IPWSO
International
Prader-Willi Syndrome
Organisation

Adults with Prader-Willi syndrome

Medical care: Overview
Medical Care: Evaluation

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ADULT MEDICAL CARE FOR PRADER-WILLI SYNDROME
Guidance for Physicians

Prader-Willi syndrome (PWS) is a complex genetic disorder with several manifestations including short stature, obesity, hyperphagia, intellectual disability, growth hormone deficiency, hypogonadism and behavioral problems. PWS is due to absence of expression of genetic information on chromosome 15 caused by one of three genetic changes (paternal deletion at chromosome 15q11.2-q13; maternal uniparental disomy 15; and imprinting defect on chromosome 15). It is important to confirm a clinical PWS diagnosis with genetic testing. A DNA methylation analysis confirms the diagnosis in >99% of cases. However, if testing was done with less reliable methods, repeat genetic testing with DNA methylation analysis should be considered as some other conditions overlap clinically with PWS. IPWSO can be of assistance.

As a result of improved knowledge about PWS in the past few decades, many adults are healthy and living to old age, particularly when they are on a rigorously supervised, calorie-restricted diet and comorbidities are prevented or actively treated. Periodic medical examinations and blood tests are essential and annual examinations are recommended.

However, IPWSO recognizes that access to health care services and specialists may vary considerably worldwide. This document summarizes the main health care needs in adults with PWS.

Most Common Symptoms and Comorbidities:

- **Hyperphagia** - an uncontrollably strong drive to eat, leads to severe obesity if food is not restricted, controlled and supervised
- **Hypotonia and reduced muscle mass** - often combined with a low level of physical activity resulting in low-calorie needs. This affects metabolism and is a major cause for scoliosis and kyphosis. Body fat is higher than normal, even with normal BMI (Body Mass Index, kg/m^2)
- **Severe obesity** - leading to high risk for type 2 diabetes, hypertension, respiratory and cardiac insufficiency, obstructive sleep apnea, obesity hypoventilation syndrome, hypercholesterolemia, venous thrombosis, and joint abnormalities
- **Pituitary Hormonal Insufficiencies** - such as hypogonadism, growth hormone deficiency and central hypothyroidism
- **Gastrointestinal** - the vomiting reflex is reduced in most individuals with PWS due to dysfunction of the autonomic nervous system. Many have chewing and swallowing difficulties leading to risk for reflux and choking. Chronic constipation is frequent and caused by delayed intestinal passage. Vomiting could be a sign of severe illness

- **Skin picking** - often related to stress and lack of occupation and associated with risk for infections and scars. Skin picking can lead to serious illnesses if post-surgical wounds are not well protected
- **Rectal picking** - often related to constipation and when severe can lead to rectal ulcers, severe bleeding, anemia, fistulas, and infections
- **History of global developmental delay/ intellectual/learning disabilities and behavioral disorders** - ranging from mild to severe, often requiring support to manage daily living
- **Psychosis and/or mood disorders** - can arise unexpectedly and require psychiatric evaluation. Sudden and persistent changes of behavior or loss of appetite may indicate physical or psychiatric illness
- **Stress intolerance** - affects relationships and can lead to skin picking and temper tantrums
- **Respiratory problems** - sleep apnea is common and should be evaluated as it is associated with cardiovascular diseases

Additional Issues:

- **Temperature regulation abnormalities** - sometimes cause hyperthermia, hypothermia, and lack of febrile response even with severe infections
- **High pain threshold** - can cause an increased risk of neglecting symptoms and their severity. Radiology examinations must be considered even if the symptoms observed are not severe
- **Gastroparesis and gastric necrosis** - in rare cases a distended stomach can develop after overeating or with constipation and gastroenteritis. Pain and vomiting can be absent. A gastric tube can be lifesaving as progression to gastric necrosis can occur necessitating acute intervention

Careful Medical History, with emphasis on the following:

Adults with PWS often have difficulties describing their health care needs and a careful medical history taken from the family/caregivers is essential.

