# PWS Information for Psychiatrists

Janice Forster, M.D., and Linda Gourash, M.D., The Pittsburgh Partnership (2018).

Prader-Willi syndrome (PWS) is a rare chromosomal disorder unique among developmental disabilities. Core features include hypotonia, hyperphagia (food seeking and lack of satiety), hypothalamic abnormalities, obesity, cognitive impairment and behavior problems. Detailed medical information is available at www.pwsausa.org. Cognitive and behavioral characteristics include a spectrum of learning disabilities and/or intellectual deficiency, inflexibility and perseveration, repetitive speech and behaviors, tantrums and oppositionality, collecting and hoarding, and skin-picking.

These features impede optimal daily living and pose significant management challenges. Stress sensitivity is life-long for the person with PWS, and families or caregivers experience the most stress compared to any other intellectual developmental disability. Families often seek psychiatric treatment for anxiety, tantrums, repetitive behaviors, skin picking, mood lability, and psychosis. People with PWS display impaired judgment regardless of age, IQ or verbal abilities. They have limited insight into the impact of their behavior on others, are prone to confabulation, and are unreliable historians. Parents and caregivers should provide the history without the patient present (a companion to act as a "sitter" will keep the patient occupied during this interview). This helps to establish the physician-parent partnership early in the process. Patients with PWS will require extra time for the initial evaluation as they will also need to be heard and affirmed. Over the counter (OTC) supplements are popular in this population and should be included in the history.

A controlled and structured environment is the foundation of good mental health for this syndrome and decreases anxiety for these individuals. A typical day should include a scheduled meal plan, supervised/restricted/locked food access, planned daily activities, mandatory exercise, opportunities for sensory experiences, low expressed emotion by caregivers, and clear behavioral expectations with reinforcement. Emphasis on incentives and natural consequences are recommended; punishment is not effective, and food reinforcers are never advised. Not everyone with PWS has a relentless drive for food, but food security is essential for all and is a powerful tool in decreasing anxiety. Counterintuitively, knowing that food is not freely available relieves stress for individuals with PWS.

**Case Formulation**

Predisposing Factors: PWS is a genomic imprinting disorder caused by the absence of expression of paternally derived genetic material on chromosome 15q11-q13. Most cases are due to a deletion of the PWS region, while 25-40% of cases are due to maternuniparental disomy (mUPD). 1-2% have a rare imprinting defect. Those with mUPD have a higher risk for mood disorder and psychosis and are more likely to have symptoms of autistic spectrum disorder. Beyond genotype, the major predisposing factors are stress sensitivity, cognitive impairments, problem solving deficits, speech/language disorder, impaired social skills and coping strategies, and family history of psychiatric disorders.

Precipitating Factors: STRESS; environmental changes including increased food access; change of expectations, structure, consistency, supervision, or caregiver attitude; drug interactions or iatrogenic side effects (introduction of sex hormone replacement, polypharmacy, excess doses); sexual abuse or exploitation; undiagnosed medical conditions which may not be experienced as pain in this population. Looking to the environment for clues (e.g., loss, grief) is often helpful but not predictive.

Perpetuating Factors: Environmental mismanagement (inconsistent food access, unrealistic expectations, inappropriate caretaker behavior), chronic interpersonal problems, secondary gain from repeated hospitalizations or trips to the emergency room, involvement of law enforcement, inadvertent reinforcement with food. Intrinsic factors include chronic communication problems due to speech and language disorders, undiagnosed learning disabilities, and unrecognized drug reactions (mood activation).

Protective Factors: Environmental stability; food security; deletion subtype; a favorable cognitive profile; easy going temperament; flexible and resourceful caretakers; well-developed leisure interests and hobbies; ongoing involvement with an informed family; opportunities to practice religious beliefs; and a good working relationship between the parent/guardian, school and residential provider.

**PSYCHIATRIC SYMPTOMS AND DIAGNOSIS IN PWS**

Psychosis, catatonia, delirium, narcolepsy, mood and anxiety disorders may present in a typical fashion. Change in mental health may be noted as a decline in level of functioning - changes in self-care or grooming; sleep pattern; level of interest in eating, social behavior, or usual preoccupations. Mood changes and psychotic symptoms may be missed due to unusual premorbid social functioning or reduced ability to articulate thought process or mood state. Perseveration, excessive repetitive behaviors and skin picking are common in PWS and should not be confused with true OCD. ADHD may manifest as the predominantly inattentive type. PWS is associated with disorders of maintenance of both sleep and wakefulness. Central and obstructive sleep apnea occur independent of obesity, so excessive daytime sleepiness may present a more complex differential diagnosis. Become familiar with the core features of the PWS personality (ICD-10-CM: F07.0, Personality change secondary to a medical condition-PWS) and establish the individual's unique behavioral baseline to distinguish between an exacerbation of syndromic behaviors and the emergence of psychiatric symptoms.

**INTERVENTIONS**

Environmental:

Environmental interventions are the cornerstone of management of persons with PWS. If the patient presents with an exacerbation of syndromic behaviors, the most effective treatment is to optimize the environmental management plan. Common examples are: unrealistic expectations for independent function; deterioration in daily structure; decreased consistency or predictability in a group home as occurs when key staff depart and new uninformed staff fill in.

PWS Intervention Pyramid

Behavioral: Behavioral and environmental interventions are generally effective for problematic syndromic behaviors and medications will not be required. The goal of intervention will be to alter the environment and caregiver communication rather than to expect the person with PWS to change. Positive behavioral strategies are helpful; punishment or punitive critical tone is counterproductive. Environmental optimization can be augmented with behavioral management using the individual's interests and hobbies as incentives.

