Welcome

to the

1st Ciliopathy Alliance Family Conference 2013

'Speaking Up for Children with Ciliopathies'

Ciliopathy Alliance

Promoting care and improved quality of life for those with ciliary diseases

Supported by

Jeans for Genes

Genetic Disorders UK

Hilton Hotel, Northampton

31 May – 2 June 2013

CONTENTS

This is the first Family Conference run by the Ciliopathy Alliance. We hope you enjoy the weekend.

We look forward to your participation, to hearing your views and learning from your knowledge and experiences of living with or caring for children affected by ciliopathies.

We would like to thank everyone who helped in the planning of the conference and all the helpers/carers assisting on the day.

We are very grateful to Jeans for Genes (Genetic Disorders UK) who provided the conference grant.

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CONFERENCE PROGRAMME

8:30 am	**Registration and refreshments for day delegates**
9:15 am	**Conference opens in the Collingtree**
9:30 am	**Welcome and Introduction to the Day** Tess Harris, *Ciliopathy Alliance and PKD Charity*
9:45 am	**About Cilia and the Ciliopathies** Professor Phil Beales, *Institute of Child Health/Great Ormond St Hospital*
10:15 am	**A Family Story** Faith Douthwaite, Joubert Syndrome UK
10:30 am	**What is the Current Clinic Experience for Children with Ciliopathies?** Fiona Copeland, *Primary Ciliary Dyskinesia Family Support Group* Julie Sales & Tonia Hymers, *LMBBS (Laurence-Moon-Bardet-Biedl Society)* Kerry Leeson-Beevers, *Alström Syndrome UK* Dr Claire Hogg, *Royal Brompton Hospital, London*
11:00 am	**Refreshment break**
11:20 am	**Life Beyond the Clinic – School, Family, Friends** Sarah Borrows, *Queen Elizabeth Hospital* Kerry Leeson-Beevers, *Alström Syndrome UK*
12:00 noon	**Research and the Role of Patient Organisations and Support Groups** Dr Miriam Schmidts, *Institute of Child Health*
12:30 pm	**What can an Alliance of Patients and Professionals Achieve?** Vicki Hedley, *EUCERD & University of Newcastle*
1:00 pm	**Lunch**
2:00 pm	**The 'Ciliopathy Café' opens in the Collingtree** Conversations & discussions about the morning talks
3:40 pm	**Break & conference group photo**
4:00 pm	**Review of the Café conversations** Interactive session involving all delegates 'Route Map' action plan
5:00 pm	**Next steps**
5:30 pm	**Conference closes**

***Please note**: The conference talks will be recorded and posted on the Ciliopathy Alliance website. The outputs from the afternoon sessions will be recorded graphically (not on video) for publication in the conference report.*

SPEAKERS' PROFILES

Professor Phil Beales
Institute of Child Health, Great Ormond St Hospital, London

Phil obtained his degrees in Genetics and Medicine from University College London. He undertook postgraduate training in both general medicine and paediatrics before specializing in Clinical Genetics. Phil now works jointly as a Consultant Clinical Geneticist at Guy's Hospital and the Institute of Child Health, Great Ormond St Hospital, London. He leads a laboratory research group at the latter. Together with collaborators from Europe and North America, his group has made major advances in understanding the structure and function of the cilia and how the defects in cilia give rise to many ciliopathy conditions, in particular Bardet-Biedl Syndrome. He is now addressing the next research challenges: to design treatments to prevent or ameliorate the progressive deterioration of children and adults affected by ciliopathies. Phil is President of the LMBBS and leads the multi-disciplinary clinics commissioned by the NHS for the diagnosis and care of people with Bardet-Biedl Syndrome.

