Prader-Willi Syndrome
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Also Known As
Prader-Labhart-Willi Syndrome and Polysardia.

Definition
Prader-Willi Syndrome is a rare genetic disorder characterised by symptoms that result in a debilitating physical and developmental disability in adolescence and adulthood. First described by Prader, Willi and Labhart in 1956 (Gilbert, 1997).

Prevalence and Incidence
1 in 10 000 live born infants.
1 in 15 000 people up to the age of 25 years.
Affects both males and females equally.

Cause
Approximately 50% of sufferers have a small deletion on the long arm of the chromosome 15 inherited from the father. See Angelman Syndrome.

Classification/Diagnosis
Diagnosis of Prader-Willi Syndrome is based on symptoms that change with age. There are no consistent biological markers available to diagnose the disorder and personal experience of clinicians are relied upon. Many symptoms are not present until older childhood or adolescence and vary in severity between individuals. As a result, criteria have been categorised into three groups: main criteria (apply to all age groups), minor criteria (apply mainly to older children and adolescents), and supporting criteria (may or may not be used for diagnosis).

Main Diagnostic Criteria
• Neonatal and infantile hypotonia (poor muscle tone) improving from 6 months of age.
• Feeding problems in infancy due to poor sucking technique.
• Poor weight gain and failure to thrive in first 6 - 12 months post-birth.
• Excessive or rapid weight gain between 12 months and 6 years of age.
• Narrow bifrontal diameter (measurement between temples across forehead).
• Almond-shaped eyes.
Minor diagnostic criteria

- Limited fetal movement, infantile lethargy.
- Weak, high-pitched cry in infancy.
- Behavioural problems (from the age of 3 years) including an assortment of:
  - temper tantrums
  - violent outbursts alternating with calm periods
  - obsessive-compulsive behaviour (particularly relating to food and eating)
  - argumentative, oppositional, rigid, manipulative, possessive, stubborn
  - verbal repetition and perseverance
  - tendency for lying and stealing (particularly food).
- Sleep disturbances including excessive daytime sleeping (lethargy).
- Short adult stature compared with other family members (mean adult height males = 155 cm, females = 147 cm).
- Hypopigmentation compared with other family members.
- Small hands and feet for height.
- Eye abnormalities (including myopia, esotropia).
- Thick viscous saliva with crusting at corners of mouth.
- Speech articulation problems (hypernasal voice).
- "Skin picking" of lesions resulting in skin ulcers.

Supporting criteria

- High pain threshold.
- Body temperature variation (infancy).
- Limited temperature sensitivity (older children, adults).
- Non-ketotic Diabetes Mellitus.
Prader-Willi Syndrome

- Scoliosis (lateral curvature of the spine) and kyphosis.
- Osteoporosis.
- Strong visual perceptual-motor skills demonstrated by above average skill with jigsaw puzzles (Holm et al., 1993).
- Normal neuromuscular development in childhood with failure of growth in adolescence.

(Simonoff, 1996)

Treatment/Intervention
- Weight loss in obese individuals is recommended to reduce the risk of obesity-related diseases.
- Growth hormone replacement may be administered to aid sexual development in males.
- Prevention of obesity has been suggested to minimise the characteristic reduction in IQ with age (currently researched).
- For individuals with non-ketotic Diabetes Mellitus, insulin therapy may be required.

(Simonoff, 1996)

Educational Implications
- IQ is not necessarily an indicator of the academic ability of the individual as Prader-Willi children with a normal IQ have been found to exhibit behaviours that are seemingly indicative of an intellectual disability. The teacher will therefore need to assess academic ability with subjective measures in addition to IQ score.
- Teachers should be aware of the child’s particular behavioural problems and be given instructions on how to deal with them.
- Teachers of Prader-Willi students with mild to moderate intellectual disabilities should consider the appropriateness of integrating these children into mainstream classrooms on an individual basis.
- Teachers should be prepared to negotiate with parents or carers of these students in relation to behaviour management.
- Teachers should be aware of the observable decline in IQ over time.

(Gilbert, 1997).
Association
Contact: Western Institute of Self Help (WISH)
Telephone: (08) 9228 4488
Hours: 9am to 4pm Monday to Thursday

Websites
http://www.kumc.edu/gec/support

http://www.pwsyndrome.com

References

Department of Human Services, Disability Branch of the Department of Human Services, 555 Collins St, Melbourne. 3001. *Guidelines for the Management of Prader-Willi Syndrome."


