



Bardet-Biedl Syndrome

Medical Information Booklet

Bardet-Biedl Syndrome UK

Registered Charity 1027384 & SCO41839



...more than meets the eye



The Origins of Bardet-Biedl Syndrome



John Zachariah Laurence

The earliest formal description of Bardet-Biedl Syndrome was provided in a paper published by John Zachariah Laurence (1829-1870), an eminent 19th century ophthalmic surgeon based in London, and his then House-surgeon, Robert Moon (1845-1914), whose own father, William, invented one of the first raised alphabets for the blind. There was no further mention of the syndrome until 1920, when Georges Bardet submitted his MD thesis on hypothalamic obesity. Bardet had worked with Louis Pasteur in Paris and recognised that a number of his cases had unusual features, in particular hexadactyly, retinitis pigmentosa and obesity.



Robert Moon

In 1922, Artur Biedl, a Hungarian working as a professor of pathology and endocrinology in Austria, published a short independent account of two siblings with congenital abnormalities, retinitis pigmentosa and polydactyly. Neither Bardet nor Biedl made any reference to Laurence and Moon's paper previously published in *Ophthalmic Review*, a publication which by then was no longer in circulation.

It was in 1925, when Solis-Cohen and Weiss 'rediscovered' the paper by Laurence and Moon and went on to consider these conditions to be the same. Until the 1980s, the syndrome was known as LMBS (Laurence-Moon-Biedl syndrome, with no reference to Bardet. More recently this condition has been split once again on the basis of clinical features, into the Laurence-Moon and Bardet-Biedl Syndromes. Bardet-Biedl Syndrome (BBS) has as the main features, rod-cone dystrophy, obesity, postaxial polydactyly, learning disabilities and hypogenitalism (males). BBS represents by far the majority of published cases and is now the more generally recognised term within the medical and scientific community.



Artur Biedl

This booklet has been funded by NHS England and produced by Bardet-Biedl Syndrome UK, Registered Charity No. 1027384 and SCO41839.

It is important to note that there are many symptoms and conditions listed within this booklet that may affect those who have BBS, but they will not necessarily affect everyone and the severity of individual symptoms can vary greatly among patients.

Our grateful thanks go to the clinicians from the BBS Specialist Clinics Teams at Queen Elizabeth Hospital, Birmingham; Birmingham Children's Hospital; Great Ormond Street Hospital, London and Guy's Hospital, London, for their contribution to this publication.

Our heartfelt thanks also go to the generous individuals living with BBS who contributed to this booklet; their guidance and personal perspective have been invaluable.

www.bbsuk.co.uk





Introduction

It is estimated that Bardet-Biedl Syndrome (BBS) affects approximately 500 people in the UK. Many GPs, doctors and health professionals will not have come across BBS before and there are many who have not heard of the syndrome.

This booklet has been produced by Bardet-Biedl Syndrome UK to promote a greater understanding of Bardet-Biedl Syndrome and the recommended care pathway. It is aimed at the medical and healthcare professionals involved in the care of Bardet-Biedl Syndrome patients and also those living with the syndrome, their parents and carers, with the aim of encouraging better self-advocacy and health care management.

The information contained within this booklet has been provided and checked by the BBS Specialist Clinics team and where possible is supported by research and published articles. A bibliography of references and useful publications can be found at the back of the booklet. For further information, contact: tonia.hymers@bbsuk.org.uk.

Bardet-Biedl Syndrome is a rare, recessively inherited ciliopathy (see later section explaining the term 'ciliopathy') which affects approximately 1 in 100,000 babies born. Features of the syndrome include rod-cone dystrophy, a progressive eye disorder that leads to blindness, characterised by tunnel vision and night blindness; obesity; renal abnormalities; developmental delay; speech and language difficulties; extra fingers and/or toes and learning difficulties. Not all of the features are always present in those diagnosed as having BBS and each one can vary in severity and appearance. The variability in presentation and severity of the syndrome, together with the rarity of the condition can lead to delayed diagnosis and a lack of adequate local health care.



"There's no-one else who knows our child like we do, and we have to take this on board and make ourselves heard. We have to be an equal partner with medical, social and educational teams and believe that we're an equal partner. We have to use the resources available to us to give our children the confidence, courage and self-esteem to know that they have a great deal to contribute to this world."
Parent

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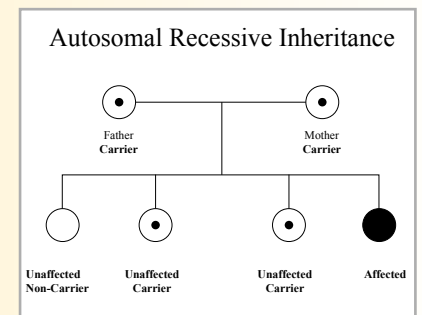
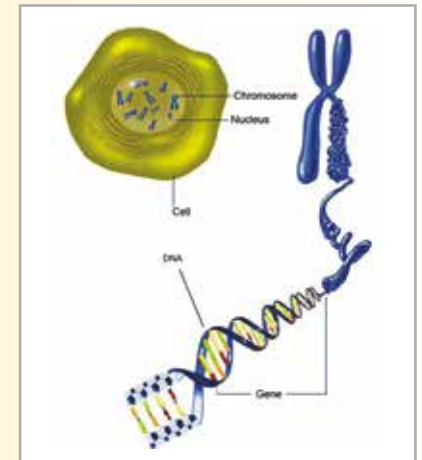
Beales et al (1999 and 2001) suggest that the presence of four primary features or three primary features plus two secondary features is necessary for a clinical diagnosis of Bardet-Biedl Syndrome.

