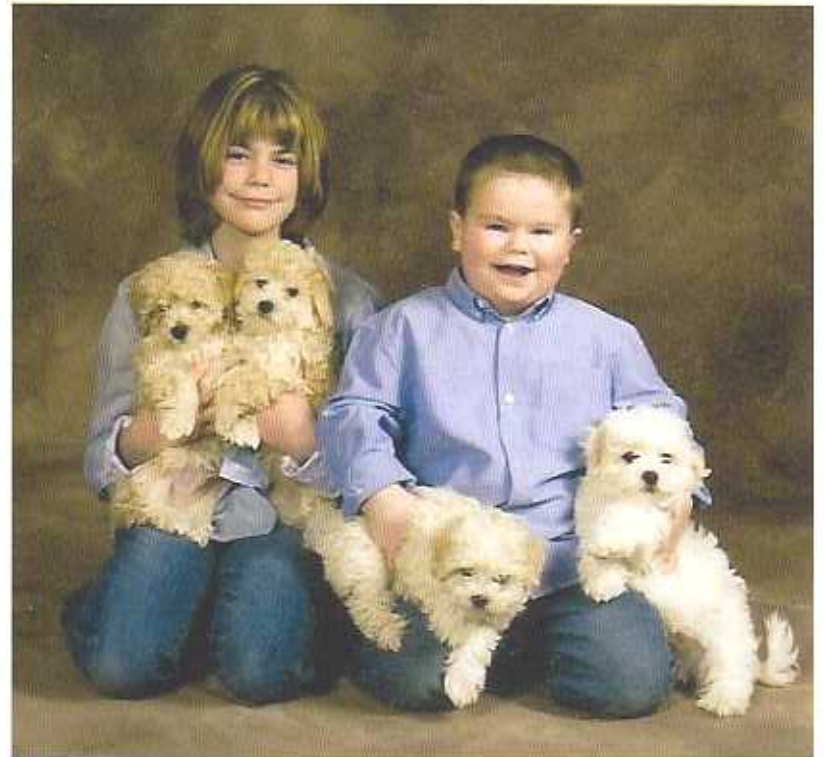


Bardet- Biedl Syndrome



John Shannon, age 5 (right), has BBS. He is pictured here with his sister Briana, age 9, and the family pups.

Chances are that you have never before heard of Bardet-Biedl Syndrome. This medical condition is often called BBS for short. It may be included with Laurence-Moon Syndrome (LMBBS for short). BBS is rare, perhaps one in 50,000 births, but there are no reliable figures for the frequency of occurrence in the U.S.

What is a syndrome?

A syndrome is a group or cluster of physical features that, when they appear together in the same individual, define a medical condition. BBS is considered a syndrome. It is always caused by alterations in the genetic material. It is **not** the result of any environmental event, such as exposure to an abnormal diet, a drug, a virus, or an infection during pregnancy. Historically, it was thought that BBS was always a recessively inherited condition—that each parent contributed one BBS gene so the child would inherit BBS equally from each parent. However, recent intensive research has shown that this syndrome is not always a classic recessive condition. Mutated or abnormal genes must be present for the many features of BBS to develop.



Liz Hannoun

There are at least thirteen different pairs of genes that can cause BBS. In addition, in about 15% of all cases of BBS in which the known genes can be analyzed, a combination of **both** a pair of one recessive gene **and** a third mutated copy of another gene must be present either to cause the syndrome to appear or to make its features more severe. Some researchers feel that some isolated features of the syndrome, such as obesity, may occur in carriers.

What are the signs of BBS?

The features of BBS may vary both between affected persons in the same family and between different affected people in unrelated families. To make the diagnosis of BBS,

your physician will look for several features that occur most frequently in BBS, but to have a firm diagnosis of the syndrome, a person must exhibit at least four of the primary features or three primary and two secondary characteristics. Because of the complex nature of the genetic alterations, each person with BBS will not necessarily exhibit every feature. Also, some features are not present at birth but may evolve or develop.

