LMBBS Conference Report 2012

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Foreword

What a difference a year can make… Last year I was enjoying the delights of the NHS, this year I was back, amongst friends old and new – and how great it was to be back!

Those of you who attended, will agree that this year's Family Weekend was 'one of the best', with the highest attendance ever. As a result, the hotel has been booked in its entirety for 2013 and we have had to make a decision regarding the way future conferences are booked and paid for.

Conference 2013 will see a new system in place whereby all delegates will contact the Hilton Hotel direct to make and pay for their own reservation. Meals and conference costs will be payable to the Society, at a subsidised rate. Delegates with LMBBS will only have to pay for their bed and breakfast. All other meals and conference costs will be paid for by the Society. We will of course provide assistance to those who require help with making their booking, full information is in the enclosed letter and booking form.

Back to Conference 2012 and we had an excellent mix of speakers, with 'something for everyone', largely made possible from the comments made on previous evaluation forms and I cannot stress enough the importance of this feedback. It is your conference and we strive to provide you with the information, help and support you have requested. The edited

presentations make up this report, enabling all of our members to benefit from the weekend and we give our heartfelt thanks to all the speakers and facilitators for their contribution before, during and after the weekend.

Over the weekend, a great time was had in the food tasting workshops with Waseema Azam and Sarah Flack, our BBS Dieticians. Ray Perry, our Benefits Officer, was understandably extremely busy and stayed an extra day to accommodate all our delegates on an individual basis and Sue King refreshed the guiding skills of our Care team, and provided a table to display visual aid resources.

I would like to say a big 'thank you' to Dr Helen May-Simera, ardent supporter and fundraiser for LMBBS. Helen flew in from Washington DC on Friday morning, jetlagged after a night flight, but nevertheless thrilled to be with us once again, to tell us all about her work in the USA. She then travelled back on the Sunday morning! Thanks also to our other speakers, Dr Barbara McGowan, Dr Marie Tsaloumas, and Professor Tim Barrett, all giving up valuable family time to speak at our conference. LMBBS wouldn't be where it is now without Professor Philip Beales, whose tireless work and quest for answers and dedication have brought us to the forefront of research. There was much praise too from members for the designated LMBBS Clinics and the difference it has made to the management of their condition.

We must not, of course, forget our carers, who work tirelessly throughout the weekend, ensuring that the children and young adults are well cared for and thoroughly enjoying 'their weekend'. Without their commitment each year, the Family Weekend would not run as smoothly. THANK YOU from us all.

Our heartfelt thanks must now go to the Hilton and all staff who make this weekend extra special. Their attention to detail is exemplary and the many requests we have are always dealt with promptly, ensuring that the weekend runs like clockwork from the time members walk through the door, until they leave. It is always warming to arrive and find familiar faces ready and waiting to welcome us.

Finally, a big thank you to you, our members, for without you and your continued support, our Annual Weekend Family Conference would not be the resounding success it has become.

We look forward to seeing you again in 2013

Chris Humphreys

Welcome and Introduction to the Day
Professor Philip Beales

Professor Beales welcomed everyone to the LMBBS Family Conference 2012 and briefly outlined the programme for the day. It was, he said, a record year with 200 delegates attending the day conference and 267 staying over the weekend. He welcomed back Chris Humphreys who was unable to attend Conference 2011 due to

ill health, saying how much she was missed and what a sterling job she had done, not just in organising Conference 2012, but with the BBS Clinics as well.

Professor Beales welcomed the international visitors, from Norway, USA, Switzerland, Guernsey and Australia, before moving on to invite delegates to take part in a research project that was taking place during the day. New research has shown that cilia in the brain helps the brain to function properly and to form memories, and Professor Beales, Dr Baldeweg and their team were interested in exploring how this might affect the daily lives of those with LMBBS. The research involved taking part in a five minute memory test to see if, as a group, people with LMBBS retain information differently from those without. We look forward to hearing the results of the tests in due course.

Professor Beales introduced the first item on the programme, which was the Laurence-Moon-Bardet-Biedl Society's Annual General Meeting.

Annual General Meeting
The Hilton Hotel, Northampton
Saturday 21st April 2012

Minutes of previous Annual General Meeting

The Minutes of the Annual General Meeting on Saturday 16th April 2011, previously circulated, were agreed and signed.

Apologies for Absence

Apologies for absence were received from James Moran, Chief Executive of the Bradbury Centre in Liverpool, the Stone family, Jonny and Sharon Fegan, Graham Longly, Beverley Barrass, Adele and Alan Fricker; Michelle and Terry Begley and Shehnaaz Jinwalla

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), Richard Zimbler and Tina Hickey were due to retire this year. We thank both Richard and Tina for their contribution to the Society over the past few years. Richard chose to stand for re-election and a nomination was received for Emma Oates. In the absence of any further nominations, both were elected to the committee unopposed.

Chairman's Report

The Chairman's Report was as follows:

We have had a very busy year, building on the successful start-up of the Bardet-Biedl Syndrome Multi-Disciplinary Clinics, which continue to be held across four centres: Birmingham Children's Hospital, Queen Elizabeth Hospital, Birmingham, Guys Hospital, London and Great Ormond Street Hospital for Children, London. LMBBS Clinics Limited, a subsidiary of the Laurence-Moon-Bardet-Biedl Society, continues to employ three support workers, who facilitate and attend these clinics, providing support to those who attend, before, during and after the appointment.

LMBBS Clinics Ltd manages the patient database, with 382 affected adults and children listed. This is an increase of 90 patients in the past year alone and an increase of approximately 180 patients since the clinics first started. All four centres have booked additional clinic dates to cope with the increase in patient numbers and, at present, appointments are running at 18 monthly. Over the past year, we have encouraged volunteer involvement in the clinics and now have several individuals who are willing to attend and provide additional support when needed; all expenses are of course paid.

Feedback has again been excellent and the first four-centre meeting was finally held on 30th September 2011, to take stock of the first year. All four centres came together to compare clinic structure and findings and plans were made to standardise the clinics across the service. Plans were also made to develop a national database within the NHS of those with Bardet-Biedl Syndrome and their symptoms. We have been involved in a research project aimed at linking genotype with phenotype, which is already producing interesting links. The long-term aim of the study is to improve diagnosis, disease prediction and long-term management of the syndrome.

Both the BBS Clinics database and the LMBBS membership database are updated regularly to ensure all records are accurate, in line with the Data Protection Act. The LMBBS membership database has increased to 515 members and 154 professionals, and these numbers are likely to continue to grow over the coming year.

In respect of Fundraising, and as reported last year, we had a good start to the year, receiving grants totalling £8,000 from the Foyle Foundation, the Hedley Foundation and VICTA. These were for our Annual Weekend and Conference in April 2011 and we thank them for their generous support.

Subsequent applications for funding were unsuccessful but donations received and the fundraising efforts of members and friends, many in response to the SOC(K) Appeal, raised around £25,000. Our very grateful thanks to everyone who had a part in raising such a fantastic sum of money for the Society, including those who gave matched funding. At the end of the year, we were delighted to receive a most generous donation of £10,000 from a friend of one of our members and we are considering how to put this to the best possible use. Our very grateful thanks to him for helping the Society in this way.

Finally, we have applied to become members of the Fundraising Standards Board (FRSB). The FRSB is the independent self-regulatory body for UK fundraising and is backed by the Office for Civil Society, the Scottish Government and the Welsh Assembly Government. The FRSB helps members comply with fundraising best practice in order to raise standards and build public confidence in fundraising; members are able to use the 'give with confidence' tick on all fundraising materials

In April 2011, we had another very successful Family Conference, with an excellent line-up of speakers and workshops. The LMBBS Family Conference 2012 is 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. We expect this event to continue to grow and have booked the Hilton Hotel, Northampton, in its entirety for 2013 and 2014.

A major consideration during the organisation of the annual Conference is the safety and well-being of the children during the weekend, in the crèche and on the trip to the theme park. Considerable time has been spent updating our child protection measures and this will be continued throughout the coming year, with key members of the team undergoing child protection training.

In March 2011, we were invited to attend a reception at Westminster to mark Rare Disease Day 2011, together with other members of the Ciliopathy Alliance. We also had an attendance at Sight Village in Birmingham and London and Sight Support in Wales, raising awareness of the Syndrome and Society. 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.
We continue to have an active presence on the board of the Ciliopathy Alliance; our thanks go to our representatives, Drina and Michael Parker, for their excellent contribution on behalf of the Society. The Alliance has achieved charitable status and planning is well under way for its first major event in May - "Cilia 2012 Conference". Although the Conference is intended to stimulate and encourage drug companies, medics, researchers and other cilia scientists, and is not aimed at patients or support groups, representatives of LMBBS will be attending the evening reception and will be on site throughout the Conference, manning an information desk at the adjoining exhibition. This very high profile, international Conference is expected to generate significant impetus to the fast-developing research into ciliopathies and their treatment.

The LMBBS website has been very busy, receiving 7,380 visits by 5,554 people between 1st January 2011 and 31st December 2011. This is an increase of 2,500 visits on the previous year. 23,757 pages were viewed including the following:

Home page	8602	visits
Publications	1722	visits
Research	1172	visits
Clinics	964	visits
About LMBBS	713	visits

As reported last year, the chat forum was underused and has therefore been removed from the site. In 2011, the Society launched its Facebook page and this has been very well

received. New families have gained much support and information from older members and it has also proven an effective communication tool for the Society.

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.

Finally, we have begun the long process of reproducing our medical booklet, with the aim of making it more patient focused. Relevant clinicians have been approached to update the content and we hope to have the new booklet completed and distributed over the coming year.

I would like to thank Professor Beales for his continued support and dedication to the Society, without whom we would not have achieved the current status. My thanks also go to the members of our Committee for their unstinting work and their ever increasing workload; as always we will strive to work together to ensure the Society continues to go from strength to strength.

Before I finish, many of you will have heard or read about the fantastic achievements of a young man from Southern Ireland, Shane Ryan, who was a member of the successful Irish rowing team. Shane has proudly informed us that he has been selected as one of the youngest members of the Irish crew to qualify for the 2012 London Paralympics. He has already been invited to the conference in 2013 to talk about his achievements.

The Chairman introduced Allan Clark who presented the Financial Report on behalf of Kevin Sales.

Financial Report

For the financial year, 1st January 2011 to 31st December 2011, the Society received an income of £58,364, an increase of £4,000 on the previous year. This included fundraising and donations of £21,970, marathon donations of £9,149, grants of £8,000 and donations from the Friends of LMBBS of £2,826. Expenses for the same period were £39,785, slightly up from the £39,000 at the end of 2010. This meant that the Society finished the year with a surplus of just over £18,000, an increase of nearly £3,000 on the previous year. The Society received an income of £13,874 from conference delegate contributions, however the cost to the Society for the weekend event was £28,917, a loss of £15,043. Over the past two years LMBBS Clinics has covered the cost of all newsletters and conference reports. In addition to the leaflet printing, which equates to approximately £6,000 per year, this has clearly assisted with the Society's financial growth, however it cannot be relied on in the long-term. The LMBBS Clinics account experienced a short-term deficit in June 2011 and £2,500 was transferred from the Society account to the Clinics account as a temporary measure. It is the intention of the trustees that this will be repaid shortly. In April 2011 the Society's Accountant, Michael Bannister, left Thompson & Co. and started his own business, Fryzer Bannister Financials Ltd. It was agreed at last year's Annual General Meeting that the Society would stay with Mr Bannister and move to the new company with him. The transition

went smoothly and we continue to benefit from Mr Bannister's knowledge of the Society and his good relationship with the trustees.