Sarah Borrows
Sarah qualified as a Nurse in 1989 and went into nephrology nursing. She has worked in all areas of nephrology which include pre-dialysis management, acute nephrology, dialysis, transplantation, anaemia management and end of life care. She supported this educationally by obtaining her nursing degree and nurse prescribing qualification. In 2010, she took 2 years out of renal nursing and went to work in a clinical research facility, gaining in-depth knowledge of the research process. In 2012, she came back into renal nursing to take up the post of Clinical Nurse Specialist in Renal Genetics, where she supports and coordinates the renal genetic clinics and liaise closely with clinical genetics and paediatric nephrology. She runs a nurse-led clinic service for patients with diagnosed renal genetic conditions. She also supports a specialist national multidisciplinary clinic for patients with Bardet Biedl Syndrome. At present she is undertaking a Masters Degree and PG Cert in Clinical Genetics. She lives in Birmingham and is married with 2 children.

Fiona Copeland
Primary Ciliary Dyskinesia (PCD) Family Support Group

Fiona Copeland had a long successful career with HSBC, one of the UK's clearing banks. During this time, she undertook a variety of roles including retail banking (serving customers at the counter etc.), nationwide ATM implementation, training, supplier and contact centre management. Since the arrival of son number two, she has balanced family life with being a Director of Stonac Ltd. This is very much a part time role but in which she specializes in project management and training. Following the diagnosis of both her children with Primary Ciliary Dyskinesia she became the chairman of the Primary Ciliary Family Support Group. She is chair of the Patient Representatives for the NIHR Biomedical Research Unit, Royal Brompton Hospital, London as well at the Patient Representative for Chronic Supparative Lung Diseases. She is a patient representative for the European Respiratory Society, Patient Advisor for NIHR Health Technology Assessment Programme,

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University of Southampton and a regular speaker on 'Living with a Genetic Condition' at UCL Medical School.

Faith Douthwaite
Joubert Syndrome UK

Faith is the parent of a child with Joubert syndrome and Chair of JSUK. Her son was diagnosed with JS in 2001, at the time of diagnosis there was no information or support for families in the UK. She contacted the Foundation in the U.S. and quickly volunteered to become a UK contact as she was desperate to speak to other families in the UK. In the last 12 years, Faith has been able to connect with many UK families and help families to keep in touch by forming JSUK. Although JSUK has no input from health officials in the UK, the US Foundation offers them current information and guidelines to pass along to families. The internet has been a valuable resource to Faith where she can learn from other parents around the world and at the same time keep families in touch with each other. The speed of contact via the internet is especially valuable for newly diagnosed families in the UK who are often still given grim prognosis for their children.

Tess Harris
Ciliopathy Alliance (CA) and Polycystic Kidney Disease Charity (PKDC)

Tess is p/t CEO of the PKDC and manages the CA on behalf of the members and trustees. She joined the board of PKDC in 2005 and was chair until 2012, before taking on the executive role. She is also President of PKD International, the global alliance of patient groups representing 12.5million adults and children affected by all forms of polycystic kidney disease: ARPKD (autosomal recessive) and ADPKD (autosomal dominant). Tess is a member of the NHS Clinical Reference Group for Renal Transplants; she also chairs the Renal Association ADPKD Study Group and is a member of the RADAR ARPKD Study Group. Prior to working for PKDC, she practised in business and marketing. She is affected by ADPKD, along with several siblings, a niece and nephew.

Victoria Hedley
MRC Centre for Neuromuscular Diseases at the Institute of Genetic Medicine (Newcastle University)

Victoria Hedley is the Assistant Manager of the EUCERD Joint Action: 'Working for Rare Diseases'. Her team coordinates this collaborative, EU-wide project, which is designed to support the European Union Committee of Experts on Rare Diseases (EUCERD) in advising the European Commission on how to formulate and implement its rare disease policies.

Dr Claire Hogg
The Royal Brompton and Harefield Foundation Trust, London

Claire is a consultant in paediatric respiratory medicine. Her specialist area is non-cystic fibrosis bronchiectasis, and in particular Primary Ciliary Dyskinesia [PCD]. She has run the National PCD diagnostic service at The Brompton since 2006, and in 2012 successfully led a bid for a National PCD management service. These combined services diagnose and care for the largest paediatric cohort of PCD patients in Europe. Research interests include, research and development into all areas of PCD and other ciliopathy diagnostics. She is a partner in

BESTcilia, a European Framework Programme 7 grant, which aims to be part of the first multicentre therapeutic trials in PCD.

