Prader-Willi Syndrome

Description/Etiology
Prader-Willi Syndrome (PWS) is a complex, multisystem genetic disorder which occurs in both males and females of all races. It is characterized by infantile central hypotonia, or low muscle tone, along with poor suck which improves with age; feeding difficulties or failure to thrive; hyperphagia, which results in rapid weight gain between the ages of 12 months and 6 years; developmental delay; and mild to moderate intellectual disability. PWS is the most common genetic cause of obesity.

It is believed that hypothalamic-pituitary dysfunction is responsible for most of the physiologic and behavioral abnormalities typically reported with PWS, especially the hyperphagia and disruption in appetite control. Morbid obesity is a major medical problem in individuals with PWS, and it can lead to respiratory compromise, obstructive sleep apnea (OSA), type 2 diabetes mellitus (DM2), atherosclerosis, hypertension (HTN), and death.

The criteria for diagnosis of PWS include failure to thrive and inconsistent feeding patterns during infancy, followed by rapid weight gain in childhood; and characteristic craniofacial features (e.g., almond-shaped eyes, turned-down mouth). Diagnosis is confirmed with genetic testing. No specific treatment exists and there is no cure for PWS. Management of patients with PWS focuses on symptom control and prevention of obesity and concomitant diseases. Because it has lifelong, multisystem implications, patients should be treated with a multidisciplinary approach that includes primary care, endocrinology, behavioral health, nutrition, and other clinicians as appropriate. Medical nutrition therapy is essential for patients with PWS, as reduced energy and fat intake is essential for weight management; other dietary interventions may reduce the risk for concomitant diseases.

Facts and Figures
› The incidence of PWS is believed to be between 1 in 15,000 and 1 in 25,000 live births. The death rate is approximately 3%. PWS occurs as a result of a genetic error, likely at the time of conception, but usually is not hereditary
› Leading causes of death in patients with PWS are due to complications of obesity and include coronary occlusion, stroke, heart failure, shock secondary to gastric dilation, and pneumonia and hypoventilation associated with aspiration. Choking on foods is a reported cause of death in approximately 8% of those with PWS
› Individuals with PWS may have a very high pain and vomiting threshold
› The metabolic rate in patients with PWS is much lower than in typical individuals. Energy requirements are found to be 20–30% less than the general population
› Although there is no cure for PWS, growth hormone (GH) therapy has been shown to increase height and lean body mass, and decrease fat mass. Studies have also demonstrated improvements in flexibility, mobility, quality of sleep, and resting energy expenditure from GH therapy
› Up to 25% of adults with PWS, especially those who are obese, have DM2, with a mean age of onset of 20 years
› Individuals with PWS are at increased risk of osteopenia and osteoporosis
Risk Factors
The occurrence of PWS is sporadic. It affects individuals of all races; females and males are affected in about equal numbers. Older maternal age may be a risk factor.

Signs and Symptoms/Clinical Presentation
› Infants may demonstrate hypotonia and hyporeflexia, which results in poor sucking and swallowing ability
› Toddlers may demonstrate delayed major milestones
› Characteristic facial features include strabismus (e.g., crossed eyes), almond-shaped eyes, thin upper lip with downward slant of the mouth, narrow temples with narrow nasal bridge, and hypopigmentation of the hair and eyes compared to other family members
› Children begin to demonstrate hyperphagia (i.e. abnormally large appetite) and excess water consumption between the ages 1 of 6
› Behavioral disorders are common and include signs of obsessive-compulsive disorder (OCD) (e.g., picking one’s skin), temper tantrums, and stubbornness. Up to 10% of young adults with PWS have features of psychosis
› Food preoccupation, binge eating, and food-seeking behavior are common in PWS. Individuals may eat garbage, spoiled food, or frozen food, or steal to obtain food
› Dental caries may be present due to decreased or thick saliva

Nutritional Assessment
› Patient Medical History
  • Review patient’s medical chart and ask patient/caregiver about any eating problems, signs of disordered eating, and weight history
  • Ask about any concomitant diseases such as DM2, HTN, cardiovascular disease, and gastrointestinal diseases
  • Review any prescribed medications and compliance with them
  • Assess patient’s social history, including family living conditions, and access to food
› Patient Dietary History
  • Conduct a diet analysis by asking the patient to complete a diet history
  – Useful tools for evaluating the patient’s dietary strengths and weaknesses include a food frequency questionnaire and a 3-day diet recall (i.e., patient recall of all foods and beverages consumed in a 3-day period) that includes 1 weekend day
  – Assess diet for overall energy intake and carbohydrate, protein, and fat intake in relationship to established and recommended dietary guidelines
  • Ask about binge-eating behaviors, including type(s) of food consumed, quantity, length of time of the binge, and any purging behaviors
  • Ask about personal habits as appropriate, including alcohol, caffeine, and soda consumption and frequency; smoking; eating at night; and frequenting vending machines or fast food
  • Ask about use of any nutrition supplements and herbs
  • Assess the amount and type of physical activity
› Anthropometric Data
  • Obtain patient’s height and weight
  • If appropriate, obtain patient’s waist circumference
  • Evaluate weight and calculate body mass index (BMI) by dividing body weight (kilograms) by height (meters squared); or 703 multiplied by weight (pounds) and divided by height (inches squared)
    – Underweight < 18.5; normal 18.5-24.9; overweight 25-29.9; obese > 30
  • Patients who are overweight/obese are at increased risk for concomitant diseases, including cardiovascular disease (CVD) and poor glycemic control
› Laboratory and Diagnostic Tests of Particular Interest to the Nutritionist
  • Fasting serum insulin-like growth factor-1 and insulin-like growth factor binding protein -3 levels can be measured to assess for growth hormone deficiency
  • Fasting lipid profile may reveal elevated total and LDL cholesterol and elevated triglycerides
  • Fasting serum glucose or A1C may be elevated with prediabetes or diabetes
  • Blood pressure may be elevated with obesity
  • Genetic testing can confirm a PWS diagnosis
Other Diagnostic Tests/Studies
• MRI can be performed to evaluate for hypopituitarism
• Serial dual energy X-ray absorptiometry (DEXA) scanning can be performed to assess for body composition and osteoporosis