To sum up, it is clear that the main costs to the Society are the Annual Family Conference and its various publications and it is good to see that there are sufficient reserves at the year end to maintain these activities for the coming year. However, we can't just maintain our present activities, we need to keep driving forward. Our leaflets all need reprinting and we want to seek new diverse ways of providing support to all members and to do this we need the continued support of the wonderful band of fundraisers and supporters. It is only with their help that we can further develop the objectives of the Society and move forward with purpose.

Appointment of Auditor
The Committee proposed that the Society continue 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 20th April 2013.

Update on Research and Study of LMBBS
Professor Philip Beales

For the benefit of the delegates attending their first LMBBS Conference, Professor Beales began by talking briefly about the recently introduced BBS Clinics.

"In 2010 we were successful in receiving the thumbs up to develop clinics specifically for LMBBS across the UK. The Advisory Group for National Specialised Services (AGNSS) is a component of the NHS, in charge of advising ministers of health on the types of specialised services that are required in the UK. The service is UK wide and is funded by the Department of Health in England; there are automatic arrangements in place for Scotland and special arrangements for Northern Ireland and Wales. Anyone in the British Isles can come and see us if they go through the requisite route. The service is an integral cohesive organisation, essentially split up into a number of partner organisations and partner services. There are four hospital trusts involved, two in Birmingham and two in London; children go to Birmingham Children's Hospital or Great Ormond Street Hospital and adults go to the Queen Elizabeth Hospital, Birmingham or Guys Hospital, London. The fifth partner is of course, the LMBBS Society and their integral involvement is something that was really important to obtaining agreement from the ministers and commissioners from AGNSS."

“Another aspect of the service is our DNA laboratory, a diagnostic laboratory, for doing molecular tests, which is pretty much a first for this kind of service. We started mid 2010 and have now seen almost 400 patients across the whole of the service, which is well above my predictions. Those of you who have attended the clinics will know that it’s what we call a multidisciplinary team. We have at least six different specialists at any one clinic, including an endocrinologist, ophthalmologist, nephrologist, clinical psychologist, geneticist and dietician. We are all coordinated by the BBS Family Support Workers and also by our Clinical Nurse Specialists. Each patient not only has access to the various clinicians, but also has a full blood profile taken as well, including genetic testing.”

“As I’ve said previously, the clinics could not run without the LMBBS Society, because from the very outset they helped us to design the service itself; they are our advocates and know more about the complexities of this condition than most clinicians do. We know about individual components and so forth, but you guys know best about the actual condition itself. We also rely on the feedback from the service as well to enable us to improve as we go along. The Society also provides support and information via publications, the website and of course events such as this Family Conference.”

Professor Beales explained that to learn from the clinics, an audit meeting is held annually where all four hospitals come together to discuss their findings from the previous year, some of which was presented at the conference and is detailed later within this report. Professor Beales discussed some of the dietetic results from Waseema Azam, the Birmingham Children’s Hospital Dietician.

“Waseema found that 50% of the children measured had a BMI in the ‘obese’ category and 20% were ‘overweight’, which is a significant problem for this group. They also found that although 25% have a ‘normal’ body fat composition, a significant number have almost 50% body mass taken up by fat, which is really important and an area in which we have to focus a lot of our efforts. Sarah Flack, Great Ormond Street Hospital Dietician, has also reported some interesting data. Of 16 children seen at the London clinic, only one of these actually falls within the healthy weight range, whereas 15 had a BMI that was in the overweight or more range. However, 8 out of the 15, or 53% were actually able to achieve a reduction in that Body Mass Index after having seen a BBS Dietician. Studies have shown that you have to at least have a quarter of your Body Mass Index standard deviation to improve not only weight loss, but metabolic health. It is therefore encouraging that in the children who are under 10, we are seeing that 75% of those lost more than, or equal to this amount. Again, in the over 10 group, 50% lost more than the target, which is very encouraging.”

Professor Beales briefly touched on the renal aspect of the service, outlining the findings of Dr Lukas Foggensteiner, who runs the adult service in Birmingham and David Goldsmith, who runs the Guys renal component. They have reported the results of 111 patients who had been seen at clinic, a number which has increased slightly now. They found that 51% essentially had normal renal function, which means that just under 50% have abnormal renal function. However the majority of these have a very mildly reduced kidney function with only about three percent having severely impaired kidneys.

Professor Beales moved on to discuss the findings to date of the clinical psychologists, he said " I'm going to give one piece of information that was gathered by Diane Gumley at the London Children's clinic. She administered various standardised questionnaires and showed that about 22% of our children accessed mainstream education without support and 48% accessed mainstream education with support, which is great, because if we went back about 20 years ago, that figure would be completely different. Dianne also highlighted a number of behavioural problems, especially in the young, which I won't go into right now. She also administered some special tests, the SCQ test which measures a number of things, including autism and I was surprised to see that just under a third fell within the autism range. Quite a significant number, 35%, and these are children don't forget, exhibited stress and anxiety, which I think is something we need to focus on. Other emotional difficulties were present in about 45% of the children assessed."

Over the past few years at the LMBBS Conference, Professor Beales has heard from parents, that speech and language seems to be an issue in some individuals who have BBS, so he asked Caroleen Shipster, Speech and Language Therapist, to come along to the BBS Clinic at GOSH to investigate. Caroleen has determined that over 60% of children who have LMBBS have either speech delay or dyspraxia, which is leading to some of the speech impediments seen. This is something that needs to be addressed, and a decision has to be made on whether Speech and Language assessments should be rolled out to Birmingham Children's Hospital and what should be done in terms of managing this aspect of the syndrome.

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Professor Beales finished the BBS Clinics aspect of his presentation by talking about the genetics discoveries. He said "as you know, there are many BBS genes, about 16 or 17 different genes, any one of which can have a fault in it, and give rise to LMBBS, which presents a big problem in terms of testing. As of September 2011, we have been able to confirm, molecularly, a BBS diagnosis for about 50% of 221 patients tested. Most of the time, Diagnosis is made clinically, but very occasionally we have difficulty in deciding whether or not someone really has LMBBS, so molecular testing can really help with those patients. We have also managed to confirm carrier testing in 20 relatives, which is important for family planning reasons and so on."

It was reported that out of the 16 or so genes found to date, the ones most commonly affected in those of North European extraction, are BBS1 and BBS10. At clinic, we have been conducting a study to look for genotype/phenotype correlations (e.g. are there certain clinical problems that only arise if one carries a certain gene mutation). It's still very early days, but so far, some loose correlations have been identified. Those with faults on the BBS1 gene tend to be taller; those with a fault on the BBS10 gene, might have a slight increase in thyroid dysfunction and again this is very preliminary data, but if you have a fault in BBS1, visual deterioration seems to be delayed into the 20s. Professor Beales reiterated that this is very preliminary data and needs to be confirmed, however it could prove to be very useful data that can be used to improve patient management at clinic.

Professor Beales displayed a chart highlighting our 'very multicultural service.' Although the majority of those attending clinic are of white Northern European extraction, a significant

proportion, over 20% are from some other ethnic background, with at least 15 or 16 different ethnic backgrounds represented. Of that 20%, the biggest group are patients of Pakistani origin, from the Midlands region. This information is useful because within those particular communities we know that the patients we see are just the tip of the iceberg and there are people out there who are not getting access to this service. As a service, we are now in discussion with the Department of Health to see whether we can establish some way of developing multicultural workers to go out into the community to reach these isolated groups.

The discussion moved on to outline the involvement of LMBBS in the Ciliopathy Alliance. The Alliance is a grouping of all of the conditions that are affected or shown to be determined by faulty cilia and the reason for pulling all of these support groups together is because individually, the conditions are rare, but with around 1 in 800 people in this country having a ciliopathy, by pushing them all together we have a more powerful voice with which to lobby parliament, the Department of Health and generally take our cause forward.

Professor Beales said, “We have coming up in just three weeks time, in London, the first international scientific conference on “Cilia in Development and Disease”. We have lined up lots of really high quality talks from scientists from all around the world, almost 300 delegates attending from 20 different countries, coming to that meeting, as the first of its kind in the world.

The presentation was brought to a close with some background information regarding the memory study that was being conducted throughout the day. Professor Beales reported that there have been two or three recent scientific papers indicating that cilia are really important for an area in the brain called the hippocampus. It used to be thought that the brain, once grown, was fixed, however in recent years it has been shown that there are certain parts of the brain that can actually keep re-growing. One area is in the hippocampus; every time we’re faced with a new stimulus from outside, we have to lay down a memory and the cells in the hippocampus, the neurones wakes one of these stem cells, which then matures into dendrites to make little connections, synapses with the rest of the brain to lay down a memory. Professor Beales said they are now wondering whether problems in the way the cilia is functioning in LMBBS could be leading to some of the memory deficits reported in those with the Syndrome.

Maybe Two Wrongs do make a Right?
Dr Helen May-Simera

Many of you have heard the terms ‘cilia’ and ‘cilium’ and know that LMBBS is a genetic syndrome. Many of you might be wondering what this actually means? What is a genetic disorder? Our bodies are made up of millions of cells and every single cell has got a nucleus, inside which there are chromosomes. Chromosomes are made up of long strands of DNA; they are absolutely tiny, smaller than microscopic, in fact they are so small you need *specialised* microscopes to see them.

A gene is a certain part of that DNA, and is the instructions for the cell to make proteins, which are the building blocks of the cells. The genes and the DNA tell the cell what kind of a protein to make; there are lots of different types of proteins which come in lots of different shapes and do lots of different things. Some look like stars, some look like barrels, some look like sheets and they all fold together in specialised ways and are really important for the function or structure of a cell.

So the way I like to explain it, is that the proteins are like a Lego brick. To build a Lego house you need lots of different bricks, which all need to fit together to make a proper structure. In genetic syndromes, there is a change in the DNA that causes a change in the protein. Suddenly a Lego brick that was nice and square might now look round or flat. The shape of the protein can change, but also the characteristics and the property of that protein. So going back to the Lego brick analogy, whereas before, a green brick may have liked to stick together with a red brick, it might not be able to do that anymore. These are the kind of events that can happen in human diseases.