The primary features are:

- Visual Impairment caused by abnormalities in the retina;
- Obesity typically apparent the end of the first year of life;
- Polydactyly (extra fingers and/or toes on the side of the hands or feet);
- Hypogonadism (underdeveloped genitals);
- Renal Anomalies (kidney malformations/malfunctions);
- Learning difficulties.

Among the secondary features are:

- Developmental delay;
- Behavioral problems;
- Neurological problems;
- High blood pressure (hypertension);
- Speech and pronunciation disorders;
- Dental anomalies;
- Lack of sense of smell (Anosmia);
- Flat and wide feet with no arches;
- Thyroid problems;
- Strabismus (often called lazy eye, i.e. eyes not tracking together);
- Short stature, shorter than average height (not always present);
- Variations in fingers and toes;

- short and stubby (brachydactyly)
- mildly webbed (syndactyly, particularly between the second and third toes)
- curved (clinodactyly, especially the fourth and fifth fingers);

Many other characteristics have been associated with BBS with varying frequencies, among them: ataxia (unsteady gait), anomalies in the development of the heart including the heart on the right side of the body, heart enlargement, occasional blood vessel anomalies, hepatic fibrosis (scarring in the liver), difficulties with hand, eye, balance and muscle coordination (children have difficulty riding bicycles or performing activities requiring balance) and frequent ear infections sometimes resulting in hearing problems.



**Tom Marker (right), a Baptist Minister,
and his wife Debby**

Each of the primary features and some secondary features are discussed in this pamphlet. However, this is not meant to be a comprehensive resource for a person with BBS, a parent, teacher, or medical practitioner. This is an overview only.

If you suspect that you or someone you know has BBS, you should seek the advice of a medical professional.

The syndrome, taken as a whole, has no cure. Treatment is available for some of the individual features.

Visual Impairment

BBS is often diagnosed in childhood when problems with eyesight are first discovered, especially difficulties in dim light or at night, or when changing from a bright to a dim setting. In the back of the eye, the retina transmits light images using cells called rods and cones to the brain. The eye condition associated with BBS is a breakdown in the function of the rods and cones in the retina, somewhat similar to a condition called retinitis pigmentosa (RP for short). Because RP is more common than BBS, you can find quite a bit of information about RP which may be helpful. However, in BBS the retinal condition is often more subtle and difficult to detect, so it often is missed when it is looked for early, especially in infants and children. Nonetheless, the retinal condition is progressive like RP.



Vickie Weir on Reno

The conclusive medical test in diagnosing the retinal condition is an electroretinogram (ERG). Since two of the primary features of BBS can be confirmed visually in females and three in males, a confirmation of malfunctioning of the retina is a definite indication of the presence of the syndrome when other features are present. Since the retinal changes are subtle, the average age at which an ophthalmologist may see the changes in the retinal appearance is about age 7 years (although the ERG may detect the changes earlier).



Ashley Morris

Nonetheless, any child in whom a diagnosis of BBS is being considered should be examined by an ophthalmologist.

The early symptoms of this eye condition are night blindness, loss of peripheral (side) vision, sometimes reduced central focus, and often poor contrast definition, i.e. stairs can look like ramps as the children cannot locate the stair edge contrast differences.

Symptoms progress at different rates for each individual but often will lead to severe visual impairment during the teen years and into the twenties, almost always leading to legal blindness. Many adults, however, retain some ability to perceive light, some color and medium to large objects, and some have only slightly or moderately limited vision. At this time, there is no known cure or effective treatment for these visual impairments. Visual aids and adaptive training can make many life-functions easier. Each state has a governmental department to provide services and a resource center for the blind and visually impaired. Modern optical and computer technology has greatly improved the options for people dealing with visual handicaps. While the aids are too numerous to give a complete list, here are a few suggestions.