Tonia Hymers
Laurence-Moon-Bardet-Biedl Society (LMBBS)

Tonia has two sons, the oldest of whom has LMBBS. With husband Rob, they went to their first Conference in 1998 and were both coerced onto the Committee soon after that. Tonia was Fundraising Co-ordinator for five years, before taking on the role of Newsletter Editor. Tonia worked for Barclays Bank for fifteen years before leaving to concentrate on raising her family. In 2005, she enrolled with the Open University and in, 2010, she completed her studies, gaining a BSc in Social Sciences. In April 2010, Tonia became the Admin/Clinic Co-ordinator for LMBBS Clinics Ltd and the Family Support Worker for BBS Clinics at Great Ormond Street Hospital, London, and Birmingham Children's hospital. Tonia is also a director of LMBBS Clinics Limited (non-remunerative).

Kerry Leeson-Beevers
Alström Syndrome UK (ASUK)

Kerry became a successful Licensed House Manager at the age of 21. However, following the birth of her first son she had to resign from the post as he was extremely ill and later diagnosed with Alström Syndrome. Kerry was a single parent for three years before returning to education and employment. She then had her second child and married her partner Scott. She joined the board of Alström Syndrome UK and soon became chair. She later resigned from the board to take up the post of Child Development Manager and then became the manager of the Asian Mentoring Scheme. Kerry is a member of the Council for Disabled Children and is a School Governor. She is also on Observer on behalf of EURORDIS and attends the Paediatric Committee at the European Medicines Agency. Kerry has recently been promoted to Acting Chief Executive Officer of ASUK and is enjoying the challenges that this new role entails. She feels very passionately about ensuring the holistic needs of people with Alström Syndrome and their families are being met and she is fully supported by a wonderful team at ASUK.

Julie Sales
Laurence-Moon-Bardet-Biedl Society (LMBBS)

Julie is Secretary of the LMBBS. She has two daughters with LMBBS. She and her husband Kevin (Treasurer of the LMBBS) were made aware of LMBBS when the girls were diagnosed in 1997 and became involved on the committee in 1998. Julie has worked in various professions, including secretarial, catering, physiotherapy, and learning support. She has undertaken independent study with the Open University and has completed a counselling course. Julie is now the LMBBS Family Support Worker, co-ordinating BBS clinics at Guys Hospital, London, and QEH Birmingham. She is a director of LMBBS Clinics Limited (Non-remunerative). Julie joined the LMBBS Committee in 1999 and has been Secretary for five years. She is Childcare Co-ordinator for the Conference Weekend Outing and has previously helped with the Society's Helpline.

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Dr Miriam Schmidts
Institute of Child Health

Miriam studied medicine at the University of Freiburg in Germany and undertook paediatrics specialist training at the Centre for Pediatrics and Adolescent Medicine in Freiburg from 2005 to 2009. In 2009, Dr Schmidts joined Professor Philip Beales and Dr Hannah Mitchison's research group at the Institute of Child health, University College London as a clinical Research Fellow funded by the German Research Foundation (DFG) and is supported by an Action Medical research Clinical Training Fellowship since 2011. Dr Schmidts has a longstanding interest in both motile and non-motile hereditary ciliary diseases with special emphasis on disorders with renal involvement and skeletal dysplasias such as Jeune Asphyxiating Thoracic Dystrophy.

ABOUT CILIA & CILIOPATHIES

What are cilia?