So what is happening with the LMBBS proteins? We know that LMBBS proteins are really important for the formation and function of a thing called the cilium. Cilia are little hairs that stick out of your cells, sometimes you can have one cilium or sometimes you can have multiple cilia and what we know is that all the proteins that are involved in LMBBS come together and make cilia. There are actually two types of cilia, motile cilia and primary cilia. Motile cilia for example, can be found in our lungs and for a long time people have known that they are important. However, there is another type of cilia, the primary cilia (sometimes called the sensory cilia) and what is amazing is that for decades, people thought they weren't important. They thought they were just left over from evolution; we didn't need them anymore and they didn't do anything. It was only about ten or fifteen years ago that researchers realised that they are important; they are really, really important.

Not only are they important, but they are on so many different types of cells in the body and rather than actually being motile and moving things around like the motile cilia, these sensory cilia are more like an antennae, they can talk to other cells and feel what is out there. We don't really know exactly what these are all doing, but we do know they are important. One of the places that we have primary cilia is on the cells in our nose, which help us to smell. In the ear we also have a certain number of these cilia that bend backwards in response to sound waves hitting the ear drum and because these bend in certain ways, the cells then fire and send the signals further up to the brain enabling us to hear. Arguably one of the most important places in the body where we have cilia is in the eye. Although it might not seem likely that cells in the eye have cilium, the very crucial cell that is needed for seeing, actually has a cilium inside it. The cell has got two parts, it has got an inner part and an outer part and connecting the two parts of these cells is a cilium and that is why eyesight is so heavily involved in BBS.

We are now finding that there are a lot of other syndromes that are diseases of these primary cilium and they are termed ciliopathies. Ten years ago we didn't realise that these diseases were linked, it turns out that they are, and that there is a lot to be learnt from comparing the different syndromes.

There are several different genes that cause LMBBS and several different proteins. There are two that I have decided to focus on, for various reasons. One of them is BBS6 and that was actually the first gene to be identified. The other one is a protein called BBS14. BBS14 and BBS6 come together in a very special way and that particular interaction is something that I have been trying to investigate further. BBS6 is at the bottom of the cilium and it anchors the cilium to the cell and BBS14 is just above it. We now know that they are holding on to each other.

When we look at cells that have both of these proteins, BBS6 and BBS14, they look fine and they are all uniform and they work very well. However, when we look at cells where we have disrupted BBS14, there are a few differences but they are still pretty well aligned. Now if we take cells where we have removed BBS6, so there is no BBS6 protein in these cells, suddenly we get really weird shapes, for some reason these cilia aren't anchoring very well. We decided to see what would happen if we were to take both of these proteins away, expecting to make the situation even worse. So we did the experiment and we took these cells and we removed both of the proteins and it turned out that actually these cells started to look a little bit better.

This is where it got really confusing. My professor didn't believe me, he said I must have made a mistake and to go back and do it again and it was only after about the third time that he started believing that what I had done was actually real. What we were seeing is that these two proteins are obviously coming together in very certain ways and this connection is important.

One of the areas in which we investigated this further was the eye. One cell in the eye that really helps us to see is the photo receptor which, as I mentioned previously, has got two parts, the inner and outer segment, connected via the cilium. In BBS one of the reasons that eyesight can be compromised is because this cilium isn't functioning. In these cells, what we noticed was that when you take away either BBS14 or BBS6, the photoreceptors don't look very well. However, although they don't look great when you remove both, it does not seem to be as bad as when you take away one or the other separately.

Although we don't know why this is happening, we are beginning to understand that the proteins that cause LMBBS and are important in LMBBS are working in complex ways and are working with each other; you can't view them in isolation. This is really important in understanding the biology behind what is going on. For the last ten years or so we have been focusing on cilia in general, now we are realising that although different parts of the body might all share the same structures, they all work slightly differently. It is going to be really important in the future to understand each cell and how unique each cell type can be to understand, not just on a genetic level, but on a protein level, what is going on.

EURO-WABB

Professor Tim Barratt

Leonard Parsons Professor of Paediatrics

University of Birmingham

Professor Tim Barrett leads the Bardet-Biedl service at Birmingham Children's Hospital. He also leads a laboratory research team studying the genetics of rare diabetes syndromes and a clinical team undertaking clinical trials in children with diabetes. In 2010 he successfully gained a European grant to set up an international register for Wolfram, Alstrom and Bardet-Biedl syndromes. Professor Barratt explains what EuroWabb is all about:

"The purpose of this project is to try and put together a registry, to pull together all the doctors looking after people with Bardet-Biedl Syndrome and other conditions across Europe, to try and improve diagnosis, help people to access genetic testing and to improve patient and doctor information.

The project is funded by the European Union. We brought together Wolfram Syndrome, Alstrom Syndrome and Bardet-Biedl Syndrome, which is why this project is called Euro WABB; It is a three year project, uniting partners across Europe: Spain, Italy, France, Poland, Estonia, Romania and others including Denmark and Sweden now as well; Professor Beales is a UK partner.

The three diseases, Bardet-Biedl Syndrome, Wolfram Syndrome and Alstrom Syndrome, have an overlap of symptoms; they all feature eye disease, diabetes and deafness and many doctors mix them up or make mistakes with diagnosis. The aims of the project are to try and get doctors to collect information about people with these conditions, about the medical information, the genetic information and conduct investigations according to a common dataset.

A big part of the project is to actually try and identify all the genetic mistakes in all the different genes that have been published, to provide a mutation database freely available on the website. This would enable any doctor in Europe who gets a report from a laboratory with a genetic mistake on it, to look up that mistake, find out where it has been published before and what sort of children or people it was published in. Parents and patients could also have access to the database, so it is about everybody being able to share the information.

A further aim is to try to write information for families and health professionals to explain what Bardet-Biedl Syndrome is, so that people will recognise it better. Alström Syndrome UK have produced a handbook, and LMBBS are also producing really good information. Sharing information around the rest of Europe will help people in countries such as Romania or Greece and so on.

We are trying to collect at least 300 anonymous records of people affected by Bardet-Biedl Syndrome and other conditions. The registry contains genetic data and medical data but nothing that will identify the patient; no names or addresses, just a centre number and a patient number. The clinical partners are the doctors around Europe who will ask you as

patients for your permission to include your data anonymously in a record in the register. The patient's role is that you can register yourselves on the website if you want to, to take part in the project so that you can see your own data record. You can also put in some data of your own, particularly about quality of life, patient experience, what it's like going to the clinics and having the diagnosis.

We are trying to build a genetic testing network, so that any patient with BBS in Europe and their doctor will know where to go for a genetic test. A lot of those are going to come to Professor Beales, because that is where the major centre in Europe is. We hope that if we can get information on enough people with Bardet-Biedl Syndrome we can understand the natural history of it; we want to know if one particular genetic mistake can predict when the eye disease is going to happen and the more information you have, the better the picture you can build up about it.

We are only able to carry out this project because of the support of the family support groups. I am really grateful to Chris Humphries and others from LMBBS for their enthusiasm. The worldwide Wolfram Syndrome Families Group, Alström Syndrome UK, the French Alström Group are also involved and there is also a German Bardet-Biedl Group who are very keen to take part in this as well. Bringing these groups together will enable us to get enough people together to do some really good research. At present we only know of approximately 400 people with Bardet-Biedl syndrome in the UK and because there are so few it is so much harder to set up new research studies looking at new treatments for this. What we really hope is that with Euro Wabb pulling everybody together, we will get enough people to do clinical trials of new treatments when they come along.

So far we have had about 2,500 hits on the website and expressions of interest from many countries all around Europe. We have also made connections with doctors looking after people with Bardet-Biedl Syndrome in Spain, Italy and Romania as well, areas where we haven't had contact before. The web address is www.euro-wabb.org: it has been written by web designers especially for people with low vision or no vision for full accessibility. It is also available in eight different languages.

We have developed an ethics form, which asks the patient whether they are willing to take part in the project and have their anonymous data stored electronically on the register. The information is held in a secure facility in the University of Glasgow because they have experience of these sorts of projects and we know it is safe that way. We also ask for permission to add the data to the UK National Disease Registry, to put all the information together from all four BBS centres. We also ask if this can be shared with other disease registries across Europe. We are trying to pull everybody's efforts together to speed up the research and one day, if there's a big Bardet-Biedl Syndrome registry in North America and they need to put European work and North American work together to speed up the research, we need patient permission in advance to allow that. I think this international collaboration will really help further research in the future."

Q. At what age does the registry include children?

A. Professor Barratt: The registry can take children from any age, from birth upwards, but we have to have permission from their legal guardian. From 16 years of age, patients can

give their own permission, however between 16 and 18 we like to have mum and dad's permission as well. Over the age of 18 patients can give their own consent.

Q. Will the patient information from the multi-disciplinary clinics be fed into the project?

A. Professor Barratt: Not without patient consent because this is a research project. We are very keen to try and build that process in to the clinics, to be able to offer patients the consent forms and the information as they come to the clinic.

Q. Are you going to be able to update the information?

A. Professor Barratt: We have designed the website with the National E-Science Centre in the University of Glasgow so that every entry is dated and every time we see a patient we can update that information. We hope to keep the project going and over time, follow the progression of the condition in individual people.

Q. How far off are clinical trials and how you would select people for them?

A. Professor Beales: It is too early to say when trials will begin There are a number of groups around the world looking at gene therapy, however none of them have been taken into humans yet. There are also a number of drug type research projects involving animals. Over the next couple of years, we are validating everything in animals but watch this space, you'll be the first to know.

A. Professor Barrett: Our aim is that as soon as a drug company is ready for trials, we are prepared with a cohort of people that might be interested in taking part. The drug company won't be able to approach patients directly, it has to be through your doctor; companies wanting to use this registry have got no direct access to the families. Further, if families want to take part in a trial, separate consent is required. Consenting for the registry doesn't commit the patient to anything else.

Q. Will we be able to see about the symptoms of specific genes, like BBS10 or BBS9 on the website?

A. Professor Barratt: Only from what's been published in the literature. You can look up all the mutations for a gene and it will direct you to the relevant publications.

Weekend Round-Up

It was suggested last year that we may have delegates sleeping in tents in the car park but we are pleased to say that it didn't quite come to that. At one point we did have ten rooms booked at another local hotel; however the Hilton were fortunately able to release some more rooms to us at the last minute. Needless to say, we have booked the hotel in its entirety for 2013. Prior to the weekend, we were a little nervous as to how we and the hotel would cope with the extra numbers, but we needn't have worried, for the majority of the weekend, everything ran like clockwork once again. Things became a little hectic during the Friday afternoon with so many delegates arriving at once and some of us became ad hoc 'baggage boys' and porters for an hour or two, but things soon calmed down. It is such a special time for us and feels like a big family reunion, catching up with old and new members; there is a great atmosphere all weekend, so warm and festive.