What is Prader-Willi Syndrome?

- A disorder of chromosome 15
- Prevalence: 1:12,000-15,000 (both sexes, all races)
- Major characteristics: hypotonia, hypogonadism, hyperphagia, cognitive impairment, difficult behaviors
- Major medical concern: morbid obesity

Cause and Diagnosis of PWS

The genetic cause is loss of yet unidentified genes normally contributed by the father. Occurs from three main genetic errors: Approximately 70% of cases have a non-inherited deletion in the paternally contributed chromosome 15; approximately 25% have maternal uniparental disomy (UPD)—two maternal 15s and no paternal chromosome 15; and 2–5% have an error in the "imprinting" process that renders the paternal contribution nonfunctional.

Diagnostic testing: Individuals who have a number of the clinical findings should be referred for genetic testing. DNA methylation analysis confirms diagnosis of PWS. FISH and DNA techniques can identify the specific genetic cause and associated recurrence risk. (See ASHG/ACMG Report, *Am J Hum Genet* 58:1085, 1996.) Patients who had negative or inconclusive tests with older techniques should be retested.

Recurrence risk: Significant only for rare cases with imprinting mutations, translocations, or inversions. All families should receive genetic counseling.

Major Clinical Findings

The following common characteristics of individuals with PWS raise suspicion of the diagnosis. Published diagnostic criteria include supportive findings and a scoring system (Holm et al, *Pediatrics* 91, 2, 1993).

- Neonatal and infantile central hypotonia, improving with age
- Feeding problems and poor weight gain in infancy
- Excessive or rapid weight gain between 1 and 6 years of age; central obesity in the absence of intervention
- Distinctive facial features—dolichocephaly in infants, narrow face/bifrontal diameter, almond-shaped eyes, small-appearing mouth with thin upper lip and down-turned corners of mouth
- Hypogonadism—genital hypoplasia, including undescended testes and small penis in males; delayed or incomplete gonadal maturation and delayed pubertal signs after age 16, including scant or no menses in women
- Global developmental delay before age 6; mild to moderate mental retardation or learning problems in older children
- Hyperphagia/food foraging/obsession with food

http://www.pwsausa.org/basicfac.htm 12-Nov-01
Minor Clinical Findings:

- Decreased fetal movement, infantile lethargy, weak cry
- Characteristic behavior problems—temper tantrums, violent outbursts, obsessive/compulsive behavior; tendency to be argumentative, oppositional, rigid, manipulative, possessive, and stubborn; perseverating, stealing, lying
- Sleep disturbance or sleep apnea
- Short stature for genetic background by age 15
- Hypopigmentation—fair skin and hair compared with family
- Small hands and/or feet for height age
- Narrow hands with straight ulnar border
- Eye abnormalities (esotropia, myopia)
- Thick, viscous saliva with crusting at corners of the mouth
- Speech articulation defects
- Skin picking

Weight and Behavior

Appetite Disorder

Hypothalamic dysfunction is thought to be the cause of the disordered appetite/satiety function characteristic of PWS. Compulsive eating and obsession with food usually begin before age 6. The urge to eat is physiological and overwhelming; it is difficult to control and requires constant vigilance.

Weight Management Challenge

Compounding the pressure of excessive appetite is a decreased calorie utilization in those with PWS (typically 1,000-1,200 kcal per day for adults), due to low muscle mass and inactivity. A balanced, low-calorie diet with vitamin and calcium supplementation is recommended. Regular weigh-ins and periodic diet review are needed. The best meal and snack plan is one the family or caregiver is able to apply routinely and consistently. Weight control depends on external food restriction and may require locking the kitchen and food storage areas. Daily exercise (at least 30 minutes) also is essential for weight control and health.

To date, no medication or surgical intervention has been found that would eliminate the need for strict dieting and supervision around food. GH treatment, because it increases muscle mass and function, may allow a higher daily calorie level.

Behavior Issues

Infants and young children with PWS are typically happy and loving, and exhibit few behavior problems. Most older children and adults with PWS, however, do have difficulties with behavior regulation, manifested as difficulties with transitions and unanticipated changes. Onset of behavioral symptoms usually coincides with onset of hyperphagia (although not all problem behaviors are food-related), and difficulties peak in adolescence or early adulthood. Daily routines and structure, firm rules and
limits, "time out," and positive rewards work best for behavior management. Psychotropic medications—particularly serotonin reuptake inhibitors, such as fluoxetine and sertroline—are beneficial in treating obsessive-compulsive (OCD) symptoms, perseveration, and mood swings. Depression in adults is not uncommon. Psychotic episodes occur rarely.

