LMBBS Conference Report 2011

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Foreward

When 'thank you' is not enough…..

I would like to sincerely thank all members, friends and colleagues for their immense support during my recent illness; the flowers, cards, e-mails and telephone calls were greatly appreciated, not only by me, but also by my family. I was finally discharged in May after spending 102 days holidaying with the NHS. I am no nearer to having an actual diagnosis so, for the time being, I retain my tracheostomy and loss of use of my right leg but, hopefully, by 2012, all will be well.

Unfortunately, I was unable to attend the LMBBS Weekend Family Conference 2011, as I was still in hospital; however, I was there with you all in spirit, every step of the way. A big 'thank you' to the Committee, for taking on the extra workload and for making it such a success; it was our biggest Conference to date and it was lovely to hear that so many new families attended as a result of the successful clinics.

Of course, this very special weekend would not have been able to take place without the generous support of our fantastic fundraising members and generous donors; our sincerest

thanks go to them, to the listeners of our BBC Radio 4 Appeal, the Foyle Foundation, the Hedley Foundation and VICTA.

Conference 2012 is already in the planning stages and, as always, we have taken note of your suggestions from the evaluation forms. I cannot stress how important these are to the Committee to ensure you have the speakers of your choice; so, if you didn't fill one in this year, please ensure you complete one next year.

Once again, the staff at the Hilton Hotel were excellent in their overall care for the visually impaired and blind, ensuring that, not only their needs but those of all attending were met; it is so pleasing to be greeted by familiar faces at the hotel annually.

Our thanks go to the excellent speakers and facilitators, who were all again so willing to give up their time to bring us up to date with the latest research and development. Special thanks to Professor Katsanis and Professor Dollfus, who flew in from the USA and Strasbourg respectively.

Research is immensely important and we thank Professor Beales for giving us such an interesting update. We must also congratulate him on the success of the Specialist Clinics, now celebrating their first year. Members who have attended have been very vocal in their praise and appreciation.

Our thanks go to Sue King, Rehab Officer for Guide Dogs for the Blind, Gloucestershire and Ray Perry, Benefits Officer, from Kent, who both annually give up their time for the benefit of our members.

We must not forget the 'unsung heroes' of the conference, our volunteer carers, who work tirelessly, ensuring that parents are able to concentrate on the Conference, knowing their children/young adults are being safely cared for. Our most heartfelt thanks go to all of you and we look forward to seeing you all again next year.

Finally, our thanks go to the Members and Professionals who attend, because it is their continued support and appreciation that makes the conference such a resounding success; we look forward to seeing you all, faces old and new, in 2012.

Chris Humphreys

Welcome and Introduction
Professor Phil Beales



Professor Beales welcomed everyone to the LMBBS Family Conference 2011 and began by wishing Chris Humphreys, LMBBS Conference Co-ordinator, a speedy recovery. Speaking on behalf of everyone, he said that our prayers and our good luck were with Chris, Phil and the rest of the family.

He went on to welcome the overseas delegates to the conference which, this year, saw visitors from Russia, France, Germany, Portugal and Guernsey. It was a busy weekend, with over 200 people staying at the hotel and nearly 130 delegates attending the day conference. Among these, were many new faces, attending for the first time or for the first time in many years, as well as families and adults who attend year after year. Professor Beales rounded up his introduction by asking all the attending professionals to stand up, saying, “these are the guys you need to have a chat with and ask them all the questions..”, which, I’m sure, turned more than a few of their faces a little pale!

Annual General Meeting

The Hilton Hotel, Northampton
Saturday 16th April 2011

Minutes of previous Annual General Meeting

The Minutes of the Annual General Meeting on Saturday 24th April 2010, previously circulated, were agreed and signed.

Apologies for Absence

Apologies for absence were received from Chris Humphreys, the Stone family and the Fegan family.

Election of Officers

The current officers, Phil Humphreys (Chairman), Terry Crotty (Vice Chairman), Julie Sales (Secretary), Kevin Sales (Treasurer), Chris Humphreys (Conference and National Co-ordinator), Anne Crotty (Fundraising Co-ordinator) and Tonia Hymers (Newsletter Editor) were all eligible for re-election and were duly elected unopposed.

Election of Committee

Of the current committee members, (Richard Zimbler, Tina Hickey, Steven Burge and Allan Clark), Steven Burge and Allan Clark were due to retire this year. They were both eligible to stand for re-election and, in the absence of any further nominations, were elected to the committee unopposed.

Chairman’s Report

The Chairman’s Report was as follows:

“First of all we have some good news from Jonny and Sharon Fegan, of Newry, Northern Ireland. Their daughter, Caitlin, had a successful kidney transplant back in December, donated from Sharon, and they’re both doing well. Jonny and Sharon were planning to be here this weekend but unfortunately had to drop out at the last minute; our congratulations, love and best wishes go to them all. Congratulations also to Paul and Emma Turnball on the birth of their fourth child, Oskar, a brother for Nikita, John and Summer. They’re all here this weekend and I should imagine that Paul and Emma are enjoying a much deserved rest. Congratulations also to Jean and David Hubberstey on the birth of their granddaughter, Helena Grace, a daughter for Michaela and Sean.

On a sad note, as mentioned previously, the Stone family are unable to attend this year as Mark is awaiting a new kidney; they all send their apologies and I’m sure we’ll certainly miss them. Also, our condolences go to Penelope and Catherine Vagg, whose mother, Joan, sadly passed away in January. Our thoughts are with them and their family at this time.”

The Chairman presented the LMBBS Trustees’ Annual Report and Accounts:

‘We have had an incredibly exciting year, with the successful start-up of the Bardet-Biedl Syndrome Multi-Disciplinary Clinics, across four centres: Birmingham Children’s Hospital; University Hospital, Birmingham; Guys Hospital, London and Great Ormond Street Hospital for Children. The LMBB Society has set up LMBBS Clinics Limited, employing three support workers to facilitate and attend these clinics, providing support to those who attend, before, during and after the clinics. Feedback has been excellent and the first four-centre meeting will be held in June, to take stock of the first year. LMBBS Clinics Ltd manages the patient database, with 290 affected adults and children listed. As a direct result of the clinics, through patient referrals and meeting new families affected with the syndrome, our patient database has increased by around 90 individuals since the clinics began in April 2010.

The LMBBS membership database is updated regularly to ensure all records are accurate, in line with the Data Protection Act. Following a recent update, each adult now has their own entry, more accurately reflecting membership numbers, whereas, previously, they may have been included on their family page. This has resulted in a big jump in numbers and we now have 432 members and 155 professionals on our database and these numbers are likely to continue to grow over the coming year.

In respect of Fundraising, 2010 was a much better year and our thanks go to everyone who helped the Society to achieve this. We had a Silver Bond runner in the London Marathon and the ‘Big “S” Summer Sundae’ fundraising initiative was well-supported and raised over £10,000. The BBC Radio 4 Appeal was a success, raising another £10,000, and we thank the staff at the BBC and their generous listeners for the chance to raise awareness and for enabling this year’s Annual Weekend to take place. We are also pleased to report that, since the beginning of this year, we have been successful in obtaining grants for £5,000 from the Foyle Foundation, £2,000 from the Hedley Foundation and £1,000 from VICTA, all towards this year’s Annual Weekend and we thank them for supporting us so generously.

In April 2010, we had a very successful Family Conference, with an excellent line-up of speakers and workshops. The LMBBS Family Conference 2011 looks set to be bigger than ever, due to increased interest as a result of the families and professionals we have met through the Specialist Clinics. It is gratifying to see this very important event continue to go from strength to strength.

We had an attendance at Sight Village, Birmingham and London, raising awareness of the Syndrome and Society and also had a presence at the Rare Disease Reception at Westminster. We will continue to seek out and attend such events as they provide ideal opportunities for both raising awareness and for linking up with other like-minded groups or individuals.

Unfortunately, very few of us managed to attend the Launch of the Ciliopathy Alliance in November, due to adverse weather conditions, a tube strike and ill health. It was a successful day, however, and has generated much interest. The Alliance is about to become a Charitable Company Limited by Guarantee and will have a board of Trustees/Directors on which we will be represented by Drina and Michael Parker.

The LMBBS webpage has been redesigned, improving accessibility, and now includes a separate page for the new NHS Clinics, outlining the service and including feedback and comments received. There is also a chat forum, although this is underused at present. All LMBBS publications are available via the website. The overall number of visits to the web site from 1st May 2010 to 31st December 2010 was 4,853, with 16,028 page views, including the following:

Home page	5,825
Publications	872
Research	888
Clinics	704
About LMBBS	882

We have produced two newsletters and a Conference Report, with a further newsletter in progress. All of our publications are committed to the health promotion and lifestyle management issues of those with LMBBS and their families/carers and are distributed to our members in accessible formats, as well as being available on the LMBBS website. We have updated the LMBBS Medical Booklet, incorporating recent research findings, and have updated and reprinted the LMBBS 'Who are We?' leaflet. We have also had wallets printed which are filled with leaflets and newsletters to welcome new families to the Society.'

The Chairman, Phil Humphreys, continued, "All of this couldn't happen without the hard work and commitment of a few individuals. Thank you to Chris, Julie and Tonia for their contribution to the LMBBS Clinics over the past year; they have worked extremely hard and, as mentioned previously, the feedback has been excellent. Individually, my thanks go to Julie for maintaining our web page and for her work as Conference Childcare Coordinator; to Tonia for her work as Newsletter Editor and Crèche Childcare Facilitator and to Chris for her work as National Co-ordinator, often the first point of contact for our members and professionals. As you have probably gathered, we have quite a full conference this year which is due to the new clinics raising the charity's profile and making more people aware of us and the work we do. We expect next year to be even busier, so I would urge you to return your booking forms promptly, to guarantee your room at the hotel. We were lucky this year that some rooms were made available at the last minute, otherwise some of us would have been staying at the local Premier Inn.