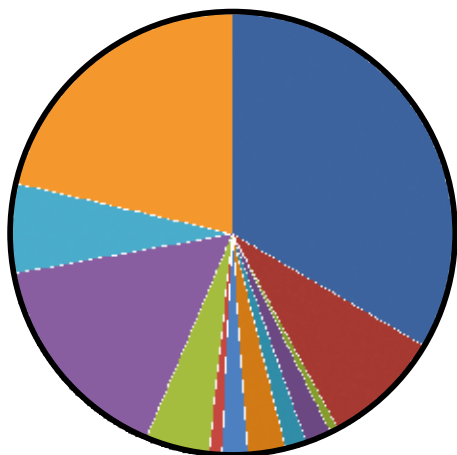
Primary Features	Secondary Features
Rod-cone dystrophy Polydactyly Obesity Learning disabilities Hypogonadism in males Renal anomalies	Speech delay/disorder Developmental delay Brachydactyly Polyuria/polydipsia Ataxia Poor co-ordination Diabetes mellitus Left ventricular hypertrophy Hepatic fibrosis Hypertonia Hearing loss



Genetics

In most cases of BBS, both parents carry a normal gene and a faulty, recessive gene. Although the parents have one copy of the faulty gene and are called carriers of the disease, they are unaffected by the presence of the faulty gene. For a recessive disease to occur, a child has to inherit two faulty copies of the gene; one from each parent. The child from each pregnancy has a 1 in 4 chance of being affected. If a new born child is not affected then there is a 2 in 3 chance that he/she will be a carrier of the faulty gene for BBS. As the syndrome is rare, a gene carrier is unlikely to have affected children unless their partner is also a carrier. This risk of encountering another carrier increases if people marry close relatives. As some BBS genes are more common than others, there is variation in the frequency with which they are being carried, known or unknown, in the population. For the most common BBS genes, BBS1 and BBS10, the frequency is estimated to be 1 in 250, whereas for a rarer gene such as BBS9, the frequency is closer to 1 in 820.





Pie chart showing relative frequency of mutations in 12 BBS genes tested (courtesy of North Thames Regional Genetics Service)

To date, (2015) mutations in 19 BBS genes have been identified in 85% of BBS patients (see <http://www.ncbi.nlm.nih.gov/books/NBK1363/> for updates on new genes). It is known that there are still more genes to find since not all patients have an identified mutation in any of these identified BBS genes, indicating that these patients must have mutations in other genes. Some genes are more common than others; a quarter of patients have mutations in BBS1 and another quarter have mutations in BBS10. However, patients who carry mutations in the same BBS gene can display quite different symptoms of the syndrome: one might have extra digits at birth whereas another person with an identical mutation may not have extra digits at all. It is hoped that comprehensive genetic testing will improve predictions about disease progression in the future.

Cilia

Mutations in BBS genes cause changes in the proteins that are needed for the correct functioning of a particular part of the cell called a primary cilium. For this reason, BBS has been categorized medically as a ciliopathy.

Ciliopathies are a range of human disease syndromes all caused by defects in primary cilia function. Examples of other ciliopathies include Alström Syndrome, Primary Ciliary Dyskinesia, Polycystic Kidney Disease, some forms of Retinitis Pigmentosa, Nephronophthisis, Joubert Syndrome and Meckel Syndrome, which have overlapping symptoms, all caused by defects in cilia proteins.

Cilia are long thin, hair-like projections that stick out of the surface of a cell. There are two types of cilium, motile and non-motile or primary cilia (also called sensory cilia). Many cell types in the body rely on having a fully functional primary cilium. Important examples include the retinal photoreceptor in the eye, and cells in the kidney. The scientific community is trying to understand exactly what roles the BBS proteins play in cilia formation and function.

Carrier Testing

Where BBS is confirmed genetically, a simple carrier test is possible in at-risk adult relatives (e.g. siblings) to help determine their own risk of having affected children if their partner is also a carrier. Knowledge of the BBS mutations can also provide the basis for prenatal screening tests, should parents need to know in early pregnancy if the foetus is affected.

“During the early days of diagnosis, it is important to allow time to come to terms with all that has happened and to give yourself time and space to adjust.”

Parent



Where both parents are carriers of a change in the same BBS gene, every pregnancy has a 1 in 4 risk of the child having Bardet-Biedl Syndrome. If the genetic changes are known in the parents, there are several options available to them, should they wish to have more children.

Prenatal Testing

Couples who are already pregnant may consider prenatal testing (e.g. chorionic villus sampling/amniocentesis). It involves testing either the tissue or fluid around the baby in early to mid pregnancy (10-16 weeks). There is a small risk to the pregnancy with prenatal testing; couples who wish to pursue this option should discuss it with their geneticist and obstetrician.



