

## REASONS FOR CONSULTATION AND REFERRAL

Prader-Willi syndrome (PWS) is a rare chromosomal disorder that is unique among all developmental disabilities. The core features of PWS include hypotonia, hyperphagia (characterized by food seeking and lack of satiety), obesity, cognitive impairment and behavior problems. Cognitive and behavioral characteristics include: learning disabilities or mental deficiency, cognitive inflexibility and perseveration, repetitive speech and behaviors, oppositionality and tantrums, collecting and hoarding, and skin-picking. Most parents and caregivers express more concern about the impact of these behavioral features of PWS because they impede optimal daily living and pose significant management challenges. Many families caring for children and adults with PWS will seek psychiatric treatment for problems such as mood lability, tantrums, skin picking and repetitive behaviors. Although the psychiatrist is usually asked to prescribe psychotropic medication, the psychiatrist's role as a consultant to the treatment team is equally important. The multidisciplinary team may include behavioral, educational, residential, and occupational specialists. Most psychiatrists will not have treated more than one or two cases with PWS. More important than previous experience is a willingness to learn about the clinical features and management of PWS. Clinical experience with other developmental disabilities is helpful, but it is important to know that all persons with PWS display impaired judgment regardless of IQ and verbal language skills.

## APPROACH TO EVALUATION

Patients with PWS will require more time for the initial evaluation. Often they have limited insight and social judgment, and while they can share their thoughts and feelings, they can be unreliable historians. *Regardless of the patient's age or IQ*, parents and caregivers must serve as co-informants to validate all aspects of the history (identification of problems, symptom severity and time course, level of impairment, family and medical histories) *in the patient's absence*. Patients must be supervised during this collateral interview. As with other developmental disabilities, it is best to take the lead from the parents as to how to communicate most effectively with the patient for the clinical interview and mental status examination. It is essential to establish a physician-parent (caretaker) partnership early in the process. In PWS, more than any other developmental disability, it is essential for the psychiatrist to evaluate the *environmental structure of living*. The following are the *essential* components for the management of syndromal behaviors: a scheduled meal plan, restricted food access, a plan for daily activities, mandatory exercise, opportunities for sensory experience, low expressed emotion, and clear behavioral expectations with reinforcement (emphasis on incentives and natural consequences).

## CONSIDERATIONS FOR CASE FORMULATION

**Predisposing Factors:** PWS is an imprinting disorder caused by the absence of expression of paternally derived genetic material on chromosome 15q11-q13. The missing genes appear to be responsible for regulating hypothalamic function during development. Psychiatrists need to know the patient's genetic subtype because behavioral characteristics and psychiatric symptoms can vary. Most cases are due to a deletion of the PWS region on the paternal chromosome 15, while 25-40% of cases are due to maternal uniparental disomy (UPD). A subset of those individuals with UPD shows autism spectrum disorder. As persons with UPD approach adulthood, the risk for psychosis and mood disorder increases. Family history of psychiatric illness increases the risk for psychiatric disorder in both subtypes. The major predisposing factors for both behavior problems and psychiatric symptoms are stress sensitivity, cognitive impairments resulting in problem solving deficits, language disorder, impaired social skills and poor coping strategies.

**Precipitating Factors:** Psychiatric symptoms can be precipitated by stress, and looking to the environment for clues (e.g., loss, grief) is often helpful but not predictive. Major precipitating factors for *both psychiatric and behavioral crises* are changes in food access, expectations, structure, consistency, level of support, supervision, and caretaker attitude. Less frequent but important to rule out are drug interactions or side effects (e.g., the recent introduction of gonadal steroid hormone therapy), sexual abuse or exploitation, and undiagnosed sources of pain or medical conditions. PWS persons have diminished pain sensitivity and atypical inflammatory response.

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

Protective Factors: The following protective factors can minimize the risk for psychiatric and behavioral symptoms:

environmental stability (predictability, consistency); food security; deletion subtype; an even 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 and residential provider.

## PSYCHIATRIC SYMPTOMS AND DIAGNOSIS IN PWS

It is essential for the psychiatrist to be familiar with the core features of PWS (310.1 Personality change secondary to a medical condition- PWS) and to establish the individual's unique behavioral baseline in order to distinguish between an exacerbation of syndromal behaviors and the emergence of psychiatric symptoms. Psychiatric symptoms may be typical in presentation and indicate an underlying psychiatric illness such as psychosis, catatonia, delirium, narcolepsy, mood and anxiety disorders. Sometimes affective and psychotic symptoms may be missed due to unusual premorbid social functioning or reduced ability to articulate changes in thought process or mood state. However, impairment is always indicated by a loss in level of functioning demonstrated by changes in self-care or grooming; sleep pattern; level of interest in eating, social behavior, or usual preoccupations; and goal-directed behavior including food seeking or repetitive behaviors. Perseveration and excessive, repetitive behaviors are common in PWS and should not be confused with true OCD. Severe skin picking may be a manifestation of Impulse Control Disorder, NOS. ADHD may manifest as the predominantly inattentive type. Central sleep apnea occurs independently of obesity, so excessive daytime sleepiness may be related to a more complex differential diagnosis.

