Williams Syndrome (WS) — Symptoms and Treatment
See online here

Williams Syndrome results from a microdeletion in region q11.23 of chromosome 7. It mostly results from de novo mutations and follows an autosomal dominant pattern. Affected individuals have characteristic elfin facies. Common clinical abnormalities related to Williams Syndrome are cardiovascular diseases (elastin arteriopathy, peripheral pulmonary stenosis, supravalvular aortic stenosis, and hypertension), connective tissue abnormalities, developmental delay, short stature, endocrine abnormalities (hypercalcemia, hypercalciuria, hypothyroidism, and early puberty), transient neonatal hypercalcemia, and mild to moderate intellectual disability. Fluorescence in situ hybridization (FISH) test is used to diagnose the syndrome. Treatment includes a multidisciplinary approach.

Overview and Definition of Williams Syndrome

Williams syndrome, also known as Williams-Beuren syndrome, results from a microdeletion in a small region of chromosome 7 (q11.23). The deleted region includes 26–28 genes, and researchers believe that a loss of several of these genes contributes to the characteristic features of this disorder. This syndrome occurs in 1 in 10,000 live births.
Typical genes that are deleted in Williams syndrome are:

- CLIP2
- GTF2I
- LIMK1
- GTF2IRD1
- ELN

Williams syndrome is inherited in an autosomal dominant pattern. The mutations are mostly de novo. The learning disabilities and cognitive difficulties in people with Williams syndrome are due to the loss of several genes, especially CLIP2.

The gene, ELN, which encodes for elastin protein, is typically absent in this syndrome and results in cardiovascular disease and connective tissue abnormalities. The absence of genes LIMK1, GTF2I, and GTF2IRD1 causes difficulties regarding spatial visualization ability; furthermore, the absence of these genes explains the characteristic difficulties with visual-spatial tasks, unique behavioral characteristics, and other cognitive difficulties seen in this population.

Loss of GTF2IRD1 may also contribute to the distinctive facial features often associated with this condition. Researchers believe that the presence or absence of the NCF1 gene on chromosome 7 is related to the risk of hypertension in people with Williams syndrome. When NCF1 is included in the part of the chromosome that is deleted, affected individuals are less likely to develop hypertension; therefore, the loss of this gene appears to be a protective factor. People with Williams syndrome whose NCF1 gene is not deleted have a higher risk of hypertension.

**Signs and Symptoms of Williams Syndrome**

Deletion of multiple genes in Williams syndrome results in a wide range of physical and mental problems. Some commonly found signs and symptoms are:

- Connective tissue abnormalities
- Developmental delays
- **Short stature**
- Distinctive facial features (characteristic elfin facies)
- Broad forehead
- Short nose and broad nose tip
- Full cheeks
- Wide mouth with full lips
- Long philtrum
- Flattened nasal bridge
- Cardiovascular disease
- Supravalvular aortic stenosis
- Supravalvular pulmonary stenosis
- Insufficient elastin leading to hernias, bladder diverticula, full cheeks, and hoarse voice
- Transient neonatal hypercalcemia
- Intellectual disability (mild to moderate)
- Difficulties regarding spatial visualization ability, such as solving puzzles and drawing; however, these individuals do well in language and rote memorization
- Outgoing and engaging personality
- Attention deficit disorder
- Problems related to anxiety and phobias
- Dental problems like hypodontia, diastema, and malocclusion
- Cocktail type personality which includes low IQ, higher verbal IQ, and a lack of social inhibition

Other symptoms include:

- Failure to thrive
- Low muscle tone
- Gastrointestinal problems, such as colic
- Urinary difficulties
- Nocturnal enuresis
- Hyperacusis and phonophobia are often seen in affected individuals
- Higher prevalence of left-handedness
- Strabismus in about 75% of cases

Diagnosis of Williams Syndrome

Diagnosis is made based on the recognition of physical symptoms and a genetic test. Developmental delays, stellate iris pattern, long philtrum, and puffiness around the eyes are the initial signs which should prompt testing for the disease.

**One of the following 2 types of tests are used:**

1. Microarray analysis
2. Fluorescence in situ hybridization (FISH) test

FISH involves probing chromosome 7 to find 2 copies of the elastin gene. The absence of 1 copy strongly suggests Williams syndrome.

Genomic testing methods that determine the copy number of sequences can include chromosomal microarray or targeted deletion analysis by FISH.

Note: Williams syndrome cannot be identified by routine analysis of G-banded chromosomes or other conventional cytogenetic banding techniques.

Treatment of Williams Syndrome

Treatment is mainly aimed at improving the quality of life and alleviating other conditions associated with Williams syndrome. To achieve this, the following tests are conducted:

- Annual cardiology evaluation
- Ophthalmology evaluation
- Auditory examination
- Thyroid function tests
- Renal ultrasound
- Administration of calcium at birth and during the first few months
- Developmental and growth evaluation
- Examination for inguinal hernia
- Blood pressure measurement
- Orthopedic assessment on joints and muscle tone
Treatment:

- Cardiovascular issues are treated on an individual basis
- Hypercalcemia is treated along with the avoidance of extra calcium and vitamin D
- Physical therapy for joint problems and low muscle tone
- Behavioral treatments
- Speech therapy to improve the social interactions of affected individuals

References


Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our legal information page.