Huge thanks go to our Fundraising Co-ordinator, Anne Crotty, who has had a very successful year. Anne is launching a new fundraising initiative this year to raise funds for the 'Save Our Conference Kitty' otherwise to be known as 'SOCK'. Thank you to all those

who have raised money for the Society this year; your donations have been very much appreciated for, without you, the Society will not survive."

The Chairman continued by congratulating Allan Clark, who, earlier in the week, had successfully completed the West Highland Way, covering over 100 miles in five days, raising a fantastic sum of money for LMBBS. Look out for the full report in the autumn newsletter. He finished his report by thanking Professor Beales, the Honorary Officers and members of the Committee and the many volunteers who had given up their time to support the society for all their support and sterling work over the past year.

Before moving on to the Financial Report, Phil had a personal message to read out from himself and Chris.

"Most of you will know that the LMBBS is like an extended family and, to us, this has never been more so than in the last five months during Chris's illness. We have been overwhelmed by cards, messages, emails and offers of help and genuine concern from so many people, members, professionals and those in the community. At one point, we had 17 bouquets in the home and we had no idea people cared so much. However, there are three people, Julie, Tonia and Anne, who have supported us over and above, taking on Chris' workload when they were already so busy with their own roles and their families. They are the sisters we never had."

With tears and hugs all round, Phil presented Julie, Tonia and Anne with the most beautiful bouquets of flowers, before handing over to Allan who, in the Treasurer's absence, (he was helping out with the Drayton Manor trip), was to read out the Financial Report.

Financial Report

The financial year 2009-2010 saw a big decline in the Society's finances, leaving the charity without funds, following the Weekend Family Conference in 2010. Preparing for the start of the LMBBS Multi-disciplinary Clinics involved using money from the LMBBS account, which meant that the final payment owed to the Hilton Hotel was delayed, until these funds were repaid by the National Commissioning Group. This is something that has never happened before and cannot happen again. We're pleased to report that all costs incurred by the start-up of clinics, paid for by the Society, have now been repaid in full and are shown on the accounts for 2010. It was reported in last year's annual report and accounts that there had been a financial loss and that fundraising and support was desperately needed. This must have had a profound impact as donations and fundraising have risen substantially compared to previous years, as can be seen in the accounts, so a big thank you goes to all those who have raised money on behalf of the Society because, without their efforts, we would not have been able to hold our Annual Weekend Family Conference this year. Our Annual Weekend was also saved by the BBC Radio 4 listeners who responded so generously to our Appeal in June, which, with Gift Aid, raised well over £10,000. Our heartfelt thanks go to them and all the staff at the BBC.

We do, however, still need the continued help of our supporters, if we are to maintain the momentum and keep driving the Society forward. Thanks to the loyal band of fundraisers, donors and 'Friends', the Society can maintain its present activities; however, with more support, more fundraising and more funds, the Society will be able to develop its objectives and be able to support its members in more diverse ways.

Appointment of Auditor

It was reported that the Society's accountant, Michael Bannister, had recently left Thompson & Co to start his own business, Fryza Bannister Financials Ltd. The Committee proposed that the Society continued to appoint Michael Bannister under his new company, Fryza Bannister Financials Ltd, for the coming financial year and this was duly agreed.

Any Other Business

In the absence of any other business, the meeting was closed. The date of the next meeting was set for Saturday 21 April 2012.

Update on Research and Study of LMBBS

Professor Phil Beales
Professor of Medical and Molecular Genetics
Wellcome Trust Senior Research Fellow in Clinical Science,
Honorary Consultant in Clinical Genetics, Molecular Medicine Unit,
Institute of Child Health/Great Ormond Street Hospital for Children and Guys and St Thomas' NHS Trust,
President of the LMBB Society

Professor Beales obtained his degrees in Genetics and Medicine from University College, London. He undertook postgraduate training in both general medicine and paediatrics before specialising in Clinical Genetics.

Professor Beales and his team, together with collaborators from Europe and North America, have, in recent years, made major advances in our understanding of the causes of the syndrome. This includes the notion that abnormally functioning cilia lies at the heart of LMBBS. The challenges that lie ahead involve understanding how dysfunctioning cilia contribute to various syndrome aspects. These discoveries bring closer the ultimate goal for the design of potential treatments to prevent further visual deterioration or weight gain.

Professor Beales has been medical advisor to the LMBB Society since 1996 and was made President of the Society in 2005. In 2010, he succeeded, with the help of the Society, in attracting funding from the DoH to establish national multidisciplinary clinics and a comprehensive genetic testing platform for all persons with LMBBS.

At last year's LMBBS Conference, Dr. Matthew Hind, a respiratory consultant from the Royal Brompton Hospital, spoke about respiratory difficulties in those with LMBBS. Over the past year, some of our members have taken part in a study at the Royal Brompton, with Dr Hind and Dr Robin Quinlan and, in Dr Hind's absence, Professor Beales presented the findings to date.

Professor Beales began by showing a picture of the lungs and describing it to the delegates. The trachea goes down into the middle of the chest and divides into two tubes called bronchi. These tubes divide into smaller and smaller tubes with small air balloons at the end, called alveoli. The passive process of gas exchange takes place in the alveoli, and involves oxygen moving across into the cells and carbon dioxide being released from them. This process depends on surface area and it is thought that, in those with LMBBS, this surface area may be reduced. Professor Beales explained further that cilia line the upper airways and are simply there to move out all the junk that we breathe in every day and so the question is also whether those cilia are working efficiently.

Those of you who attended last year's conference, or read the report, will remember that, from talking to delegates at previous conferences, it became clear to Professor Beales and his team that many people with LMBBS were experiencing symptoms of general respiratory disease, such as coughing, breathlessness, wheezing, snoring, daytime sleepiness and morning headaches; subsequent testing has indeed shown a degree of reduced lung function in many of those tested.

Around 30 people have been to the Royal Brompton Hospital for tests, which begin with the doctor taking a very detailed history. Many took part in the sleep study, which involved an overnight stay to enable the team to measure the exchange of gasses, heart rate and oxygen levels. Lung function tests, involving breathing in and out of various machines and a high definition CT scan, to look at the structure of the lungs, were also undertaken. Some had an echocardiogram, an ultrasound looking at the functioning of the heart, because the heart is closely allied with the lungs, and some had a brush swab taken from the inside of the nose, a painless process that allows the doctors to examine the cilia on those particular cells. The study found that many were experiencing all of these respiratory symptoms, suffering repeated infections, often leading to being prescribed frequent courses of antibiotics. Many of the patients tested, also had sinusitis and other nasal problems and there were quite a few people experiencing breathlessness and wheezing.

As mentioned earlier, some took part in the sleep study to check for sleep apnoea. This occurs in twice as many men as women and is becoming much more common in the general population, due to a general increase in weight, which is clearly a major problem. Symptoms of sleep apnoea can be snoring, daytime sleepiness and difficulty in waking up. There can also be periods of night time choking where people stop breathing for a short while; the brain then wakes up a little to trigger breathing, which means poor quality sleep. As Dr Matt Hind explained last year, sleep apnoea can be treated with CPAP, Continuous Positive Airway Pressure, a machine that pumps oxygen into the airways by means of a mask worn overnight. Nearly everyone who attended the Royal Brompton as part of this study demonstrated disordered sleep breathing at night and 70% were given a CPAP machine to take home. We are hopeful that Dr Hind will come back next year to give us a full update; however, those who have been managing to use the machine successfully have reported much better rest and sleep as a consequence.

The lung function tests gave surprising results, with many of those with LMBBS unable to physically perform them. The test requires the patient to purse their lips around a tube fairly

tightly and blow, which caused a lot of difficulty for some. It was found that there was a general reduction of between 30 and 50% in the ability to complete the test successfully. Moving on to the CT Scans and X-rays, 26 patients were tested and the results showed that lung volume was a little smaller in those with LMBBS, with one or two people showing unusual configuration of the lungs; one patient had an extra lobe and airway, which is very unusual and something the team hadn't seen before.

Finally, the last test that was undertaken was a motile ciliary test, where the nasal brushings were investigated under a microscope to measure the beating of the cilia. It was found that the frequency of the beating was about half what it should be; the cilia were all present, which is good and most of them were completely normal; however, they were beating much slower and were not in coordination with each other.

From this study, it is clear that respiratory function tests need to be checked routinely to determine whether someone has got sleep apnoea or a reduced lung function, to enable them to benefit from the available treatments. This study also reinforces the necessity to maintain a healthy diet with lots of exercise because, although as we know it can be difficult, it will help ease the symptoms of respiratory disease hugely.

Moving on to other research, many of you will be aware that there is much research going on at present, using gene therapy and stem cell therapy, in particular regarding the correction of retinal dysfunction; however, Professor Beales and his team have been trying to focus on what is probably a more practical and more immediate type of approach to some aspects of living with LMBBS, for example kidney cysts and the problems they can cause. In the lab, they have been looking at whether there are some medications already licensed and in use, that might actually be able to prevent cysts forming or at least reduce the size of the cysts and improve the function of the kidneys.

One of the animal models used in the lab is the zebra fish, a freshwater fish found in the rivers at the bottom of the Himalayas. The zebra fish was the first fish to have its whole genome sequenced so it is known that there are many genes that are similar, if not identical, to ours; not so surprising considering we all evolved from fish. This provides the opportunity to study their genetics and also to remove the function of certain genes; so, for example, when they removed the function of the BBS genes in the fish, they developed kidney cysts.

Professor Beales explained that they were able to exploit this system by administering a library of drugs, about 1,000 or so of approved prescription drugs that are already in the chemist. This means that they have already been through the 15 years, and the billions of dollars it costs, to bring a compound to the market. Their idea was to see whether they could re-badge some of the drugs that are already out there and put them to some other use, in this particular case the treatment of kidney cysts; could they prevent them? Having worked through the 1000 or so drugs, administering them to BBS zebra fish engineered to have kidney cysts, they narrowed it down to a few that seemed to be working. The next stage was testing on mammals, in this case, BBS mice and, although they lost some of the drugs, a handful of them still worked. This process isn’t limited to the kidneys but can be used for other aspects of the syndrome too.