A fantastic aspect of the weekend is that we have dieticians, a benefits advisor and a rehabilitation officer all available for informal or private consultations. These very special individuals are conference regulars, great supporters of the Society and really understand LMBBS and its implications. Sarah Flack and Waseema Azam, our dieticians, laid out a table of different healthy foods on the Friday night to allow the children to explore different flavours and textures. There were stickers and little prizes to encourage participation which was a big hit. They also held food tasting workshops for adults on the Saturday, which was very popular, great fun as well as entertaining, with a learning curve of the good, the bad and the healthy'. Every day snack foods were offered varying in taste and calories, with some very interesting responses. 'Yuck' followed by 'I like that one' came from some of our Visually Impaired members. It was good to see that a few were quite knowledgeable about calorie content.

Sue King, rehabilitation officer, provided a table of equipment for the visually impaired. It is a great way for parents and young people to have a look at what is available, as the setting is so relaxed and informal. Anyone can just wander over and chat with Sue or try out some of the items on display. As Chris Humphreys mentioned in the Foreword, Sue also provides sighted guide training to our volunteer care team and this year she was also able to give some guide training to a VI delegate.

We know from our experience at BBS clinics that many people plod along, kind of feeling that they are not getting adequate benefits, however don't really know what to do about it or

where to go for help. During the conference weekend, Ray Perry, our benefits advisor, is on hand to help whoever needs it. He has been helping our families for years and as Chris mentioned earlier, he was in so much demand this year, that he extended his stay so he could help more people. These are just some of the benefits to attending the fabulous weekend family conference.

The formal Saturday programme continues to blow us away year after year. The syndrome is entirely different now to what we thought we were dealing with, when my family attended our first conference some fourteen years ago. Over the years, parents and those affected have reported so many symptoms that they felt must be part of the syndrome, however so little had been researched or documented and their questions were left unanswered. We are in an extremely exciting time right now, with discoveries happening frequently and lo and behold, all those niggling issues are coming to light. Every year, we learn more about BBS and research is promising a brighter future, in particular for our very young children affected with the syndrome. We must surely be coming to a point soon, where babies born with BBS, need not be affected by such a severe degree of visual impairment, kidney disease and weight management issues, which is incredible and very exciting.

Another aspect of the weekend that proves invaluable is the informal peer mentoring and family support that is provided amongst our members. Steve Burge has provided support and encouragement to parents and young adults affected by BBS year after year. This year was no exception; a young delegate said 'it was good speaking to Steve as he understood what it was like to be diagnosed with this syndrome.' Richard Zimbler is another great advocate of the Society and most years hosts a music jamming session with the older kids; he is such a great role model. Over the past couple of years, Laura Dowswell and Claire Anstee, both BBS mums, have provided support at the New Families Meeting and also made themselves available throughout the weekend to help those struggling with their diagnosis or overwhelmed at their first conference. Taking a step back during the weekend, and observing the comings and goings, I realised what an amazing community the BBS membership has become. If a VI member seems lost, someone quickly steps in to help out. If someone is upset, a friendly arm is soon around them and if someone is sitting alone, it won't be for long. So thank you to all of you, you are very special people.

Hormones and BBS: What have we learned from Clinic?
Dr Barbara McGowan

Dr Barbara McGowan is a consultant in Diabetes and Endocrinology at Guy's and St Thomas's Hospital, London. She was awarded a PhD from Imperial College London in 2007, investigating the role of gut hormones and other neuropeptides in appetite control. Her main areas of research interest are in obesity and appetite control. Dr McGowan leads the obesity bariatric service at Guys and St Thomas Hospital and has been part of the Bardet-Biedl Clinic team since its inception in 2010, reviewing patients for their endocrine and diabetes problems.

“I am a diabetologist and an endocrinologist. An endocrinologist studies hormones, chemical messages that are secreted by several glands in our body. We have several glands, for example the pituitary and thyroid gland. At the out-patient visit, patients have a blood test and we take a history, asking questions related to hormone function. We now have data for about 143 patients; I am going to share with you what we have learned from the specialist BBS clinics.

What are the hormone issues that we are interested in? Number one is weight management, because weight is controlled by hormones. This is of interest because if we are overweight or obese, then our risk of being diagnosed with diabetes increases. We are also interested in reproductive function, and issues such as fertility and general well-being. We may ask male patients questions about their energy levels, how often they are shaving and we may ask female patients questions about their periods, whether they are regular, and check for symptoms of polycystic ovarian syndrome such as excessive hair growth also called hirsutism, menstrual regularity and fertility problems. Another gland we monitor is the thyroid gland, which sits in the neck and produces thyroxine. Thyroxine is an important hormone because if we don't make enough of it we will feel tired and lethargic, we put on weight and may feel constipated. If we make too much of it, all metabolic processes in our body speed up and we may get palpitations, feel hot and sweaty and may lose weight. Finally, we are interested in water balance, which is again controlled by hormones secreted by the pituitary gland. In clinic we may ask questions such as ‘are you drinking too much, do you feel thirsty, do you get up at night to pass urine’, to try and have an idea of how the pituitary gland is working.

Body Mass Index (BMI) is a measure of weight, calculated by dividing our weight in kilograms by our height in metres squared. A normal weight is a BMI of 20 to 25, below 20 is defined as anorexia, a BMI of 25 to 30 indicates that an individual is overweight, a BMI of over 30 is obese and a BMI of over 40 is morbidly obese. We have data from 143 patients, 77 males and 66 females with an average age of 31. The average BMI of the 143 patients that we have seen in clinic is 35.5, which is in the obese category. If we look at the spread of the BMI, most of the 143 patients are in the obese range with 36% having a BMI of over 40, in the morbidly obese range, which is of course an issue. Why is it an issue? Because obesity is associated with a number of conditions and medical problems, amongst which is diabetes; the more our weight goes up, the more likely the chance that we will develop diabetes.

What is diabetes? The pancreas makes insulin and insulin is very important to regulate the sugar levels in our blood. There are two types of diabetes, type 1 and type 2. Type 1 diabetes is the one that children and young people usually suffer with; the pancreas does not make any insulin and patients usually have to start insulin straight away and take it for the rest of their lives. The type of diabetes associated with BBS, is type 2 diabetes. This is where the sugar levels increase, but not initially because of a lack of insulin. The pancreas still makes insulin but the insulin doesn’t work very well; we call this insulin resistance. With type 2 diabetes, the body is making more insulin than the normal person would be making, it is just not working very well. To improve sugar levels or diabetic control, the first step is to diet and lose weight, because by losing weight, the body becomes more sensitive to the

insulin that is being made. The next step is to prescribe Metformin, because this drug will help the body to become more sensitive to its own insulin. Without successful intervention, eventually the pancreas may fail and insulin may be needed.

In our BBS population, we have found that 19 out of 121 patients, around 16%, have type 2 diabetes, so how does that compare to the general population? Some of the incidence rates quoted in the general population are between 4 and 7%. We have got data for 12 of the 19 patients, and looking at how we are treating that diabetes, 6 are being treated through diet alone, 4 take Metformin and 2 take insulin.

Another condition that we are interested in is called metabolic syndrome which is a collection of medical conditions, which when added together, puts the patient at a higher risk of developing heart disease and type 2 diabetes. To have metabolic syndrome, one needs to have central obesity, high blood pressure, high triglycerides and low levels of high-density lipoprotein (HDL), which is the good cholesterol. When we see a collection of these conditions, we may diagnose metabolic syndrome. By looking at the data collected in clinic, we found that about half of BBS patients seem to have the metabolic syndrome. Around 25% of the general population have the condition, so once again it seems to be more common in the BBS population.

Moving on to polycystic ovarian syndrome, this is a syndrome where females may experience issues, irregular periods or no periods at all. They may also have fertility issues and experience difficulties with becoming pregnant. They may have excessive androgens, male hormones, which can cause hirsutism, excessive hair around the chin or on other areas of the body. A pelvic ultrasound will often show lots of cysts on the ovaries. We found that just under 17% of females with BBS have polycystic ovaries.

Let's move on to another organ, the liver, and a condition called 'non-alcoholic fatty liver disease'. The majority liver disease is caused by excessive alcohol, however in this case alcholo is not the culprit, rather, it is the deposition of fat in the liver. So, why are we interested? We are interested because over time, a fatty liver can become inflamed, leading to hepatitis and then onto cirrhosis. We have found that around 25%, about a quarter of BBS patients, have raised liver enzymes which may be a sign of a fatty liver. In the future, we will need to investigate this more closely.

Earlier on, I mentioned the pituitary gland, which is a really important gland. It sits just behind the upper part of the nose at the base of the brain and produces a number of really important hormones, such as growth hormone, which children need to grow; the thyroid stimulating hormone, which acts on the thyroid to produce thyroxine. The pituitary gland produces sex hormones which we need to feel well, to reproduce, to menstruate and to produce testosterone. It also produces a hormone called prolactin. Prolactin is a hormone that females usually produce when they are breastfeeding. Sometimes however, the pituitary gland decides to make a little too much prolactin, causing galactorrhea, which is production of milk from the breast. Too much prolactin can also shut down the reproductive axis. Finally, the pituitary gland also produces an antidiuretic hormone which controls water balance.

In clinic, we often ask BBS patients relevant questions to try and find out whether the pituitary is working well. A previous study looking at the pituitary gland in BBS children found some subtle abnormalities in some of these hormones. But what did *we* find?

We were very pleased to find that three quarters of BBS patients had absolutely normal pituitary function, which is really reassuring. Just over 10% had a slightly low insulin growth factor 1 (IGF1), which is essentially a marker of growth hormone. However, low levels of IGF-1 are quite common in obesity so we are not too concerned about this. Some patients had slightly raised levels of prolactin and some had low prolactin levels. One patient had a very high prolactin, so we scanned the pituitary gland and no abnormality was found. The significance of this is unclear, because prolactin is a stress hormone, so when we take blood and the patient is a little bit stressed, prolactin levels may be a little raised, with no real clinical significance. We will, however, continue to monitor levels.

More interestingly, around 41% of BBS males have low testosterone levels, which is quite important because testosterone helps us feel well and protects against osteoporosis. It is, of course, also important for sexual function. When we identify a low testosterone level we try to assess if the problem is at the level of the pituitary or the testes: either the testes are not making enough testosterone or the pituitary gland is not making enough sex hormones to talk to the testes to make enough testosterone. We found that in most of our BBS patients, the problem was at the level of the pituitary, and this is something we need to study further. Some of our patients are indeed on testosterone replacement.

Finally, the thyroid gland. As mentioned earlier, the thyroid is an important gland which sits in the neck and makes thyroxine; If one makes too much thyroxine, all our metabolic processes speed up and if we don't make enough thyroxine they all slow down. The good news is that we found that in three quarters of our patients, the thyroid works perfectly well. Seven percent had an underactive thyroid and need to take thyroxine, and this is probably a little bit more common than the general population. We found that about 14% had a slightly abnormal thyroid, but not quite abnormal enough to need thyroxine, so we need monitor thyroid function over time. We found only one patient with an overactive thyroid, but overall, in about 25% of BBS patients, there was some sort of a thyroid issue, which may be linked to one of the BBS genes. However this needs further study.

