Prader–Willi Syndrome (PWS)

Genetic Basis: Paternal deletion + maternal imprinting

1. Chromosomal Region Involved

- Chromosome: 15q11–q13
- This region contains imprinted genes where:
  - Paternal copy is normally active
  - Maternal copy is normally imprinted (inactive)

2. Causes of PWS

PWS occurs when functional paternal genes in 15q11–q13 are missing or inactive.

A. Paternal Deletion (≈70% cases)

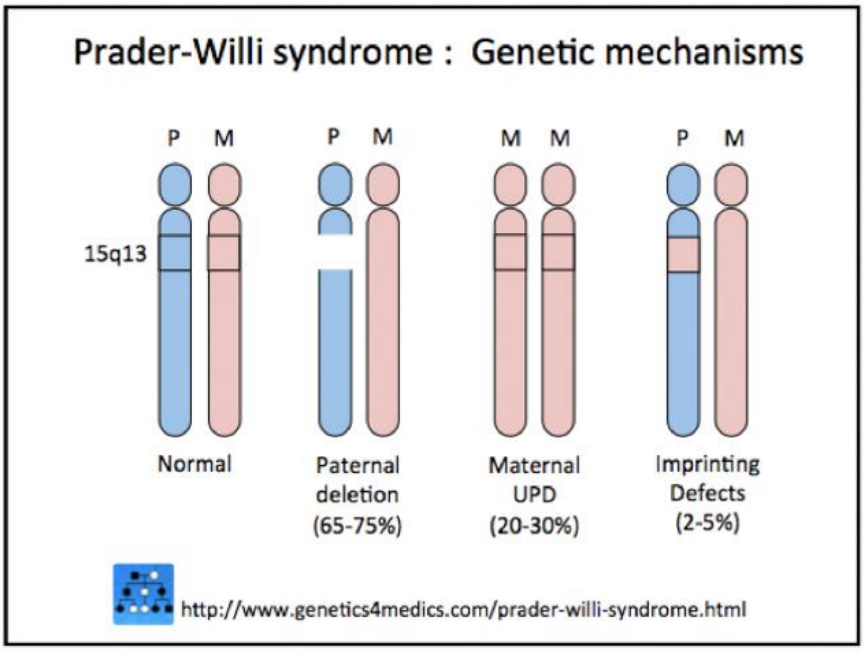
- • Part of the paternal chromosome 15 is deleted.
  • Maternal copy is imprinted → no active gene → PWS.

B. Maternal Uniparental Disomy (UPD) (≈25–30% cases)

- • Child inherits two maternal chromosome 15 copies.
  • Both are imprinted → no active paternal gene.

C. Imprinting Defect (≈1–3% cases)

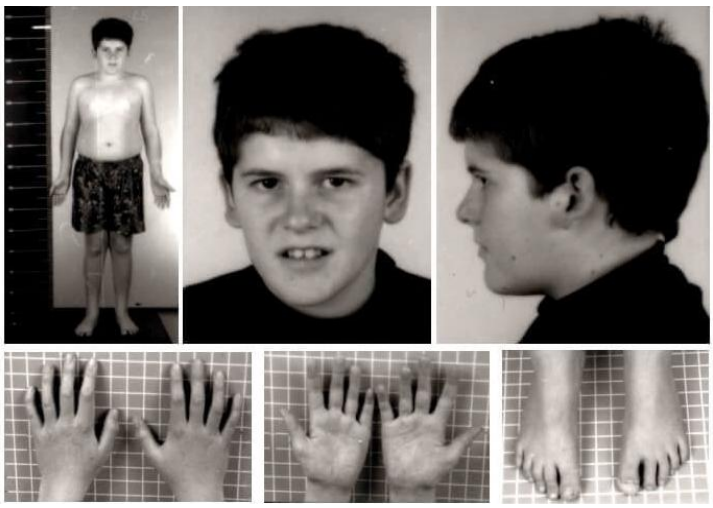
- • Paternal chromosome 15 is present but incorrectly methylated.
  • It behaves like a maternal (silent) chromosome.



3. Pathophysiology

Loss of paternal expression affects:

• Hypothalamus development
• Endocrine regulation
• Appetite control



4. Key Features

Infancy:

- • Hypotonia
  • Poor feeding, failure to thrive

Childhood → Adulthood:

- • Hyperphagia (excessive eating)
  • Obesity
  • Mild–moderate intellectual disability
  • Short stature
  • Hypogonadism
  • Behavioral problems (temper tantrums, skin picking)
  • Small hands and feet
  • Almond-shaped eyes, narrow forehead

5. Diagnostic Testing

• Methylation analysis → gold standard (detects all mechanisms)
• FISH / microarray → detects paternal deletion