

# The University of Chicago Genetic Services Laboratories



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## Prader-Willi Syndrome Testing

### Clinical Features:

Prader-Willi syndrome (PWS) [OMIM #176270] is a genetic disorder which causes hypotonia and poor feeding in infancy, followed by the development of hyperphagia and subsequent obesity. Physical characteristics of PWS also include short stature, small hands and feet, and a characteristic facial appearance consisting of a thin upper-lip, down-turned mouth, dental crowding, and almond shaped eyes. Developmental milestones are delayed, and learning disabilities are always present, but may vary in severity. Behavioral problems include temper tantrums, obsessive compulsive tendencies, and skin-picking. Psychosis occurs in 5-10% of patients as young adults (1). Individuals with PWS do not undergo spontaneous pubertal development and are infertile (1, 2).

### Inheritance:

PWS is an imprinting disorder caused by the lack of expression of the paternal copy of 15q11-q13. This can occur by one of several mechanisms including a de novo paternal deletion in this region, maternal uniparental disomy (UPD), an imprinting center defect, or a paternal chromosomal translocation. The recurrence risk depends on the mechanism involved and may be up to 50%. PWS affects approximately 1 in 25,000 births and displays no ethnic or gender preference (2, 3).

### Molecular Genetics:

- Approximately 70% of individuals with PWS have a de novo deletion of 15q11-q13 on the paternally contributed chromosome, corresponding to a less than 1% recurrence risk (2).
- Approximately 25% of PWS is due to maternal UPD15, corresponding to a less than 1% recurrence risk (2).
- 2-5% of patients have an imprinting center (IC) abnormality of which 10-40% are deletions of the IC region. A recurrence risk of up to 50% applies to the IC deletion group and a low recurrence risk of less than 1% applies to the remainder of the IC abnormality group (2).
- Less than 1% of PWS is due to a paternal chromosome 15 translocation, which may result in a recurrence risk of up to 25% (2).

### Additional Resources:

#### Prader-Willi Syndrome Association

5700 Midnight Pass Road, Suite 6  
Sarasota, FL 34242  
Phone: 800-926-4797  
email: [national@pwsausa.org](mailto:national@pwsausa.org)  
[www.pwsausa.org/index.html](http://www.pwsausa.org/index.html)

### Test methods:

We recommend methylation-specific (MS)-MLPA as the initial test for PWS. This testing will identify patients with abnormal methylation, large deletions and imprinting center deletions. Those patients with abnormal methylation, but no deletion, should pursue UPD testing for UPD15.

#### Methylation-specific MLPA (MS-MLPA)

Sample specifications:	3-10 cc of blood in a purple top (EDTA) tube
Cost:	\$525
CPT codes:	81331
Turn-around time:	4 weeks

#### Microsatellite analysis for UPD15 testing

Sample specifications:	3-10 cc blood from patient and BOTH parents in purple top EDTA tubes
Cost:	\$540 (total for a patient's and both parents' blood samples)
CPT codes:	81402
Turnaround time:	2 – 4 weeks

#### Imprinting center deletion analysis

Sample specifications:	3-10 cc of blood in a purple top (EDTA) tube
Cost:	\$450
CPT codes:	81403
Turn-around time:	4 weeks

#### **Results:**

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

#### **References:**

1. Chen C, Visootsak J, Dills S et al. Prader-Willi syndrome: an update and review for the primary pediatrician. Clin Pediatr (Phila) 2007; 46: 580-591.
2. Driscoll D, Miller J, Schwartz S et al. Prader-Willi Syndrome. In: Pagon R, Bird T, Dolan C, eds. GeneReviews [Internet]. Seattle: University of Washington, 1998.
3. Whittington JE, Holland AJ, Webb T et al. Population prevalence and estimated birth incidence and mortality rate for people with Prader-Willi syndrome in one UK Health Region. J Med Genet 2001; 38: 792-798.

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