To sum up, we found that after reviewing all the clinical and biochemistry data over the last two years, there seems to be a prevalence of obesity in the BBS population, with type 2 diabetes more common for the age of the patients. There is an increased prevalence of metabolic syndrome and polycystic ovaries and there is an increased prevalence of non-alcoholic fatty liver disease. In terms of pituitary function, this seems to be relatively well preserved in patients with BBS but there is a reduced level of testosterone in about 40% of male BBS patients. Although a low level of testosterone is quite common in obese patients, a level of 40% is over and above what we would see in routine clinical practice. We have also seen that an underactive thyroid is also common in the BBS population."

If this article has made you want to try and lose some weight or adopt a healthier lifestyle, don't forget you can contact your BBS Dietician for support. Past newsletters contain helpful hints and tips and are available on our website: www.lmbbs.org.uk. The next newsletter, due out at the end of the year, will feature a healthy living article by Sarah Flack, BBS dietician. If you would like to receive a copy of the article before then, send an email to toniahymers@btinternet.com.

Bardet-Biedl and the Eye: What do we know? What do we see?
Dr Marie Tsaloumas

Dr Marie Tsaloumas was Clinical Lead for Ophthalmology at University Hospital Birmingham (2004-2008) and now leads the Medical Retina Service. She has published and lectured at length on retinal disorders, including diabetic eye disease, retinal vein occlusion and macular degeneration

As well as general ophthalmology and cataract surgery, Dr Tsaloumas has a sub speciality interest in diabetic disease, age related macular degeneration and vascular diseases of the eye; the medical retina service she runs at the Queen Elizabeth Hospital, is recognised for Advance Sub-speciality Training. She has extensive experience in the diagnosis, management and treatment of macular diseases, including age related macular degeneration, diabetic eye disease and other retinovascular diseases.

Dr Tsaloumas also takes part in multidisciplinary genetic services. She runs Von Hippel Lindau Retinal Angioma Service and is a member of the National Bardet-Biedl service based in Birmingham and London, providing, with her team, the ophthalmology service for the adult Bardet-Biedl service in Birmingham.

Dr Tsaloumas began her talk by introducing herself and telling the delegates how she had become involved in running the Ophthalmology side of the adult Bardet-Biedl clinics in Birmingham.

She then went on to tell us about the eye and how the visual impairment is caused in Bardet-Biedl Syndrome. She explained that the eye is like a camera; at the front of the eye is the lens and at the back of the eye is the photographic film, the retina. On the retina are photoreceptors, or the rods and the cones and their function is to signal to the nervous system that light is in the visual field, by moving vital proteins.

We know that Bardet-Biedl is a ciliopathy and specifically in the eye we've heard that the defective cilia are found in the photoreceptors of the retina. This means that there is a defect in the transportation of proteins in the photoreceptors and a defect in the transmission from the photoreceptors, which leads to them degenerating and dying. In Bardet-Biedl Syndrome, this defect is called a rod/cone dytstrophy.

The photoreceptors are the rods and the cones and in Bardet-Biedl Syndrome they are damaged due to defective cilia and don't work properly. The rods provide us with night vision and peripheral vision and the cones provide us with colour vision and central vision, so if a patient has damage to their rods, they will have limited peripheral and night vision and if they have damage to their cones, colour and central vision are impaired. As the rods and the cones, the photoreceptors in other words, degenerate, they do it in a haphazard pattern which causes the retina to present in a certain way, this is known as rod/cone dystrophy and should not be confused with Retinitis Pigmentosa, which is in many ways a completely dissimilar condition. Dr Tsaloumas also explained that there are other eye related problems which can occur in Bardet-Biedl Syndrome, namely cataracts, glaucoma, squints and nystagmus (wobbly eyes) but it is the rod/cone dystrophy which is the preliminary cause of vision failure within the condition.

Dr Tsaloumas explained that the Birmingham adult clinics have seen many different patients with differing degrees of visual deterioration. The Ophthalmology team realised that it was essential to document their findings in a systematic way and so everything to do with each individual patient is recorded at every clinic. This information includes at what age the patient was diagnosed and when there was a noticeable deterioration in vision and it has been recognised that these two factors vary considerably from one patient to another. Other aspects which are considered when recording this information are practical things like where a patient has been educated, in mainstream or in special education; whether a patient has access to IT support like voice recognition software; do they use Braille; have they had eye surgery, or trauma to the eye and are they registered blind.

Once in the clinic, the patients have their eyes examined for refraction; that is to see whether the patient requires glasses. Eye drops are used to dilate the pupil so that the retina and the back of the eye can be examined in detail. Additionally patients are able to undergo the electrodiagnosic testing which measures the pathway between the eye and the vision area at the back of the brain. Dr Tsaloumas also showed a slide of a macular scan of the eye, which patients undergo in clinic; this gives a structural picture of what the eye looks like.

Sixty-two patients have already been seen in the Birmingham adult clinics, most of these are white British/Irish with two Pakistani patients, one Indian and a few Eastern European patients. Of these, the age of diagnosis ranges from six months to fifty years and the age of visual deterioration within the same group of people ranges from six months to forty years, with most people having significant visual deterioration by the time they were twenty. Forty-three of these patients are registered blind, most use canes and only a few have a guide dog. 72% of those patients have vision of 3/60 or less, which is sufficient lack of vision to be registered blind and four of those patients have no vision at all. Almost half of the patients have nystagmus or wobbly eyes, indicating poor vision from early childhood; and eighteen patients have cataracts.

Dr Tsalmoumas explained that when she looked into the back of the eye, most patients had a rod/cone dystrophy. Six patients had a healthy appearance to the back of the eye, fourteen had macular scarring or scarring to the central vision which Dr Tsalmoumas said she felt was a feature of Bardet-Biedl, and two patients had good vision. She showed us a slide showing the difference between a healthy eye and the eye of a Bardet-Biedl patient and she explained the differences, stating that in Bardet-Biedl syndrome, the optic nerve is pale and

the blood vessels are thin and stringy, compared to those in a healthy person. She went on to explain that visual scientist, Dr Good, is analysing the differences in scans of Bardet-Biedl patients and those with Retinitis Pigmentosis and is picking up obvious differences, confirming the two conditions are quite different.

So what are the future plans? The ocular findings and the genetic findings have not yet been correlated, so this is the next step. Dr Tsalmoumas said that she hoped Professor Beales and others would correlate the findings to ascertain similarities and differences between the specific gene and ocular condition. She also talked about the possibility of conducting a patient satisfaction questionnaire to find out what patients would like from the eye clinic in the future.

Regarding treatment, Dr Tsaloumas explained that there is research going on worldwide which is addressing general rod/cone dystrophy; so applying to Bardet-Biedl syndrome and other conditions which have problems with the retina. Gene therapy and retinal transplantation or implantation are being researched and experiments are being carried out on mice. Currently there are no clinical trials being carried out in the UK, although research is moving forward all the time.

Dancing with LMBBS: a personal perspective
Emma Oates

My story begins when I was 30 weeks pregnant with our oldest child, Tom, when a routine scan showed that he had a kidney abnormality; I was told that this would have to be closely monitored after he was born. After a healthy pregnancy thus far and with all the excitement of the impending birth of our first child, I took the news rather badly and became increasingly anxious about the health of our unborn baby. On the 8th of March 1997, Tom arrived safely. He was born with an extra finger on his left hand and an extra toe on his right foot. I remembered thinking that I'd never before heard of a child being born with extra digits but none of the doctors or nurses seemed to be concerned about it and, a few months after he was born, Tom had these removed. Tom's kidney function was monitored for the first few months of his life and we were told that they appeared to be fine. He was discharged from the kidney clinic aged six months, shortly after his extra digits had been removed and we were left with what appeared to be a perfectly healthy baby boy.

Things ticked along quite nicely for a while and family life settled into a routine but Tom was not as advanced as other children of his age. I put this down to his placid nature but, deep down, I suspected there was something not quite right. I was, at that time, totally in awe of the people in the medical profession who looked after Tom. I hung on their every word and they all told me not to worry as Tom would catch up. I wish I had had the confidence and strength to listen and act upon those inner feelings I had in those very early days.

I finally lost my temper when Tom was about 20 months old or so. At a meeting at Harrogate Hospital, I was told that Tom was just a bit slow and that I should accept that this was the way things were and that he probably would be fine. At that time, there were many words I

could have used to describe Tom but slow was definitely not one of them. At our request, Tom was transferred to the care of another paediatrician and this is when things began to change for the better for us. Dr Cubitt made sure everything was in place for Tom and continues to do so both medically and educationally. I will always be grateful to her for this.

By the time Tom was 2½, he began attending Pre-School. From very early on, it was clear that Tom was, indeed, different and it wasn't long before I was invited in for a chat about his development. Within this environment, which was very free play, Tom struggled both with the actual play side of things and interaction with his peers. He would choose to sit and look at books on his own and was not a bit interested in imaginary play. I remember on one occasion I was called in because he refused to climb into a cardboard box and pretend it was a fire engine. When the teacher asked him in front of me why he wouldn't do it, he looked at me and said it's a box…not a fire engine. I looked at the teacher and explained that Tom did have a point and that, indeed, it was a cardboard box and not a fire engine. However, I understood her concern. Tom was not complying with the social interaction which was expected of him and which his peers were enjoying. Tom was never unhappy in the environment of pre-school. He was just in his own little world. We called it Tom's bubble of happiness and, even now, Tom still lives in this little happy bubble.

Against the wishes of some of the committee, Tom continued at pre-school and we secured support for him from Barnardo's Charity. A lovely lady came in to help him and they formed a great bond and got on well. I shall always remember her kindness and it was this lady who put us in touch with the Education Office so that, by the time Tom started school, he had a statement of special educational needs which covered 25 classroom hours and 5 non-classroom hours and this remains in place now some 11 years on. Tom continued into reception and Year 1 and was seen by various therapists. Speech and occupational therapists soon discharged Tom saying there was really not much else they could offer me to help him.

It was a physiotherapist who one day asked me whether I had considered genetic testing. At that time, I didn't really understand what she meant but I agreed to a meeting with Dr Cubitt to discuss it. In about March 2004, we had a meeting with a genetic doctor and discussed Tom in depth. I remember lots of blood being taken and he tried to explain genetics to me in a very simple way but I couldn't really get my head around it. Dr Crow said it was all necessary to make sure nothing had been missed. I was convinced nothing had been missed, I was to be proved very wrong. I was called back in at the end of May for the results. I remember this day vividly because this was the day which changed everything for me, for us as a family and, importantly, for Tom. I remember hearing the words Bardet-Biedl Syndrome for the first time and not having a clue what it meant. I certainly had no idea how much a part of our lives it would become. I was in shock and fell silent. This must have shown on my face because Dr Crow asked me if I was okay and that's when the tears came, but these were not tears of sadness or anything like that. It was pure relief…at last, some kind of answer. I asked Dr Crow to write it down for me and, when I came home, I researched it and researched it. It was as if everything I had read, had been written about Tom. I couldn't stop reading. I read and I read and I read.