Mobility and Braille training are usually available through public schools, low vision centers, Lions, or local blind centers, or at a state school for the blind. Learning how to travel in a safe manner and to use a cane can provide confidence and independence and are particularly useful for children and adolescents. Many low vision aids (LVA) are available and can improve productivity and assist education. Devices like a CCTV (closed circuit television) can greatly magnify objects or printed material. Standard computer operating systems (Windows XP and OS X Tiger) provide disability options to make school and professional work easier.

Computer programs that translate type written word into spoken language are becoming easier to use and more accessible.

Strabismus is a common feature and can be corrected with eye muscle surgery and sometimes with covering the better eye to force the "lazy" eye to work. Strabismus is often seen at birth or in early childhood. If not corrected early, it can often lead to total loss of vision in the "lazy" eye as the brain turns off the image from that eye.

A confirmation of malfunctioning of the retina is a definite indication of the presence of the syndrome.

Obesity

Obesity is a common characteristic of BBS. It is usually noticeable near age one year, sometimes earlier. In shorter than average individuals, the disproportion accentuates the weight in the torso. At present, the reason(s) for the obesity are unclear. Some individuals say they are unable to know when to stop eating. Many feel hungry all the time and they constantly think of food. Some obesity may be caused by how the food (calories) is processed by the body.

Weight control is a common BBS concern even without overeating. Many cases show up where the children were not excessively fed and they still continued to gain weight, particularly around the middle. Several of the possible BBS mutations allow one to control weight with considerable exercise and food intake control, while several of the other



Carly Morris

possible BBS mutations do not allow this weight control to work very well. Many people without BBS struggle with weight issues, and information regarding a healthy lifestyle is plentiful. Professional guidance from dietitians, nutritionists, and exercise professionals is available to manage food intake and caloric distribution. Success can be achieved to maintain acceptable ratios of height to weight. Prescription medicines may help suppress appetite or aid weight loss.

Weight-loss surgeries may be discussed with a physician, although this option has not been successful with other genetic obesity syndromes, and its benefits and risks must be disclosed fully by the doctors.

Polydactyly (extra fingers and/or toes)

Obvious at birth, extra digits are typically on the side of the small finger or small toe. These can vary from small skin tags to fully formed and functional digits. Skin tags can be tied off shortly after birth and will fall away. More fully formed digits have bones and movement. Extra digits can be surgically removed at an early age.

Slight webbing (syndactyly) between fingers or toes (particularly the second and third toe) is common. Fingers tend to be short compared to the palm (brachydactyly), and feet are often short, wide, and flat with no arch. These features can challenge either dexterity (of fingers) or balance (of toes), which can be improved with therapy and properly fitting shoes. Check the Internet for businesses that sell very wide shoes.

Hypogonadism

Males with BBS can have small genitalia (testes and penis). The testes may not descend appropriately into the

scrotum after birth. Surgical intervention is available. Testosterone treatment for adolescent BBS boys has been used to accelerate sexual development and maturation if it is delayed.

Because female genitals are more difficult to “measure”, underdevelopment here is more difficult to assess in girls; it is not known how frequent this feature is among women with BBS. Both late onset of menstruation and irregular menses may occur. There is occasional evidence of hormonal imbalance but, like many matters concerning BBS, this has been poorly and inconsistently documented. Some girls with BBS have been placed on oral contraceptives to smooth out the irregularities in the frequency of periods. Some females also have malformations of the uterus, vagina, and the drainage system from the bladder. In the more severe variations, these anomalies have been labeled as “McKusick-Kaufman Syndrome”.

While it is infrequent that a male with BBS will father a child, BBS women have given birth.

