Prader-Willi Syndrome

Condition Description: **Prader-Willi syndrome (PWS)** is caused by abnormal expression of genes on chromosome 15 due to abnormal imprinting.[1] This is most commonly due to a deletion of the paternally-derived chromosome 15q11-q13, but can also be due to uniparental disomy[1] (UPD) or a mutation involving the imprinting center on chromosome 15[2]. Recommended testing strategy is presented as an algorithm at the end of the sheet[3].

Diagnostic Criteria:

1. Severe Hypotonia
2. Feeding problems until age 2 at which time insatiable appetite develops leading to increased obesity risk
3. Short stature with small hands and feet
4. Hypogonadism (small penis, undescended testes)
5. Characteristic behaviors (obsessive, temper tantrums, skin picking)
6. Global developmental delay, mild to moderate cognitive impairment
7. Hypopigmentation compared to family background

Other associated findings: Growth Hormone deficiency, hypogonadotropic hypogonadism, risk for insulin resistance and diabetes, sleep apnea (obstructive and central), high pain threshold

Differential diagnosis[3]: Infantile Hypotonia: Spinal Muscular Atrophy, Congenital Myotonic Dystrophy or other myopathy/neuropathy, other chromosomal abnormality.
Older children (obesity/cognitive impairment): Fragile X, Bardet Biedl syndrome, chromosomal abnormality

Action required: Follow diagnostic algorithm to confirm diagnosis. Consider referral for clinical genetics evaluation (link to clinics) and endocrinology. Follow management recommendations.[2,3]

Specialty Clinic: Prader-Willi syndrome Clinic 801-712-0501
http://www.medicalhomeportal.org/resources/services/provider/13155

Reference/Resources

1. http://www.ghr.nlm.nih.gov/handbook/inheritance/updimprinting.
2. Ramsden et al. Practice guidelines for the molecular analysis of Prader-Willi and Angelman syndromes. BMC Med Genet 11:70, 2010. http://www.biomedcentral.com/content/pdf/1471-2350-11-70.pdf.
3. McCandless et al. Clinical Report—Health Supervision for Children with Prader-Willi Syndrome. Pediatrics 127:194-204, 2011. http://pediatrics.aappublications.org/content/127/1/195.full.pdf+html
4. Genetics Home Reference Prader-Willi Syndrome http://www.ghr.nlm.nih.gov/condition/prader-willi-syndrome.

Patient Resources:
Prader-Willi Association (USA): http://www.pwsausa.org/index.html
Utah Prader-Willi Syndrome Association: http://www.upwsa.org/
PWS Basic Information and Medical Concerns:
http://www.upwsa.org/downloads/prader_willi_syndrome_basic_info_medical_concers.pdf.

Prader-Willi Syndrome Diagnostic Algorithm[3]

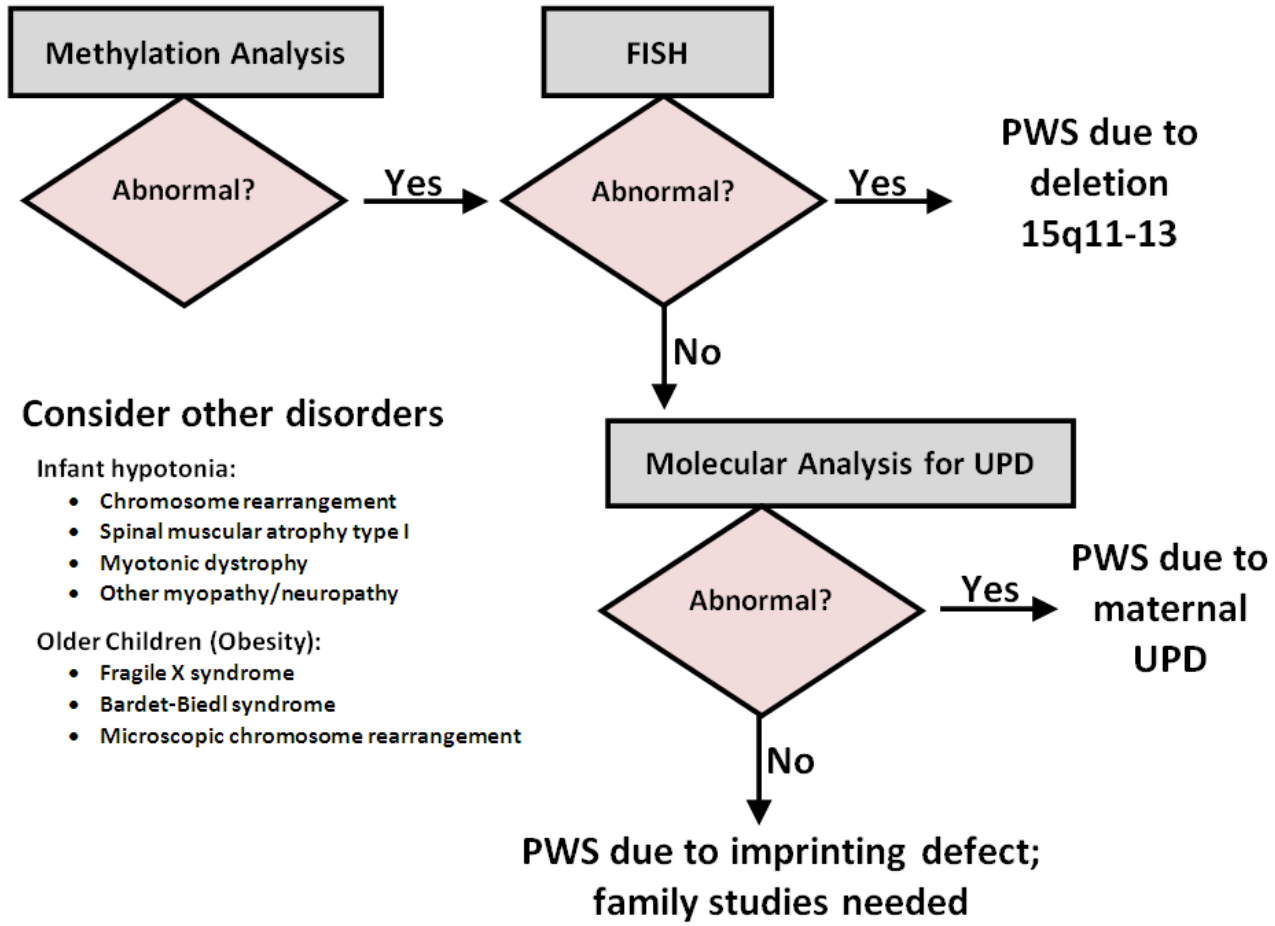

FIGURE 1
Flowchart of recommended molecular testing strategy for PWS.

UPD = Uniparental Disomy

From McCandless et al. Clinical Report—Health Supervision for Children with Prader-Willi Syndrome. Pediatrics 127:194-204, 2011. http://pediatrics.aappublications.org/content/127/1/195.full.pdf+html