Pre-implantation Genetic Diagnosis (PGD)

A couple can be referred to be considered for PGD via a clinician provided that they fulfil a number of criteria. These can vary between NHS centres, however common requirements are that they do not already have a healthy child and that they do not smoke. Couples who wish to pursue this route should contact their GP or geneticist.



Couples who are not interested in either of these options, or do not know the genetic change that has caused BBS may opt to have a detailed scan throughout pregnancy to assess if there is evidence that the baby is affected. This should be done in a specialist centre by an ultrasonographer who is familiar with the features associated with BBS. Features of BBS may be difficult to pick up before 20 weeks gestation and, as already mentioned, may not be present in all babies with BBS.

Prospective parents who have Bardet-Biedl Syndrome

Those who have BBS, who wish to have children, may also have several options available to them, including the options outlined above. The first step is for the partner of the person who has BBS to be tested for carrier status, to determine whether he or she carries the same change in the same gene.

The children of a BBS affected parent will all be carriers of the affected gene, but will not have the syndrome, provided that the other parent does not have any changes in the same gene. If the other parent is a carrier of a change in the same gene, then each child has a 50% chance of having the syndrome. If both parents have BBS, then all children will be affected with BBS.



Bardet-Biedl Syndrome UK
www.bbsuk.org.uk

Genetic Alliance UK
www.geneticalliance.org.uk
020 7704 3141

Contact A Family
www.cafamily.org.uk
0808 808 3555

"It is not the end of the world when it comes to being diagnosed with a medical condition. Everybody is their own unique person. It doesn't matter how fast or slow they are at achieving their goals in life, as long as they've enjoyed trying, they will get there at their own pace."

Parent

The ocular findings seen in BBS are similar in clinical appearance to retinitis pigmentosa. However, BBS is a different genetic condition. The correct term for the retinal findings in BBS is rod-cone dystrophy and clinically, upon examination of the retina (the light sensitive tissue lining at the back of the eye) a pigmentary retinopathy is often seen.

The rods and cones are the names of the photoreceptor cells found in the retina and in BBS, the rod and cone photoreceptors degenerate because of defective cilia. The rods provide night vision and peripheral vision and therefore, as the rods degenerate, the BBS individual will experience nyctalopia (poor night vision) and loss of peripheral vision. The cones provide colour vision and central vision, so if a patient has damage to their cones, colour and detailed vision will be impaired.

Onset is usually during primary school years and initially shows itself as night blindness. However, in some cases, visual symptoms can be delayed into the late teens or beyond. As the retina degenerates and the condition progresses, the affected individual may lose some ability to see through the whole visual field. Loss of peripheral vision is frequently referred to as tunnel vision. As the visual fields 'close in' the young person may begin to appear clumsy, especially at night time. A young person's functional vision will also be affected by changes in lighting. Low lighting and dark evenings will make it much more difficult for the individual to use residual sight and daytime glare will also affect central vision.

A recent study found rod-cone dystrophy in almost all patients who had a genetic diagnosis of BBS. A significant number of patients have clinically evident retinopathy while in some patients, where the retina can appear normal, clear evidence of retinopathy can be found on electro-diagnostic testing, for example an electroretinogram (ERG).

A recent study has shown the mean age at which symptoms or signs of visual loss was reported was at twelve years of age, although night blindness was often noted earlier. The mean age of registration of blindness was approximately fifteen years. Other ocular manifestations of BBS include nystagmus (wobbly eyes), high astigmatism (irregularly shaped cornea), strabismus (abnormal alignment of the eyes/squint), glaucoma and cataracts.



"No one should ever put limitations on what they think someone will be able to accomplish just because of a diagnosis of BBS."

BBS Patient



Clinical Features

Treatment

Gene Therapy may one day be used to treat rod-cone dystrophy in BBS, but there is no such treatment available at present. In the meantime ophthalmic advice and support should be offered to maximise the quality of life of patients with low vision.

Correction of refractive error (myopia, astigmatism) and tinted glasses (for photophobia) can assist in maximising useable vision. Cataract surgery should be offered where appropriate and where it will be of actual visual benefit. Low vision aids and mobility training can improve independence and confidence. Magnifying glasses, digital systems and voice systems may also be helpful.

Consideration should be given to educational planning and if there are disrupted sleep patterns and nocturnal apnoea, sleep studies should be considered. Referrals to local low-vision clinics and organisations assisting the visually impaired are recommended. Partial sight and blind registration (certificate of visual impairment) should be carried out in the first instance where any visual impairment is diagnosed.

Visual Assessment

At diagnosis:

- Visual acuity assessment and refraction
- Visual field testing
- Dilated fundal examination
- Electro-diagnostic testing
- OCT scanning

Follow-Up

Yearly eye examination:

- Visual acuity
- Visual field testing (where possible)
- Fundal examination
- Electrodiagnostic testing if indicated
- Screening for cataract, glaucoma and diabetic retinopathy as appropriate



RNIB

www.rnib.org.uk
0303 123 9999

VICTA

www.victa.org.uk
01908 240831

Action for Blind People

www.actionforblindpeople.org.uk

Blind Children UK

www.blindchildrenuk.org
0800 781 1444

Look

www.look-uk.org
0121 450 7754

Sense

www.sense.org.uk
0300 330 9250

Obesity is reported to occur in 72%-92% of affected individuals. Weight issues usually begin in childhood and, with age, increase in severity. Many children exhibit rapid weight gain within the first year of life, but others may not present with weight concerns until puberty. It must be remembered that BBS symptoms cover a spectrum, so everyone needs an individual assessment of their weight or dietary concerns. The majority of adults who have BBS, have a BMI greater than 30 which is often accompanied by other health issues, for example, hypertension (high blood pressure), dyslipidaemia (an abnormal amount of lipids, such as cholesterol and/or fat in the blood) and type 2 diabetes mellitus. Fat tends to deposit within the abdomen, which is a cause for concern as this distribution can be linked to high blood pressure and elevated triglycerides (a type of fat found in the blood).