Professor Beales and his team have now started to look at going through this process for the retina, to see whether there are drugs already out there that could slow down degeneration of the eyes; however, he said that they have to be honest and don't want to give false hope because it is still early days. Excitingly, they are also in conversation with colleagues about the possibility of using stem cells and there are other groups, outside of the UK, working on gene therapy for this condition as well. Before taking questions, Professor Beales thanked Dr Miriam Schmidt and Dr Dan Osborne, who have just completed the initial drug screen and who will be going on to test the drugs further, in different systems, in due course; we will look forward to hearing more about those in future years.

Questions:

Q. If you are on dialysis, would you still get cysts on your kidneys?

A. The idea is not to provide a cure, but to try and delay or slow down the progression of the kidney problems, so we are talking about someone who hasn't gone onto dialysis and someone whose kidneys haven't failed just yet.

Q. How do you test for problems with cilia?

A. We use a very tiny brush to take a sample from the inside of your nose, which is then put onto a slide and examined under a microscope. We can then take a movie of it, slow it down and count the number of times it is beating in a second.

Q. The cilia that you're taking from the nasal area, is the pattern the same throughout the body?

A. There are motile cilia and non-motile cilia. Motile cilia beat, such as those that line the bronchi and the oviducts that help the egg move down into the uterus, and they are there mainly to shift fluid around. The non-motile cilia are more abundant and are perhaps even more important as we think they may be the eyes, ears and antennae for the cells.

Q. But, if there's dysfunction in one area, is it likely to map across to the other?

We think it is all related in terms of the basic ciliary function; however, it obviously manifests differently according to where it is.

Q. How do you go about getting to hospital to have these tests?

A. The referral will come via the BBS Multi-disciplinary clinics.

Q. Would emphysema come from this?

A. We tested everyone involved in the study and found no evidence of emphysema or bronchiectasis, which is great. It really seems to be a case of reduced lung volume in general, with the added fact that the cilia are not beating in quite the way they should, which is probably responsible for a lot of the recurrent chest infections that people are experiencing.

The Bardet-Biedl Syndrome Clinic

Dr Elizabeth Forsythe
Academic Clinical Fellow, Molecular Medicine Unit
Institute of Child Health, London.

Dr Elizabeth Forsythe is an Academic Clinical Fellow, based in the Molecular Medicine Unit at the Institute of Child Health in London and is one of the doctors working for Professor Phil Beales' research group. Although originally trained in paediatrics, Elizabeth has a special interest in genetic conditions, including Bardet-Biedl Syndrome. She attends all the Bardet-Biedl Syndrome clinics in London as part of the genetics team and spends the rest of her working time in the laboratory, researching rare genetic conditions. Elizabeth's presentation was about the LMBBS clinics and what to expect from them.

Dr Forsythe began by explaining that she attends the London clinics and therefore her presentation is centred on that experience, although the clinics in Birmingham are very similar in structure. She said there were a few familiar faces amongst the delegates who had already been seen at a clinic; however, there were many more still to be seen. Dr Forsythe explained that the clinics started in April 2010, with the aim of being a 'one-stop-shop' for those with LMBBS, to enable the patient to see all the relevant clinicians either in one day or over two days. At each clinic, the patient may see a geneticist, such as Professor Phil Beales, who deals with conditions that are hereditary or where there's a change in genetic material; a kidney specialist (nephrologist); a dietician, who can help with any diet and weight issues; an ophthalmologist, who will carry out very detailed tests specific to BBS; also present will be a hormone doctor (endocrinologist) and a clinical psychologist. At the London clinics, the patient will also meet the specialist BBS Nurse, Kath Sparks, who has already built up strong ties with the LMBB Society, developing an excellent understanding of the children and adults with BBS, especially with regards to the emotional difficulties experienced by many with the syndrome. Linking all four services are the LMBBS Support Workers, who facilitate the clinics, helping the patients with travel and accommodation and generally providing support and information before, during and after their appointments.

On the clinic day, in addition to seeing the doctors and clinicians, the patient has some investigations performed, such as recording the height, weight and blood pressure. A blood test is also carried out to check for a number of things, in addition to screening for any genetic change that might have caused BBS. To date, around 103 patients have been seen and, out of all the patients who have given blood, a genetic change has been found in about 65%, which is pretty much what was expected. If a mutation isn't found, it doesn't mean that the patient doesn't have BBS, as there are still BBS genes to be found. The patient also has a detailed eye examination and may be referred for an ultrasound scan.

Dr Forsythe suggested that some people might question the importance of, or need for, specialist clinics. To begin with, she explained that it is very useful for looking after the eyes, as the Ophthalmologist has seen lots of people with BBS and can give specialist advice.

There is help and support with weight, diet, blood pressure and kidney or hormone problems. Dr Forsythe explained that, in particular, it can be difficult to know whether someone has got kidney or hormone problems because the symptoms can be very vague, so it's really useful to go along and be checked for these particular things. The BBS patient can also address any issues to do with mood or behaviour or any concerns they may have about the genetics of BBS. Last but not least, Dr Forsythe suggested that the clinic also provides a good opportunity for patients to discuss a health problem that maybe hasn't been resolved by the local health care team. Without making any promises, she said they see a lot of people with BBS and so might be better placed to know the right way forward.

A major advantage of the clinic is obviously that it cuts down on appointments, giving patients the chance to see everyone under one roof, rather than seeing many different clinicians at different hospitals at different times, which is quite a big disturbance for most people's lives. It is a very friendly clinic compared to most other clinics; everyone has lunch together and it's very relaxed. (Many of the delegates were nodding in agreement which certainly confirmed the positive feedback received to date.) Dr Forsythe explained that the BBS Clinic is a very patient focused clinic; the patients get their own consulting room and the doctors have to move between the patients. One of the major benefits is that all the doctors know about BBS and most have seen lots of people with the syndrome already. The aim is to see everyone annually for a check-up and this also provides a good opportunity to meet other people with BBS. For some patients and their families, it is their first experience of meeting someone else with BBS and it has been so nice for them to meet other people who have similar experiences.

Dr Forsythe continued with the explanation that the more people that attend the clinics, the more knowledge the clinicians will gain about BBS. This information will then feed back to the patients, and, over the years, knowledge of the syndrome will accumulate with obvious benefits. Everyone involved with the clinics is understandably proud of the first year's outcomes and a patient satisfaction survey, courtesy of LMBBS, shows a high level of patient satisfaction, from the first point of contact and the help and support provided beforehand, through to the clinical service and support available on the day.

So how does a BBS patient get to attend one of the new clinics? If they are already on the LMBB Society mailing list, they will automatically be added to the clinics database and will be contacted by one of the Clinic Support Workers to make an appointment. For those not on the mailing list, they can get a referral from their doctor, either a GP, or a specialist doctor. Following the appointment, letters containing the results and information from all the different specialists are sent to the patient, the patient's GP and any other doctors that are involved in the patient's care, so that everybody is up to speed.

Dr Forsythe finished her presentation by reiterating that a key aim of the clinics is to be patient focused and to make life a little easier by having all the clinicians in one place. She urged everyone to use the feedback questionnaires to ensure they remain patient focused. Questions were then invited from the delegates:

Q. “My daughter attended the clinic in July at Great Ormond Street; they took her blood but I haven’t heard anything back, so should I presume that no genetic changes have been found? We have received the report but no genetic results and I wondered, will you keep checking her DNA?”

A. Professor Beales: “We are experiencing a backlog in the testing at the moment, which will hopefully be resolved soon, so it may be that your daughter’s sample is yet to be tested; however, if we fail to find a mutation in any of the known genes, we would keep the DNA sample so when a new BBS gene is found we can then check that gene.”

Understanding Bardet-Biedl Syndrome: The Strasbourg Contribution
Professor Hélène Dollfus
Professor of Medical Genetics, Strasbourg Medical School
Head of the Medical Genetics Department, University Hospital of Strasbourg
Coordinator of the Centre for Rare Genetic Eye Disorders, University Hospital of Strasbourg Director of the laboratory EA 3949, Strasbourg Medical School, Université Louis Pasteur

As an Ophthalmologist trained in France and having specialised in Paediatric Ophthalmology, Hélène Dollfus has a particular interest in inherited eye diseases and retinal inherited disorders. This led her to train in Medical genetics and molecular biology, applied to genetic conditions.

Since 2003, Professor Dollfus is Professor of Medical Genetics and head of the Medical Genetics department at the Hôpitaux Universitaires de Strasbourg. Since 2004, Professor Dollfus is the director of the research medical genetic laboratory of the Strasbourg medical school (INSERM AVENIR label), and, since 2005, is the coordinator of the centre for rare genetic eye disorders (CARGO) in Strasbourg.

Professor Dollfus’ presentation was based on one she gave to the French BBS Society a few months ago; she began with some background information. There are three teams working together in Strasbourg, the Department of Medical Genetics, where genetic counselling and diagnosis is centred; the National Centre for Rare Eye Diseases, which focuses more on inherited eye disorders, especially retinitis pigmentosa in BBS; and the third is the research laboratory where the fundamental research on Bardet-Biedl Syndrome is carried out. Professor Dollfus stressed that the presentation was on behalf of all the collaborators, who, she said, were extraordinary and extremely involved in the medical and scientific care of Bardet-Biedl Syndrome.

Professor Dollfus explained that the syndrome was probably described for the first time in France in 1756, in a small village in the south, where it was reported that a person was found to be overweight, with eye problems and extra digits. There has also been another description of the condition by Laurence and Moon; however, it is believed that this is quite different from the traditional Bardet-Biedl Syndrome description of symptoms that may include retinitis pigmentosa, weight gain, polydactyly, cognitive disorders and renal,

urological and genital abnormalities. As we know, the syndrome is a ciliopathy and Professor Dollfus showed a fascinating slide of a diagram which placed some ciliopathies on a spectrum according to severity and type of symptoms.

