Prader-Willi SYNDROME ASSOCIATION (USA)
SAVING AND TRANSFORMING LIVES

TESTING AND DIAGNOSIS

Prader-Willi syndrome (PWS) is diagnosed using a series of very specialized genetic tests which are ordered specifically to diagnose this condition. Common chromosome tests, like a karyotype, do NOT reliably detect the genetic changes of PWS. The physical examination and history are very important parts of making the diagnosis and should be done before genetic testing.

Genetic tests for PWS can be expensive and may require sending samples to specialized laboratories; blood samples (sometimes saliva) are often mailed by the blood drawing lab to such specialized labs. Be certain that your insurance company has approved any test prior to having it done.

A positive DNA methylation test result is >99% accurate proof that the individual has PWS

A negative methylation test result means that the individual almost certainly DOES NOT have PWS

DNA Methylation Testing – The BEST INITIAL TEST

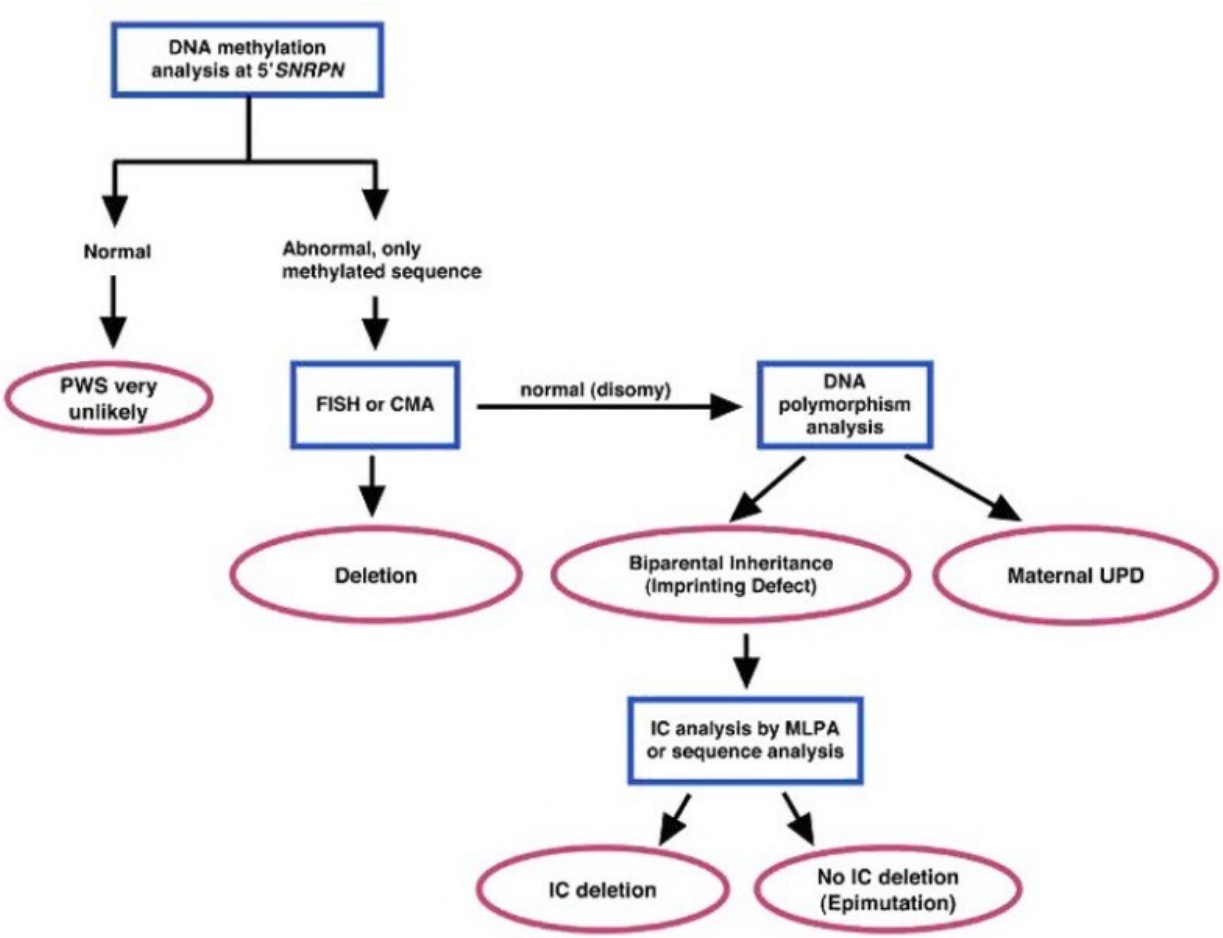
All persons suspected of having PWS should be tested with a **DNA methylation analysis**. This test detects nearly all (>99%) cases of PWS. *(It also detects Angelman syndrome which involves the same region of chromosome 15. This test may be called "Prader-Willi/Angelman DNA methylation Panel").* There are 3 major genetic changes that can cause PWS (sometimes called molecular class or genetic subtypes), and all 3 types will have a positive DNA methylation analysis for PWS.

FISH – Historically, this test was often used after a positive DNA methylation test to determine whether the individual has the deletion subtype of PWS (the most common). It is not the best first test, as it will not detect the two other subtypes of PWS. Even if this test is negative, the individual could still have PWS.

Chromosome Microarray – Chromosome microarray (CMA) testing is a relatively new test, but becoming the test of choice to detect most chromosome deletions, even many small "atypical" sizes, and it will also detect many cases of uniparental disomy 15 (UPD), another genetic subtype of PWS. It does not detect all cases of PWS and specifically those with imprinting defects.

Uniparental disomy (UPD) and imprinting defect testing – This is a specialized DNA test that usually requires blood from the patient and both parents for accurate interpretation.

Comprehensive testing strategy for PWS



Important terms:
FISH = fluorescence in situ hybridization
CMA = chromosomal microarray
UPD = uniparental disomy
IC = imprinting center
MLPA = multiplex ligation probe amplification

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