X-linked Hydrocephalus with Aqueductal Stenosis: \( L1CAM \) Gene Deletion/Duplication

**Condition Description**

Mutation of the \( L1CAM \) gene (Xq28) is characterized by hydrocephalus, mental retardation, spasticity of the legs, and adducted thumbs. The phenotypic spectrum \( L1CAM \) mutations includes X-linked hydrocephalus with stenosis of the aqueduct of Sylvius (HSAS), MASA syndrome (mental retardation, aphasia/delayed speech), spastic paraplegia (shuffling gait, adducted thumbs), SPG1 (X-linked complicated hereditary spastic paraplegia type 1), and X-linked complicated corpus callosum agenesis. The group of conditions as a whole can be referred to as L1 syndrome.

Hydrocephalus in L1 syndrome may be present prenatally and result in stillbirth or death in early infancy. Males with HSAS are born with severe hydrocephalus and adducted thumbs. Seizures may occur. In less severely affected males, hydrocephalus may be subclinically present and documented only because of developmental delay. Mild-to-moderate ventricular enlargement is compatible with long survival. Mental retardation is usually severe and is independent of shunting procedures in individuals with severe hydrocephalus. In MASA syndrome, mental retardation ranges from mild (IQ of 50-70) to moderate (IQ of 30-50). The degree of intellectual impairment does not necessarily correlate with head size or severity of hydrocephalus; males with severe mental retardation and a normal head circumference have been reported. All phenotypes can be observed in affected individuals in the same family. Females may manifest minor features such as adducted thumbs and/or subnormal intelligence. Rarely do females manifest the complete L1 syndrome phenotype.

While mutation detection rates are unknown, point mutations, partial gene deletions, and partial gene duplications have all been reported. Although uncommon, de novo disease-causing mutations have been reported.

[X](https://www.genetests.org) for the GeneTests summary on this condition.

**Genes**

\( L1CAM \)

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of L1 syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of L1 syndrome who have tested negative for sequence analysis

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

*Submit only 1 of the following specimen types*

**Type: DNA, Isolated**

**Specimen Requirements:**

- Microtainer
- Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**

- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

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Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Special Instructions
Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests
- Sequencing analysis of the L1CAM gene is available and is required before deletion/duplication analysis.
- ACGH array-based test for deletion/duplication analysis of 109 different X-linked intellectual disability genes is available.
- Prenatal testing is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.