Covering the basics of the condition, she explained that Bardet-Biedl Syndrome is recessively inherited with parents usually being unaffected carriers. Genes are inherited in two copies, one from the mother and one from the father and in this condition, to be affected, two copies of the gene have to be present. For a couple with one child affected by Bardet-Biedl Syndrome, there is a 25% risk of having another affected child.

Since 2002, Professor Dollfus and her colleagues have been concentrating on two main tasks, the first of which is a national protocol looking at the different clinical manifestations of Bardet-Biedl Syndrome, in a core of approximately 40 BBS patients, which, she said, has provided interesting data on the natural history of the disorder. The second part of their work is laboratory research where their main aim is to find new BBS genes, to understand the mechanisms of the condition and to relate what is happening at a cellular level to clinical manifestations of BBS.

For example, they have discovered that Hydrometrocolpos, a malformation of the lower part of the abdomen and the genital organs of females, is not only implicated in one type of BBS gene, but in all of them; however, it is, she explained, a very rare malformation for BBS patients. Secondly, they have shown that part of the brain called the hippocampus is of a particular shape in nearly 40% of patients with BBS (also shown by Professor Beales' team). This part of the brain is specific for memory and emotion; however, in the French study, they have not, as yet, been able to correlate the findings with clinical manifestations. Professor Dollfus explained that their patients have been doing really well with cognitive performances which, she said, should be reassuring for parents. On a practical note, she explained that they are just finishing their national guidelines for follow-up for Bardet-Biedl patients, which will be useful across the country for GP's and others involved with medical care, who are less informed of the condition.

At the present time, they are able to identify BBS genes in 70% of BBS patients, roughly the same as the British team and, where they are unable to identify a known mutation, they are trying to identify new ones, which, unfortunately, is a little like looking for a needle in a giant haystack. The aim is to one day be able to find mutations in 100% of patients. As has been mentioned previously, a major aim of research is to link genotype to phenotype to aid diagnosis and care and, interestingly, Professor Dollfus' team believe they have identified that patients with the BBS16 gene will not have extra digits.

She explained that the aim of the laboratory in Strasbourg is to try to understand why there are different clinical manifestations in the ciliopathy that is Bardet-Biedl Syndrome. They are concentrating on three different targets, obesity, retinitis pigmentosa and renal disease. They are trying to understand why there is a problem with maintaining a healthy weight in Bardet-Biedl Syndrome, a question that has been asked since way back in 1922, when George Bardet hypothesised that there could be a problem with the control of eating behaviour caused by a malfunction of some kind within the brain. Professor Dollfus agreed that indeed

the brain is essential to regulating eating behaviour and body weight. She explained that adipose tissue, (fat tissue), communicates with the brain and together they interact with hormones. Leptin, a hormone that comes from the adipose tissue, informs the brain about the state of the body with regards to food intake and the state of the adipose tissues. There are, she said, a lot of different groups around the world working on the hypothesis that the part of the brain responsible for controlling eating behaviour is defective in patients with Bardet-Biedl Syndrome, the results of which could potentially explain why there may be some eating behaviour dysfunction in BBS and why patients may have more difficulties in controlling their food intake.

This research may explain certain food behaviours; however, there may be more to it than that. Professor Dollfus explained that they questioned in Strasbourg whether the adipose tissue itself, the fat cells, could be involved in obesity in BBS. They have shown that, although the adipocyte is not ciliated, when it grows from a preliminary cell to a mature cell, it does carry cilia which, in BBS, are defective, meaning the biological pathways for the maturation of the adipocyte are altered when there are BBS mutations.

To sum up, this means there may be two aspects to obesity in Bardet-Biedl Syndrome, to do with brain function and eating behaviour and also at a cellular level. However, it was stressed that many BBS patients have greatly improved their weight through diet and exercise so it is important to keep in mind that this does work, even though there may be underlying issues for weight gain.

Moving on to briefly talk about the renal aspect of BBS, Professor Dollfus explained that the basic function of the kidneys is to filter blood and produce urine, which doesn't work very well in some patients with BBS. They have shown that, in the cilia of the tubular cells in the kidney, there is a defect causing dysfunction at the level of BBS proteins of a receptor that is specific for a hormone that concentrates the urine. She concluded that, although this is only one aspect, it probably does contribute to kidney disease in BBS.

Rounding up the presentation, Professor Dollfus touched on her speciality, ophthalmology, which she planned to cover in more depth during the afternoon workshops. She explained that photoreceptor cells, some of the cells that make up the retina, have a ciliated structure and in Bardet Biedl Syndrome, where there is a defect at the level of the BBS protein, the photoreceptor cells do not function well, which explains why there may be retinal degeneration. The photoreceptor cell has two parts that are related to the connecting cilium. It was explained that they think the proteins necessary for visual phototransduction are made in one part of the cell; however, their function and use is in the other part of the cell and therefore all the proteins have to go from one part, the inner segment, to the other part, the outer segment through the connecting cilium. When this connecting cilium has a deficiency, as is the case in BBS, all the proteins get stuck, inducing retinitis pigmentosa and all the related difficulties such as night blindness and tunnel vision.

In the laboratory, they are studying the mechanisms that lead to retinal degeneration and have been using different models, involving retina from mice and also human retina and, at present, have some very interesting data from the In Vitro mice retina studies. The aim, she

said, is to develop gene therapy for retinal dystrophy in BBS, as there have been some successes in other retinal dystrophy conditions. To conclude the presentation, Professor Dollfus reiterated that they are trying to contribute the best they can to improve knowledge of the clinical manifestations of BBS and to understand why they occur. Of course, further research is needed; however, she stressed that international connections, such as the ones between Professor Dollfus, Professor Beales and Professor Katsanis are extremely useful in this respect. The final aim, she said, is to improve the care and wellbeing of their patients.

An Update on the Genetics and Functional Studies of BBS Genes

Professor Nicholas Katsanis
Director, Centre for Human Disease Modelling
Professor of Cell Biology
Brumley Professor of Paediatrics, Duke University

Dr. Katsanis obtained his first degree in Genetics from UCL in London in 1993 and his Doctorate from Imperial College, University of London in 1997. He then joined the laboratory of Dr. Lupski at Baylor College of Medicine, where he initiated his studies on Bardet-Biedl Syndrome. In 2002, he relocated to the Institute of Genetic Medicine, John Hopkins University.

In 2009, he moved to Duke University to become a Distinguished Brumley Professor and to establish the Center for Human Disease Modeling, where he is the Director. This new structure aims to facilitate collaboration across disciplines and to develop physiologically relevant tools to study variation found in human patient genomes. In parallel, the Katsanis lab pursues questions centred on the signalling roles of vertebrate cilia, the translation of signalling pathway defects on the causality of ciliary disorders, and the dissection of second-site modification phenomena, as a consequence of genetic load in a functional system.

Professor Katsanis attended the LMBBS annual conference in 2007 and began his presentation this year by saying how wonderful it was to be back and to see some familiar faces, as well as new ones, and invited everyone to catch up with him during the day for a chat. As he said in his previous talk, attending conferences such as this are one of the highlights of his year as they remind him of his purpose, which can sometimes be missing when stuck in the lab for long periods. He brought greetings from the BBS group in the United States; they hold a biannual conference, which, last year, broke its record with around 150 people attending. It has grown from what used to be a small affair, which is reflective of the research taking place in the field and the efforts of many with regards to raising awareness. Professor Katsanis said they have learned a lot from the way the UK LMBBS meetings are organised and hoped to see a stronger interaction between the European and American Societies because, although there may be cultural differences, the fundamental problems that everybody is faced with and the struggle of trying to inform the medical establishment about what the disorder means and what the challenges are, are very common and the themes that we are learning from each other, he said, are going to be very, very valuable.

He continued, “When I started looking at this disorder in about 1997, we had zero genes, we didn’t have a clue about what might be causing this disorder. In 2011, we’re actually now up to 17 genes that can account for up to 80% of the mutations; we have a pretty decent basic understanding of what the biology is. The word ‘drug target’ is beginning to appear, but let’s not get ahead of ourselves, we are not there yet. However, just cast your mind back to where we started about a dozen or so years ago and look at where we are today. It’s kind of easy to forget because you’re focusing on day to day life and your battle with this syndrome, and all the challenges that it throws at you; however, this is a very good moment to pause and to look back and take some encouragement about where we used to be and where we are today and anticipate what may happen in the next ten to twelve years. I know it is a long time, I know that this is going to be a very frustrating time for all of you; however, we are making progress and sometimes, even though it feels as if we’re moving along at a very slow pace, it’s only when you look back that you begin to appreciate how far along we’ve come. It is important to stress that the vast majority of lessons that we’ve learned, we’ve learned them because you push us, because you participated, you provided your energy, your enthusiasm, your raw emotion and your time, because we cannot do this without active and bold patient participation; so, please, do not give up, please carry on pushing us because that’s the only way to go.

One of the things that I care about is to understand the variability of BBS at the genetic level, to understand the pathology of the disorder at the fundamental biochemical and cellular level: ‘What are these proteins doing?’, ‘Why they are defective?’ and ‘How is it that they’re giving rise to different pathologies, where they are defective?’ Humans have a remarkable capacity to receive and process bad news; we all have a much greater difficulty receiving unknowns: ‘I do not know what’s wrong’, ‘I don’t know what’s going to happen to your son or to your daughter or to your brother or to your sister’, ‘I can’t even name what’s wrong’ or ‘I have found a mutation in one of the BBS genes but I don’t know what this means for the future of your child’. The biggest failing in genetics, and not through lack of trying, is to take genetic data and make predictions, other than sometimes to say, ‘Yes, this child will have BBS’, ‘No, that child will not have BBS’. But this disorder, like most other genetic disorders, comes in many, many flavours and challenges, and it is important that we begin to understand how genetic variation tracks with those challenges, so we can make predictions: ‘Yes, you need to be looking after your kidneys more’, ‘You have a high likelihood of going to end stage renal disease’ or ‘No, you’re one of those BBS patients who will not face major challenges with your kidneys’, ‘You might lose your sight over a decade’ or ‘You might lose your sight over 30 years’ and so on and so forth. These questions are important; they don’t speak of a cure but they speak of something which is considered to be just as important which is management, information, understanding and, of course, acceptance about what is yet to come.”

