BARDET-BIEDL SYNDROME (BBS): A RARE GENETIC DISEASE OF OBESITY

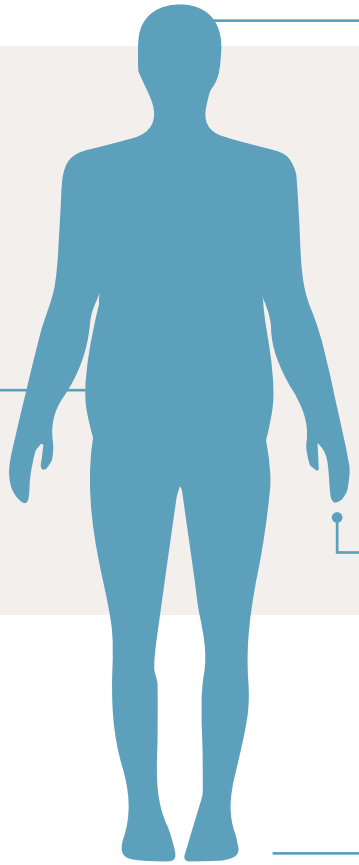
Estimated prevalence (US): 1500 to 2500*

Common features of BBS[1-3]

Obesity (72%-92%)
- typically early onset by age 5

Hyperphagia (insatiable hunger)
- preoccupation with food
- excessive food-seeking behavior

Renal anomalies (53%)



Visual impairment (93%)
- typical onset: 5-10 years old

Cognitive impairment (>50%)
- learning difficulties
- speech delay
- developmental delay

Postaxial polydactyly (63%-81%)

BBS has a highly variable phenotype that evolves significantly during childhood and/or adolescence[4]
- Phenotype can vary between siblings

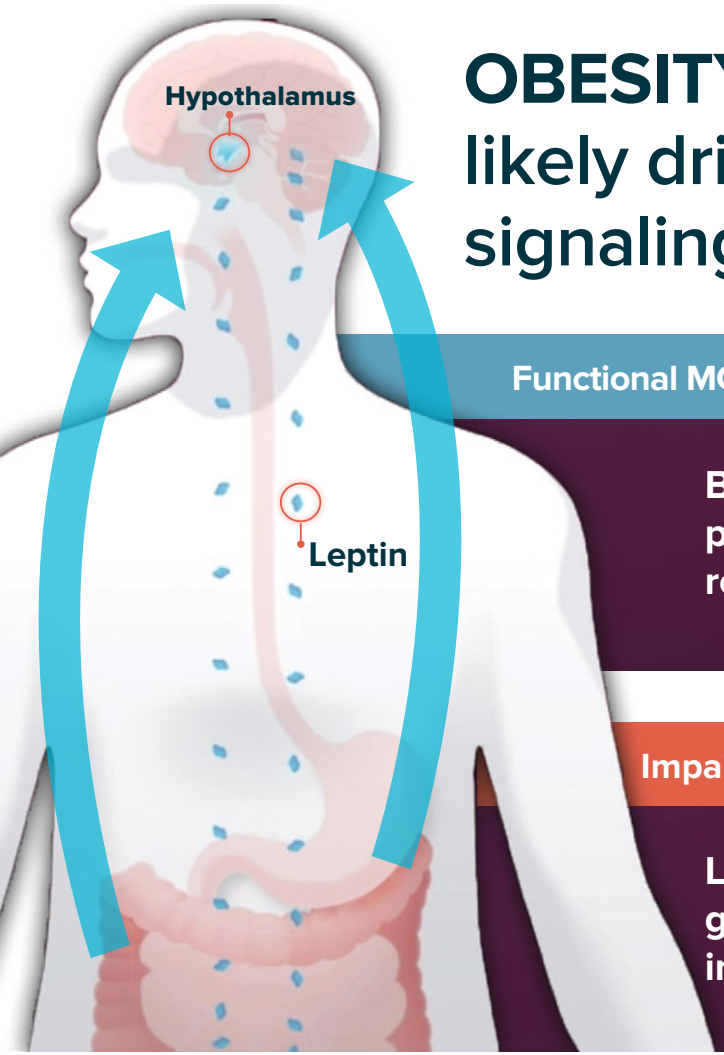
Learn more about the most common clinical features of BBS ›

*Company-estimated number of affected individuals.

Hyperphagia and obesity can seriously impact overall health and quality of life for individuals living with BBS.

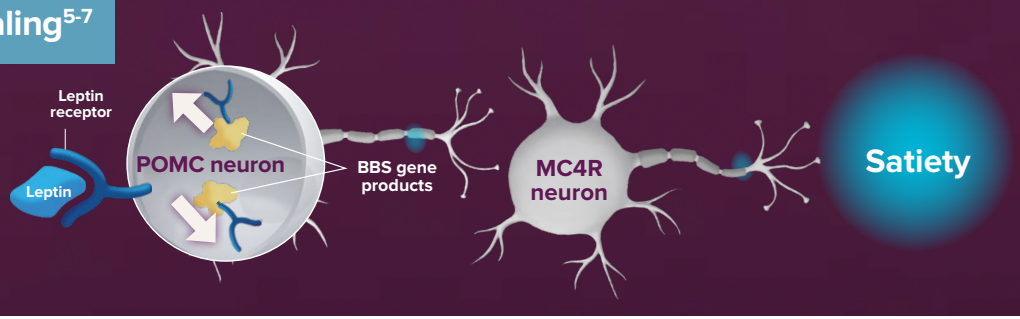
RARE Genetic Diseases of OBESITY

OBESITY AND HYPERPHAGIA IN BBS:
likely driven by impairment of a key signaling pathway that regulates hunger[5]



