

A 4-year-old boy is brought to the physician for evaluation of binge-eating. He complains constantly of hunger and has temper tantrums when his parents refuse to give him additional snacks. Past medical history is significant for hospitalization during the first month of life for nasogastric feeding due to weak suck and hypotonia. The patient is status post orchiopexy for bilateral cryptorchidism at age 1 year. He also receives physical and speech therapies twice a week. His height is <5th percentile and weight is >99th percentile. On examination, he has a narrow forehead, a down-turned mouth, almond-shaped eyes, and small hands and feet. He has low muscle tone and a microphallus. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Disregulation of imprinted gene expression in chromosome 11p15
- ☐ B. Loss of the maternal copy of 15q11-q13
- ☐ C. Loss of the paternal copy of 15q11-q13
- ☐ D. Nondisjunction resulting in an extra X chromosome
- ☐ E. X-linked mutation of the fragile X mental retardation 1 gene
- ☐ F. X-linked mutation of the hypoxanthine-guanine phosphoribosyl transferase gene

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- ☐ A. Disregulation of imprinted gene expression in chromosome 11p15 [4%]
- ☐ B. Loss of the maternal copy of 15q11-q13 [14%]
- ☒ C. Loss of the paternal copy of 15q11-q13 [76%]
- ☐ D. Nondisjunction resulting in an extra X chromosome [1%]
- ☐ E. X-linked mutation of the fragile X mental retardation 1 gene [3%]
- ☐ F. X-linked mutation of the hypoxanthine-guanine phosphoribosyl transferase gene [2%]

Proceed to Next Item

Explanation:

User Id: [REDACTED]

Prader-Willi syndrome	
Clinical features	<ul style="list-style-type: none"> • Hypotonia • Weak suck/feeding problems in infancy • Hyperphagia/obesity • Short stature • Hypogonadism • Intellectual disability • Dysmorphic facies <ul style="list-style-type: none"> • Narrow forehead • Almond-shaped eyes • Downturned mouth
Diagnosis	<ul style="list-style-type: none"> • Deletions on paternal 15q11-q13

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Diagnosis	<ul style="list-style-type: none">• Deletions on paternal 15q11-q13
Complications	<ul style="list-style-type: none">• Sleep apnea (70%)• Type 2 diabetes mellitus (25%)• Gastric distension/rupture• Death by choking (8%)

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This patient has the characteristic features of Prader-Willi syndrome (PWS), a sporadic disorder due to **maternal uniparental disomy**. Normally, people inherit 2 active copies of each gene - 1 from the mother and 1 from the father. Patients with PWS inherit both copies of a section of chromosome 15 from their mother. The **deletion of the paternal copy of chromosome 15q11-q13** results in **poor suck and feeding problems in infancy** followed by a life of compulsive **binge-eating** and obesity-related problems. Other common manifestations are shown in the table.

Genetic testing is required to confirm diagnosis and begins with karyotype and methylation studies, followed by fluorescence in-situ hybridization, and then microsatellite probes. Management revolves around **obesity** and its complications. Patients benefit from a structured eating environment and strict limitation of food intake (eg, locks on refrigerator, close supervision). They should be screened for **sleep apnea** (central and obstructive) as well as **type 2 diabetes mellitus**. Some patients undergo growth hormone therapy to improve linear growth and body composition, including fat-free mass and bone density.

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(Choice A) Beckwith-Wiedemann syndrome is a congenital disorder due to dysregulation of imprinted gene expression in chromosome 11p15. Characteristic physical findings include macroglossia, rapid growth, hemihyperplasia, and umbilical hernia or omphalocele.

(Choice B) Patients with **Angelman syndrome** suffer from paternal uniparental disomy (eg, deletion of the maternal copy of chromosome 15q11-q13). As in PWS, these patients may have short stature and intellectual disability. However, other unique features include frequent **smiling/laughter**, hand-flapping, ataxia, and seizures.

(Choice D) Klinefelter syndrome (XXY) is the most common sex chromosome abnormality causing primary hypogonadism. However, newborns typically have normal male external genitalia and no apparent dysmorphic features. After puberty, small testes and tall stature become apparent.

(Choice E) Fragile X syndrome is the most common X-linked inherited cause of intellectual disability. Affected boys have a prominent forehead and macroorchidism in contrast to PWS.

(Choice F) Lesch-Nyhan syndrome results from a deficiency of the hypoxanthine-guanine phosphoribosyl transferase enzyme, resulting in marked hyperuricemia. It is characterized by self-mutilation, mental retardation, and extrapyramidal symptoms (eg, dystonia, choreoathetosis).

Educational objective:

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Educational objective:

The main features of Prader-Willi syndrome are hypotonia, hyperphagia, and obesity. Patients are at risk for sleep apnea, type 2 diabetes mellitus, and gastric rupture.

References:

1. [Prader-Willi syndrome: an update and review for the primary pediatrician.](#)
2. [Recommendations for the diagnosis and management of Prader-Willi syndrome.](#)
3. [Clinical report—health supervision for children with Prader-Willi syndrome.](#)