Professor Katsanis showed the delegates a slide of a BBS family, with two girls known to have mutations in BBS1; however, the clinical presentation of the two children was vastly different which, he said, was representative of the tremendous variability seen in the disorder, which presented a major challenge, as little was understood about variability. A number of years ago, they were able to show that there was another mutation in this particular family in BBS6, with which, if affected alone, the person would not develop BBS.

However, if BBS6 was affected in addition to BBS1, the mutational load would be more severe. Of the two children mentioned previously, one had no evidence of obesity, very mild retinal degeneration, no cognitive defects, normal development and normal speech, whereas the child who inherited the mutation in BBS6 in addition to BBS1 was very obese, had severe retinal degeneration, and had delayed development.

Professor Katsanis explained that, in the United States, when you send a sample off for genetic testing, about 30% of the time, the results will come back 'VUS', Variant of Unknown Significance, which, he said, was an absolute killer for families, not least because, in the United States, the patient has to pay for the test, which costs around $1,000. VUS means they were not able to find a mutation, or a BBS gene, *so far*. What they want to do is start developing tools and assays to become a lot more predictive with regards to the mutations in genes and the potential effect they may have. The first step is to find all the BBS genes or, if not all, then almost all of them and, fortunately, the technology has improved enough to help this move forward. Professor Katsanis has data from around 500 patients in the United States which, together with the families that Professor Beales and Professor Dollfus are working with, provides data from around 1,000 families. Their collective goal is to identify mutations in 90% plus of these families, which will, hopefully, give them the ability to explain who is going to get what, when, why and how long it's going to take, which will have major implications for the health management of those with the syndrome.

Professor Katsanis moved on to discuss the cilia aspect of the syndrome and said that they have a fairly good idea of all the proteins that are required to build, maintain and make cilia function and, it stands to reason, he said, that, if they query all those proteins, they will probably be able to identify the vast majority of BBS genes. They will then be able to develop fast, functional assays that will tell them whether the mutation identified is a BBS causing mutation, which will be extremely important to the family who wish to have further children. Put simply, they need to find out a way to assess for these mutations.

Professor Katsanis continued, "A number of years ago there were a whole host of studies that used the entire gamut of the toolkit that we have as biologists, evolutionary tools, protein identification studies, gene identification studies and so on and so forth, and we built what we call the ciliary and basal body proteome, which is around 1,000 proteins, the amount needed to build, to maintain and for a cilium to function. I'm sure we're missing a few and I'm sure that a few in this list of 1,000 proteins are false positives, but it's okay, we can tolerate that. This was converted into an online database so we can manage this data and share this data with our colleagues across the world and move forward and systematically sequence the whole thing. To put this into perspective, in 2001 the first draft of the human genome sequence was published, which cost somewhere in the region of two billion dollars and took, depending on your point of view, somewhere between two to four years. Today it takes about 700 bucks and about 72 hours to sequence, not the entire human genome, but at least the fraction of a human genome that I care about, which is all the ciliary genes. So, for that kind of cost and for that kind of money, I can afford to query every single BBS patient ever recruited, which started in around 1985. We anticipate that we will have sequenced all 500 patients in the year's cohort by September of this year, which then gives us an analytical problem. There is a torrent of data and it is like the old adage of trying to drink from a fire

hose, but that's okay; I'd rather have the fire hose and then figure out a better way to drink from it because, until about a month ago, I didn't even have the fire hose.

It is our expectation that the gene discovery portion of the work will continue to accelerate very hard over the next year, year and a half and then it will probably peter out because we will have reached the point where we have identified almost all the genes, not all of them but most of them. So where are we now? We actually have, we think, up to 17 BBS genes; in some populations, we can explain 80-100% of the disease, in others, only about 25%. If you happen to hail from Kuwait, we're only about 25% of the way; however, if you happen to be from Newfoundland, it's 100%; every single family from Newfoundland has had these prime mutations discovered. If you happen to live in the United States, we can explain probably about 75-80% of the disease, which is not bad. We are also beginning to identify genes that might not cause BBS itself, but might affect the presentation of BBS and this is something that really excites me personally because it's the beginnings of prediction."

He then explained that a major challenge with identifying relevant mutations is that every single human being, irrespective of disease status, will carry in their genome between 150 and 200 changes that have never been seen before, so the challenge is to be able to differentiate between those 200 changes that might be irrelevant to the clinical problem and the smaller number of changes that are relevant. To model one change, one mutation, takes about a year and costs around $100,000, so to model the 200 changes would be impossible. Fortunately, they are able to model the changes in fish, which costs around $50 per mutation and takes 72 hours, which still has to be done 200 times over; however, it can be done. The expectation is that, with experience, the cost will drop and the speed will increase.

Professor Katsanis showed the delegates some slides from his lab research involving the now famous zebra fish. As mentioned in Professor Beales' presentation, the paradigm is very straightforward; you eliminate a BBS gene from the fish, and then you put a BBS gene back in, which provides data that is reproducible over and over again. He explained this, using the car as an analogy, that, if your car won't start, take the battery out, put a new one in and, if it starts, then it was obviously the battery. In the lab, the BBS fish have reduced spine length and it has been demonstrated that, by putting a normal copy of BBS1 in the fish, spine length can be restored. If, however, a copy of the BBS1 that carries a mutation is put in and the spinal length is not restored, then that particular mutation is clearly a problem. If spinal length is still restored, despite the mutation, then it obviously does not have a deleterious effect. This means that, from not knowing the effect of a mutation, they can show biologically that a certain mutation cannot repair the loss of BBS1, which has been done with over 150 BBS mutations that account for around 90% of all mutations found to date. Professor Katsanis and his team have reported on every single mutation of every family they have sequenced and have input the data onto an online database that people can access very easily. This has enabled them to make some headway into interpreting the mutations that were found in primary BBS genes, which will aid diagnosis.

It is well known now that BBS is a ciliopathy which means it isn't such a rare disease after all; 1 in 1,000-1,500 live births will be affected by a ciliopathy. Professor Katsanis pointed out that not being a rare disease is a good thing when trying to get pharmaceutical companies to

fund research as, the more people affected, the more profit there will be in them finding a treatment. Moving forward, the idea is to sequence around 500 patients affected by one of the range of ciliopathies in about 800 genes, to build genetic models that look at causality, the genes that cause disease and the variations that determine who gets what disease and the rate of progression into what aspect of the clinical phenotype.

In collaboration with two genome centres at Baylor College of Medicine and the National Institute of Health, Professor Katsanis and his team were able to sequence 752 individuals that had a ciliopathy of some kind, in addition to a control group of 300 individuals who did not have a ciliopathy. They found 40/50 mutations but couldn't tell, just by looking at the mutations, their relevance to protein function. However, by doing the fish studies, they were able to sort out which mutations had a detrimental effect on protein function and which mutations had no effect. They discovered that around six percent of patients with ciliopathies will have a mutation in a particular gene, not sufficient to cause disease but likely to contribute to the mutational load. From their research, they have found a particular mutation in a small number of BBS patients where every single one has had severe renal problems, which may assist with diagnosis and condition management in the future.

Professor Katsanis moved on to talk about a hypothesis they are working on that suggests primary cilia regulate the degradation of proteins required for signalling pathways. Cells are placed in a special saline, in which, if protein degradation is not working, the cells turn green, so the more green that is visible, the less efficient protein degradation is. He reported that, many years ago, they were able to show that, if BBS4 was removed from cells, the amount of green in the cells increased, so the question was, 'Where protein degradation is defective, if they were able to improve the efficiency of the protein degradation machinery, they may be able to remove some of the toxic effects of BBS.' They have found an experimental cancer drug, approved by the FDA for use in very advanced cancer patients, that reduced the severity of the effects in cells; however, transferring results from cells to humans has an extremely high failure rate, although they have had some success with fish. They have shown that this drug works for BBS1, 2, 4, 7, 8 and 9, but not for BBS3, 5, 6, 10 and 12 and they are still testing others; it is clearly a work in progress. They are working with mice and, if that is successful, they will be able to start a very small clinical trial in around 2013-2014.

Professor Katsanis understood everyone's frustration, but emphasised the need for caution; he said, "If we get this wrong the first time, it's going to be ten times harder to persuade anybody to participate. We've got to be sure that it's safe, we've got to be sure that it has a chance of working and we have to understand it a little bit because, if we have a catastrophe first time around, although we might shave a couple of years off the process, it could push us back a decade." He finished by saying that he agreed with Professor Beales in that he didn't think there would be one drug that solved the problem; however, in time, there would probably be multiple treatments for the various symptoms of the syndrome.



Weekend Round-Up!

Wow! What a fantastic weekend we had this year, with lots of new faces as well as old – if we keep growing at this rate, we will soon be pitching tents in the car park! Well, maybe not, but it is very likely that we will have to start using other local hotels as 'overflow' accommodation, so be sure to get your booking form in early to secure a room for next year.

The weekend guests started arriving from lunchtime on the Friday, to be welcomed by Richard Zimbler and Steve Burge, who did a fantastic job on the LMBBS Reception Desk; by mid afternoon, there was already a lovely buzz throughout the fabulous lobby that tends to be the focal point of the weekend. Dinner was served in the restaurant from 6pm and was delicious; three courses, with a range of healthy options to choose from. During the evening, the childcare team met the children and young adults and, later, they had the chance to brush up on their guiding skills. There was a meeting for 'New Families' hosted by Steve, who has BBS, and Laura, Claire and Allan, all of whom have children with the Syndrome. It is an informal get together for individuals and families and gives everyone a chance to ask questions and swap stories. It also means that newcomers have familiar faces to turn to over the weekend.