Psychological: Psychological therapy to manage stress by enhancing coping strategies can be effective if techniques are adapted for the unique cognitive attributes of the person with PWS. Interventions can be written down, scripted and cued by the caregiver, as it is unlikely that the person will be able to utilize these interventions independently. A therapeutic relationship with an individual counselor can be extremely helpful to the person but must be augmented by regular contact with the caregiver for factual validation. Treatment goals can include problem solving for misunderstandings; support for losses, life transitions, and changes; ongoing assessment of mood and thinking processes; and gaining the patient's interest and investment in behavior plans. Social stories can be adapted for PWS and are an effective way of presenting new concepts and working toward acceptance of change. Insight therapy to achieve behavioral change has limited benefit.

**PHARMACOTHERAPY**

If a person with PWS presents with the clinical signs of a psychiatric disorder, the use of appropriate classes of psychotropic medication is indicated. Caution is needed in dosing as response characteristics and side effect profile are often atypical.

General Guidelines: START LOW; GO SLOW. Medications are more likely to have side effects at standard doses in persons with PWS due to impaired drug metabolism or neurosensitivity.

Pharmacokinetics effects include abnormal intestinal motility and delayed gastric emptying altering drug absorption; diet may be rich in cruciferous vegetables affecting CYP1A2 metabolism; greater fat mass at all BMIs delaying clearance of lipophilic agents.

Pharmacodynamic effects such as initiation of estrogen replacement concurrent with SSRI treatment causing mood activation; testosterone replacement has been associated with behavioral activation. Nausea or appetite change are rarely reported, and weight gain is less common due to the close supervision of food intake essential to the management of all persons with PWS. Judge the efficacy of one medication before adding other. Use regular acting agents before using extended release preparations.

Expected benefits, possible adverse reactions, or potential drug interactions need to be shared with caregivers so they can monitor medication efficacy. Most individuals with PWS are not competent to give informed consent; they may say they understand benefits and

risks, but their judgment is impaired regardless of age or IQ. The use of medication may carry secondary gain for this population, and individuals with PWS should not be responsible for administering pills or prn agents.

**SPECIFIC MEDICATION PRECAUTIONS**

All classes of psychotropic medications have been used successfully to treat psychiatric symptoms in PWS. Some medications, despite their efficacy, carry a higher risk for adverse effects. Atypical neuroleptics are associated with metabolic and motor side effects that require close monitoring. Risperidone has not been found to cause weight gain in this population when food security is in place. Extrapyramidal effects are more difficult to assess in patients with PWS due to syndromic hypotonia: look for loss of emotional expression or hands down by the side. Symptoms of neuroleptic malignant syndrome may be atypical due to decreased lean muscle mass, syndromic hypotonia, hypothalamic abnormalities causing temperature dysregulation at baseline, and excessive daytime sleepiness.

SSRI medications, atypical neuroleptics, modafinil and stimulants have been associated with mood activation. Patients should be monitored closely for increased anxiety, irritability, emotional reactivity, self-injurious behavior, or increased goal directed behavior including food seeking or skin picking. SSRIs, atypical neuroleptics, carbamazepine, and oxcarbazepine have been associated with hyponatremia, serious enough to cause seizures. Valproic acid has been associated with hyperammonemia in late adolescents and adults. SSRIs have not been helpful with skin picking, food seeking and food preoccupation, but they have been useful in low doses for mood and anxiety-related symptoms.

N-Acetylcysteine (NAC) has been found effective for reducing skin picking in many individuals but may have significant GI side effects. Exacerbation of psychiatric symptoms has also been reported. Topiramate can cause dose dependent, reversible renal tubular acidosis (hypochloremic acidosis). Topiramate is associated with cognitive dulling, irritability and worsening of syndrome associated osteoporosis. At low dose, it has been helpful in reducing skin picking in some individuals.

Families should keep a diary of every pharmacotherapy visit including the medication prescribed, dosage used, targeted symptoms and reasons for discontinuation. Checklists and anecdotal records may track information about mood, sleep, behavior and thought content between appointments. Patients with PWS should be expected to give feedback on how they feel, but specific response to dose changes of medication may be beyond their understanding. Some persons with PWS will believe that more medication or higher doses are better and decreasing doses or stopping medication may be upsetting to them, even when the drug is ineffective or causes side effects. Change of any kind is stressful. Listening carefully to their feedback can help ensure compliance with your recommendations and successful ongoing management.

Hospitalization: Hospital units are not prepared for the needs of the person with PWS. Strict food security must be established immediately. Staff will require specific guidance on how to manage the syndrome. A weight gain of 20 pounds is not uncommon during a brief stay, and gastric dilatation, necrosis and death have resulted from failure to control access to food. PWSA | USA provides resources for managing food and other issues on hospital units www.pwsausa.org.

**Resources:**

Call PWSA | USA to arrange consultation with an expert on the Clinical Advisory Board or to obtain printed materials. Visit the website for extensive information about PWS.

Psychiatric Primer - A comprehensive booklet available on line at www.pittsburghpartnership.com and www.pwsausa.org.

The Mental Health of People with Prader-Willi Syndrome with Specific Focus on Mood Disorders and Psychotic Illness, by Tony Holland and the Clinical and Scientific Advisory Board of IPWSO, January 2017 www. ipwso.org and www.pwsausa.org.

www.theNADD.org - Diagnosing, treating and supporting people with intellectual disabilities and psychiatric or behavioral concerns.

But ler MG , Manzardo AM, Forster JL. Prader-W Syndrome: Clinical Genetics and Diagnostic Aspects with Treatment Approaches. Curr Pediatr Rev. (2016)12(2):136-66.