Beckwith-Wiedemann Spectrum and Isolated Lateralized Overgrowth

Also called: Beckwith-Syndrome, BWS, Macroglossia-Omphalocele-Visceromegaly Syndrome, Isolated Hemihypertrophy

What is Beckwith-Wiedemann spectrum and isolated lateralized overgrowth?

Beckwith-Wiedemann spectrum is a genetic disorder that can cause overgrowth of body parts (hypertrophy) along with other medical findings (described below). The overgrowth may be limited to one body area, such as the legs, head or tongue, or it may involve several different areas of the body. When overgrowth is limited to only one side of the body, it is called lateralized overgrowth. When a person has lateralized overgrowth with no other signs of Beckwith-Wiedemann spectrum, that person may be considered to have isolated lateralized overgrowth.

People with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth also have an increased risk of developing certain cancers during childhood. These are usually cancers of the kidney or liver. Less commonly, cancers can arise from muscle or other tissues, or from the adrenal glands.

Most children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth grow up to be healthy adults. By the time the children are teenagers, their growth tends to become more typical and their cancer risk falls to that of the general population. Adults with these syndromes usually have normal intelligence and lifespan.

What is the cancer risk for people with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth?

Children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth are at increased risk of developing a kidney tumor called Wilms tumor. Most Wilms tumors develop before the age of 5 years, but some children can develop Wilms tumor later. Children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth also have an increased risk of developing a liver cancer called hepatoblastoma. Most hepatoblastomas develop by 2 years of age.

Rarely, children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth develop other types of cancer, including the following:

- Tumor in tissues with similar origins of nerve cells (neuroblastoma)
- Tumor in the adrenal glands (pheochromocytoma, adrenocortical carcinoma)
- Tumor in the muscle tissues (rhabdomyosarcoma)

The estimated risk for all types of tumors in children with Beckwith-Wiedemann spectrum is between 4% (about 1 in 20) and 21% (about 1 in 5). The estimated risk for all types of tumors in

children with isolated lateralized overgrowth is about 6% (about 1 in 17). The greatest time of risk is in the first 8 years of life.

What are other physical findings seen in people with Beckwith-Wiedemann spectrum?

Children with Beckwith-Wiedemann spectrum may have the some of the following additional physical findings.

- Creases or pits in or around the ear lobe
- Omphalocele, a birth defect in which organs that are normally in the abdomen poke out through the belly button (navel). These organs are covered in a sac made of a thin layer of body tissue. This condition is corrected surgically during infancy.
- Umbilical hernia, a birth defect in which there is a bulge near and under the belly button (navel). Correcting this through surgery may or may not be required, depending on the size of the hernia.
- Larger than normal organs in the abdomen (visceromegaly)
- Abnormal kidney(s)
- Abnormal heart
- A gap in the roof of the mouth (cleft palate), which is corrected surgically
- Blood sugar levels that are too low as a newborn (hypoglycemia)

Other, minor physical issues may include: excessive amniotic fluid during pregnancy (polyhydramnios); separation of the right and left sides of the main abdominal muscle (diastatsis recti); noncancerous blood vessel growths (hemangiomas); or port-wine stain birthmarks (nevus flammeus).

What causes Beckwith-Wiedemann spectrum or isolated lateralized overgrowth?

Most cases of Beckwith-Wiedemann spectrum and some cases of apparently isolated lateralized overgrowth are caused by changes known as “methylation defects” on a region of chromosome 11 called 11p15. Chromosomes are the thread-like structures that carry genetic information telling cells within the body how to function. The genes located at 11p15 help control how and when cells grow, divide and die. The methylation defects seen in Beckwith Wiedemann spectrum or isolated lateralized overgrowth interfere with how these genes work. As a result, cells with 11p15 methylation defects can grow and divide in an abnormal manner. Researchers believe this contributes to the enlarged body parts and possibly also to tumor formation. Pregnancies conceived using in vitro fertilization (IVF) are at higher risk of having Beckwith Wiedemann spectrum caused by a methylation defect. The risk of Beckwith Wiedemann spectrum in children conceived using IVF is between 1/4000 and 1/1000.