The cause of the obesity associated with BBS is unknown but is the subject of current research. There is certainly a dysfunction of appetite regulation which can lead to hyperphagia (excessive appetite) and energy intake exceeding requirement, which makes dietary management challenging.

Treatment

Understandably, diet and weight concerns are a major source of stress for patients and their families. The knowledge that untreated obesity can lead to multiple health problems, for example, metabolic syndrome, diabetes mellitus and cardiovascular disease, adds to this stress.

Unfortunately there is no single treatment approach for obesity in BBS, just as for obesity in general but those with BBS can successfully lose weight, or in younger children, control their rate of weight gain, whilst ensuring height growth is maximised. A healthy well balanced diet and active lifestyle approach is advocated and for some, considering the glycaemic index of foods may also be useful. Portion control strategies are important, because of the excessive appetite that can be associated with BBS. Very low calorie diets, as used to manage Prader Willi Syndrome are not warranted, as this is an over restriction of energy intake. Dietary advice should be tailored for an individual to address their weight or dietary concerns.

It is important to intervene and educate with dietary strategies to control weight gain in childhood as these are more likely to have a lasting effect into adulthood. A multi-disciplinary approach is needed and should include dietary advice, behavioural management and exercise. Early referral to a registered dietitian with either an interest in BBS or experience in obesity management is important and attendance at the Multi-Disciplinary Team BBS clinics is strongly advised.



“I’m really into sports and when I found out I had BBS, I didn’t think playing sports would be possible. However, a whole new world opened up for me after I went along to a vision impaired cricket event. To my delight, I won the best new player award at my first match.”

BBS Patient



BBS Specialist Clinics: Dietetics

Contact your dietitian for advice and ongoing support.

For more information about BBS Specialist Clinics, go to:

www.bbsuk.org.uk

Obesity (Continued)

Pharmacological and surgical management approaches for obesity are available, but associated risks and benefits need to be carefully considered. These treatment options can be advocated only if strict criteria are met and when traditional methods have failed.

Bariatric surgery is considered only for life-threatening obesity and its use in young patients with genetic syndromes of obesity is rare, with only a very limited number of cases reported in the literature. However, Bariatric surgery may offer an alternative treatment option, when traditional non-invasive methods of weight control fail. It is important to note that specialist dietary advice and support is needed post surgery and compliance with these dietary restrictions is imperative. It is not an easy option and is not suitable for all individuals.



Polydactyly and Brachydactyly

The presence of extra digits is by no means universal with 68% to 81% of patients affected. The most common form is post-axial polydactyly (an extra digit next to the little finger or toe) ranging from a single skin tag to a fully formed digit on all four limbs. Brachydactyly (shortness of the fingers and toes) is common, affecting 46%-100% of patients and is more frequently found in the feet than in the hands. When present in the hands, it may affect dexterity and the ability to use keyboards or Braille. Syndactyly (webbing) is less frequently seen and is usually partial and confined to the feet.

Treatment:

Rudimentary skin tags can be tied off at birth after documentation by a discharging paediatrician or GP. Larger accessory digits are often non-functional and should be excised within the first year of life by either an orthopaedic or plastic surgeon. Bony malformation in already wide feet can lead to ill-fitting shoes and it is important to seek podiatric/orthotic advice and special fitting.

"I keep myself fit by going to my local gym, which I attend three times a week. I am good at rowing, I can do two thousand metres in ten minutes. I also enjoy the cycling machine and running on the treadmill. I use the weights as well to keep fit."

BBS Patient



*Although Bardet-Biedl Syndrome (BBS) can affect the kidneys in a number of ways, significant kidney problems and kidney failure are seen in only a **small** proportion of patients. Nevertheless it is important to monitor all patients regularly.*

Minor kidney problems and high blood pressure are more common. Therefore blood and urine tests and ultrasound scanning of the kidneys should be a routine aspect of renal management in BBS. Kidney manifestations can be quite variable in BBS: patients can have kidneys that have not formed correctly (renal malformations), kidney cysts or other variations in the shape and size of the kidneys. Generally these abnormalities do not cause too much trouble. In about 5% to 10% of people with BBS the kidney function declines progressively, causing a rise in the serum creatinine and a fall in the eGFR (estimated glomerula filtration rate, a measure of the function of the kidneys). This may culminate in kidney failure and the need for dialysis or a kidney transplant. This usually occurs in the first few decades of life and in general, if kidney function is normal at the age of twenty then it is unlikely to decline later in life. Patients with BBS seem to do very well with dialysis and kidney transplantation, so even if kidney failure does develop there are very good treatments to support patients.

