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.

Reasons for Consultation and Referral

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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).

Consideration 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,
Psychiatric Alert for Psychiatrists on Prader-Willi Syndrome (cont’d)

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.

Psychodynamic 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

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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 or www.pittsburghpartnership.com.

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