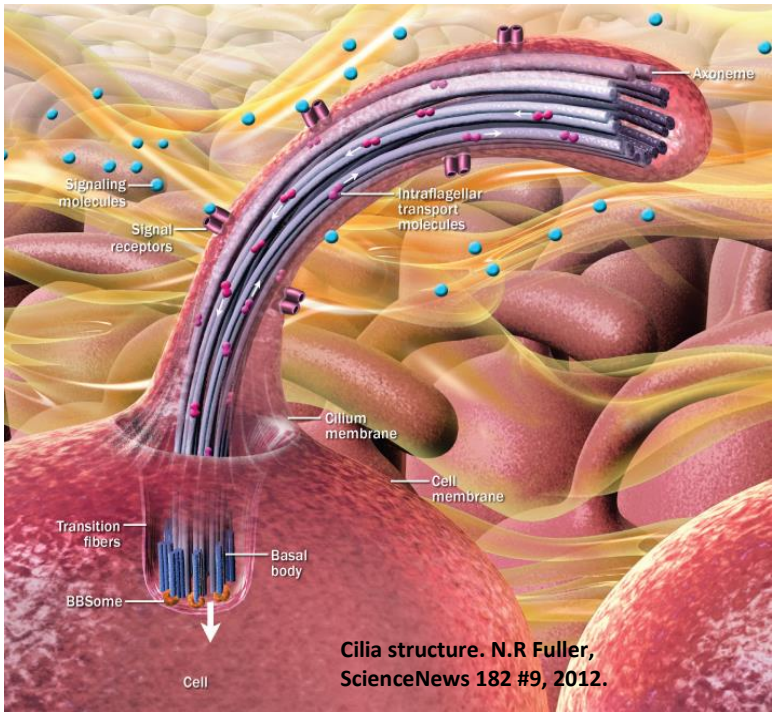

Figure 1

Cilia are microscopic hair-like structures extending from the surface of nearly all our cells that play a vital part in embryonic development and in everyday life (see figure 1). They can be motile, functioning to move fluids in the body, for example moving lung mucus to help get rid of inhaled germs, or to propel sperm. Non-motile cilia have a sensory function acting as the cell's antenna, receiving signals from other cells or fluids nearby. In the kidney, for example, cilia bend with urine flow and send a signal to alert the cells that there is a flow of urine. In the eye, non-motile cilia are required for involved in sensing light signals for vision**.**

What are ciliopathies?

Cilia are widespread and present in most of our organs and when defects occur in them, often as a consequence of inheriting a genetic mutation, this can cause a wide range of symptoms (see figure 2). A range of diseases have been linked to genes that direct the growth and development of cilia and the control of signalling within them; these often result in developmental deformities as well as kidney cysts and failure. Disorders that occur when cilia function is abnormal are known as '**ciliopathies**' (a single word meaning 'diseases of cilia'), and these are thought to affect more than 1 in 200 people. In summary, the ciliopathies are devastating genetically inherited conditions which carry a heavy economic and health burden on the patients, the affected families and on society more widely. Some of the ciliopathies are described briefly below.

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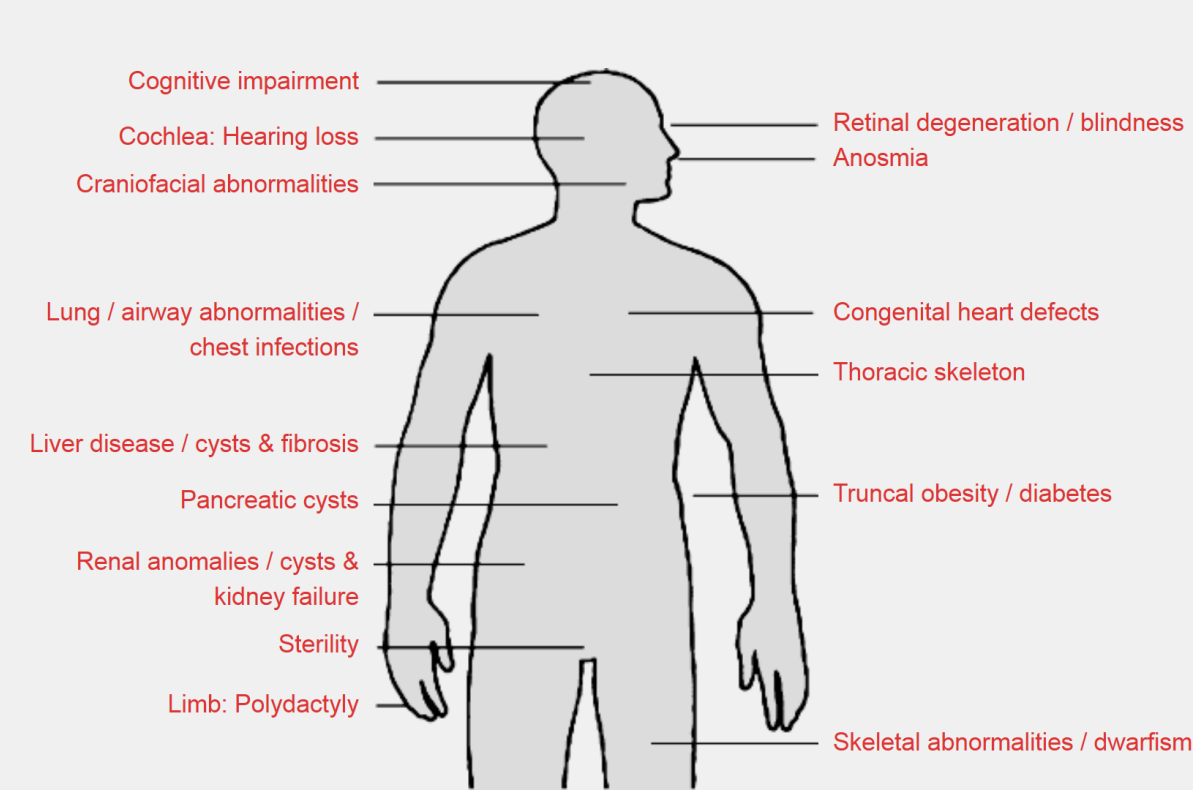

