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. All hypotonic children in the Neonatal Intensive Care Unit (NICU) who do not have a diagnosis should be tested for PWS.

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 ~80% of individuals with 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 types), 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 type of PWS (the most common). It is not the best first test, as it will not detect the two other subtypes of PWS and will not give information on the size of the deletion. Even if this test is negative, the individual could still have PWS.

Chromosome Microarray/Oligo-SNP array (OSA) – Is a relatively new test, but becoming the test of choice to detect most chromosome deletions, even many small "atypical" sizes. It will also detect many cases of uniparental disomy 15 (UPD), another genetic type 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 involving DNA polymorphisms that requires blood from the patient and both parents for accurate interpretation.

More detailed information on genetic testing for PWS can be found at:
https://www.ncbi.nlm.nih.gov/books/NBK1330/

Comprehensive Testing Strategy for PWS

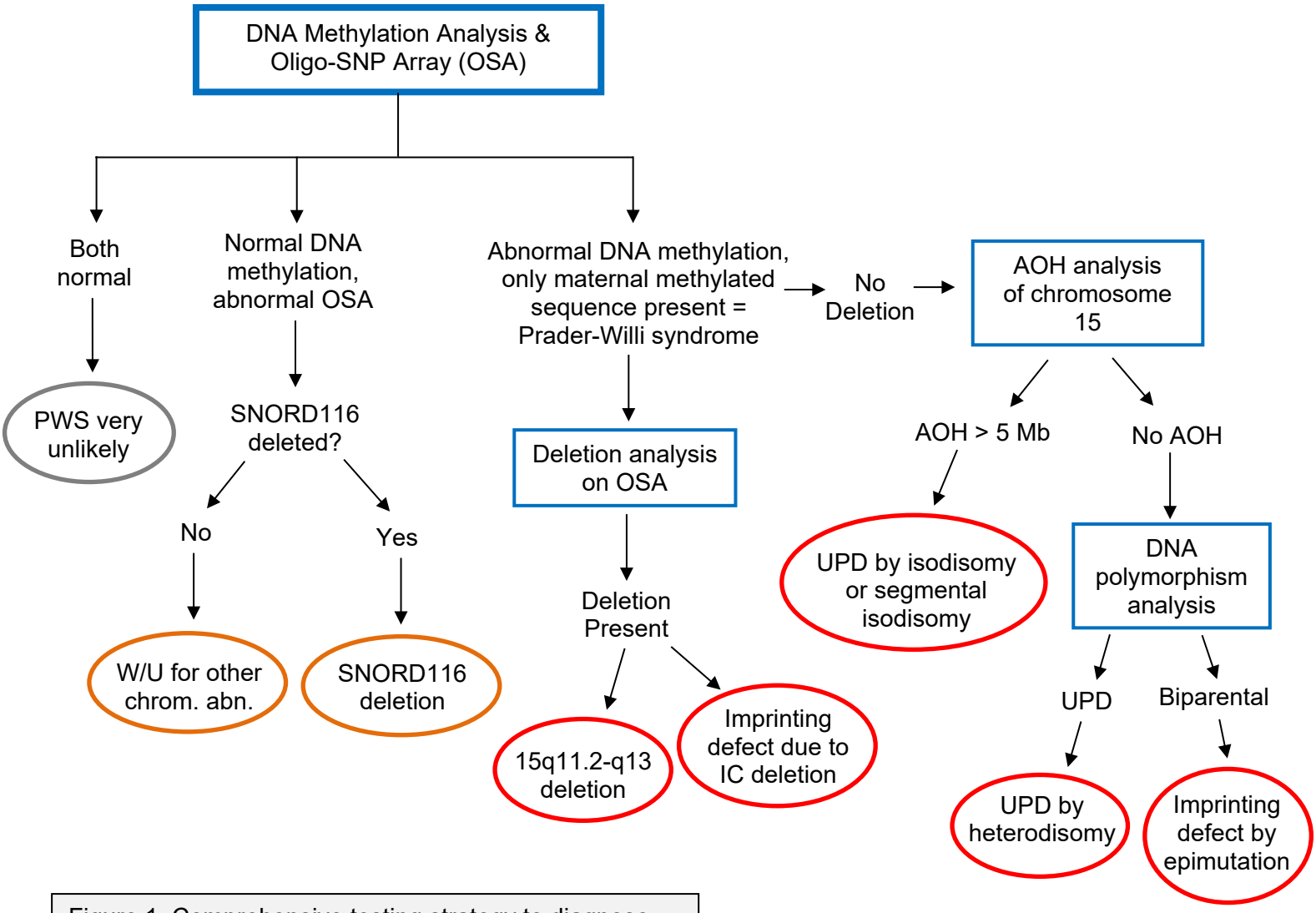

Figure 1. Comprehensive testing strategy to diagnose PWS and to establish the genetic mechanism
AOH: absence of heterozygosity
chrom. abn.: chromosome abnormality
IC: imprinting center
PWS: Prader-Willi syndrome
UPD: uniparental disomy
W/U: workup

Source:
Driscoll DJ, Miller JL, Cassidy SB: Prader-Willi Syndrome, 2023. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1330/