

Prader-Willi/Angelman: Methylation

Test Code: PW

Turnaround time: 2 weeks

CPT Codes: 81331 x1

Condition Description

Prader-Willi (PWS) syndrome is characterized by severe hypotonia and feeding difficulties in early infancy, followed in later infancy or early childhood by excessive eating and gradual development of obesity (unless externally controlled) [1-2]. Motor milestones and language development are delayed. All individuals have some degree of mental retardation. A distinctive behavioral phenotype (temper tantrums, stubbornness, and obsessive-compulsive characteristics) is common [3]. Hypogonadism is present in both males and females and manifests as genital hypoplasia, incomplete pubertal development, and, in most, infertility. Short stature is common; characteristic facial features, strabismus, and scoliosis may be present.

Confirmation of a PWS diagnosis is obtained by DNA-based methylation testing to detect abnormal parent-specific imprinting within the Prader-Willi critical region (PWCR) on 15q11-13. This testing determines whether the region is maternally inherited only (the paternally contributed region is absent) and detects >99% of affected individuals. Methylation studies would also diagnose ~80% of patients with Angelman syndrome which is allelic (genetically related) to PWS, but clinically distinct, and results from the absence of maternally contributed region.

In all patients with a clinical presentation of PWS, it is important to begin testing with methylation studies first. If abnormal, further testing such as FISH (70% of the causes), uniparental disomy (UPD) studies (30%) and sequencing of the imprinting center (<1%) may be considered.

PWS is caused by absence of the paternally derived PWS/AS region of chromosome 15 by one of several genetic mechanisms. The risk to the sibs of an affected child of having PWS depends upon the genetic mechanism that resulted in the absence of the paternally contributed PWS/AS region. The risk to sibs is less than 1% if the affected child has a deletion or uniparental disomy, up to 50% if the affected child has a mutation of the imprinting control center, and up to 25% if a parental chromosomal translocation is present [4].

References:

1. Holm *et al.* Prader-Willi syndrome: consensus diagnostic criteria. *Pediatrics* 91:398-402 (1993).
2. Gunay-Aygun *et al.* The changing purpose of Prader-Willi syndrome clinical diagnostic criteria and proposed revised criteria. *Pediatrics* 108:E92 (2001).
3. Dykens E and Shah B. (2003). Psychiatric disorders in Prader-Willi syndrome: epidemiology and management. *CNS Drugs* 17:167-78
4. Cassidy and Schwartz. (2006). Prader-Willi syndrome. www.genetests.org

[Click here](#) for the GeneReviews summary on this condition.

Indications

This test is performed for:

- Confirmation of a clinical diagnosis of PWS
- Prenatal diagnosis of PWS in a family with an affected individual who was confirmed to have the PWS deletion.

Methodology

Methylation sensitive PCR.

Detection

Approximately 99% of PWS cases and approximately 70% of AS cases will be detected by this assay.

Reference Range

Normal: Both unmethylated and methylated allele detected. Prader-Willi Syndrome: Only methylated allele detected. Angelman Syndrome: Only unmethylated allele detected.

Specimen Requirements

Submit only 1 of the following specimen types

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

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ 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.

Related Tests

- EmArray Cyto 60K can be used to detect microdeletions/microduplications throughout the genome.
- Congenital Hypotonia Panel is available to test for common causes of isolated congenital hypotonia in neonates.