Figure 2

Retinitis Pigmentosa (RP): a large group of inherited diseases of the retina (also called retinal dystrophies) that are marked by progressive loss of vision. RP affects about 1 per 3,500 people and several forms of RP are understood to be ciliopathies. RP can form part of a syndrome combined with other disabilities. Symptoms usually start with problems in night vision and peripheral vision ('tunnel vision'). Later the detailed and colour vision is affected, often leading to blindness. RP is currently incurable, and can arise from flaws in any of approximately 200 genes, many still not identified. Gene therapy trials are in process, in addition to research into stem cell replacement therapy.

Usher syndrome: Usher syndrome is an autosomal recessive genetic or inherited condition that affects hearing, vision and balance variably. Nice genes are implicated and Usher is divided into three clinical types, in the UK Usher one and Usher two being the most common. Usher type one patients are profoundly deaf from birth with balance problems, developing retinitis pigmentosa-related vision problems between 8-12 years old, which will progress to blindness. Type two are born with moderate to severe hearing impairment and normal balance, balance and visual problems develop but progress more slowly. Sign language and cochlear implants can help, but the continually degenerating senses are incurable.

Alström Syndrome: a very rare recessively inherited condition that occurs with close to a 1 in a million chance. There are about 700 cases worldwide (50 in the UK), although it is likely underdiagnosed. Disease is caused solely by mutations in the ALMS1 gene. Many major organs, particularly the heart, lungs, kidneys and liver, are affected. The key features are retinal degeneration (Rod Cone Dystrophy, nystagmus, photophobia), hearing loss, obesity, diabetes, heart muscle dysfunction, kidney and liver disease, disturbed fat metabolism. The symptoms get progressively worse from birth, with variable expression of symptoms

between different affected individuals. Correct diagnosis is often delayed, which is associated with poor disease outcomes.

Bardet-Biedl Syndrome: a rare, recessively inherited complex disorder that involves many body systems and occurs in about 1 per 100,000 people. There is progressive visual impairment (rod-cone dystrophy) often diagnosed as retinitis pigmentosa that causes impaired night-vision, then tunnel vision, and ultimately blindness. There is obesity from early childhood, extra fingers and/or toes and/or partially fused digits, kidney abnormalities, often leading to renal failure. Development is delayed, with speech delay and learning difficulties. Affected boys can have underdeveloped genitals. Correct diagnosis of this complex syndrome is often delayed and there are no treatments yet for the retinal degeneration or developmental problems, the obesity is hard to treat. Extra digits can be successfully surgically removed.