One particularly common problem related to the kidneys can be a reduced capacity to concentrate the urine. This leads to higher than average urine output and sometimes excessive thirst, although few patients notice this. Infections of the bladder (cystitis) and, occasionally, of the kidneys themselves can also occur and are treated in the conventional way with antibiotics.

Hypertension (elevated blood pressure) may be evident in patients with kidney disease of any type and in BBS hypertension is often present and should therefore be regularly checked and treated if necessary. Hypertension can also put further strain on the kidneys so in BBS patients, where there is known kidney involvement, it is particularly important to monitor and treat this.

As already noted, obesity is a very common problem in people with BBS and excessive body weight can put additional strain on the kidneys and make high blood pressure worse. This can exacerbate any underlying kidney problems or can even occasionally cause kidney damage on its own. The rationale for managing weight in BBS therefore extends to protecting the kidneys from damage.

Assessment

At diagnosis:

- Check symptoms of anaemia, polyuria and polydipsia
- Baseline blood pressure assessment: 24 hour blood pressure monitoring
- Measure plasma creatinine, urea, electrolytes, GFR
- Bladder and renal ultrasound examination

Follow-Up:

- Yearly for symptoms, baseline blood pressure
- Yearly early morning urine analysis for albumin creatinine ratio and dipstick testing for microscopic haematuria
- Yearly monitoring of plasma creatinine, urea and electrolytes, GFR



National Kidney Federation

www.kidney.org.uk

0845 601 02 09

British Kidney Patient Association

www.britishkidney-pa.co.uk

01420 541424



Individuals with BBS often have mild to moderate learning disabilities. Some early studies over-report the level of difficulties, as they used tests which were not tailored to visual impairment. Although studies conclude that a significant number of patients experience significant learning difficulties, only a minority have a severe impairment on IQ testing.

Often, a patient with BBS, and their parents alike, report a deficit in short term memory which is counterbalanced by excellent long term memory. The majority of children with BBS are able to remain in mainstream education, provided adequate classroom assistance and/or low vision aids are available.

Developmental delay is common in children who have BBS. Several components of development are often delayed, including speech and language development, general motor skills and, to a lesser extent, fine motor skills. In particular sitting, standing and walking may be delayed by up to one year.

Sometimes a child or young person with BBS will be labelled as rude or intellectually impaired because a requested response is delayed. There does seem to be some delay in the speed at which information can be processed. However, once decoded, the question is mainly answered in a reasoned and appropriate way. The 'delayed response' phenomenon is widely reported by parents and teachers of children with BBS.

Some common difficulties for children with BBS are:

- o Emotional immaturity
- o Poor reasoning

- o Poor communication
- o Psychological inflexibility
- o Obsessional thinking
- o Rigid routines
- o Challenging behaviour
- o An inability to form friendships

Some children who have BBS receive a diagnosis of autism. There is a great variation in learning difficulties among the BBS population, with some individuals seemingly unaffected by learning/behavioural difficulties and others who have severe autism and global developmental delay. For some children, much of this improves as they mature. However, emotional immaturity, poor reasoning, inflexibility and obsessional thinking can carry through into adulthood.

Between the ages of 7 to 12, there is typically an increasing awareness of the disability and the feeling of being different is starting to emerge, particularly in the school setting. At this sensitive age, young people may have difficulty with friendships, obesity and bullying, resulting in low self-esteem. Fears, such as the daily management of any behaviour difficulties, education, living an independent life and having a relationship, start to set in for both the person affected by the syndrome and their family. Fitting in socially is very important and the teenage years are when relationships and sexual functioning are major issues. Emotional detachment is common for any teenager, so suddenly not wanting to share everything or discuss things openly anymore can be difficult for parents who want to help. As with the general population, hormonal changes can also contribute to developing emotional difficulties, with people feeling lonely and unhappy.

In **adulthood**, common concerns are: worrying about medical conditions, not feeling in control of emotions, apathy and social skills problems, such as lack of a social life and finding a job. Individuals with autistic traits may have difficulty understanding other people's emotions and difficulty reading social cues, which makes it harder to relate to others. Independence is an issue for some, but not for others. Some people are able to do anything they want to do, whereas others find themselves understandably frustrated about the limitations that come with BBS.

Depression, anxiety, panic attacks, anger and poor emotional control commonly affect adults and young people with BBS. It is unclear whether this is a part of the syndrome or an indirect result of it. In reality, it is probably a combination of both.

A small number of patients experience delusional thoughts and some develop periods of frank psychosis. If this is suspected, prompt referral for a psychiatric opinion and therapy is warranted.



For **adult patients**, isolation can lead to anxiety and depression and it is vital that appropriate support is in place. There are many ways to access support:

- Ask GP to arrange a Social Services Assessment and Occupational Therapy Assessment.
- Ask GP/Social Worker about local support groups for the disabled or visually impaired.
- Ask GP about counselling if more support is needed for low mood or anxiety.
- Talk to staff at a local disability centre/Social Worker about activities in the area.
- Contact BBS UK (formerly LMBBS). It may help to talk to others in the same situation.
- Exercise is vitally important for emotional and physical wellbeing.
- Local Disabilities Team/Social Worker will be able to help with claiming benefits, arranging support workers, carers or respite, and linking individuals with local services in the area.