Renal Anomalies

Again, not every person with BBS has kidney problems. The nature of kidney irregularities associated with BBS is neither specific nor unique; the same anomalies occur without BBS. However, their frequency in persons with BBS makes investigation and periodic monitoring part of prudent annual medical care. Sometimes, the structure of the kidney is unusual; the kidney is larger than normal or contains cysts. Sometimes these cysts are large enough that the size is documented on ultrasound examinations of the fetus during pregnancy. The cysts cause unusual echoes on the ultrasound study, creating a so-called “echogenic kidney” (meaning a kidney that produces excessive echoes from the ultrasound examination). Sometimes these fetal anomalies disappear later in pregnancy or after birth.

The structure of the kidney could be abnormal without necessarily causing any functional difficulties. Sometimes the kidney may not function normally or may have an inability to concentrate urine properly. An indication of functional difficulty may be excess urine production (polyuria) or excessive thirst (polydipsia). Another indication in children may be the inability to control urination during the night or persistent bedwetting, or even loss of control after it was established.



Monique Lamb and Sabrina: mom was a kidney donor for her daughter.

Many people with BBS have kidney problems, which should be treatable or adaptable. A few people with BBS have developed kidney failure which requires dialysis or even a kidney transplant. A complete renal evaluation should be done upon diagnosis of BBS. That evaluation may include blood tests of kidney function: a "Blood Urea Nitrogen" or BUN, a creatinine level, and a "creatinine clearance", urinalysis for abnormal substances in the urine (such as excessive protein or amino acids), and sometimes an ultrasound examination of the

abdomen and kidneys ("renal ultrasound"). The blood and urine tests are simple and inexpensive and may be repeated each year or two to assure that there are no new or progressive problems.

Learning

Some medical literature says that mental retardation is part of BBS but this may not always occur. As mentioned earlier, not every feature occurs in every person with the syndrome. Also the severity of any feature may vary widely, even between two affected people in the same family. Not every person with BBS has cognitive impairment but some developmental delay or learning disability occurs frequently.

Developmental delay means a slower progress to develop certain functions, sometimes called "meeting milestones". Acquiring certain physical abilities during the first few years of life, like rolling over, sitting alone, walking, and talking, are standard comparisons for infant development. Certain developmental delays for a child with BBS may be attributed, in part, to other features such as visual impairment or hearing impairment. Learning to walk can be more difficult due to extra weight, wide flat feet, or differences in visual perception. For most children with BBS, there does seem to be some delay in acquiring both gross and fine motor, speech, and language skills. Most BBS children need speech therapy for difficulty in



Brandon Young at his 2007 graduation with a Bachelor of Arts degree in Political Science



Joy Ravenel after receiving her AA degree in Business in 2007

forming certain sounds. However, developmental progress is not necessarily indicative of intelligence. Learning disabilities associated with BBS range from needing just a little extra time with specific concepts to severely impaired comprehension. Again, it may be difficult to separate the challenges presented by the physical issues from those that truly relate to cognition or intellect. Is the child not learning her colors because of learning problems or because she cannot see the colors? Every child diagnosed with BBS should receive careful evaluation and formal testing, and an individual education plan (IEP) should be developed with parents and teachers. Optimal educational provisions will assist

each BBS individual to reach full potential. Many of our BBS children have average or above average IQ's and many grow up to complete college and some have advanced degrees!

Social Aspects

For persons with BBS, impaired vision can hinder the use of non-verbal cues in their relations with other people. They may appear rude or may make inappropriate comments and yet may be genuinely unaware of the resulting social alienation. The limitations of the side vision can cause them to bump into obstacles or to walk into half-open doors so the person may be labeled "clumsy" or "careless." Research has shown that many children with visual disabilities do not develop friendships in the usual manner and may need encouragement to pursue neighbors and school mates, especially in younger years of education.

Obesity may be perceived as of lack of self-control and may accentuate awkward physical movement. Most people do not truly understand that being overweight is not always a result of overeating. Adding up all these concerns, children with BBS may have even greater challenges living in our social environment.