- **Medications and dosages** - assessment for medications that are no longer necessary, drug interactions and medication side effects (for example hyponatremia)
- **Weight** - changes in weekly measurements, in particular recent changes
- **Food environment** - access to food at home, at work and in between, extent of supervision, dietary interventions
- **Physical activity/exercise** – routines, hours per week
- **Breathing** - shortness of breath with activity, particularly if new onset
- **Sleep abnormalities** - snoring, signs of apnea, insomnia, daytime drowsiness

- **Gastrointestinal problems** – dysphagia, reflux, constipation and its treatment, rectal picking
- **Bed-wetting** – exclude urinary tract infection, particularly if new onset
- **Sexuality, relationships and education** - menstrual cycles, sexual activity, contraception, potential sexual victimization
- **Skin picking** - can cause infections and include aggressive nail and lip biting
- **Dental problems** - damage from reflux, teeth grinding, periodontitis
- **History of low impact fractures** - consider bone mineral density assessment (DEXA), new onset gait pattern changes warrant radiographs to rule out a fracture
- **Mental/emotional/psychological states**
    - Behavioral problems can be extensive when every-day structure is lacking, plans are changed or in other situations with insecurity. Support and a daily schedule are needed
    - Unusual habits - e.g., perseveration, repetitive behavior, autistic features
    - Psychiatric symptoms – psychosis, depression, mood disorders. Psychiatric evaluation and medication can be needed. Low doses of antipsychotics are usually sufficient and help to mitigate adverse effects
- **Living situation** - e.g., living at home with family, in mixed or PWS-specialized group homes? Assess the patient's social and economic situation and the caregivers' knowledge about PWS
- **Work situation/day program** - educational input and satisfying activity?

Physical Examination (yearly):

- **Height, weight, and body mass index** (BMI, kg/m^2)
- **Blood pressure, pulse, heart and lung auscultation**- hypertension? Heart failure? Arrythmia?
- **Leg edema**- accumulation of fluid or lymph, or secondary to obesity? Accumulation of fluid (dependent edema) is treated with diuretics and compression stockings. Only compression stockings are effective for treatment of lymphedema, and size measurement of stockings is preferably performed by a trained occupational therapist. Weight loss in an obese individual helps reduce leg edema
- **Abdominal examination** - constipation? cholelithiasis? Consider rectal examination and abdominal radiographs when severe abdominal distention
- **Back and joint inspection** - scoliosis, kyphosis, joint abnormalities?
- **Skin** - Ulcers? Infections?
- **Feet and foot position** - severe pes planus? special shoes/shoe inserts needed?
- **Male genitals** - cryptorchidism? Consider referral to urologist. Inguinal-crural fungal infection due to poor hygiene

Blood Tests (yearly):

- Hemoglobin and blood cell count
- Na+, K+, creatinine, liver enzymes
- Fasting blood lipids
- Hemoglobin A1c and fasting blood glucose
- Vitamin D (25-OH), calcium
- Thyroid function testing (TSH, free T_3, free T_4)
- Sex hormone profile (LH, FSH, Estrogen in women and fasting Testosterone in males)
- IGF-1: for those treated with growth hormone, confirming dose and compliance

Other recommendations:

- **Ophthalmology examination** - every 2 to 3 years
- **Dental examination and hygiene** - twice yearly or more often if needed
- **Hearing evaluation** - in those with poor speech and those over 50 years of age
- **Mental state** - If there has been a sudden and persistent change in mental state or behaviour assess for the presence of abnormal mental beliefs or experiences suggestive of the onset of mental illness
- **Echocardiography** - every 2 to 3 years particularly if obese
- Participation in **national disease screening programs**

If possible, the following is also recommended:

- **Endocrinologist** - to assess hypothalamic/pituitary function and risk for diabetes. Growth hormone and sex hormone treatment is recommended in the absence of contraindications
- **Medical geneticist** - to confirm genetic testing and for genetic counseling of parents and family members
- **Dietician (or equal)** - to assure knowledge of PWS requirements
- **Physiotherapy** - to assess joints, muscles and recommendations for motor activities and as adjunct in management of edema
- **DEXA (Dual energy x-ray absorptiometry)** - to assess bone mineral density and body composition
- **Bioelectrical impedance** - for body composition measurements
- **Standing spine radiographs** - for those with scoliosis and/or kyphosis, to monitor for progression Can also reveal severe constipation.
- **Sleep studies** - if sleep apnea is suspected or when daytime sleepiness is present
- **ENT specialist** - if excessive snoring
- **Speech pathology** - for swallow function assessment and management if significant concern for dysphagia

More information can be found on the International Prader-Willi Syndrome Organization (IPWSO) website that includes information about family support organizations in over 100 countries: http://www.ipwso.org

Advice in acute situations: for health professionals and families:
https://ipwso.org/information-for-medical-professionals/important-medical-facts/

A source of detailed information about PWS on the internet is in GeneReviews:
https://www.ncbi.nlm.nih.gov/books/NBK1330/