For **young patients** of pre-school/school age, an Education, Health and Care Plan (previously called a 'Statement') will ensure the child is fully supported. Parents/carers should contact the school/pre-school and request a plan be commenced. The school/pre-school's SENCo (Special Educational Needs Co-ordinator) will co-ordinate the process and arrange for educational psychologist and sensory team involvement. Possible interventions for children would include:

- Assistance with school integration
- Behaviour therapies
- Speech therapy
- Family support
- Management of symptoms
- Sensory support
- Emotional support

It is important to get any associated learning difficulties, such as autism diagnosed, as diagnosis could then lead to help from other areas.



It is really important that **parents and carers** receive support too. Parents and carers of BBS patients of all ages with health conditions can often become stressed and anxious about the condition and the difficulties of caring for someone with additional needs. There are many ways parents and carers can seek support:

- Ask GP to arrange a Social Services Assessment and Occupational Therapy Assessment.
- Ask GP about individual or couples counselling if more support is needed for low mood or anxiety or conflict arising in the family.
- Talk to staff at a local children's centre or child development centre about activities in the area for parents/carers.
- Contact BBS UK: It can sometimes help to talk to other parents/carers in the same situation.
- Exercise is important for emotional and physical wellbeing.
- Parents/carers should try to find some time for themselves: it is important to have 'me' time, whether alone, with friends or each other. Relationships often suffer when caring for someone with a health condition.
- Local Children with Disabilities Team/Social Worker will be able to help with claiming benefits, arranging support workers, carers or respite, and linking families with local services in the area.



"We sometimes need to find a little time for ourselves. This normally involves 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 parents of newly-diagnosed Bardet-Biedl children, is to allow yourselves this time too, in whatever form it takes."

Parent



Male Reproductive System

Hypogonadism (lack of production of sex hormones) is common amongst males, affecting up to 30% of BBS patients; a small buried penis with reduced volume testes is common. 10% have undescended testes at birth. In the majority of cases this is due to a partial failure of the hypothalamus/pituitary gland with low or inappropriately normal luteinizing hormone (LH) and follicle stimulating hormone (FSH), with low circulating testosterone levels. In a small number of individuals there may be primary gonadal failure. There is usually sufficient testosterone production to permit normal pubertal development. The timing of male puberty is often slightly delayed but with normal progression and secondary sexual characteristics. Puberty is a particularly stressful time for those with BBS, regardless of their sex, and, where possible, referral to a counsellor with experience in this field can be of help.

Adult male patients with hypogonadism may be prescribed testosterone replacement by an endocrinologist. This may take the form of either injections or daily gel preparations. While this may help with sexual function and libido, an important benefit is the preservation of bone mineral density and reducing the risk of fractures. Although affected males are likely to be infertile, several have fathered children.

Female Reproductive System

Hypogonadism is much less frequent in women. However, structural anomalies of the female genitourinary tract are documented, including vaginal atresia (abnormally closed or absent vagina), hydrometrocolpos (collection of watery fluid in the uterus and vagina), ectopic urethra (urethra that terminates somewhere other than the bladder), hypoplasia (underdevelopment) of the uterus, ovaries and fallopian tubes, and septate vagina (vagina that is divided). Women with BBS tend to have a normally timed puberty, and although there is little evidence to suggest secondary hypogonadism, polycystic ovary syndrome (PCOS) may be present in up to 20% of women with BBS. This can lead to problems with menstrual irregularity, acne and hirsutism (excessive hair). For those patients who are considering fertility, polycystic ovary syndrome needs to be considered should there be a delay in conception. Several females with BBS have given birth successfully to healthy children.



Patients affected by any of these issues should speak to their GP for a referral to an endocrinologist and/or counsellor where appropriate.

Patients of the BBS multi-disciplinary clinics should speak with their endocrinologist or BBS Clinical Psychologist.

Diabetes UK can offer information and support to those affected by diabetes:
www.diabetes.org.uk
0345 123 2399

Diabetes

Diabetes mellitus is present in nearly 16% of adult patients with BBS. It rarely presents before adolescence and in this age group occurs in those with the highest BMI scores. A higher proportion of patients may have abnormalities of glucose tolerance and regular screening for the development of diabetes is recommended.

The underlying BBS ciliopathy and high BMI scores contribute increased risk factors for Diabetes Mellitus. This can be controlled with combinations of diet and medicine including insulin. Newer therapies, for example, GLP-1 analogues and DPP-IV inhibitors are also potentially useful to try to optimize glycaemic control. Regular diabetes assessments are important and should be carried out at least annually. Preventable diabetic retinopathy can lead to rapid deterioration of vision already compromised by rod-cone dystrophy.

Alongside monitoring for complications of diabetes, it is important to adequately control blood pressure and all patients with diabetes over the age of 40 should be on lipid lowering therapy. Both of these measures are aimed at decreasing long-term cardiovascular risk. Up to 19% of patients may have subclinical hypothyroidism and it is possible that they may benefit from monitored thyroid hormone replacement.