The Birmingham Children's Hospital Dietician, Waseema Azam, was available all weekend, to give help and advice where needed, as was Ray Perry, our benefits advisor. Rehabilitation Officer and LMBBS Conference regular, Sue King, displayed a range of visual aids and Francis Lestel, Vice President of the French 'Association of Parents of Visually Impaired Children' demonstrated free and low-cost computer software for the visually impaired, in the lobby area, over the weekend; It was great for the new families in particular, to have access to such a wealth of information in an informal setting.

As usual, for the children, there was a range of activities, crafts and gaming available throughout the weekend. This always comes into its own on the Saturday evening, when everyone is relaxed and ready for some fun. This year, the conference fell a week before Easter, so we had a craft table making Easter bonnets, Easter cards and baskets with chocolate eggs in. There were also table football, snooker and other games being put to good use – in some cases by the parents! A special highlight was watching the Hughes and the Mapleys play a game of table football, girls versus boys; well done girls, you did us proud! It was also very entertaining watching Emmy and Holly's dad 'helping' them make a very girly, pink Easter bonnet; ten out of ten for effort.

Saturday evening's Family Quiz and Grand Raffle were held in the Collingtree Room this year, as we were just too many for the lobby. Dennis Clark provided another challenging quiz, generating fierce competition among the teams. The atmosphere was electric, with much laughter and it was clear that everyone was having a great time.

Thank you, all of you, who generously donated so many tombola and raffle prizes and bought so many tickets. The Petty family donated not one, but two, magnificent hampers

and the Oates family donated the star prize of a week's holiday at their caravan site in Yorkshire. Conference Photographer, Doug, donated three of his beautifully-framed photographs, adding considerably to the monies raised. The tombola was enjoyed by all ages and our thanks go to Ray, Doreen and everyone else who helped, enabling us to raise the magnificent total of £685.

All too soon, it was Sunday morning and, following another delicious breakfast, time for everyone to say their farewells for another year. However, it wasn't really goodbye as new friendships had been made and support networks established, which would carry on throughout the year. The LMBBS Facebook page lit up with messages and comments about the weekend and, from these and the evaluation forms received, it was clear that everyone felt the same; it had been an amazing weekend.

Our Day in the Creche

Sandra Dale

This year we had eight gorgeous little people as our guests for the day, ranging in age from 4 months to 7 years. They were Carla, Bethany, Lucas, John James, Summer Jane, Mia, Noah and Oskar. No two years are ever the same and this year it was a case of nappies, bottles, cups and dummies all lined up ready to 'go'!

On the crèche care team this year were Linda, Karen, Nathan, Mel and myself. Linda and Karen are becoming old hands, with a few years experience behind them, they were the nappy changers; Linda has no sense of smell so was perfect for the job! For Nathan and Mel, it was their first year and they were naturals. They had great fun with the children, painting and doing Play Doh, they were such fun and so helpful, I hope they will join us again next year.

We have a wonderful choice of toys in the crèche, put to very good use by all the children. This year, the playhouse became a hospital; Carla, 7, in a white coat and stethoscope was the doctor and injections and blood pressure were the order of the day, a very serious business. Summer, 21mths, brought her baby walker with her but decided not to use it, however the wheels were in motion very quickly. Noah, 20mths, is a climber and very quickly clambered in and put it to good use, whizzing around the room. Mia and Lucas, 3, were chefs for the day with Nathan's help and spent a lot of time playing with the kitchen. Mia looked so cute with her hair in bunches and a very serious expression on her face as she played. John James, 3, loved the videos and kept himself busy with all the toys.

Bethany, 3, Carla's sister, was such a happy little girl and a very willing patient for Carla in the hospital, as was Mia. Summer, liked to be with one of us at all times and we soon discovered that a sure way to get her laughing was to blow raspberries on her feet. She loved listening to music and wiggled her bottom when the music is on. We mustn't forget baby Oskar, the youngest at just 4mths, he had three doting ladies ready to jump to his every whimper – what more could he ask for? I am still waiting for my cuddle!

The hotel wraps itself around a square that has a fenced-off duck pond and tables and chairs. All the children loved the baby ducks and trips outside were in high demand. The walk was just perfect for toddlers and enabled them to get outside for some fresh air. Dinner time was wonderful, with all the children sitting around the table, they were all so well behaved. Mia's mummy and daddy came to see her and volunteered to stay while the carers had lunch, our thanks to both of them.

I have been in the crèche for a number of years now and watching the children grow up is so rewarding, we all have so much fun together. At the end of the day, the parents collect their children and take them away, tired but happy and we look forward to seeing them again next year. Huge thanks to Linda, Karen, Mel and Nathan, a fantastic team.

Welfare Reform
Ray Perry
Area Benefits Officer
Kent County Council Social Services

Ray Perry is an Area Benefits Officer with Kent County Council Social Services Department, based in Tonbridge, and has over 30 years' experience, giving advice and training on Social Security Benefits.

He is a member of the National Association of Welfare Rights Officers (NAWARA) and the London Welfare Rights Officer Group (LWROG). He has a particular interest in LMBBS and has already successfully taken many LMBBS and registered-blind cases to appeal.

Ray can provide LMBBS members with a benefits check to ensure that their benefits are being maximised. He is also able to offer advice on procedures and tactics if you are considering taking a case to appeal.

The purpose of the presentation was to outline some of the government's plans for welfare reform which, year on year, will make savings of up to 18.5 billion pounds and will change profoundly the welfare system in the UK. The focus was on three main areas that are causing problems and a lot of worry for people at the moment, the reassessment of Incapacity Benefit claimants; the reassessment of Disability Living Allowance and the scrapping of Disability Living Allowance which is going to happen in 2013; and, finally, the introduction of Universal Credit.

Ray reported that the government have just started the reassessment of 1.5 million people who are currently in receipt of Incapacity Benefit, Income Support on the grounds of

sickness, and Severe Disablement Allowance. The aim is to migrate them from Incapacity Benefit onto the new Employment and Support Allowance (ESA). ESA now has a new work capability assessment which is, he said, tougher than the assessment that previously existed under the old scheme and has recently been updated again to make it even tougher. Trials in Burnley and Aberdeen found that 30% of those assessed were 'fit for work'. Rolled out nationally, this will equate to 450,000 people losing their entitlement to Employment and Support Allowance and being forced to claim Jobseekers Allowance.

These new changes started in February 2011 and will be completed by 2014. It was reported that everyone, apart from the terminally ill, will be reassessed, which may well be a new experience for those currently on Incapacity Benefit, as many have been automatically exempt from the assessment process.

Ray explained that the new process is about moving on from Incapacity Benefit, which was for those who were considered *incapable of work*, to Employment Support Allowance, which is for those with *limited capacity for work*. The form that is to be completed, the ESA50, is key to receiving this benefit and involves a point scoring process. Following that will be a medical
assessment which will be undertaken by Atos Origin, who are occupational therapists rather than doctors. Those proven to have limited capacity for work and able to claim ESA will be placed in one of two groups. The first one is the support group, which is for those with very severe conditions and will account for approximately 5% of claimants; they will not have to engage in work related activity at all. Ray stated that, for the other 95%, the journey is just beginning and will involve work related activity and many more interviews with agents of the Department of Work and Pensions. It is possible to appeal against the decision and already, Ray said, they are clogging up the appeal system and it is falling apart. So much so, that it is now taking ten months just to get a tribunal date and they are holding Saturday and Sunday appeal tribunals in an attempt to catch up. He continued, "This is only going to get worse because it has just started; from February, the number of extra medicals increased by 7,000 a week and, starting from the end of March, there will be 11,000 extra on top of those, which is quite a worrying number to look at." He continued, "A worrying development is that, following the work capability assessment, the report is being forwarded to the DLA unit, who may then, depending on the contents of the report, reassess the client's DLA award."

Ray moved on to talk about Personal Independence Payments, PIPs, which are going to replace Disability Living Allowance for people of working age from 2013. Ray claimed that, although the government says it is a fairer objective assessment, in reality it is a 20% cut in expenditure. There will be two components, 'Mobility' and 'Daily Living', and two rates, 'Standard' and 'Enhanced'. The assessment, like ESA, will have a points scoring process and there is a longer qualifying period of six months. Ray reported that, in addition, the government is 'medicalising' DLA, by introducing a medical with a DWP approved healthcare professional, with all awards subject to periodic review. Under the present system, some recipients are on indefinite awards; however, even those will be reviewed; everyone will be reassessed.

On a positive note, PIPs will not be means-tested, not taxable and will continue to be a passport to other benefits; special rules for the terminally ill will remain. There will, Ray said, be a greater duty to report changes in a health condition, which may be difficult for those with a fluctuating illness or disability; even so, there will be legal and financial penalties if these changes are not reported. It is still unclear, at this point, whether PIPs will replace DLA for children.

Finally, looking ahead, Ray reported that the next step will be for all existing means tested benefits and tax credits for people of working age to be replaced by a Universal Credit, which will be assessed and paid on a household basis. For those in employment, entitlement will automatically be adjusted as earnings vary, using real time PAYE data from Her Majesty's Revenue and Customs, through the introduction of two new IT systems. What this means, Ray said, is that the average family will have their income capped at £26,000, regardless of how big their family; there will also be limited help for mortgage interest.

Ray stated that introducing Universal Credit will be a huge and complex undertaking and suggested that the government has set itself a very tight deadline; however, it is an integrated benefit and households who claim will automatically receive everything they are entitled to. He argued that, although the object of a simpler, more transparent scheme, which is easier for claimants to understand, with a clear work incentive, commands widespread support, there is concern over the lack of detail on key elements.

