoke on “Advances in treating the CNFS defects of lysosomal storage diseases”. Particularly interesting was the work that her group had done using AAV-4 virus to get the gene product (in this case a [lysosomal enzyme] into the endothelial (the cells lining the inside of the blood vessels) cells of the brain. From there the enzyme spread to other areas of the brain. This was achieved by intravenous injection, which is a significant breakthrough; most previous attempts had involved direct intracerebral injection.

Chaperone Therapy

Dr Jeffrey Kelly (Scirrps Research Institute, California) spoke about “Therapeutic strategies against gain and loss of function misfolding diseases”. This included the exciting new area of chaperone therapy. Dr Kelly explained that chaperone therapy, while certainly offering promise, seemed to be more effective against certain genetic mutations than others. However, the reasons for these differences were becoming clearer and hopefully one day it would be possible to overcome them.

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Europe Task Force for Neuronalopathic Gaucher Diseases
On Thursday July 6th 2006, a Charity Golf Day was held at Upminster Golf Club, in Essex, to raise funds for the Metabolic Unit at Great Ormond Street Children’s Hospital, and in particular for Type 3 Gaucher’s Disease. Daniel Hannaway suffers from Gaucher’s Type 3, (and by chance Daniel celebrated his 5th birthday in great style the day before the event). The Golf Day was arranged to benefit Daniel and other children who suffer from this disease, writes Alan Gardener, Daniel’s maternal grandfather.

‘As Captain of the Golf Club in 2006, I was able to organise the day and obtain tremendous support from the Club and its members. 24 teams of four players signed up to play. After a slightly threatening morning the weather brightened into a beautiful sunny afternoon. The day was won by the “Jolly Sailors” consisting of four ex-colleagues closely followed by “The Premier Team” led by the Lady Captain, Brenda Brind. The first four teams won a prize, which were kindly donated.

‘Everybody taking part – family, friends and club members enjoyed a wonderful afternoon’s golf followed by a dinner, complete with a magician to entertain everyone at their tables as they dined.

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Severity Scoring Tool for NGD

Type 3 or Neuronopathic Gaucher Disease (NGD) is one of the three recognized subtypes of Gaucher disease. Typically there is a wide spectrum of signs and symptoms affecting the visceral organs, the brain and the central nervous system. Enzyme replacement therapy is very effective in managing the visceral disease; however, the neurological disease remains a more challenging obstacle. There is currently no method to reliably monitor neurological disease and equally possible response to treatment. Elin Haf-Davies and Neurologist Dr Catherine Deville at Great Ormond Street Hospital, London have developed a Severity Scoring Tool (SST) for this purpose. Elin Haf-Davies writes:

‘Initial development consisted of identifying the neurological domains presenting in neuronopathic Gaucher disease. Domain identification was established based on a retrospective study of patient notes in one hospital and a systematic review of numerous relevant publications. Thirteen different neurological features were identified.

‘Detailed description and classification of each individual neurological feature then took place, allocating scores between 0 and 3 depending on the severity of the presentation. This led to the first draft of the SST.

‘Forty five patients with NGD across four centres in Europe were then assessed using the tool to establish the clinical and statistical reliability and validity of each domain and the SST overall. Assessment of each patient on average took between 20 and 30 minutes.

‘Content validity of the SST was established through a process of systematically asking the opinion of five European experts. This complete process allowed for a revised and validated version of the SST to be developed which hopefully will be published in the near future. We hope that this tool will make patient assessment more standardised, allowing doctors to objectively monitor the progress of each individual patient, as well as assessing patients as a group. There is further work to be done in developing the SST, in particular identifying which neurological features have a heavier burden on disease than others. This will be done through a combination of statistical assessment, seeking the opinion of leading experts in the field and of course the patients and families themselves. There will also be a need to identify what score change in the SST is clinically important. Again this is likely to be based on the opinion of experts in the field.