

# BECKWITH-WIEDEMANN SYNDROME (BWS)

## OVERVIEW

### What is Beckwith-Wiedemann syndrome (BWS)?

Beckwith-Wiedemann syndrome (BWS) is a rare overgrowth disorder involving genetic and epigenetic changes on chromosome 11p15. BWS occurs approximately every 1 in 10,500 births (Mussa, Di Candia et al. 2016). Since BWS was first described by Drs. Beckwith and Wiedemann in the 1960s, we have come to understand that not all children with BWS present in the same way. Patients with BWS may only have one or more of the most common (cardinal) features or perhaps only a handful of suggestive features.

#### Common Features (Cardinal Features)

- Macroglossia (large tongue)
- Omphalocele (abdominal wall defect that causes internal organs to protrude outside of the body)
- Hemihypertrophy/lateralized overgrowth (one side of the body/body part is larger than the other)
- Hyperinsulinism (persistent low blood sugar requiring medications/surgery)
- Multifocal Wilms tumor/nephroblastomatosis (kidney tumor)

#### Suggestive Features

- Large birth weight
- Facial nevus flammeus (red marks on the forehead, nose, and/or eyelids)
- Polyhydramnios (increased fluid during pregnancy)
- Placentomegaly (large placenta)
- Ear creases/pits
- Umbilical hernia
- Diastasis recti (weak abdominal muscles)
- Organomegaly (enlarged organs – most commonly kidneys and/or liver)
- Embryonal tumors, most commonly Wilms tumor (kidney tumor) or hepatoblastoma (liver tumor)

BWS is a **mosaic** disorder, which means that some cells in the body may be affected and others may not. This results in a range of features. Because of this, BWS doctors and researchers are beginning to refer to classical BWS as one end of the 11p Overgrowth Spectrum or Beckwith-Wiedemann spectrum. The spectrum describes a range of features due to changes on chromosome 11p15, from isolated hemihypertrophy/lateralized overgrowth to classical BWS.

### What causes BWS?

BWS is caused by changes on part of chromosome 11p15. Some of these changes act directly on the DNA itself (**genetic** changes). Other changes affect the regulation of the growth genes and whether they are turned on or turned off (**epigenetic** changes). These changes disrupt the normal balance of growth gene expression and lead to the overgrowth seen in patients with BWS. Most cases of BWS (~85%) are not inherited (meaning that it is not usually passed down from parent to child) but there are some instances of familial BWS.

### How is BWS diagnosed?

Despite advances in genetic testing, BWS is still primarily a clinical diagnosis. Careful examination by a geneticist can help identify the presence of common and suggestive features. Genetic testing can be performed, which may identify whether any chromosomal abnormalities or genetic or epigenetic changes are present. Due to mosaicism, some patients with BWS may have a negative

genetic result. This can occur depending on the tissue tested. A negative result does not exclude a BWS diagnosis.

### What management is available for BWS?

Management for patients with BWS will vary depending on the clinical features present in each child. Therefore, it is important to treat each child with BWS on an individual basis. Health care providers can include:

- Pediatrician – management of general pediatric concerns
- Geneticist – diagnosis and care coordination for BWS features
- Endocrinologist – management of hypoglycemia
- Feeding specialist – feeding evaluation and optimization
- Oncologist – management of tumor screening
- Orthodontist – evaluation of tooth and jaw development
- Orthopedic surgeon – evaluation and management of hemihypertrophy
- Otolaryngologist – evaluation of the airway, tonsils, and adenoids
- Plastic surgeon – evaluation for and management of macroglossia
- Pulmonologist - evaluation for obstructive sleep apnea
- Speech therapist – speech therapy

### What tumor screening is recommended in BWS?

All patients with BWS have an increased risk for the development of tumors. Based on the American Association for Cancer Research (AACR) guidelines, all patients should receive routine screening to monitor for kidney and liver tumors.

#### Ultrasound Screening

- Full abdominal ultrasound every 3 months until age 4 years
- Renal ultrasound every 3 months from age 4 – 7 years

#### Alpha-fetoprotein (AFP) Screening

- AFP measurements every 3 months until age 4 years

In BWS patients with *CDKN1C* mutations, additional screening for neuroblastoma is recommended. These include urine HVA/VMA and chest x-rays. Tumor screening tends to lead to earlier detection and more favorable outcomes, which is why tumor screening is so important in children with BWS.

### Summary

- BWS is a rare overgrowth disorder caused by changes on chromosome 11.
- Some major features include macroglossia, omphalocele and hemihypertrophy/lateralized overgrowth.
- BWS is mosaic so patients can present with a wide range of clinical features.
- Evaluation for BWS is done by both clinical assessment and genetic testing.

### References:

Mussa, A., S. Di Candia, S. Russo, S. Catania, M. De Pellegrin, L. Di Luzio, M. Ferrari, C. Tortora, M. C. Meazzini, R. Brusati, D. Milani, G. Zampino, R. Montirosso, A. Riccio, A. Selicorni, G. Cocchi and G. B. Ferrero (2016). “Recommendations of the Scientific Committee of the Italian Beckwith-Wiedemann Syndrome Association on the diagnosis, management and follow-up of the syndrome.” *Eur J Med Genet* **59**(1): 52-64.

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