



JOUBERT SYNDROME &
RELATED DISORDERS FOUNDATION

The faith to believe, the hope to dream, the love to see it through

Joubert Syndrome

(Cerebellar vermis agenesis/hypoplasia)

Joubert syndrome refers to a disorder in which there is a specific abnormality in the part of the brain called the cerebellar vermis. There is a group of genetic conditions and syndromes that may share this cerebellar malformation, and they are known as Joubert syndrome and related disorders (JSRD). These conditions have some characteristics in common, but there is a spectrum of symptoms and abilities in affected individuals. For additional information regarding this family of conditions, please refer to the Joubert Syndrome & Related Disorders Foundation website at www.jsrdf.org.

Individuals diagnosed with classic Joubert syndrome traditionally exhibit the following features:

- Underdevelopment (hypoplasia) or complete lack (aplasia/agenesis) of the cerebellar vermis, usually indicated by the “Molar Tooth” sign found on an axial view of a brain MRI scan.
- Developmental delays/mental retardation—variable severity.
- Difficulty coordinating voluntary muscle movements; uncoordinated movements (ataxia).
- Decreased muscle tone (hypotonia).

The following features are often present:

- Facial features may be abnormal in appearance (eyes far set from each other, small ear lobes, broad forehead, arched eyebrows, broad mouth).
- Oculomotor apraxia (OMA), which is a specific eye movement abnormality in which it is difficult for children to track objects smoothly. Eyes may appear to jump, with jerky eye movements.
- Abnormal breathing pattern with episodes of rapid breathing or panting (hyperpnea), which may be followed by pauses in breathing (apnea).
- Abnormal collections of cerebrospinal fluid in the posterior fossa that may resemble Dandy-Walker malformation.
- Difficulty processing and reacting to information received through their five senses.

While less common, the following features may also be present in some individuals and may be useful to define a JSRD (see Parisi and Glass “Joubert syndrome” GeneReview at www.genereviews.org for more information).

Many of these features are not present at birth:

- Rapid, involuntary movements of the eyes (nystagmus).
- Severe visual impairment, or Leber congenital amaurosis
- Retinal dystrophy, particularly increased pigmentation of the retina or flattened electroretinogram (ERG).
- A malformation of the retina or other regions of the eye (coloboma)
- Renal insufficiency, particularly juvenile nephronophthisis or cystic dysplastic kidneys.
- Abnormalities of the liver, including hepatic fibrosis.
- Extra fingers and/or toes (polydactyly).
- Extra strands of tissue between the gums, tongue, and mouth (oral frenulae) or nodules on the tongue.
- Other conditions not listed here may also be observed

Explanation of features:

Individuals diagnosed with Joubert syndrome have an absence or underdevelopment of part of the brain called the cerebellar vermis which controls balance and coordination. The severity of the resulting ataxia (uncoordinated movements) varies from person to person.

Decreased muscle tone is common in children with Joubert syndrome. As a result of the poor muscle tone, developmental delay (usually in gross motor, fine motor and speech areas) is common.

Some children have also been noted to have abnormal eye and tongue movements. Developmental delays are usually treated through physical therapy, occupational therapy, speech therapy, and infant stimulation. Most children diagnosed with Joubert syndrome are able to achieve standard milestones, although often at a much later age.

Some individuals experience difficulties resulting from an inability to appropriately process information received through the five senses - hearing, seeing, tasting, touching, and smelling - as well as from their poor sense of balance and muscle movement. Some families have found that sensory integration therapy can help to minimize these sensory issues.

Mild to moderate mental retardation is typical, but overall health and growth are not known to be severely affected by this condition unless significant liver or kidney failure occurs.

Management and treatment:

Presently, there is no cure for Joubert syndrome. It is recommended that individuals with Joubert syndrome see the appropriate specialists necessary to help monitor their various clinical features. Suggested specialists include a nephrologist (kidney doctor), ophthalmologist (eye doctor), geneticist, and neurologist, as well as any others recommended by your doctor.

Screening for some of the complications associated with Joubert syndrome-related disorders, such as liver, retinal, or kidney involvement that may become progressive over time, is recommended on an annual basis. Please refer to the Joubert Syndrome Foundation & Related Cerebellar Disorders website's "Evaluation Recommendations" link for a complete listing of recommended annual tests.

Inheritance and recurrence:

Joubert syndrome is passed down from parents to offspring as an autosomal recessive trait, which means that both parents have one altered copy of the gene(s) responsible for this disorder in their DNA. (In order for a child to be born with JS, both the egg and the sperm must contain the same altered gene in question). The odds of having a child born with Joubert syndrome to parents who carry the altered gene involved are 1 in 4, or 25%, in each pregnancy that they share.

Genetic cause:

Presently, three genes for this disorder have been identified, *NPHP1*, *AHI1*, and *CEP290*. These genes are associated with the complications of retinal dystrophy and/or nephronophthisis in the majority of individuals with causative mutations. However, these genes are not the cause in many individuals with Joubert syndrome, and the genetics of these disorders remain complex. It is likely that alterations in other genes cause this condition.

Research is currently underway to assist medical professionals in developing a greater understanding about this disorder. For more information about genetic research, please contact the Joubert Syndrome Foundation & Related Cerebellar Disorders.

Additional resources for families:

- Joubert Syndrome & Related Disorders Foundation: www.jsrdf.org
- The ARC, an advocacy organization for individuals with disabilities: thearc.org
- United Cerebral Palsy: www.ucp.org/ucp_generaldoc.cfm/1/3/43/43-43/5807 offers One-Step Resource Guides which list resources for people with disabilities. Guides are available for every U.S. state/territory
- American Liver Foundation: www.liverfoundation.org/

Resources used in the creation of this document:

- Gleeson, J.G. et al. (2003). Molar Tooth Sign of the Midbrain-Hindbrain Junction: Occurrence in Multiple Distinct Syndromes. *American Journal of Medical Genetics*, 125A, 125-134.
- Joubert Syndrome & Related Disorders Foundation website: www.jsrdf.org
- Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database: http://www.nlm.nih.gov/cgi/jablonski/syndrome_cgi?index=96
- ORPHA.NET database on rare diseases and orphan drugs: www.orphanet.net
- Parisi, M.A. and Glass, I. A. "Joubert Syndrome". GeneReviews, Online publication of expert-authored disease reviews: www.genereviews.org

The information presented is intended to summarize this condition as it is presently understood by medical professionals. The statements included in this document are for information only and should not be considered as medical advice. Please always consult your physician for medical advice.