

Adults with Prader-Willi syndrome

Medical care: Overview

Medical care: Evaluation

**Approved by the Clinical and Scientific Advisory Board of IPWSO
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ADULT MEDICAL CARE FOR PRADER-WILLI SYNDROME

An Overview of Medical Problems for Physicians

Prader-Willi syndrome (PWS) is a complex genetic disorder with many manifestations and potential medical and psychiatric complications. Genetic testing is available to confirm the diagnosis. Because of cognitive dysfunction and behavioral problems, adults with PWS might have difficulty describing how they feel, and their capacity to make judgments about their condition may be impaired. Therefore, a careful medical history taken from the family/caregivers and relevant examinations are important.

As a result of improved knowledge about PWS in the past few decades, many affected adults are living to old age, particularly when rigorously supervised, energy-restricted diet and prevention and/or treatment of comorbidities occurs.

The following potential complications make it valuable for adults with PWS to have an annual general physician evaluation. IPWSO recognizes that access to health services and to specialists may vary considerably due to factors that include poor transport, limited financial resources, or great distances. This document summarizes the main health needs that are recommended in the context of available resources.

Most Common and/or Serious Medical Findings:

- Small muscle mass and hypotonia - often associated with little physical activity and therefore low calorie needs. Even if weight is normal for height, the fat mass is high.
- Uncontrollably strong biologically determined drive to eat - leads to massively increased fat mass if food is not controlled externally through constant lifelong supervision and support concerning access to food.
- Severe obesity - complications of which include type II diabetes, hypertension, respiratory and cardiac insufficiency, sleep apnea, hypercholesterolemia, skin changes and ulcers, and joint abnormalities.
- Hormonal insufficiencies such as hypothyroidism, growth hormone deficiency and often hypogonadism with attendant complications (e.g., osteoporosis).
- Gastrointestinal problems - chronic constipation, reflux, choking, and the risk of catastrophic cascade of gastric distention, necrosis and deadly rupture.
- Many are unable to vomit, and pain threshold is high.

- Spinal deformities - scoliosis, kyphosis or kyphoscoliosis, present in up to 80%.
- Intellectual disability and behavioral disorders - can be mild but are often severe, requiring constant personal assistance and support (as for food control).
- Psychosis and/or mood disorders - can arise unexpectedly, requiring psychiatric evaluation and medication. Sudden changes of behavior or loss of appetite may indicate physical or psychiatric illness.
- Respiratory problems - responsible for a high proportion of deaths in PWS.

Additional Issues:

- Temperature regulation abnormalities - sometimes causes hyperthermia, hypothermia, and lack of febrile response even with severe infections.
- Communication difficulties - causes inability to express feeling ill and/or in pain.
- High pain threshold - increases the risk of underappreciating the presenting symptoms and overlooking several diseases and fractures. X-ray and abdominal scans must be considered even if symptoms observed are not severe.
- Gastroparesis and gastric necrosis - a distended stomach can be seen both after overeating and with other conditions, including constipation. Gastric necrosis can occur with a distended stomach, and symptoms can be few. Vomiting and loss of appetite can be signs of life threatening intra-abdominal disease. Medical evaluation and treatment can be lifesaving.

Concerning Medication:

Many patients with PWS are treated with several daily medications, the necessity for each of which should be periodically re-evaluated. Due to their small lean body mass and, often, increased sensitivity to drugs, a low starting dose is suggested, especially for psychotropic drugs and antihistamines. Respiratory complications can result from the use of standard doses of benzodiazepines.

Psychiatry:

It is valuable to have people with PWS who are on medication for psychiatric or behavioral problems, even those who are well controlled, be seen by a psychiatrist periodically.

General remarks:

This document is designed to address the medical problems encountered in adults with PWS in an effort to reduce serious medical problems and improve quality of life. A separate IPWSO document addresses evaluations during regular medical visits.

PWS is due to absence of genetic information on chromosome 15 due to one of three genetic changes (deletion at chromosome 15q11.2-q13; uniparental disomy 15; an imprinting defect on chromosome 15). It is very strongly recommended that the diagnosis be confirmed through genetic testing. A DNA methylation analysis confirms the diagnosis in >99% of cases.

IPWSO can be of assistance in identifying sources of testing. Some other conditions can overlap in signs and symptoms with PWS.

Much of the medical care needed in PWS is not expensive or difficult to obtain in most countries and is not different from the medical care of other patients with similar findings.