Behavior

Anecdotal evidence from many families indicates that the behavior of people with BBS cannot be completely attributed to visual disabilities or learning issues alone. Many behaviors associated with BBS also fit within some of the "autism features" similar to other genetic syndromes that mimic autistic features. Autistic behavior could be part of the developmental delay, the communication deficits, and socialization issues. Many methods of behavior modification which are successful with the autistic are beneficial for people with BBS. Having a structured environment, advance preparation, and elimination of surprise or change in routine will minimize some negative interpersonal behaviors. Positive reinforcement of appropriate behaviors, as with most people, will improve interactions and socialization. Opportunities to socialize with adults or older children often improve BBS social behavior. BBS children feel more comfortable socializing with adults than with their peer group.



Sarah (left) and Stephanie Knob



Grace Miller

Dental, Smell, & Ear, Nose and Throat Issues

Many people with BBS have dental or jaw issues that can affect their chewing and, therefore, their digestion. Many of these concerns can be corrected with braces.

Oral surgery has been needed in some cases due to gum tissue irregularities. Many BBS people have nose blowing,

coughing up sludge and/or whistling difficulties.

Recently, an absence of or a diminished sense of smell has been found in people with BBS. In fact, more than half of all people with BBS have either no sense of smell or a profoundly reduced sense of smell (called either "anosmia" or "hyposmia"). This altered or lack of smell may have life consequences since smell is both a part of eating behaviors and a sense of fullness and also a warning for several threatening situations, such as spoiled food and smoke. At this time, no treatment is known.

Ear infections are common in unaffected young children as their ear canals mature. It is also common, but possibly more frequent, in children with BBS. Ear infections should, as for any child, be treated with appropriate antibiotics and decongestants. Chronic fluid behind the eardrum (glue ear) can affect hearing. An Ear, Nose, and Throat specialist (otorhinolaryngologist) should be consulted and surgical insertion of ear tubes should be discussed. Usually, as the child grows, these ear difficulties will fade.

Thyroid irregularities can occur but can be controlled with thyroid medication.

Living Full Lives

Hearing the medical terminology and seeing clinical information can be scary for those newly introduced to BBS. The syndrome is rare, and many medical practitioners are not familiar with BBS and may not have full sensitivity to the wide range of BBS characteristics. Many doctors tell BBS patients and their parents that the family is the expert on the subject because they live with the condition and are aware of so many of the issues that are out of the ordinary.

Generalizations, especially with BBS, can be misleading. With that caveat, many people with BBS are affectionate, eager to please and, like everyone, enjoy cheerfulness and encouragement.

The L M B B S Association will give you the opportunity to communicate with families who are warm, intelligent, compassionate — and living with BBS. Many organizations generously offer services to help meet the needs from issues associated with BBS. Many parents of older children and adults with BBS have been down these many paths without the support and knowledge that we have now. We encourage you to become part of the network of BBS families as we all learn more and help each other.

The challenges should not be minimized, but life with BBS can be full.



Jessica Zaza on her way to prom in 2007

The LMBBS Association helps connect people who are living with LMBBS. Request to join our e-mail group at:

<http://groups.yahoo.com/group/LMBBS/>
or contact our group moderator:

Claudia Parker
9688 Oaktree Terrace
Midwest City, OK 73130-3538
405-736-0600 or ClaudiaCParker@sbeglobal.net

Information & personal stories can be found at
<http://lmbbsa.com>

Or at the site of the British LMBBS Society at:
<http://www.lmbbs.org.uk>

You may be able to find a genetic counselor in your area
at <http://www.nsgc.org>

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The information in this pamphlet is designed for educational purposes only. The contents are not medical, legal, technical or therapeutic advice and must not be construed as such. The information contained herein is not intended to substitute for informed professional diagnosis, advice or therapy. Readers should not use this information to diagnose or treat Bardet-Biedl Syndrome or related disorders without also consulting a qualified medical or educational professional.

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