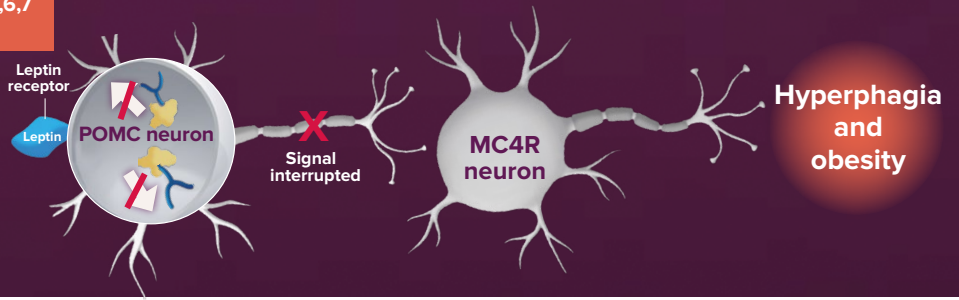
Functional MC4R pathway signaling[5-7]

BBS genes play a critical role in signaling



Impaired signaling in BBS[3,6,7]

Loss of BBS gene function impairs signaling



The MC4R pathway[5,6]

- Plays a key role in regulating hunger, satiety, and energy expenditure, and is activated by leptin

BBS genes play a critical role in signaling[5-7]

- Help traffic leptin receptors to the cell surface of POMC neurons, which can activate MC4R neurons

Loss of BBS gene function impairs signaling

- Individuals with BBS inherit 2 nonfunctional copies of a BBS gene, which are the result of a disease-causing variant in each copy[4,8]

Learn more about the MC4R pathway ›

BMI=body mass index; MC4R=melanocortin-4 receptor; POMC=pro-opiomelanocortin.

HYPERPHAGIA AND OBESITY CAN IMPACT OVERALL HEALTH AND QUALITY OF LIFE FOR INDIVIDUALS WITH BBS

Many patients with BBS suffer from hyperphagia, exhibiting extreme food-seeking behavior[3,9]

Hyperphagia often has an early onset, typically by age 5

General dimensions of hyperphagia

Behavior
Excessive food-seeking behavior

Drive
Preoccupation with food

Severity
Significant distress when denied food

Hyperphagia and food-seeking behavior are different in BBS[3]

- Overall, hyperphagia impacts patients with BBS significantly more when compared to matched controls with similar age, sex, and BMI z-score
- Patients with BBS are more likely to exhibit extreme food-seeking behaviors such as sneaking and stealing food when compared to matched controls

Obesity is common in BBS and can worsen comorbidities[1,4,10,11]

As many as 9 out of 10 patients with BBS are affected by obesity

- Severe obesity has an early onset, typically beginning in childhood by age 5, and persists into adulthood

Obesity further complicates management of comorbidities

- Diabetes
- Renal impairment
- Hypertension

Consider the *Understanding the Impact of Hyperphagia* tool for discussions with patients and their families

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BBS CAN BE DIAGNOSED BASED ON CLINICAL FEATURES

Clinical Features of BBS[2-4]*

Hallmark features of rare genetic diseases of obesity

- Early-onset, severe obesity
- Hyperphagia

Other clinical characteristics of BBS

- Visual impairment (rod-cone dystrophy that presents as atypical retinitis pigmentosa)
- Cognitive impairment (learning difficulties, speech delay, developmental delay)
- Renal anomalies
- Postaxial polydactyly
- Genital anomalies
- Diabetes mellitus
- Anosmia or hyposmia
- Ataxia
- Dental anomalies
- Congenital heart disease

*BBS has a highly variable phenotype that evolves significantly during childhood/adolescence.[4]

Genetic testing can help provide additional evidence to support diagnosis[4,12]

Order test kits through the Uncovering Rare Obesity® program–the only no-charge,† comprehensive genetic testing program for rare genetic diseases of obesity, including BBS.

Learn more about diagnosis ›

A Rhythm Territory Manager is here to support you and your BBS multidisciplinary care team ›

†Rhythm Pharmaceuticals covers the cost of the test and supplies sample collection kits. Patients are responsible for any office visit, sample collection, or other costs.

References: 1. Forsythe E et al. *Front Pediatr.* 2018. doi:10.3389/fped.2018.00023. **2.** Pigeyre M et al. *Clin Sci* (Lond). 2016;130(12):943-986. **3.** Sherafat-Kazemzadeh R et al. *Pediatr Obes*. 2013;8(5):e64-e67. **4.** Forsythe E, Beales PL. *Eur J Hum Genet*. 2013;21(1):8-13. **5.** Eneli I et al. *Appl Clin Genet*. 2019;12:87-93. **6.** Huvenne H et al. *Obes Facts*. 2016;9(3):158-173. **7.** Seo S et al. *Hum Mol Genet*. 2009;18(7):1323-1331. **8.** National Institutes of Health. MedlinePlus® Genetics. Accessed October 27, 2021. https://medlineplus.gov/genetics/condition/bardet-biedl-syndrome/#inheritance. **9.** Heymsfield SB et al. *Obesity (Silver Spring)*. 2014;22(01):S1-S17. **10.** Pomeroy J et al. *Pediatr Obes*. 2021. doi:10.1111/ijpo.12703. **11.** Forsythe E et al. *Clin Genet.* 2015;87(4):343-349. **12.** Beales PL et al. *J Med Genet*. 1999;36(6):437-446.

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