Please also see medical and other information, most of which is written for a lay audience, on the International Prader-Willi Syndrome Organisation (IPWSO) website that includes information about family support organizations in over 100 countries: <http://www.ipwso.org>

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

ADULT MEDICAL CARE FOR PRADER-WILLI SYNDROME

Evaluation Guidance for Physicians

Prader-Willi syndrome (PWS) is a highly variable, complex genetic disorder with many manifestations and potential medical and psychiatric complications that are most effectively treated early in their course. Adults with PWS can be healthy, but are at risk for potential complications, which are detailed in the companion document *An Overview of Medical Problems for Physicians*. It is therefore valuable for them to have a general physician evaluation and blood tests at least annually. The below listed examinations are recommended during the medical visits. IPWSO recognizes that access to health services and to specialists may vary considerably. This document summarizes the main health needs that are recommended in the context of available resources.

Clinical diagnosis of PWS should be confirmed by genetic testing. A single genetic test, DNA methylation analysis, can conclusively make the diagnosis in >99% of cases.

Careful medical history, with emphasis on the following:

- Medications and doses - assess for medications no longer necessary and drug interactions.
- Weight - assess for recent changes and comparison to the last examination.
- Food environment - access to food at home, at work and in between. Extent of supervision. Dietary interventions.
- Physical activity/exercise - routine hours per week.
- Respiratory difficulties - shortness of breath with activity.
- Sleep abnormalities - snoring, signs of apnea, insomnia, daytime drowsiness.
- Gastroenterological problems - reflux, toilet habits, constipation and its treatment, rectal picking (common and potentially resulting in fistulas or infection in PWS).
- Bed-wetting - and possible sign of urinary tract infection.
- Sexuality, relationships and education - menstrual cycles, contraception in both sexes.
- Skin picking - can cause infections.
- Mental/emotional/psychological states.
 - Behavioral problems - e.g., severe temper tantrums.
 - Unusual habits - e.g., perseveration, repetitive behavior, autistic features.
 - Psychiatric symptoms – psychosis, mood disorder, severe behavior changes.

- Living situation - e.g., living at home, with other intellectually delayed individuals, or in a special center? Assess the patient's social and financial situation and the knowledge of the caregivers about PWS.
- Work situation/day program - Is there educational input and satisfying activity?

General relevant body examination, including:

- Height, weight, and body mass index (BMI, kg/m²).
- Vital signs - evaluate for hypertension or possible medication induced arrhythmias.
- Dental - inspection of teeth for signs of reflux, teeth grinding, severe decay.
- Heart auscultation - evaluate for cardiac insufficiency, cor pulmonale.
- Lung auscultation - irregular ventilation/atelectasis?
- Abdominal exam - evidence of constipation?
- Back and joint inspection - scoliosis, kyphosis, joint abnormalities?
- Leg edema? Ulcers?
- Feet and foot position - special shoes needed?
- Skin examination - signs of skin picking, sores, infections?
- Genitals in men for cryptorchidism (if present, refer for surgical evaluation)

Blood tests (yearly or every two years):

Recommend as fasting blood test at 8am, for lipids, glucose and diurnally active Testosterone

- TSH, free T3, free T4 (i.e., thyroid function tests).
- Hemoglobin A1c or fasting blood glucose.
- Vitamin D (25-DH), calcium, phosphorous.
- Hemoglobin and blood cell count.
- Na⁺, K⁺, creatinine (hyponatremia may suggest excess fluid intake or side effects of medications).
- Blood lipids, cholesterol, liver enzymes.
- Men: testosterone, LH; Women: estradiol, FSH (if not given sex hormone treatment).
- IGF-1: for those treated with growth hormone, confirming dose and compliance.

OTHER recommended examinations:

- Ophthalmology examination every 2 - 3 years.
- Dental examination and hygiene twice a year or more often if needed.
- Hearing evaluation in those with poor speech and those over 50 years.

If possible, the following is also recommended:

- Evaluation by an endocrinologist to assess pituitary/hypothalamic function and risk for diabetes.
- Evaluation by a medical geneticist to ensure the correct genetic testing has been accomplished and for genetic counseling for future recurrence risks for the family.
- Dietician (or equal) every 6 months, assuring knowledge of PWS requirements.
- Physiotherapy assessment of joints, muscles and recommendations for motor activities.
- DEXA (for bone mineral density and body composition) every 3 years.
- Sleep studies to evaluate central or obstructive sleep apnea or narcolepsy, if indicated.

Please Note:

Some other conditions can overlap in signs and symptoms with PWS. It is optimal to assure that the diagnosis is correct through genetic testing. IPWSO can be of assistance in identifying sources of testing.

A source of detailed information about PWS diagnosis, symptoms, evaluation, and management is GeneReviews: <https://www.ncbi.nlm.nih.gov/books/NBK1330/>