CONDITION

Beckwith-wiedemann syndrome

Learn about Beckwith-Wiedemann syndrome, including overgrowth, low blood sugar, tumor risk, genetic testing, treatment, and childhood surveillance.

WHAT IT IS
Genetic overgrowth condition beginning before birth

BODY SYSTEM
Growth and development

MAIN SYMPTOMS
Large tongue, abdominal wall opening, uneven body growth, newborn low blood sugar

WHAT CAUSES IT
Altered genetic regulation on chromosome 11

HOW IT IS DIAGNOSED
11p15.5 methylation and copy-number testing

MAIN TREATMENT
Feature-based treatment and childhood surveillance

CAN IT BE CURED?
No, no treatment corrects imprinting change

IS IT AN EMERGENCY?
Sometimes, with severe breathing difficulty or seizures

LONG-TERM OUTLOOK
Most children do well with monitoring and treatment

Overview

Beckwith-Wiedemann syndrome, often shortened to BWS, is a genetic overgrowth condition that begins before birth. It is also called Beckwith-Wiedemann spectrum because its effects vary widely. Some children have several recognizable features, while others have only one or two.

BWS affects how certain genes control growth. These genes are in a region of chromosome 11 called 11p15.5. Most changes involve genomic imprinting , a process that controls whether the copy of a gene inherited from the mother or the father is active. BWS is usually caused by a change in this control system rather than by a missing or extra chromosome.

Possible features include a large tongue, an abdominal wall opening, one side of the body growing more than the other, low blood sugar after birth, and larger-than-expected organs or

body size. Development and intelligence are usually typical, although complications such as severe or prolonged low blood sugar may affect development.

Children with BWS also have an increased risk of certain childhood tumors, especially Wilms tumor of the kidney and hepatoblastoma of the liver. The level and type of risk depend partly on the underlying molecular change. Regular tumor surveillance during early childhood can help find these tumors when they are smaller and more treatable.

Care is usually coordinated among genetics, primary care, endocrinology, surgery, and other specialists based on the child's needs.

Symptoms

BWS can look different from one person to another. Features may be noticed during pregnancy, at birth, or later in childhood.

Common or important features include:

Some children have feeding difficulty, noisy breathing, sleep-related breathing problems, or delayed speech because of macroglossia. A difference in leg length can affect walking, posture, or the hips and spine.

Growth often becomes less unusual later in childhood. Adults with BWS are not necessarily taller than other adults.

- Macroglossia , meaning a tongue that is larger than usual. It may affect breathing, feeding, speech, dental development, or jaw growth.
- Omphalocele , an opening in the abdominal wall that allows some abdominal organs to extend into a sac at the belly button.
- Umbilical hernia or diastasis recti , in which the belly button area or the space between abdominal muscles is weak or widened.
- Lateralized overgrowth , meaning one side or one part of the body grows more than the other. It may affect a leg, arm, face, or several areas.
- Low blood sugar in the newborn period. Some infants produce too much insulin, which lowers blood glucose.
- Larger-than-expected birth weight or rapid early growth. Not every child with BWS is unusually large.
- Organ enlargement , sometimes involving the kidneys, liver, pancreas, or adrenal glands.
- Ear creases or small pits near the ears.

- Large kidneys or structural kidney differences.
- A large placenta, excess amniotic fluid, or an unusually long umbilical cord during pregnancy.

Causes and risk factors

BWS results from altered regulation of growth-related genes in chromosome region 11p15.5. Important genes in this region include IGF2 , which promotes growth, and CDKN1C , which helps limit cell growth.

Several types of molecular changes can lead to BWS:

Many affected people are mosaic , meaning the molecular change is present in some cells but not others. This helps explain why one body area may be more affected and why a blood test can sometimes be normal even when clinical features suggest BWS.

Most cases occur without a previous family history. Less commonly, BWS can be inherited. The chance that another child or family member will be affected varies greatly according to the exact molecular cause. A genetics professional can interpret this risk after testing.

BWS has been reported more often among children conceived using assisted reproductive technology, such as in vitro fertilization. However, most children conceived this way do not develop BWS, and many children with BWS were conceived without fertility treatment. The condition is not caused by something a parent did during pregnancy.

- Changes in DNA methylation, a chemical marking system that helps turn genes on or off
- Paternal uniparental disomy, in which some cells have two paternal copies of part of chromosome 11 and no maternal copy
- A disease-causing change in the CDKN1C gene
- A chromosome rearrangement, duplication, or deletion involving the 11p15.5 region

Diagnosis

Diagnosis begins with a medical history and physical examination. A clinician may look for macroglossia, an abdominal wall difference, lateralized overgrowth, ear findings, low blood sugar, or characteristic prenatal findings.

Molecular testing can confirm the diagnosis and identify the subtype. Testing usually examines methylation and copy number in the 11p15.5 region. Depending on the results and family

history, testing may also look for paternal uniparental disomy, CDKN1C variants, or chromosome rearrangements.