If you are concerned about the changes and how they may affect you, support and information is available from the following sources:

Ray has kindly posted some useful information on the LMBBS web page: www.lmbbs.org.uk
Royal National Institute for the Blind (RNIB): www.rnib.org.uk
Dept for Work and Pensions: www.dwp.gov.uk
Ray Perry: ray.perry@kent.gov.uk

Workshop 1
Professor Phil Beales & Professor Nico Katsanis

Following, are a selection of discussion threads, from the many that took place during the three workshops held throughout the afternoon:

Delegate: In your presentation, you said that if you replace defective genes in a DNA strand in the fish, the DNA strand will fix itself; does this mean that you can cause the fish to grow a bad spine, replace the defective gene with a good gene and the spine will be repaired?

Professor Katsanis: It's not about repair of the spine – it's the whole fish that is repaired. Here's an example - I have two fish and, in one of them, I eliminate the BBS gene. In another one, I eliminate the BBS gene and, at the same time, I introduce the human copy of the BBS gene, hopefully showing that if you replace a damaged gene with a healthy gene, the fish that grows should be healthy.

Delegate: A human DNA strand, at some point does it stop growing? It's a building block and then a person is drawn from that building block, so why can't you take a damaged DNA strand, remove the damaged part and replace it with a healthy part?

Professor Katsanis: This is the premise of gene therapy. There are many reasons why it should work; It sounds very simple in principle, however in practice it has turned out to be harrowingly difficult. Don't think about it as a jigsaw puzzle where you take out one piece and you put a new piece in there, it's more like putting a piece of gum in and hoping it sticks, however, if you stick it on a really pretty piece of the puzzle, it's going to make a whole ugly mess. Which could translate to being cured from your particular disease, but then ending up with another, such as cancer. A few years ago there was a big gene therapy trial in France and a couple of people developed acute leukaemia and died which knocks the whole process back. Basically there should be no messing around with genes until you're 100% sure that what you are doing is going to work.

Delegate: I wondered if it would be helpful, as far as genes are concerned, to study parents?

Professor Katsanis: Yes, is the answer to that. Initially we've always been interested in gathering DNA from parents because it has been very helpful and still is for finding new genes. Although we are nearing the end, which is good news, I still think there is going to be a huge amount of benefit in collecting parent DNA.

Delegate: As parents, we've been told we carry one BBS gene, however we've not been told of the other. As we understand it, in layman's terms, is it a case of there being one gene to transfer the disease and then another to determine the severity – does it take two genes?

Professor Beales: In your particular situation, the reason why you have a single mutation is because we've found it by looking for *known* mutations. That means the other one is an unknown. We'll get there eventually, fairly soon I would hope, by sifting through the rest of that particular gene. I think it's very likely there will be two mutations in that one gene, but as Nico pointed out this morning there's quite often in many situations a third mutation elsewhere. In our cohort, of people in who we have found mutations, about 70% of them have two mutations in one gene and the other 30% only have one mutation in one gene. The way we are interpreting the data regarding the 30%, is either the second mutation is in a region of that gene that we haven't been able to query for various reasons, or that the gene we're looking at is not really the primary gene and the mutation is a modifying mutation, with the primary mutation being in a gene that we haven't yet discovered.

Delegate: If you find two mutated BBS genes, how do you know which one is the primary?

Professor Beales: It tends to be the one where we have two mutations in it. So the traditional paradigm is still true, that you must transmit a mutation in the same gene from the father and the mother to the child, you need both copies of a particular BBS gene to be defective in order to get BBS, but then you can have an additional BBS gene defective, from just one of the parents, and that will contribute to how severe the disease might be or how rapid the progression of some of the symptoms might be.

Delegate: So does the number of mutations you've got depend on the severity of your symptoms then?

Professor Katsanis: It is beginning to look like that, yes, however, there are also mutations in humans that will protect you from some defects. So you may have two, or three, or four BBS mutations, but could also have what is described as an amber mutation, that will improve the efficiency of your system in some cellular process which might shield you from some of the defects in BBS. Those mutations are extremely difficult to find because it's very difficult to identify things that make you better. Now that we're beginning to query people's entire genome, we will have the opportunity of querying everything and then the hope is that we will be able to start teasing some of these things out. This issue of multiple mutations is very important to understand because when we find a mutation in a single BBS gene, the predictions about what's going to happen next are based on epidemiology, not on the mutation. We worked with a family a few years ago with three BBS patients, two of them were blind in their teens, however the third had just started manifesting stationary night blindness at the age of 36, which is really useful information to have. It's one thing losing your vision when you're 16 and another when you're 36. We would like to understand why and we would like to see if we can mimick the reasons why, because that's an extra 20 years of light.

The conversation turned to the difficulties families faced in obtaining a correct diagnosis while their children were at a young age.

Professor Katsanis: To put it in perspective we are beginning to see the age of diagnosis dropping, and it's dropping because there have been more papers published about this disorder. To put it in perspective there's about 7000 classified genetic disorders and most physicians might see one or two people with any of those in their entire professional careers, so it's a very difficult thing to learn to manage.

Professor Beales: Collectively, ciliopathies are relatively common disorders, and so rather than expect the GP to know about different rare syndromes, they essentially should have a set of tools to be able to say "Okay, this is likely to be a ciliopathy based on retinal problems, perhaps weight problems, perhaps kidney problems, perhaps diabetes, these kinds of things." Maybe there should be better tools for them, not necessarily to know what the disease is but to know that it falls within this spectrum, and if it does, then you need to go to that particular specialist. The Ciliopathy Alliance, is aiming to bring a lot of these disorders together to raise awareness of them collectively, but also to try to use it as a platform for lobbying government, the people who make the difference. Most scientists five years ago,

would never have heard of BBS, any biological scientist worth his weight now, will have heard of BBS, unfortunately however, that's not the case for most medical doctors, so we need to focus on that group of people.

Delegate: Do you think in your life times there will be … you'll be able to say right, that genetic disorder, will you be able to stop that?

Professor Katsanis: We have to think that or we might as well pack in our jobs and go do something else! If you don't try you're sure to fail, so I would rather go down in flames having put everything into it. The biggest challenge is to make sure that, in addition to rolling that ball up the hill, we have to make sure that we get the next generation appropriately excited so that when we fall off, they will pick up the mantle and carry on. Am I going to see this in my lifetime? I sure hope so, but if not I will come back and haunt all my post docs so that they carry on. It will happen, it has happened for other disorders. A colleague of ours, Andrew Hammersley in Exeter, looking at baby diabetes, has found that people with a certain genetic disorder respond to a tablet and don't need insulin. It's one of the earliest demonstrations of how powerful genetics can be to change treatment.

Delegate: And do you, between the countries, you're not all just duplicating the same work, you're actually saying, okay, we're going to work on this, you're going to work on that, and then you're pooling it, is that what's happening?

Professor Katsanis: That's the idea, yes, we try.
Two years ago when we spoke at the various meetings here and in the United States, the words drug therapy were not in our vocabulary, other than as a distant hope and aspiration. Now they are, and all it is, is closing our eyes and throwing darts at a dartboard, but at least we have some darts, that's something. We will almost certainly crash and burn many times over, but at least we've got something going on. So when I think about, I don't know, breast cancer, when I think about HIV, when I think about hepatitis, the paradigm that has been really successful is not to eradicate these things but to convert them from acute, and in many cases lethal conditions, to chronic treatable conditions. I don't think there's going to be a cure for BBS, however I think it's going to be a transition to a long term, manageable disorder. So we may be able to slow down retinal degeneration to such an extent that it will not really become an acute problem until you're ninety-two years old, in which case you'll have other things to worry about as well. My approach is, if I have a drug that I see that has higher promise in endocrine issues or cognitive issues, I'm not going to say, oh, I'm not going to pursue that, because the vision problem is a bigger need. It's a question of, I have to take the path of least resistance. I do not wish to narrow the opportunity to discover something that is beneficial to people just by being super targeted on something. So from that point of view, if I really had a choice I would prefer to be able to deal with things that are truly life threatening, because I have seen people achieve remarkable things without sight and without hearing.

Delegate: You're talking about groups of drugs that might help to slow down the processes. Can you put timescales on ...

Professor Katsanis: I would rather come to you in a year with really good news rather than promise something today.

Professor Beales: It's probably worth saying as well that there are other researchers in other fields, Moorfields Eye Hospital and others, all working on other eye diseases and trying to find treatments for those eye diseases. Some of those have some overlap with Bardet-Biedl as well. There are other research programmes looking specifically to find treatments for the eye diseases as well, so there are people doing that.

Delegate: That's all that I need to know, that there are people working on that, that it's not been forgotten.

Delegate: Do you think that psychologically the children need a lot of help?

Professor Beales: We're learning more about that as we go along and at each clinic we have a clinical psychologist there who, correct me if I am wrong, needs to spend more time with you guys than the rest of us put together.

Delegate: You say a psychologist can help, however the experience I had with my daughter was that seeing someone was not sufficient and she needed medication. We tried several and the one that worked best was one acting on Serotonin.

Professor Beales: We have found that there is reduced Serotonin activity in connection with BBS4 and we are waiting on data for BBS1. We are now breeding mice that either make too little or too much serotonin and it will be about a year before we have a better idea of what is going on, however we think there is a shortage of Serotonin and that it might contribute to mood swings and depression in BBS.

Delegate: My middle son is 11, he's in high school and is doing really well, however he has become very emotional and cries for everything. When he's upset for a simple reason he cries like a baby, throws his glasses, saying 'there is nothing wrong with my vision', and 'leave me alone, you're stupid'. So, I needed some help and the best thing that happened was at the Birmingham clinic, where I spoke about my son to the clinical psychologist and she has arranged for us to be seen locally, and I'm so pleased, thank you.