Assessment

At diagnosis:

- Measure height and weight- calculate BMI
- Hormone levels: testosterone, gonadotropins FSH and LH, inhibin B
- Pelvic ultrasound examination (females)
- Fasting lipid profile, including triglycerides
- Fasting plasma glucose(FPG)
- Oral glucose tolerance test
- Fasting plasma insulin concentration
- Thyroid function test

Follow-Up:

- Annual measurement of weight and height
- Annual thyroid function test
- Annual fasting plasma glucose
- Annual screening for sleep apnoea



Speech and Language

Many children with BBS present with speech and language difficulties. It is very common for first words to emerge late. The difficulties may range from mild to severe and there can be problems across a range of communication skills or just in one area. Below are some examples of the types of difficulties that can occur:

- Expressive language impairment including slow acquisition of new words, difficulties putting sentences together, and difficulties describing a sequence of events or telling a story.
- Difficulties with receptive language including difficulties with understanding words and sentences; difficulties following stories and more abstract language within the classroom and at home.
- Impaired social communication skills, some children may have a diagnosis of autism.
- Speech development can be very delayed. Some children do not babble when they are young, other children do not develop speech sounds in the expected pattern or they have unusual speech patterns (disordered speech and/or dyspraxic speech patterns).
- The voice can be high pitched.
- Resonance can be hypernasal.

Treatment

A referral to speech and language therapy should be made at the first signs of speech and language difficulties. An assessment of the child's difficulties can then be made and specialist advice and treatment be provided early.

Hearing impairment, if present, will contribute to speech and language difficulties. For example, if conductive hearing loss is present during the pre-school years and is left untreated, this will have a negative impact on speech and language development. Hearing difficulties should be actively managed as soon as they are detected (see next section).



www.ican.org.uk
www.talkingpoint.org.uk
www.afasic.org.uk
www.autism.org.uk
www.dyspraxiafoundation.org.uk
www.makaton.org

"Of course the two things which inspire me the most to carry on with strength and determination are my children, two bright, funny, intelligent, kind and loving young people who have enriched our lives and made us proud parents. "

Parent



Neurological Abnormalities

Ataxia*, impaired co-ordination and mild hypertonia** are reported in a significant number of individuals. Low muscle tone is common amongst BBS patients of all ages.

Some limited brain MRI studies have shown that some patients with BBS have smaller, unusually formed hippocampi and there is a tendency towards decreased overall white matter. However, it is not clear if or how this affects neurocognition. A number of patients with BBS report difficulties with memory function.

* Ataxia is the term for a group of disorders that affect co-ordination, balance and speech.

** Hypertonia is a condition marked by an abnormal increase in muscle tension and a reduced ability of a muscle to stretch.



Hearing

Conductive hearing loss, almost always caused by glue ear, affects many children with BBS. This often resolves spontaneously or, with treatment, by adulthood. A minority of patients with BBS have sensori-neural deafness.

Assessment

At diagnosis:

- Audiogram, audiometry, tympanogram
- Auditory evoked potentials

Follow-up:

- Yearly examination: audiometry
- Detect glue ear (acute and chronic otitis media) which can lead to conductive hearing loss

Treatment

Glue ear management: myringotomy tubes and/or hearing aids.



Digestive System

Hirschsprung's disease occurs more frequently in Bardet-Biedl Syndrome than in the general population, however the incidence is unknown. In this condition, a section of the bowel is permanently narrowed and unable to relax. This causes a build-up of stool and forms a blockage. It has been reported in a number of individuals with Bardet-Biedl Syndrome and should be suspected in babies who take longer than usual to pass meconium, particularly in the context of a swollen abdomen and bilious vomit. In older children and adults, it often presents with a swollen abdomen, poor appetite and constipation that does not respond to any of the usual treatments.



Orthopaedic Abnormalities

Examination and early identification of scoliosis (curvature of the spine), genu valga (knock-knee), genu vara (bow-leg) and pes planus (flat-foot) will allow for early intervention/treatment and may avoid unnecessary discomfort.

Physiotherapy and orthotic referral should be considered; early orthotic intervention and supportive footwear/insoles will ease discomfort and protect feet against further damage.



Liver

Fibrocystic and fibrotic liver diseases have been reported in a very small number of cases of BBS. More recently, there is an awareness of the likelihood of co-existent non-alcoholic fatty liver disease (NAFLD) that is driven by obesity and type 2 diabetes. This is a chronic condition that can evolve over many years. It can manifest within a spectrum of disease that ranges from simple fat accumulation (hepatic steatosis) that has few, if any clinical consequences, to inflammation (steatohepatitis) and in some cases scarring that can lead to liver cirrhosis. It is progressive in some, but not all, patients. Managing the condition relies on staging the severity of NAFLD and treating the conditions that predispose to it, namely reducing weight and optimising blood sugar control in patients with diabetes.

Assessment

- Measurement of plasma ALT, AST and GGT concentration
- Liver ultrasonography



Cardiovascular

Congenital heart disease has been reported in a minority of BBS patients. Dextrocardia (heart points to the right instead of the left), and occasionally complete situs inversus (where organs are positioned opposite to normal position) have been reported but are rare.

However, hypertension is a common feature of Bardet-Biedl syndrome and often presents in childhood or early adulthood. It may occur as a result of other features contributing to metabolic syndrome in Bardet-Biedl syndrome, in particular obesity. It is imperative that hypertension is treated, since it can contribute to renal deterioration. Both lifestyle modification and pharmacological intervention are encouraged.