Treatment Goals
› Promote Normal Growth and Development and Reduce Risk of Complications
  • Monitor weight and dietary adequacy in infants and young children who have feeding difficulties. Support new parents as appropriate and educate about tube feedings if indicated, or other feeding techniques, such as providing small, frequent feedings to promote normal infant growth and development
› Maintain Healthy Weight and Reduce Risk of Complications
  • Educate patient or caregivers of children about appropriate energy, fat, carbohydrate, and protein needs to prevent excess weight gain and achieve nutritional goals throughout the life cycle
  • Emphasize to parents that children with PWS will require lifelong care and nutrition monitoring and follow-up
  • Work with patients and/or caregivers to develop healthy meal plans and recommend supplements as indicated to promote adequate nutrient intake and reduce the risk of any co-occurring diseases
  • Educate parents or caregivers about the importance of learning the Heimlich maneuver for choking
  • Work with the patient and/or caregivers to develop a physical activity regimen to prevent obesity or lessen the complications of obesity
  • Review appropriate techniques with patient/caregivers to minimize excessive eating and drinking and bingeing behaviors
› Provide Emotional Support and Educate
  • Assess anxiety level and coping ability of parents and older patients; provide emotional support; educate and encourage discussion of PWS pathophysiology, potential complications, treatment risks and benefits, strategies for preventing complications (e.g., obesity, choking, concomitant diseases), and individualized prognosis
  • Request a referral, if appropriate, to a
    – social worker for identification of local resources for special education programs or support groups
    – behavioral health clinician for counseling on coping strategies

Food for Thought
› Diets of children with PWS should be monitored for nutritional adequacy. Researchers who studied the diet quality of children with PWS ages 2–4 years found that although BMI was within normal limits for each age group, intake of mono- and polyunsaturated fat, iron, calcium, and vitamins D and E were below recommended intakes of the reference population (Lindmark et al., 2010)
› Researchers report that a high-fiber, macronutrient-balanced diet is more beneficial for improving weight and body composition in children with PWS than a simple energy-restricted diet. Results of a study on 63 children aged 2–10 years indicated that an energy-restricted, balanced diet of 30% fat, 45% carbohydrate, and 25% protein with a goal of 20 g fiber each day can slow the rate of weight gain and may prevent obesity associated with PWS (Miller et al., 2013)
› A small study on 49 teenage and adult patients with PWS examined the potential of a multidisciplinary cyclical residential rehabilitation program on dietary management, physical activity, and weight loss in a traditionally noncompliant population. Researchers found that subjects who attended 4-week residential programs four times per year were able to maintain a 1,500 calorie diet and 6.5 hours of daily physical activity, which resulted in a decrease in BMI of 2.1 points in every residential session (Grolla et al., 2011)
› In a study on how families manage food, hunger, and eating practices for children with PWS, researchers found that most families had a negative attitude about restricting food by denying physical access, particularly with the use of locks. Most families preferred to work toward achieving a lock-free environment. Families also reported that keeping the child with PWS occupied by engaging in activities throughout the day was helpful in controlling hunger and food preoccupation (Allen, 2011)

Red Flags
› High threshold for pain and vomiting can complicate bingeing behaviors and lead to delayed gastrointestinal treatment
› Choking is a common cause of death in patients with PWS
› Patients with PWS who demonstrate excess water consumption should be monitored for hyponatremia
What Do I Need to Tell the Patient/Patient’s Family?

- Reinforce the importance of preventing patients from becoming morbidly obese
  - Stress that collaboration between parents and school staff may be necessary to ensure that a calorie-restricted diet is maintained and any choking hazards monitored
  - Encourage ways to help the patient develop physical activity habits to minimize the risk and effects of obesity
  - Encourage regular follow-up with the dietitian and treating clinician for monitoring and early detection of complications

Related Guidelines

Encourage patents and caregivers to contact the Prader-Willi Syndrome Association for information, resources, and local support

Note

- Recent review of the literature has found no updated research evidence relevant to this topic since previous publication on November 25, 2016

References