Because BWS can be mosaic, testing blood alone may not detect the change. If suspicion remains after a negative blood test, a genetics team may discuss testing another tissue. This could include cells from the inside of the cheek, skin from an affected body area, or tissue collected during a medically necessary procedure.

A diagnosis may still be made clinically when testing does not find a molecular cause. A negative test does not always exclude BWS.

Additional evaluation depends on the person's features. It may include:

Testing may also help guide tumor surveillance because tumor risk differs among molecular subtypes.

- Blood glucose monitoring in newborns
- Abdominal and kidney ultrasound
- Measurement of arms, legs, and body symmetry
- Feeding, airway, sleep, speech, or dental assessment
- Kidney function and blood pressure checks
- Review by a clinical geneticist or genetic counselor

Treatment and management

There is no single treatment that corrects the underlying imprinting change. Management focuses on each person's features and on preventing or finding complications early.

Low blood sugar in a newborn needs prompt treatment. Initial care may include feeding support or glucose given by mouth or into a vein. Persistent low blood sugar caused by excess insulin may require medication and care from pediatric endocrinology. A small number of children need pancreatic surgery when severe hyperinsulinism does not respond to other treatment.

An omphalocele usually requires evaluation by neonatal and pediatric surgical teams. Timing and type of repair depend on its size, the organs involved, and the baby's overall health. Smaller abdominal wall problems, such as an umbilical hernia, may only need observation unless they persist or cause complications.

Macroglossia does not always require surgery. Feeding specialists, speech-language therapists, dentists, orthodontists, sleep specialists, and ear, nose, and throat clinicians may

help assess its effects. Tongue-reduction surgery may be considered when the tongue causes significant airway obstruction, feeding problems, sleep apnea, persistent drooling, speech concerns, or changes in jaw and tooth development.

Lateralized overgrowth should be measured over time. A shoe lift may help with a mild leg-length difference. Larger or increasing differences may need orthopedic treatment. The goal is to support comfortable movement and reduce stress on the hips, knees, and spine.

Tumor surveillance is an important part of childhood care. Protocols differ by country and molecular subtype. Common North American approaches use abdominal ultrasound and blood testing for alpha-fetoprotein, or AFP, during the years when hepatoblastoma risk is highest, followed by kidney ultrasound during the remaining period of Wilms tumor risk. Testing is often performed about every three months in early childhood.

AFP is naturally high in newborns and falls with age, so clinicians interpret the pattern over time rather than relying on one result. International protocols may tailor surveillance more closely to the molecular subtype. Families should follow the schedule provided by their genetics, oncology, or primary care team rather than changing testing based on a general schedule.

Complications

Most children with BWS do well with appropriate monitoring and treatment. Potential complications depend on the features present.

Severe or prolonged low blood sugar can injure the brain if it is not recognized and treated. Early glucose monitoring is therefore important, especially after birth.

Macroglossia can contribute to airway blockage, obstructive sleep apnea, feeding difficulty, speech problems, and changes in tooth or jaw position. Symptoms may change as the child grows.

Lateralized overgrowth may lead to a leg-length difference, altered walking, hip or back discomfort, or spinal curvature. Regular measurement helps identify changes before they cause major functional problems.

Kidney complications can include structural differences, calcium deposits, stones, urinary infections, or reduced kidney function. Blood pressure and kidney follow-up may be appropriate for some children.

The childhood tumor risk is higher than in the general population, but most children with BWS do not develop cancer. Wilms tumor and hepatoblastoma are the main concerns. Less common tumors have also been reported. The risk is not the same for every child, which is why

molecular test results can affect surveillance discussions.

Follow up

Follow-up is most intensive during infancy and early childhood. The care plan may include regular visits with primary care and genetics, scheduled tumor surveillance, growth measurements, and review of feeding, breathing, sleep, movement, speech, dental development, and kidney health.

Keep copies of molecular test results and the surveillance plan. This information can help new clinicians understand which BWS subtype was found and what monitoring has been recommended. Families may also benefit from genetic counseling before another pregnancy or when an affected person reaches adulthood.

Contact the child's healthcare team promptly for a new abdominal lump or swelling, blood in the urine, ongoing abdominal pain, unexplained vomiting, loss of appetite, or an unexpected change in energy. These symptoms have many possible causes, but they should be assessed rather than saved for a routine visit.

Symptoms of low blood sugar can include shakiness, sweating, unusual sleepiness, poor feeding, irritability, or confusion. Follow the child's established glucose plan and seek prompt medical advice if these occur.

Call emergency services for severe breathing difficulty, blue or gray lips, a seizure, loss of consciousness, or inability to wake the child normally. These are emergency symptoms regardless of whether they are caused by BWS.

Routine concerns, such as gradual changes in leg length, speech, tooth position, or school needs, can usually be discussed at a scheduled appointment unless they are rapidly worsening.

Sources

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