Assessment

- Blood pressure monitoring
- Auscultation
- ECG
- Echocardiography



“When I was 16, I went to the West of England College in Exeter. At the college I learnt how to be independent, doing such things as cooking, cleaning, and shopping. I also completed courses in further education, including an NVQ in administration. I also did work experience placements. I love living independently and being able to see my friends and go where I want to. I feel that I have achieved a lot so far in my life, and I look forward to enjoying life to the full.”

BBS Patient



Joints

A large number of patients with BBS report pain in weight-bearing joints, probably because of osteoarthritis. However, a small proportion also have abnormally hypermobile or lax joints, the cause of which is unknown, but may be associated with hypotonia (decreased muscle tone).



Dental

Several people with BBS have unusually short tooth roots, especially of the front lower teeth. Crowding of the teeth necessitating prophylactic removal is common. The majority of patients have a high-arched palate. Occasionally enamel dysplasia is evident. Both of these abnormalities can increase susceptibility to tooth decay and loss and regular dental supervision is advisable.



Respiratory System

Many BBS patients in the UK are affected by asthma, allergy and hay fever.

Obstructive Sleep Apnoea (OSA) is common and related to excess weight, particularly around the neck. This may be compounded by low muscle tone and soft palate dyscoordination. All patients should be questioned about their quality of sleep and the presence of daytime somnolence (excess sleepiness). Evidence suggesting OSA should lead to a referral for sleep studies and lung function assessments as many BBS patients report that treatment (e.g. nocturnal CPAP devices) results in major benefits such as increased activity, weight loss and lower blood pressure.



Bardet-Biedl Syndrome: Specialist Clinics

Bardet-Biedl Syndrome UK (BBS UK), together with Great Ormond Street Children's Hospital, Guys Hospital, London, Birmingham Children's Hospital and Queen Elizabeth Hospital, Birmingham have been commissioned by NHS England to provide multi-disciplinary clinics for Bardet-Biedl Syndrome patients. At each clinic, patients are seen by an Ophthalmologist, Nephrologist, Dietitian, Clinical Psychologist, Geneticist, Speech and Language Therapist and Endocrinologist; the aim is to provide a 'one stop' annual visit to ensure patients receive expert attention and management and should bring about a major change in how BBS is managed, with a focus on diagnosis, early intervention and good health management.

BBS UK is an integral member of this valued multi-disciplinary team (MDT) and provides information and support to the patients and their families/carers before, during and after clinics. Its involvement pre-clinic ensures patients and their families are well informed about the syndrome and feel well supported to attend. BBS UK representatives attend each clinic, offering emotional and practical support to patients and their families and ensure that they are aware of all relevant benefits and social support services. Post clinic they provide ongoing support and liaise between patient and hospital where required and generally provide an ongoing point of contact.

It is recommended that all patients with a suspected diagnosis of BBS should be referred to one of these centres. Such referrals should be addressed to:

Professor Phil Beales
Consultant Clinical Geneticist
Great Ormond Street Children's Hospital
Great Ormond Street
London
WC1N 3JH



BBS UK Clinic Support Team

Adults Service: Julie Sales 01892 685311

Childrens Service: Tonia Hymers 07805 685342

www.bbsuk.org.uk

bbsclinics@bbsuk.org.uk



"I have met so many children, young people and adults who have BBS at conference and clinics over the years, and their bravery, courage and determination in the face of disability and illness is inspiring. I have also seen so much achievement within our group, whatever their passion; we have successes in business, sport, in the workplace, music, art, as well as academic, and there is a great deal that can be achieved."

BBS Clinics Support Worker





SUPPORT

Bardet-Biedl Syndrome UK (formerly Laurence-Moon-Bardet-Biedl Society) is a voluntarily run charity aimed at protecting the health and promoting the welfare of persons affected by BBS, their families and carers. The charity also aims to advance the education of the medical and educational professions and the general public on the subject of BBS and its implications for the family.

BBS UK produces twice-yearly newsletters and an annual Conference Report, which records the highlight of the year, the annual Weekend Family Conference, which brings interested professionals and those with BBS, their families and carers, together for a formal conference programme and social weekend. The charity maintains a web site and Facebook page and through these has developed a community which self supports, with members helping each other through the challenges often faced. A general helpline, a New Family's contact, an Adult's contact and a Special Educational Needs contact are all available. Details can be found at:

www.bbsuk.org.uk

"I got in touch with two wonderful people from the BBS charity. They were a huge source of support to me and put me in contact with even more families. Sometimes I think the hardest thing for people is thinking that you are alone and that is where the charity comes into its own."

Parent

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

Conference Delegate





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This booklet is meant as a guide only. If you feel concerned about anything you have read please seek medical advice from your GP, consultant or a member of the BBS Clinics Team. We welcome your comments and feedback, please send to: info@bbsuk.org.uk or tonia.hymers@bbsuk.org.uk

Bardet-Biedl Syndrome UK

Registered Charity 1027384 & SCO41839



Bardet-Biedl Syndrome UK

Registered Charity No. 1027384 and SCO 41839

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