Developmental Concerns

Motor Skills

Motor milestones are typically delayed one to two years; although hypotonia improves, deficits in strength, coordination, balance, and motor planning may continue. Physical and occupational therapies help promote skill development and proper function. Foot orthoses may be needed. Growth hormone treatment, by increasing muscle mass, may improve motor skills. Exercise and sports activities should be encouraged and adaptations made, as needed. Proficiency with jigsaw puzzles is frequently reported, reflecting strong visual-perceptual skills.

Oral Motor and Speech

Hypotonia may create feeding problems, poor oral-motor skills, and delayed speech. The need for speech therapy should be assessed in infancy. Sign language and picture communication boards can be used to reduce frustration and aid communication. Products to increase saliva may help articulation problems. Social skills training can improve pragmatic language use. Even with delays, verbal ability often becomes an area of strength for children with PWS. In rare cases, speech is severely affected.

Cognition

IQs range from 40 to 105, with an average of 70. Those with normal IQs typically have learning disabilities. Problem areas may include attention, short-term auditory memory, and abstract thinking. Common strengths include long-term memory, reading ability, and receptive language. Early infant stimulation should be encouraged and the need for special education services and supports assessed in preschool and beyond.

Growth

Failure to thrive in infancy may necessitate tube feeding. Infants should be closely monitored for adequate calorie intake and appropriate weight gain. Growth hormone is typically deficient, causing short stature, lack of pubertal growth spurt, and a high body fat ratio, even in those with normal weight. The need for GH therapy should be assessed in both children and adults.

Sexual Development

Sex hormone levels (testosterone and estrogen) are typically low. Cryptorchidism in male infants may require surgery. Both sexes have good response to treatment for hormone deficiencies, although side effects have been reported. Early pubic hair is common, but puberty is usually late in onset and incomplete. Fertility has not been documented in either sex.
Other Common Concerns

- Strabismus—esotropia is common; requires early intervention, possibly surgery
- Scoliosis—can occur unusually early; may be difficult to detect without X-ray; curve may progress with GH treatment. Kyphosis is also common in teens and adults
- Osteoporosis—can occur much earlier than usual and may cause fractures; ensure adequate calcium, vitamin D, and weight-bearing exercise; bone density test recommended
- Diabetes mellitus, type II—secondary to obesity; responds well to weight loss; screen obese patients regularly
- Other obesity-related problems—include hypoventilation, hypertension, right-sided heart failure, stasis ulcers, cellulitis, and skin problems in fat folds
- Sleep disturbances—hypoventilation and desaturation during sleep are common, as is daytime sleepiness; sleep apnea may develop with or without obesity; sleep studies may be needed
- Nighttime enuresis—common at all ages; desmopressin acetate should be used in lower than normal doses
- Skin picking—a common, sometimes severe habit; usually in response to an existing lesion or itch on face, arms, legs, or rectum. Best managed by ignoring behavior, treating and bandaging sores, and providing substitute activities for the hands.
- Dental problems—may include soft tooth enamel, thick sticky saliva, poor oral hygiene, teeth grinding, and infrequently rumination. Special toothbrushes can improve hygiene. Products to increase saliva flow are helpful.

Quality of Life Issues

General health is usually good in individuals with PWS. If weight is controlled, life expectancy may be normal, and the individual’s health and functioning can be maximized.

The constant need for food restriction and behavior management may be stressful for family members. PWSA (USA) can provide information and support. Family counseling may also be needed.

Adolescents and adults with PWS can function well in group and supported living programs, if the necessary diet control and structured environment are provided. Employment in sheltered workshops and other highly structured and supervised settings is successful for many. Residential and vocational providers must be fully informed regarding management of PWS.

Resources for Health Care Providers

"Health Care Guidelines for Individuals with PWS" and the book *Management of Prader-Willi Syndrome* are available from PWSA (USA), as are other publications for professionals and parents.

For a more comprehensive medical description of PWS, see the University of Washington School of Medicine, Seattle, GeneClinics: Medical Genetics Knowledge