PRADER WILLI SYNDROME

A **rare genetic disorder** caused by a **methylation defect** on **chromosome 15**, leading to the loss or silencing of **paternal genes**, typically due to a **deletion**, **imprinting defect**, or **uniparental disomy** *(where the child inherits both copies of chromosome 15 from the mother).* This disrupts the function of the hypothalamus, which regulates hunger, hormones, and mood. It usually results from **a sporadic mutation** and is **not inherited**, though genetic counseling can help identify the cause.

Imprinting is a genetic process where the expression of certain genes depends on whether they are inherited from the mother or father, with some genes being activated or silenced accordingly.

CLINICAL FEATURES

Symptoms in infancy

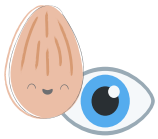
- **Hypotonia**
- **Failure to thrive**
- Lethargy
- Weak cry
- **Difficulty feeding/poor suck**

Symptoms in childhood

- **Behavioural concerns**
  - Compulsive
  - Stubborn
  - Manipulative
- **Obesity**
- **Hyperphagia**

Facial:

- **Almond-shaped eyes**
- Narrow bitemporal diameter
- Up-slanting palpebral fissures
- Thin upper lip
- Small-appearing mouth
  - Down-turned corners of mouth
  - "Triangular mouth"



Hand findings:

- Short fingers
- Partial syndactyly
- Thumb hypoplasia

Neurologic:

- **Global developmental delay**
- **Mild to moderate intellectual disability (ID)**

Genitourinary:

- **Hypoplastic genitals**

Endocrine

- **Short stature**
- **Delayed puberty**
- Osteoporosis
- Hypothyroidism
- Small hands and feet

DIAGNOSIS

- **DNA methylation studies**
- **Chromosomal microarray** to confirm microdeletions/ duplications, or paternal uniparental disomy

OBESITY-RELATED COMPLICATIONS

- Type 2 diabetes
- Heart disease
- High blood pressure

- Obstructive sleep apnea (OSA)
- Gallstones
- Liver disease

MANAGEMENT

- **Nutrition in infancy**: hypercaloric formula to promote weight gain.
- **Therapy**: physical, speech, occupational, and developmental therapies for movement, communication, and life skills.
- **Mental health care**: support for obsessive behaviors, mood disorders, and psychological issues.
- **Sleep treatment**: address sleep apnea to improve behavior and daytime functioning.
- **Weight management**: reduced-calorie diet, increased physical activity, and supervision of meals during childhood.
- **Growth hormone**: improves growth, muscle tone, and reduces body fat.
- **Sex hormone replacement therapy**: for delayed puberty.

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