The hardest part about those early pre-diagnosis days and possibly also one of the downsides of living in a desirable small Yorkshire village where everyone seems to know

everyone else's business was the attitude towards Tom by other people. Often not the children, but their parents would tittle tattle at the school gate and gossip when they thought it wouldn't get back to me. I found this very hard to deal with and often chose not to go out in the village. I became very down and insular and self-conscious. I felt lonely and isolated and felt no-one knew how desperately helpless to help Tom I felt. Even some close family members didn't know how to handle or react to it. This was a very dark time for me. I was so grateful to Dr Crow because with the diagnosis we were in the starting blocks and could plan our way forward even though the future was and still is to hold many uncertainties. At least we had some idea of what we were dealing with and, for me as his mother, I really began to understand Tom and his little traits and quirks. The diagnosis helped me really get what Tom was all about and it changed my life as his mother in a way which is very hard to express. Understanding Bardet-Biedl Syndrome to the limited degree that I do has completely changed my outlook on everything including the need to feel accepted by that bunch of small-minded people who made me feel so miserable. I'm happy to say that, whilst we Bardet-Biedl parents have our ups and downs, the dark days for me are a distant memory.

By the time Tom was 9 months old, I was pregnant with our daughter, Katie. Again, I had a routine scan at 30 weeks and it showed the same kidney abnormality which Tom's scan had shown but the doctors' reaction was completely different this time. I was admitted to hospital that very day. It was a Friday afternoon and I was told that they suspected the baby's kidneys were not working well and that the baby would be delivered on the Monday morning by caesarean section just 30 weeks into the pregnancy. I remember being given steroids to strengthen the baby but, to be honest, the rest of the weekend was a blur. I cried a lot and was so worried about the baby's health and its survival. I also desperately missed being at home. Monday morning came and they said they would leave me until Tuesday. Tuesday came and they said possibly Wednesday and so it went on until Friday. I had been in hospital a week and was beside myself. On that Friday morning, Steve and I were sent to Leeds so I could be looked at there. I was examined by four different doctors that afternoon and I will never forget the words of the last one as we prepared to leave. He said "you do understand that, when this baby is born, it's probably going to need a kidney transplant." I was inconsolable, however, I was told to go home and rest which, with a 16-month baby, was a little difficult. However, I was relieved to be home.

Katie arrived without intervention on her due date, the 10th of September 1998. She had an extra toe on her left foot. When I look back now, this next part seems extraordinary but, at the time, naivety and utter trust in all the health professionals stopped me asking questions. I was told by the same doctor who had not been alarmed by Tom's extra digits or presentation of his kidneys that Katie would not need any follow-up appointments about her kidneys as it was obvious they were just like her brother's and that, as he was fine, so she would be. I accepted this totally and without question and I remember the feeling of relief when they had told me that she was going to be okay. Her toe was removed around the time of her first birthday.

Developmentally, Katie was a different kettle of fish to Tom. She was never in the same place for very long. She walked at around 13 months and was bright and noisy, sociable and loved imaginary play. As babies, they were very different in personality and still remain so but Katie was not a well baby. Despite everything Tom had to contend with, he was always well in himself. Katie was not. She was poorly from about 9 months with asthma and ear,

nose and throat-related problems. She couldn't cope with illness and often went into febrile convulsion which became more severe as she grew. On several occasions, she was admitted to Harrogate by ambulance on blue lights and we would spend days there whilst she was stabilised and they established what was wrong. The first couple of times were caused by severe tonsillitis but, latterly, these incidents have been caused by urinary tract infections and kidney complications.

Katie began pre-school as Tom was in reception. Katie, I'm afraid, suffered at that time from second child syndrome. I was so worried about Tom and she appeared so normal that my focus was definitely on Tom. However, she progressed well at school, particularly enjoying music and showing good skill in maths and science. After Tom's diagnosis, the doctors thought that the individual symptoms should be looked at in both children, even though Katie had not had the genetic testing done. I was in complete denial about Katie because as a person she appeared to be so normal, had a lovely bunch of friends and was holding her own in the classroom. Even though she had an extra toe, had a roundness to her trunk and the kidney issue had been flagged up during pregnancy, I still believed that she couldn't possibly too have Bardet-Biedl Syndrome.

As part of the tests, we attended an ophthalmology appointment in Leeds General Infirmary. The children underwent electrophysiology tests and at the end, the doctor turned to me and told me that all the abnormalities which Tom had in his eyes were present in Katie's too. I remember this day vividly, not only because that was the first time I'd cried in front of them on the hospital steps but also because this all but confirmed that Katie too was indeed a Bardet-Biedl sufferer; it seemed so unfair. Following on from this, the children were sent for kidney scans and tests. Tom's results were reasonable but Katie's were less good and this remains Katie's primary area of concern.

The months and years after diagnosis ticked along. The children continued to develop within themselves and at school and, as a family, we learnt to live with this condition, albeit a rollercoaster journey and, with every appointment be it medical or educational, as a mum, I understood the kids more and this has made me strong and able to fight their corner. In September 2010, we were at an ophthalmology appointment in Leeds where I was told about the multidisciplinary clinics being set up in Birmingham and London dedicated to Bardet-Biedl Syndrome. Around Christmas the appointment letters arrived for us to go down in the February. I pondered over the letters during the Christmas holidays and, to be honest, when it came to it, I was not massively enthusiastic about going. I felt that I was going to go down and tell our story to a whole new bunch of people and I couldn't see the point in it when the children were seen already locally. I was very sceptical, but Dr Cubitt said I should maybe go once and, if I didn't want to go back with the children, then I didn't have to. So reluctantly, we headed down to Birmingham in early February just last year.

I remember every part of this day as this was the most life-changing day for me since diagnosis. We arrived late, frazzled from the journey, however the afternoon could not have gone better. Apart from the excellent and very personal service we received, this was the day I was introduced to the Bardet-Biedl Society. I met Tonia and Julie and discovered that they too had children with this condition just like I did. At last, I had met someone who absolutely 100% understood what it was like to live with this condition. I cannot express how grateful I am not only to Dr Cubitt who persuaded me to go, or to Professor Barratt and his

team who paid such careful attention to the children on that first appointment and since, but to find the Bardet-Biedl Society and Tonia and Julie has been brilliant and we are in regular email and text communication. I am also very grateful to have been given the opportunity to help out in the Birmingham clinics, where I'm able to get to know the families and offer the arm of friendship and support which was selflessly offered to me on that first trip down.

I'm often told by friends "you're always so cheerful" or asked "how do you cope?" Back in the dark days, the answer would have been not very well. However, allow me to answer these questions individually. First of all, I am not always cheerful. I am a mum. Mums are not always cheerful. I am also human and no matter how much we try, we all from time to time have our quiet reflective moments, times of worry and anxiety, times when we don't want to talk or be sociable and times when we are just in a bad mood. I am no different from anyone else in this way. However, most of the time, I am cheerful and centred and very happy with my lot living in a loving family environment. During the dark days, I was not like this and actually I didn't like it. Darkness didn't suit me but it's only the passage of time and understanding of BBS and trying to see life through Tom and Katie's perspective which has lifted this curtain of darkness and shown me that following the path of happiness and positivity is a much more pleasant way to live but it's not always easy given the challenges we Bardet-Biedl parents face.

Of course the two things which inspire me the most to carry on with strength and determination are Tom and Katie, two bright, funny, intelligent, kind and loving young people who have been born into the world with this thing which they can't control but who are very happy and have enriched our lives and made us proud parents. To help us, their parents, along the way, we sometimes need to find a little time for ourselves. This normally involves, for Steve and I, a bike ride, a swim, a run or simply relaxing over a drink with friends. This time is important because it makes us function better as parents and my advice to any of you here who are parents of newly-diagnosed Bardet-Biedl children, is to allow yourself this time too, in whatever form it takes.

As far as coping is concerned, there's not much option. What is the alternative? Not coping. I don't think so. To me, it's not so much do we cope but more *how* do we cope. By this I mean what tools do we use to make living with this thing as good as it can be. For me, the answer is contained in one word…acceptance. I have learned to totally accept Bardet-Biedl Syndrome. I can't change it or make it go away. It's here to stay so around diagnosis time I decided to accept it. I consider it the fifth, most stubborn and unpredictable member of our family. People talk about fighting illness but to me this implies a winner and a loser and we can never completely win with BBS and make it disappear and losing is not an option so, to me, it's like a dance. Sometimes I'm not always a willing partner and during those quiet reflective moments, or those times when we're in a bad mood, it would be easier to sit it out, but if it wants to dance with me, then I must dance with it, and look at each appointment like a new routine. Sometimes the steps are harder to learn than others but learn them I must, if I'm to keep on top of this energetic thing called Bardet-Biedl Syndrome. Bardet-Biedl Syndrome never stops dancing and nor must we.

Workshop 1: Informal question and answer session
Professor Phil Beales

Delegate: What is the general outlook, from a vision point of view in BBS?

Professor Beales: We know from studies over the years that on average, we start to see visual deterioration at around 6 to 8 years of age, and that will present itself, more often than not, as night blindness. Over the ensuing 10 to 15 years you could expect to have a reasonably steady decline but it can also just stay the same for many years. Many ophthalmologists will prescribe tinted glasses because they think that bright sunlight might actually promote the degeneration of the photoreceptors at the back of the eye, however we just don't know for sure. There are also questions regarding the benefits of using vitamins to protect against visual problems and a compound that is now being prescribed, lutein, which is found in green vegetables, is supposed to prevent macular degeneration, which can present in BBS.

Delegate: A couple of days ago, I saw a news item reporting that scientists had been putting photoreceptors in the back of the eyes of mice and they could then see in the dark again. I read on the internet that it would be available in humans in five years time.

Professor Beales: A colleague of mine, Jane Sowden, first discovered about three or four years ago that if you put stem cells into mice with retinal degeneration, those stem cells, rather than being killed off, would embed themselves and integrate themselves into the retina. Secondly, she proved that stem cells could be turned into any other kind of cell in the body, What they have to do next is produce a photoreceptor cell that can receive light and turn it into a brainwave but for that to happen you need nerve connections as well. I think other methods of treatment will come along much quicker than stem cell therapy.

Delegate: There is a buzz going on in the US right now, about TUDCA, which has shown to improve vision and lead to weight loss in mice. Do you know if that's valid or not?

Professor Beales: What we need to do is see whether this is related to some of the biological pathways that we've unearthed. One of the pathways is called the mTOR signalling pathway. And it's a pathway that senses our energy states, the amount of fat, sugar and so on. It is very important for growth and also eye development as well. A study that we've done, accidentally, recently, came from a study of polycystic kidney disease. There are big international trials using a drug called rapamycin which is derived from a fungus on Easter Island that they discovered a few years ago and it is used as an immunosuppressant for kidney transplants. We were looking at whether this drug, might prevent cysts in BBS mice. We didn't really see that great a response to the kidney cysts, but we did see a huge response in weight loss, 30% of their body weight. It just so happens that some people with LMBBS are also on rapamycin following a kidney transplant, so what we need to do, is go back to the database, see who is taking rapamycin and see whether there has been an effect on the weight and vision of these patients.