Most children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth (about 80%–85%) do not inherit the condition from a parent. These children have no history of the condition in their family. In these cases, the methylation defects on chromosome 11p15 either happened in the egg or sperm cell that formed the child or in one of the child’s cells during

pregnancy. These children are the first in their families to have Beckwith-Wiedemann spectrum or isolated lateralized overgrowth.

A smaller proportion of children with Beckwith-Wiedemann spectrum have the condition because of changes within a specific gene known as *CDKN1C* or because of an abnormal genetic makeup of chromosome 11p15 (this is called "uniparental disomy").

The risk of passing the condition to future children differs depending on what type of change is found on chromosome 11p15 after genetic testing. A genetic counselor can help to explain the risks.

How are people with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth screened for tumors?

Children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth are at increased risk of developing Wilms tumor and hepatoblastoma and have a small increased risk to develop other types of cancers. Most of these cancers can be cured with proper treatment if they are found early. Screening is recommended for all children with this condition. The goal of screening is finding and treating tumors early to allow the best outcome for patients. People with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth should be managed by a healthcare provider who knows these conditions well.

Recommended screenings for children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth include the following:

- **Yearly physical exams** by a healthcare provider who knows these syndromes well.
- **Ultrasound exams** of the abdomen. These ultrasounds should be started in infancy and repeated every three months and discontinued when the child reaches age 8 years. Until the age of 4 years, the ultrasound exam should include views of the liver, kidneys and other internal organs (abdominal ultrasound). After age 4 years, the risk of cancer in the liver or other internal organs drops dramatically, so the exam should focus only on the kidneys (renal ultrasound).
- **A blood test to check the levels of alpha-fetoprotein** (AFP). AFP is a protein that is often released by liver cancer cells. Checking a child's levels of AFP in the blood can help screen for liver cancer. Levels should be checked beginning in infancy and repeated every 6–12 weeks and discontinued when the child reaches age 4 years.

It is possible that the recommended screenings may change over time as health care providers learn more about Beckwith-Wiedemann spectrum and isolated lateralized overgrowth. Parents should discuss all screening options for their child with a health care provider who knows these spectrums well. Because Beckwith-Wiedemann spectrum and isolated lateralized overgrowth are complex conditions, it is important that parents seek out an experienced health care provider for their child.

How is genetic testing for Beckwith-Wiedemann spectrum and isolated lateralized overgrowth done?

The healthcare provider may suspect Beckwith-Wiedemann spectrum or isolated lateralized overgrowth after looking at a person's medical or family history. In most cases, a healthcare provider will ask questions about a person's health and the health of other family members.

The healthcare provider will record which family members have developed signs and symptoms of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth and at what ages these occurred. From this information they will create a family tree. If Beckwith-Wiedemann spectrum or isolated lateralized overgrowth is suspected in a child or other family members, the healthcare provider will likely recommend genetic testing.

Diagnostic genetic testing

If the healthcare provider suspects that a person has Beckwith-Wiedemann spectrum or isolated lateralized overgrowth, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person's genes are made of DNA.
- Specific areas on chromosome 11p15 are checked for possible changes. If there are differences, a genetic specialist decides if they might be associated with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth.
- If genetic changes are found that reveal Beckwith-Wiedemann spectrum or isolated lateralized overgrowth, a genetic counselor will work with the family in the following ways:
    - To help the family understand the cancer and other health risks of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth
    - To review what cancer screening tests are available
    - To find out if other family members should consider genetic testing
    - To help with decisions about prenatal genetic testing

It is important to remember that genetic testing does not always find genetic changes on chromosome 11p15 for all people with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth. This is because researchers do not yet fully understand all of the genetic causes of this condition. If no changes are found, this does not exclude a diagnosis of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth. For that reason, we recommend that all children who have a clinical diagnosis of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth receive the same medical management, regardless of genetic test results.