## INTERVENTIONS

**Environmental and Behavioral:** If the patient presents with an exacerbation of syndromal behaviors, the most effective intervention is to optimize the environment augmented with targeted behavioral therapy. Functional behavioral assessments or input from an applied behavior analyst may be helpful, but most likely the goal of intervention is to alter the environmental conditions rather than to expect the person with PWS to change. The individual's unique attributes such as personal interests and hobbies can be used in the service of treatment. Behavioral and environmental interventions should be used for problematic syndromal behaviors before psychotropic medications are considered, and they should accompany all medication trials.

**Psychotherapy:** A relationship with an individual counselor is extremely helpful; goals include assessment of mood and insight, avoiding misunderstandings, supportive therapy for losses and life changes and to assist in gaining the patient's interest and investment in behavior plans. Insight therapy to achieve behavioral change has limited benefit.

**Medication:** If a person with PWS presents with the clinical signs of a psychiatric disorder, the use of appropriate classes of psychotropic medication is indicated. However the dose response characteristics and side effect profile may be atypical.

**General Guidelines:** "START LOW; GO SLOW." Some classes of medication are more likely to have side effects at standard doses in persons with PWS, possibly due to differences in drug metabolism or neurosensitivity. Factors affecting pharmacokinetics include: abnormal intestinal motility with delayed gastric emptying that alters absorption; a diet that may be rich in cruciferous vegetables inducing CYP1A2 metabolism; and greater fat mass at all BMIs which delays clearance of lipophilic agents. There may be pharmacodynamic effects as well. Initiation of estrogen replacement concurrent with SSRI treatment has caused mood activation, and depot testosterone has been associated with behavioral activation. Individuals with PWS may not display the most typical medication side effects. Nausea or appetite change is 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. When possible, judge the efficacy of one medication before adding others. Parents and caregivers need to be informed about expected benefits, possible adverse reactions, or potential drug interactions as they monitor medication efficacy. Most individuals with PWS are not competent to give informed consent for medication trials or operative procedures; they may say they understand benefits and risks, but their judgment is impaired regardless of age or IQ. In fact, the use of medication may carry secondary gain, and individuals with PWS should never be responsible for administering prn medications.

**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. Persons with PWS appear to be prone to mood activation with SSRI medications, atypical neuroleptics and modafanil, and patients should be monitored closely for the appearance of increased anxiety, irritability, emotional reactivity, self injurious behavior, or increased goal directed behavior including food seeking or skin picking. In patient's with PWS, extrapyramidal effects are more difficult to assess due to syndromal hypotonia. Symptoms of neuroleptic malignant syndrome may be atypical due to syndromal hypotonia and hypothalamic abnormalities causing preexisting temperature dysregulation and excessive daytime sleepiness. The risk for hyponatremia appears to be increased when using SSRIs, atypical neuroleptics, carbamazepine, and especially oxcarbazepine. Valproic acid has been associated with varying degrees of hyperammonemia. Anecdotal reports from parent surveys suggest that SSRIs have not been helpful with skin picking, food seeking and food preoccupation, but

they have been useful for some anxiety-related symptoms. Topiramate, sometimes helpful for skin picking, produces renal tubular acidosis (hypochloremic acidosis) that is dose-dependent and reversible. Like topiramate, a number of psychotropic agents are known to exacerbate osteoporosis, which is associated with the syndrome.

**Hospitalization:** Although inpatient hospitalization is sometimes necessary, hospital units are not prepared for the needs of the person with PWS. The nursing and dietary staff will require *very specific guidance* on how to manage the syndrome. The PWSA-USA can provide resources for managing food and other issues on hospital units.

**Ongoing Care:** Families who seek psychiatric care should keep a diary of the outcome of every pharmacotherapy visit including the medication prescribed, dosage used, symptoms targeted and reasons for discontinuation. Regular appointments and follow-up calls during treatment are essential. Checklists and anecdotal records may track information about mood, sleep, behavior and thoughts between appointments. Patients with PWS should be expected to give feedback on how dose changes of medication affect their sleep, mood and behavior. Although the patient is a stakeholder in the process, change of any kind is stressful for them. Listening carefully to their feedback can help ensure better patient compliance with your recommendations and successful ongoing management.

#### ADDITIONAL RESOURCES:

PWSA-USA has an excellent database of archived materials, books, and manuals about PWS. The PWSA Clinical Advisory Board can help address specific concerns, make referrals or provide consultation.

Psychiatric Primer is a more detailed resource available at [www.PWSAUSA.org](http://www.PWSAUSA.org) or [www.pittsburghpartnership.com](http://www.pittsburghpartnership.com).

[www.theNADD.org](http://www.theNADD.org) (excellent books, DVDs, and other resources on diagnosing, treating and supporting people with intellectual disabilities and psychiatric or behavioral concerns)

Fletcher, R., Loschen, E., Stavrakaki, C., & First, M. (Eds). (2007). *Diagnostic manual-intellectual disability: A textbook of diagnosis of mental disorders in persons with intellectual disability*. Kingston, NY: NADD Press. (a new manual with adapted diagnostic criteria for making psychiatric diagnoses in people with intellectual disabilities)

Szymanski, L., & King, B.H. (1999). Summary of the practice parameters for the assessment and treatment of children, adolescents and adults with mental retardation and co-morbid mental disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, 1606-1610.