Delegate: Do you think one day you could reverse the damage in the eye?

Professor Beales: Reverse is unlikely. What we're focusing on in my lab is actually on prevention to slow the degeneration down. Other people are doing gene therapy, which has quite a lot of promise as well. There are two groups who have done gene therapy in BBS mice and it seems to work. I am watching this very carefully and we will implement it here if it's proven to work.

Delegate: For me, growing up with BBS, it was always about getting to the point of acceptance. Different studies and potential treatments come along, you dream and think, 'well, maybe this one will be the one', you know. I think it is more important spending that time with your child and just supporting them and helping them to accept BBS. If I could have my sight back tomorrow, would I?
The thought of getting my sight back is actually more scary now than living the rest of my life as a blind person, because I know what I've had to overcome to get here. If that could happen, I'd go for it, but I think what I've concentrated on is getting to a point of acceptance.

Delegate 1: Our son is at university and has gained a great deal of weight. Where is the cut-off point that you say, "Right, well we've tried everything else, it's not working" Because if he continues gaining weight we are concerned about his heart….

Delegate 2: Over the last 15 months I've lost 16 kilos. I have BBS1 and saw a dietician because my weight was just going up and up and I wasn't happy. I've had to make a few adjustments, but it's basically about portion control. If you read those newsletters from the LMBB Society and do what they say, it just happens. I have so many other medical things and fatigue, so I didn't do the exercise, but I followed the 'half plate veg or salad' rule and made sure my snacks were the right kind and no more than 100 calories. I also drank lots of water and was just really disciplined, but it's not a diet, it's a way of life; I've had cheese this week and I do have chocolate sometimes - nothing's forbidden.

Delegate 1: But with all due respect, you have actually been able to grasp the concept yourself and you have been able to work with it. Our son hasn't been able to grasp the concept and work with it, he's at University with access to taxis and takeaways… at what point does it become dangerous to keep the weight increase going? We are now considering bariatric surgery.

Professor Beales: We don't enter into bariatric surgery lightly, but we have done so for a handful of folks who come to our clinic. It has been effective in some, but it has also been non-effective with an initial magic weight loss which then went back on again. Unfortunately it is to do with the hypothalamus, where our appetite centre is, which means some of our guys with BBS can eat a whole plate of food and not feel full – that's a simplistic view of it. We have just recently found where the block is and we are waiting for some money to come through so that we can look at this particular area, to see whether there are certain ways we can bypass the blockage. There is a receptor called the leptin receptor, which responds to

the hormone, Leptin released by fat cells, which feeds back to the brain to tell us that we have eaten enough and should therefore stop. We have found that in LMBBS, this response is blunted. The leptin is still being produced by the fat cells but is not having an impact on the brain, so you always feel hungry. What we need to try to do in those folks where willpower alone is not enough, we need to switch that signal off that says, let's carry on eating.

Delegate: How far away are you, do you think from a treatment?

Professor Beales: When we find that something is switched on, it's always easier in biology to switch it off, you can find a chemical or a drug that can block the actions of whatever it is. Ours is the other way around, it's switched off, so we need to try to find a way to turn it on, which is more technically challenging.

Delegate: Are we looking at a few years, do you think?

Professor Beales: Years is definitely right, I would say certainly within a decade but hopefully within the next four or five years.

Delegate: I have two daughters, one who has been diagnosed with BBS and another who has the same sort of symptoms, but hasn't been diagnosed. I can't get her to the doctors, to the hospital, to the opticians, anything. She is an adult with autistic tendencies, so I can't force her to go. Is there any way of testing her without her attending hospital?

Professor Beales: If your daughter would be happy to spit into a pot, we can get DNA that way. We can send you a little pot in the post, she can spit into it, you put it back in the post, and we can do the genetic testing. As your other daughter has been diagnosed, we already know where to look for the mutations.

Delegate: My son has been diagnosed with BBS and suffers with anxiety and stress. Over the last six years he has become housebound with agoraphobia. I wondered if there was anybody that could help him to overcome these problems that could visit us at home.

Professor Beales: This is an issue that we've come across quite a lot and is an issue we want to address. Unfortunately, the service is hospital based, but what we want to do, and I wanted to do this from day one, is to be able to push the service more into the community. The Department of Health have realised this is the way we should be doing it, so we are trying to get the funding to make this happen. In the meantime, if you can go to your GP, they should be able to refer you to a local clinical psychologist for behavioural therapy for agoraphobia.

Delegate: How does one go about getting a referral for genetic testing? My nephew is getting married and he is concerned that he might be carrying the gene.

Professor Beales: Carrier testing isn't done within our clinic, it is done within the genetic service, So you just need to ask your GP to be referred to see your local geneticist, for

genetic counselling, and the sample will be sent to our lab for testing. You do, however, need to know which BBS gene is involved so you know which one to test for.

Workshop 2: Ophthalmology
Dr Marie Tsaloumas and Dr Kulshrestha

Delegate: When my daughter was first diagnosed, she was diagnosed with retinitis pigmentosa and her consultant ophthalmologist said she has RP as a result of LMBBS, however earlier you said that the eye condition in BBS isn't actually RP.

Dr Tsaloumas: It is important to understand the terminology that specialists throw around. Retinitis pigmentosa is a specific condition caused by specific genes. Bardet-Biedl Syndrome is a condition with eye problems and other problems. The eye problems are very similar to RP, but they're just not the same condition and I think it's important that they're not lumped together because they are different genes. Also, my impression is that patients who have auto-somal dominant inheritance in RP keep their central vision till late middle age. That does not seem to happen in Bardet-Biedl patients, where central vision can go a lot earlier. So I think it's just a little bit lazy on the part of clinicians to collectively say this is retinitis pigmentosa, because it isn't, the progress may be different, future treatments may be different and the progression of the disease may be different.

Delegate: So they would require different treatments or therapies?

Dr Tsaloumas: One may assume that a drug that worked in retinitis pigmentosa may work in the pigmentary retinopathy in Bardet-Biedl Syndrome. However, if you are talking about gene therapy you'd have to be talking about two different therapies, because they're different genes.

Dr Tsaloumas: When we look into the back of someone's eye, it is quite easy to tell normal from abnormal. Then, when you see something abnormal, the question is, what are you looking at? In a patient with pigmentary retinopathy, you've got to think to yourself, why have they got pigmentary retinopathy, is it retinitis pigmentosa? Could it be Bardet-Biedl? Could it be some other condition? What I have noticed in the length of time I've been doing the BBS clinic is that patients with Bardet-Biedl Syndrome, as well as having a pigmentary retinopathy, seem to get macular scarring and macular degeneration as well, quite early.

Delegate: Can you tell me what 'floaters' are?

Dr Tsaloumas: Between the lens and the retina we have what is called the vitreous jelly. As we get older and I do mean after about the age of 20, the jelly starts to wobble in its jelly mould and bits of the jelly can fly off - that's a floater. Normally, floaters have absolutely no effect whatsoever, except for the fact that they are annoying. However, sometimes when the jelly wobbles and floaters come off, it can pull on the retina and cause a retinal hole or a tear and often you get flashing lights with that. If you have a condition that makes you prone to vitreous haemorrhages, like type one diabetic eye disease, occasionally, the floaters may actually be blood floaters.

Delegate: We were told that everybody has floaters and it doesn't matter.

Dr Tsaloumas: Everybody does have floaters but that doesn't mean it doesn't matter. When you have very poor vision, you can also have visual hallucinations, a condition called Charles Bonnet Syndrome (CBS). I tend to see it more in the middle age and elderly population who have had good vision all their life and then lose vision. With CBS, you can see floaty bits, but patients have also described seeing flowered wallpaper, netting, dogs and cats. I've also got a lady who sees horses and another who sees military personnel…

Delegate: My son is totally blind. Last time I took him to the optician they said he had a cataract. What is the point of removing cateracts in the severely visually impaired?

Dr Kulshrestha: There are certain situations in which cataract extraction can be useful. If the retina shows that there is no involvement of the macula, it may well be that by taking the cataract out, the patient will be able to see a little bit centrally, although they will still have a problem with their peripheral vision. That is something that the patient will discuss with the consultation prior to surgery; nobody has an operation until every eventuality, complication and guarded prognosis has been discussed fully.

Delegate: Is there any advantage to having tinted glasses?

Dr Tsaloumas: I'm not aware of any actual research, however I look at it this way, try whatever you want, as long as it's not doing any harm.

Delegate: What about ocular vitamin supplements.

Dr Tsaloumas: There was a big study in the States called the Age Related Eye Disease Study, which showed that ocular vitamin supplements were of benefit in reducing the rate of deterioration in *Dry Age Related Macular Degeneration*, however, we are not dealing with

Dry Age Related Macular Degeneration. Do I have any objection to people wanting to spend their money on ocular vitamin supplement? No, they're great multivitamins, so if you feel like taking a multivitamin, you might as well take one of those. Omega 3 supplements can also be beneficial.

Dr Kulshrestha: A lot of people with BBS are diagnosed young, and if they were to take vitamin supplements for a very long period of time, you can have effects of toxicity, especially from vitamin A in the long term, so obviously I wouldn't advise a young person with hereditary eye disease to go on long term vitamin supplementation. Lutein is also helpful for macular disease and is something that is present within the normal diet, in spinach, kale and green leafy vegetables, so provided you already include those in your diet you don't necessarily need that in the form of a lutein supplement tablet. Fish oils help to protect against macular degeneration and are also healthy for the heart, so at least one portion of pink salmon a week can be very helpful in the prevention of macular degeneration. It is important to remember that no trials have been done so far in patients with BBS, so there is nothing to suggest in the literature at all that any vitamin supplementation or lutein will help in any way.

Delegate: Can gene therapy help?

Dr Kulshrestha: At this moment in time there is no gene therapy for this condition, however, there is a lot of work being done in the labs at the moment and the treatment of disease in general, especially in ophthalmology, is expanding all the time. There is a condition called Central Retinal Vein Occlusion. Now previously, there was no treatment for that, it's a blockage in the vein behind the eye. All of a sudden the government and NICE licensed a drug for injection for that condition, we were the first to use it in our hospital and we've been saving these people's sight to miraculous levels. So there is hope for all people with hereditary eye disease.

People have been looking at retinal implants as well, and I believe in Manchester they have pioneered retinal implantation for patients with retinitis pigmentosa. At the moment, the results are a little bit crude however the actual technology is always expanding. When I was a junior, possibly around sixteen years ago, we had a group of patients with retinitis pigmentosa and we were investigating whether colour contrast could help these patients to see. The idea was to develop a virtual headset that would adjust contrast for optimal visual processing. The original studies were based on a computer programme which had the scene of a busy street with a truck, a tree, buildings, shops, petrol station and that sort of thing. The trial showed a black and white photo, a colour photo, and a modified photo, as it would appear through one of these head sets. What was interesting, was that on the black and white and colour image, patients were only getting about ten to twenty percent of the objects correct. On the modified colour contrast image they were getting more than ninety percent of the objects correct. Unfortunately, the computer scientist who was working on the project passed away and that research has never, unfortunately, come back. I am in the process of

trying to regenerate that research, given the major advancements in computer technology over the past fifteen years.