Prenatal genetic testing

Before considering prenatal genetic testing, parents should talk with a genetic counselor to decide if there is risk of passing on Beckwith-Wiedemann spectrum or isolated lateralized overgrowth to their children. Only certain genetic types of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth are inherited. Most are not passed on to future children.

If testing would be helpful, prenatal genetic testing may take place either before pregnancy occurs or during pregnancy. People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy—Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for the non-methylation defect cause of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth before placing them into the uterus.

Testing that occurs during pregnancy—Testing can be used to see if a pregnancy is affected with the known cause of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth. A health care provider gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)—**during the first trimester (first three months)
- **Amniocentesis—**during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the cause of Beckwith-Wiedemann spectrum or isolated lateralized overgrowth identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced health care provider or genetic counselor.

Special concerns

Genetic testing for Beckwith-Wiedemann spectrum or isolated lateralized overgrowth is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with their genetics healthcare provider to be sure they understand the meaning of the results.

Sometimes children or adults with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth can feel sad, anxious, or angry. Parents who pass on changes that cause Beckwith-Wiedemann spectrum or isolated lateralized overgrowth to one or more of their children can feel guilty. Some people with changes that cause Beckwith-Wiedemann spectrum or isolated lateralized overgrowth could have trouble getting disability coverage, life insurance or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth?

Children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth have a higher risk of cancer. They should monitor their health and adopt healthy habits. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.

Other ideas to reduce the risk of cancer include the following:

- Eat a healthy diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
- Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun

People with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth should watch closely for general signs or symptoms that could signal cancer:

- Pain or enlargement of the abdomen
- Blood in the urine
- Aches, pains, lumps, or swelling that cannot be explained

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with Beckwith-Wiedemann spectrum or isolated lateralized overgrowth and their families?

Resources about Beckwith-Wiedemann spectrum or isolated lateralized overgrowth:

- Beckwith-Wiedemann Syndrome Support Group, United Kingdom (https://www.bwssupport.com/)
- Beckwith-Wiedemann Syndrome Facebook Group (*www.facebook.com/groups/78357624606/*)
- Beckwith-Wiedemann Syndrome Family Forum (*www.beckwith-wiedemann.info*)

Other resources:

- Making Sense of Your Genes: A Guide to Genetic Counseling *(www.ncbi.nlm.nih.gov/books/NBK115508/)*

- Young People with Cancer: A Parent's Guide (*www.cancer.gov/publications/patient-education/young-people*)

Sources:

1. Genetics Home Reference - Beckwith-Wiedemann Syndrome
ghr.nlm.nih.gov/condition/beckwith-wiedemann-syndrome
2. Gene Reviews - Beckwith-Wiedemann Syndrome
www.ncbi.nlm.nih.gov/books/NBK1394/
3. Cancer.net - Beckwith-Wiedemann Syndrome
www.cancer.net/cancer-types/beckwith-wiedemann-syndrome
4. Weksberg R, Shuman C, Beckwith JB. Beckwith–Wiedemann syndrome. *European Journal of Human Genetics*. 2010;18(1):8-14. doi:10.1038/ejhg.2009.106.
5. Brioude F, Kalish JM, Mussa A, et al. Expert consensus document: Clinical and molecular diagnosis, screening and management of Beckwith-Wiedemann syndrome: an international consensus statement. *Nat Rev Endocrinol*. 2018;14(4):229-249. doi:10.1038/nrendo.2017.166
6. Duffy KA, Cielo CM, Cohen JL, et al. Characterization of the Beckwith-Wiedemann spectrum: Diagnosis and management. *Am J Med Genet C Semin Med Genet*. 2019;181(4):693-708. doi:10.1002/ajmg.c.31740

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