Delegate: (…..) really appreciated the time with the psychologist, being able to speak to people on his own without mum and dad being there. This is the first time we've actually come to the conference and what we've gained today has been invaluable. We really appreciate all the help and all the work that you do. Is there another clinic this year? Will it be on a yearly basis?

Professor Beales: Everyone's going to come on a yearly basis. Whether it's exactly twelve months or fifteen months, we're not sure, because we have to get through everyone at least once, and then we can start inviting people back. So you will come within the following year at some point. But that's very helpful feedback, thank you.

Workshop 2

Professor Helene Dollfus

Professor Dollfus used her afternoon workshops to discuss, with delegates, the research and developing treatments and therapies relevant to Retinitis Pigmentosa.

Delegate: My daughter is nearly eighteen and her visual field is now down to less than five degrees. Last time they did an ERG, they said they possibly wouldn't do any more. What is your opinion on that?

Professor Dollfus: The ERG, electroretinogram, is a functional test that helps to test the photo-receptor cells, the cones and the rods, that are involved in Bardet-Biedl Syndrome. Unfortunately, the natural history of retinal involvement in BBS is that there is going to be progressive degeneration of the retina, so the answers of the ERG are going to get lower and lower through time and, eventually, although some photoreceptor cells may still be functioning, the ERG will appear quite flat. This doesn't mean there is no retina at all functioning, but that the retina is quite damaged. Doing and re-doing ERG's regularly is a burden for the patient and shouldn't be re-performed, because there is no use.

Delegate: So what would be a better way of recording the back of the retina, of being able to monitor the retina?

Professor Dollfus: We can record the visual field with different devices. Of course, when the visual field is very small, you cannot use these devices any more, but there are other methods we can use to evaluate the retina. OCT, optical coherence tomography, is a method that provides an image of the retina as a cross section, showing the different layers and can be used, for instance, when you have fluid at the back of the eye at the level of the macula, which can occur in any type of Retinitis Pigmentosa. It is also used to see the thickness of the photoreceptor layer. The basic test for an ophthalmologist is to measure visual acuity, which is the best test to see how the retina functions. Other imaging techniques look at the back of the eye and can be merged to get a very good overview of what's going on in the retina.

Delegate: In Japan, recently, they've been growing retinas; can you tell us about that?

Professor Dollfus: This is fascinating research that has been done on stem cells, putting them in a cocktail of different biological factors, using techniques for supporting development, they developed a tri-dimensional tissue that resembled an eye, which is a miracle, a breakthrough in science and very, very impressive. This is an area that is already very prolific in scientific publications of stem cell research for treating retinal diseases. In Great Britain, there are big specialists, especially James Bainbridge and Robin Ali in London, who have been the first to do stem cell research on mice with retinal degeneration,

where they saw stem cells really acting and connecting with other cells in the retina. This is a very promising area of medicine and warrants a lot of research and a lot of investment because it is regenerative medicine.

Delegate: Would this be relevant to Bardet-Biedl Syndrome, insomuch as would the receptors be re-grown as well?

Professor Dollfus: That is the hope; there is still some time before we are at that stage, but we cannot say that it is impossible. Nothing is impossible. When you see what has been done by the Japanese group, re-growing an eye artificially … it's just … I cannot tell you, I was really amazed; a lot of people were amazed by this.

Delegate: If the photoreceptor cells were implanted in someone who has BBS, would they start to degenerate or would the problem be stopped?

Professor Dollfus: Stopped.

Delegate: Would you have to do something to the patient before you put the stem cells in?

Professor Dollfus: There have been some trials using neurotrophic factors in patients with Retinitis Pigmentosa. This involves putting ciliary neurotrophic factor, or CNTF, a cone preserving factor, into the eye, with the aim being to prevent the cells dying. The other aspect is gene therapy, which is treating the cell directly for the genetic defects of the cell. As we know, there has been some very interesting and important research in the United States and in Great Britain, treating children who have Leber's Congenital Amaurosis (LCA), a type of retinitis pigmentosa that, like Bardet-Biedl Syndrome, is due to lots of different genes, one of which is RPE 65. This gene only accounts for one percent of all the patients with LCA, so it's a minority of these patients; however, it is one of the first genes for which gene therapy has been proven to be safe and non-toxic, and may be beneficial for the patients.

Delegate: How does gene therapy work? It sounds like you just throw switches and turn things on and off.

Professor Dollfus: The type of gene therapy that has been applied to LCA uses adeno-associated virus (AAV), carrying the gene that is missing from the patient. This is injected into the eye, so the virus can get the gene into the right cells and produce the protein that is deficient. For LCA, the virus has been targeted towards the pigment epithelial cells, to produce the protein there. For BBS, we have to target the photoreceptor cells themselves, using probably a similar strategy with some changes, to try and treat the photoreceptor cells.

Delegate: Has there been Bardet-Biedl Syndrome specific research into this?

Professor Dollfus: My group is working on this and there has also just been a publication for BBS4 by a group in the United States, involving mice. They are doing roughly the same thing as we are, using AAV virus, which is proof that it can work for BBS4. We are working

on BBS10 and are building a therapy which will be tested on mice first, which is very important.

Delegate: How long does it take to get from mice to humans?

Professor Dollfus: When you have a new molecule or a new type of therapy, you have to go through different agencies to get the drug approved; you have to prove the concept, usually on mice, and then you have to show that it's not toxic. Immunological data is also important because, when you introduce a foreign organism in the body, you have to look at how the immune system reacts. So there are a lot of issues to be answered before we can put this into a real treatment; we are not there at all yet but, looking back over the last fifteen years, we have moved dramatically forward and, hopefully, we will move forward faster and faster over the next few years.

Delegate: A few months ago, some people in Germany bypassed the photoreceptors altogether and implanted a camera; do you know anything about this?

Professor Dollfus: We know that, for deaf people, cochlea implants, connected to the brain, enable them to hear; however, the ear is less complex than the retina, which has a lot of interconnections and a lot of data to be analysed and transmitted to the right place in the brain for recognition. The dream is to have the equivalent of the cochlea implant for people who are visually impaired and there is a lot of research being done on artificial retinas. There are many variations on the model; a microchip can be placed in different settings, under, on top of, or behind the retina and there are also different methods used to transfer the visual input from the chip to the brain. There has been clinical research on patients that have end-stage Retinitis Pigmentosa, especially in Germany, and it has been amazing to see the results in some patients. They wrote the name of one patient on a piece of paper and held it in front of him and he spotted a mistake in the spelling, so it clearly works; however, the technology needs to be ameliorated for better resolution. The challenge now is to have chips that go to an even higher resolution with a greater number of electrodes that will be sufficient to function well.

Delegate: What's the difference between Retinitis Pigmentosa and Macula Dystrophy?

Professor Dollfus: There are different degrees of retinal degeneration. The retina is divided in two parts; the macula is the centre of the retina, where the cones are, that give us colour vision and fine vision. The other part is the periphery of the retina, where the rods are, that gives visual field perception and also vision in low-level light. Retinitis Pigmentosa starts at the periphery of the retina and progresses towards the macula and may, in some end stages, induce macula degeneration. You can have isolated macular involvement in retinal degeneration and you can have exclusively peripheral degeneration in some types of Retinitis Pigmentosa, not in BBS. In some types of RP, you can have what we call rod-cone dystrophy, or cone-rod dystrophy. Rod-cone dystrophy starts at the periphery and progresses towards the centre. Cone-rod dystrophy starts in the centre with macular involvement and will progress towards the periphery.

Delegate: Are there differences between patients who have mutations in the same gene?

Professor Dollfus: Yes, there can be differences and some patients will have more prominent macular involvement at the beginning, and others will have more prominent peripheral involvement. So it can be quite different from one patient to the other.

Delegate: Do all BBS patients have both rod and cone involvement in RP?

Professor Dollfus: I usually say, with BBS, both the cones and the rods may be affected. However, the clinical presentation may be different from one patient to the other. Some will have mainly cones at the beginning and it will progress towards the rods or it may be more peripheral at the beginning and be more prominent afterwards at the level of the cones.

Delegate: So we can't predict how Retinitis Pigmentosa will progress?

Professor Dollfus: I think, in any type of Retinitis Pigmentosa, not only BBS, but other syndromes or isolated Retinitis Pigmentosa, you cannot predict exactly what is going to happen. For some conditions, you know it's going to be very severe from the beginning and, for others, you know it's going to be a slower process. In Bardet-Biedl Syndrome, it's very difficult to predict how things are going to go; some patients stay quite stable for a long time with not much progression, we just cannot predict.

Delegate: But, if they've been stable, then it's likely to stay stable?

Professor Dollfus: Hopefully. We don't tend to see dramatic deterioration from one day to another.

Delegate's Comments

"I cannot begin to tell you what a great time we had and how moving and inspirational it has been, amazing doesn't begin to describe the people we have met and who now we will know ad infinitum. . . . "

"I feel like something inside me has changed. I have gained a new perspective."

"What an amazing weekend we had at the conference! The best yet - heartfelt thanks to ALL. We are already looking forward to next year's."

“ What a brilliant but emotional weekend. This weekend I realised what it means to have true friends and brothers and sisters in my life who just get it.”

“ Fantastic conference weekend, Chris was very much missed and we all wish her well. Thanks to everyone who works so hard to organise the weekend, you all do such a wonderful job which is what makes the weekend so enjoyable as well as informative.”

“What an amazing conference, everything was brilliant, saw some lovely old friends and met some epic new friends that I am sure I will chat to for a long time to come.”

“The carers were excellent, the children well looked after. Meals were very good. Very happy and proud of the people who took over for Chris and made the conference so good – thank you”.

“Delicious food, lovely hotel and very helpful staff.

“The whole weekend has been very instructive and we have gained a lot of knowledge relating to the condition, thank you for a wonderful weekend, it has been brilliant.”

“What a fantastic weekend, bring on next year!”

I hope you have enjoyed this conference report, don’t forget, all of the contact details can be found at the beginning.

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