Jeune syndrome (Asphyxiating Thoracic Dystrophy): a very rare (1 per 200,000 people), recessively inherited disorder included in the spectrum of short-rib polydactyly syndromes, affecting mainly skeletal development. Five genes are implicated. The chest is narrowed due to short ribs, preventing proper lung development and causing respiratory distress, often from birth, with 20-60% of cases lethal in the first 1-2 years of life due to asphyxiation. Arms, legs and fingers are shortened and the bone ends acquire bony extensions. Extra fingers and toes can occur, and retinal disease (retinitis pigmentosa, rod-cone dystrophy) leading to impaired vision progressing to blindness. Cysts in the kidneys can develop, as well as liver dysfunction. Surviving patients may "grow out" of the rib phenotype later in life, and mechanical ventilation or thoracic expansion surgery is possible.

Joubert Syndrome: a rare recessively inherited disorder affecting mainly brain development, sometimes accompanied by renal and/or retinal symptoms. Mutations in several cilia genes can cause Joubert Syndrome, including an X-linked gene that primarily affects boys. Variable brain abnormalities occur, mainly in the cerebellum (controls movement and balance), with low muscle tone from birth, delayed developmental and breathing and movement abnormalities. There can also be kidney insufficiency and extra fingers and toes. Retinal degeneration may also occur, initially as night blindness, progressing into visual loss also in daylight and blindness. No cures are available, only supportive therapy.

Nephronophthisis (NPHP): the most common genetic cause of chronic kidney disease within the first three decades of life, NPHP is inherited recessively. NPHP may occur during infancy, but more typically is first seen in late childhood, with progressive renal failure being developing from early puberty. The kidneys are of a normal size, but are abnormally formed, having cysts and other disruptions; patients experience frequent passing of urine (polyuria), excessive drinking and anaemia. Eleven cilia genes (called nephrocystins) are currently implicated, but they account for only a third of cases. Polyuria (passing large volumes of urine frequently)

Polycystic Kidney Disease (PKD): a range of incurable genetic diseases affecting children and adults, PKD can be inherited as recessive (ARPKD) or dominant (ADPKD) forms. These are multi-system conditions, affecting other organs (liver, pancreas, spleen, brain, intestines). Dominant PKD is results from the mutation of two genes (PKD1 and PKD2) and is the most common inherited life-threatening condition and most common inherited kidney disease, affecting about 1 in 400-1000 (80,000 in UK). Onset is typically in the 30s-50s; multiple kidney cysts develop, causing progressive kidney failure and ultimately leading to end stage renal failure in half of all patients. Recessive PKD affects 1 in 20,000 and is usually evident from birth – it is fatal in 30-50% of cases. Babies fail to develop kidneys and lungs properly giving rise to chronic disease, and there may be spine/limb deformities. There is liver fibrosis and kidney failure often by age 30.

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Primary Ciliary Dyskinesia: a relatively rare (affects 1 in 15,000 people) autosomal recessive disorder affecting the respiratory system's lungs, sinuses and ears with chronic infections and mucus build-up, leading to obstructive lung disease and glue ear that often requires clearance and surgical interventions. Hearing problems are frequent. Organs are displaced from their symmetry in half of patients causing spleen, heart and liver problems, and infertility occurs. The incidence can be as high as 1 in 2,500 in the Asian population and other areas where consanguineous marriages are prevalent. Over 20 genes are implicated to cause PCD, but diagnosis is frequently delayed. Treatment is similar to that used for cystic fibrosis, with lifelong physiotherapy and targeted antibiotics.

CILIOPATHY ALLIANCE PATIENT GROUPS

Alström Syndrome UK (ASUK)
www.alstrom.org.uk

Jeunes Syndrome Foundation
www.jeunes.org.uk

Laurence-Moon-Bardet-Biedl Society
www.lmbbs.org.uk

Joubert Syndrome UK (JSUK)
www.jsuk.org

Polycystic Kidney Disease Charity (PKDC)
www.pkdcharity.org.uk

RP Fighting Blindness
www.rpfightingblindness.org.uk

Primary Ciliary Dyskinesia Family Support Group
www.pcdsupport.org.uk

Sense (for Usher patients)
www.sense.org.uk

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