Accepting Bardet-Biedl Syndrome
Kathryn Murphy

Firstly I would like to say a huge thank you to the Society for having me back to the conference. For those of you who were not here when I spoke in 2006, and a little refresher for those that were, my talk then was titled “More Than Meets The Eye”. This was because I felt Bardet-Biedl Syndrome was more than just about the eye conditions. My medical condition had much more affect on my life than the retinitis pigmentosa and macular dystrophy present in my eyes. Back then, I went into each condition in some detail but this time, I’m not going to do that, I am going to talk about Bardet-Biedl Syndrome in general. Each of the conditions I have just forms my picture of Bardet-Biedl Syndrome.

Those of you that heard me speak back in 2006, probably thought I had a good acceptance of BBS, I did too. It is only with hindsight that I know differently; I just used to focus on each of the conditions. If asked about it, I would reply about my blood pressure or kidneys and so on and that has only changed in the last few years. Two interesting comments from two different specialists first started the ball rolling. At the end of a consult, one doctor said, “But who knows? We are dealing with Bardet-Biedl Syndrome”. My thoughts were, why on earth did he have to bring that up? I came about my kidneys! Then another specialist said, “but then again this is Bardet-Biedl Syndrome”. I think that was the clincher. Not him too. I just came about my blood pressure. I then became extremely unwell, which turned out to be related to my kidneys and salt loss and I realised then that there is little for me health wise that doesn’t come back to Bardet-Biedl Syndrome. I have Bardet-Biedl Syndrome.

Bardet-Biedl Syndrome brings many challenges into your life and no, I wouldn’t want to have to go through some of them again. However, without these experiences I wouldn’t be who I am today. For me this is God’s hand at work in my life as I am a Christian. For me this is my guide in my life and where I draw my strength from. God doesn’t promise us that everything will be wonderful and perfect by believing and having Him in your life. In the Bible in Romans 8, verse 28: we are told, “*And we know in all things God works for the good of those who love him, who have been called according to his purpose”*. Life can be good but that does not mean that it will be easy. Good and easy are two very different concepts altogether. Living with Bardet-Biedl Syndrome is not easy but it can be good, and full of many opportunities.

One of these opportunities has been to become an advocate for BBS in Australia, developing a website known as Bardet-Biedl Australia. I truly feel that this was and still is part of some greater purpose to having this syndrome. I studied Nursing for three years at University and worked as a nurse until the medical issues made it necessary for me to stop work. The knowledge I gained from my nursing degree laid a foundation that continues to

help me understand the functioning of the human body, and has, and continues to be a constant assistance in managing my health.

Often I wonder why I have allowed myself to be a contact for Bardet-Biedl Syndrome and promoting the syndrome. The computer work strains my eyes and adds stress and pressure to an already precious energy source. Many times when I've thought about giving it all away, I've had an enquiry or an email from someone from the society here in the UK. It restores my passion to keep going, knowing the value of the support of actually having contact with people with the condition. It doesn't matter where we live, BBS affects people throughout the world. We are the only ones who really understand how this syndrome affects our lives. The web and social media such as Facebook are wonderful tools where we can now be in touch with one another. I just hope that what I am doing makes a difference to the people's lives I come into contact with.

Although the website existed, that was all I had achieved. If someone found it, it was by good fortune and Google. Life did not hold much of interest and it was exhausting just doing the basics. Life pretty much revolved around all my medical visits, and the company of my parents. I would also go to church and a church group when able. This was until just over a year ago when the biggest change in my life occurred, when Spiritus entered. Spiritus or Anglicare, as they are now called, is a care organisation that receives funding from the government under the Home And Community Care Program. They provide domestic assistance, nursing care, social and allied health care to look after the elderly, disabled and chronically ill in their own homes. Initially I contacted Spiritus for domestic assistance. I can't tell you the difference this has made. You feel so much brighter when your place is clean. Finally I wasn't using the last ounces of my energy cleaning. Something enjoyable could be contemplated or another task achieved instead.

The real change came when I learnt, to my delight, that Spiritus was more than just domestic or nursing help, there was the social care as well. I started attending the craft group on Wednesdays, where I found a beautiful group of women who welcomed me like nothing I have ever experienced. Maybe that is because we all have a reason to be with Spiritus in the first place. One of the ladies at the group also had RP, so that was an easy starting place. I told them a little more about my health and they asked so many questions, they were so interested. This made me realise that if I wanted to be a voice for BBS in Australia the place I needed to start with first, were the people in my life. A few weeks later, I took along the brochure I wrote for the website and gave it to the women at the craft group. They were amazing and so interested in BBS and it is the support and friendship of these women that has given me the confidence to now be open and honest about BBS in my life. For the first time in so long I feel like I belong somewhere; for so long, I thought I must be doing something wrong, or maybe there was something wrong with me, because I just never felt like I fitted in anywhere.

Also, as part of Spiritus' activities, there are short trips away. Laughter truly is the best medicine. Getting away and having fun with other people for the first time since I don't know when, I felt alive again. No, these people were and are not my age, just like at craft, but what a great bunch of people and many with a wicked sense of humour. Following the BBS Conference, I have a three day trip to the Northern Rivers of NSW to look forward to in July.

At much the same time, the pastor of my church gave me the opportunity to speak about how God has been using Bardet-Biedl Syndrome in my life, and my relationship with God through my life's challenges. Ever since this I have felt my relationships in the church developing and strengthening as people now have a better understanding of my situation. When I used the phrase "More than Meets the Eye" this was because I felt people did not realise there was more to me, that I was trying to cope with this huge condition. On the other hand I didn't want them to know either. I was scared about how they would react and treat me. When is the right time to tell people in your life about Bardet-Biedl Syndrome? I don't think there is a right or wrong answer to this question, it is whenever you feel comfortable, as long as you are meeting all necessary legal and health obligations. The important word here is comfortable. Because I was never comfortable with talking about BBS, it showed. That dreaded question of what do you do? Finally, fifteen years on, I am happy and comfortable to say I no longer work because I have a rare genetic condition called Bardet-Biedl Syndrome. Guess what? Now that I am more comfortable with this answer, I find that people's responses are so much better. I am amazed at how much our own behaviour can influence our perceptions and peoples responses.

Being more open about BBS did not happen overnight, it has been a journey now of fifteen years. To start with, BBS had little effect on my life, so denial came and went throughout the development of more conditions. Now though, every day the syndrome has a constant effect on my life. I no longer have the luxury of forgetting. Without knowing about BBS, people won't really know the true me. It has helped shape who I have become today and now plays a large role in determining how much I can do. Yes, there will be periods when my life is on hold due to medical conditions, the past shows me that, but more than ever now, I am determined to make the most of my life when I can. None of us know what's in store for us round the corner. I thought travelling overseas was no longer an option; the flights and then bus tours are so full on. I have learned that it is how you approach a situation. I broke up the flight with time in the Airport Hotel in Singapore for my much needed sleep and if bus tours are exhausting then why do them? Instead I've booked all my accommodation independently and worked out areas I want to see with day tours. There are a few rest days included and if necessary, a few sights may have to go a miss, but I'm here and on a trip of a lifetime travelling by myself.

I think that also sums up how I feel about my life right now, and that is how fortunate I am. For many years I have focused on what the world or society projects to be the norm. Well I have never done the norm. My mum and I have a saying "I don't do normal". I've learnt to apply this to my health and Bardet-Biedl Syndrome, I don't know why it has taken me so long to realise that society's norms probably wouldn't be a good fit for me either. No I don't have the typical life of a mid 30 year old, married with children. That used to really upset me. Well maybe there could be a knight in shining armour one day, but I'm not holding my breath. I'm quite realistic about the rest of my life now. I am just really thankful for the friends in my life, my family and the health I have at the moment. The journey of Bardet-Biedl Syndrome over the last fifteen years has shown me how precious life is, and not to take life, health, or the people you care about for granted.

I have constantly, throughout the years, had to fight for knowing my body and continue to have to fight. Sometimes I get it wrong, but on the whole it is because of fighting to know

whatever answers are out there about BBS and what is happening with my body, and the team of specialists I have, that I am here today. I think the most important factor when dealing with health professionals and BBS is their interest in the syndrome. The other important attribute of a specialist for me, is the ability to look outside the square. In my case most of my test results are often very good, yet functionally I have effects felt daily with my eyes, kidneys and heart which cannot be explained. In many cases doctors will not accept there is a problem unless the test results show a problem. Fortunately, over time I have found exceptions to the rule and found doctors willing to manage and help me.

In Australia we do not have anyone dedicated to researching Bardet-Biedl Syndrome, nor the clinics now available in the UK. However I can say after many years, I have a great team of Health Care Specialists. It is very much a team effort of which I am part of. I felt for many years that doctors viewed me as largely a hypochondriac. All I was trying to do was get the best for my health. If I didn't research BBS or look into the signs and symptoms my body was exhibiting, then who would have? Undertaking a Chronic Conditions Self Management Course with Spiritus was so beneficial. The course reinforced that all these years I had been doing a great job. I was self-managing my chronic condition. The course from Stanford University discussed the importance of patients and carers having a partnership with their health professionals in chronic diseases. With this comes the responsibility for daily management, as we are the ones living with the condition 24 hours a day. You are the only one that truly knows your body.

I hope I have shown you, through a glimpse of my life, a slightly different spectrum of Bardet-Biedl Syndrome. No one should ever put limitations on what they think someone will be able to accomplish just because of a diagnosis of BBS. Regardless of how we are each affected, BBS will not be without its challenges. It is a hard path we walk but I hope you can see that, especially over this past year, life has been very good.

Kathryn finished by playing a CD of 'The Climb', sung by Miley Cyrus. She said, "the first time I heard it, I thought it just so accurately talked of our journey, or maybe my journey, with Bardet-Biedl Syndrome. It is about the climb, where there's always going to be a battle, going be another mountain to climb and we're going to want to make it move but it's about the climb..."

Delegates Comments

"People were so, so friendly, we have been made to feel so welcome. So many people have approached us and chatted."

“I found the whole weekend an experience I will never forget, it was amazing.”

“Great variety of speakers, aimed at everybody.”

“Excellent crèche staff, very friendly and caring, with a great variety of activities.”

“The hotel staff were just brilliant and looked after us really well.”

“The concepts of the workshops and the professionals involved were excellent, however delegates spent too much time discussing poor diagnosis, which could be discussed in separate sessions maybe.”

“Really informative, without blinding us with science.”

“The care team are brilliant and my children really enjoyed their day out.”

“Children looked after very well with lots of things for them to do,”

“This weekend has given me the knowledge needed to provide support in the best way possible.”

“Everyone was so lovely and helpful, it is a great community you have set up as well as an amazing society.”

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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