

Research Visits with the Prader-Willi Population

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Disclosures

Neither speaker has any disclosures to report.

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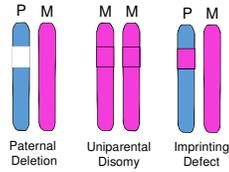
Objectives

1. Describe the most common characteristics of someone with Prader-Willi Syndrome (PWS).
2. Identify differences between clinical care and research study visits that may have an impact on someone with PWS.
3. Discuss methods that can be used to help facilitate successful research visits with the PWS participant.

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Review of Prader-Willi Syndrome (PWS)

- Chromosome 15q11-13
 - Paternal deletion: 70%
 - Uniparental disomy: 25%
 - Imprinting defect: 5%
- Occurs in approximately 1 in 12,000 to 15,000 births
- Most common genetic cause of obesity



PWS Basic Facts - Prader-Willi Syndrome Association USA 2016, Retrieved from <https://www.pwsasa.org/basic-facts>

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Characteristics of PWS

- Almond shaped eyes
- Narrow bridge of nose, narrowing of forehead at temples
- Thin upper lip and upturned mouth
- Small hands and feet



Feldman, C & Koffman, C. Genet. Mol. Biol. 2000, 23(4): 715-24

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Characteristics of PWS

- Low birth weight/poor feeding as infants
- Hypotonia
- **Hyperphagia**
- Slow metabolism
- Cognitive delays
- Obsessive/Compulsive behaviors (e.g. skin/rectal picking)
- Behavioral problems
- Short stature

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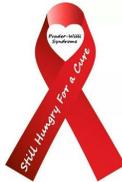
Other Associated Problems

- Sleep issues: sleep apnea, hypersomnolence
- Scoliosis
- Hypogonadism
- GI symptoms: gastroparesis, constipation, lack of vomiting
- Autism
- Hormone imbalances
- High pain tolerance

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Hyperphagia

- Increased appetite begins in early childhood (~2-5 years old) and then rapidly increases
- Patients may steal food, forage through the trash, and eat non-food items
- Excessive eating can lead to death from severe obesity, choking, or stomach rupture
- Food is a constant source of perseveration



Hyperphagia is the #1 barrier to these patients living independently

Milner, J. Diseases 2015, 3, 78-85

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Current Treatments

- Growth hormone: usually started after diagnosis (infancy)
- Other hormone deficiencies: testosterone, estrogen, thyroid
- Hypersomnolence: Modafinil, Contrave, etc.
- Skin picking: n-acetylcysteine
- Psychiatric/behavioral issues: psychotropic medications
- Weight management: low calorie diet plus exercise



There is no cure for PWS and conventional weight management treatments have not been successful

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Research in the PWS Population

- Few pharmacologic studies in the past

Current Non-Medication Trials	
PATH for PWS	Parent-focused Remote Education to Enhance Development (PRETEND)
PWS Anxiety and Stress Questionnaire (PADQ)	Developing Objective Biomarkers of Hyperphagia in Children with PWS
PWS Activity, Sleep and Eating Pattern Pilot Study	Oxytocin and the Autonomic Nervous System in PWS
Mindfulness-based intervention for temper outbursts in PWS	Web-based study of cognition

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Research in the PWS Population



- First large trial to demonstrate statistically and clinically significant improvement in hyperphagia-related behaviors and weight loss
- Families were eager to join
- 108 patients enrolled
- 3 groups: 2 different doses of Beloranib and placebo
- 5 patients discontinued due to adverse events
- Unfortunately, 2 deaths lead to the trial being stopped

McCordless, S. Diabetes Care, Metab. 2017; 19: 1751-61

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Current PWS Studies

Drug Name	GLWL-01	DCCR	Cannabidiol oral solution	Carbetocin	Livote tide
Company	GLWL Research	Soleno Therapeutics	Insys Therapeutics	Levo Therapeutics	Millendo Therapeutics
Phase ¹	II	III	II	III	Phase I/II
Type of study ²	Triple blind randomized crossover	Triple blind, placebo-controlled	Randomized, Double-Blind, Placebo-Controlled	Blinded, randomized (followed by open label)	Double blind, randomized placebo-controlled study
Route of administration	3 oral capsules twice a day	Once a day tablet	Oral solution, twice daily	Intranasal	Subcutaneous injection once per day
Eligible Ages	16-65 years old	Ages 8 and above	8-17 years of age	7-18 years old	12-65 years old

Research Announcements - PWSA USA 2018. Retrieved from <http://www.pwsusa.org/research-announcements/>

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Clinical Care Vs. Research Visits

Clinical Care

- Quarterly/semi-annual visits
- 30-60 minutes(unless multiple providers)
- Routine structure/procedures
- Known staff
- Established relationship

Research

- Weekly/monthly, possibly with added travel
- 1.5-6 hours or more
- Visit structure varies
- Unfamiliar procedures (ECG, DEXA, etc.)
- Procedures done multiple times
- Unknown to staff/facility

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Clinical Care Vs. Research Visits

Clinical Care

- Fasting not required
- "Need" driven
- Few transitions
- Labs may not be required

Research Visits

- **FASTING** often required
- Protocol driven
- Lots of transitions in single visit
- Most participants must give assent/permission
- Questionnaires (caregivers separated from patient)
- Many samples (blood, urine) are required that day

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Tips for Successful Research Visits

Hyperphagia

- Set expectations on fasting/meal times before the visit
- Send consent prior to visit for guardian/caregiver review
- Get all fasting procedures done as soon as possible
- Be prepared, be efficient, be fast (and hope the blood draw goes well!)



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Tips for Successful Research Visits

Hyperphagia

- Have family bring in their food
- Schedule meal breaks (follow typical food schedule if possible)
- Limit discussions about food
find distractions
- Be aware of surroundings: cafeteria, trash, staff lunches, etc.



Tips for Successful Research Visits

Obsessive Compulsive Behaviors

Skin Picking

- Use verbal cues
- Use distraction/redirection (coloring, puzzles, crafts)
- Find alternatives for wearing ID bands
- Cover lesions or "picking areas" (clothing, bandages, Coban wrap, etc.)

Perseveration

- Re-direct and distract—be aware of your verbal or nonverbal feedback
- Introduce a different topic or procedure
- Provide a quiet break
- Don't feed in to repetitive questions



Tips for Successful Research Visits

Obsessive Compulsive Behaviors

- What you do at the first visit may establish participant's expectations for the rest of the study
- Provide consistent staff, give notice if this changes
- Keep same routine order each visit if possible
- Provide adequate preparation for changes
- Plan ahead to limit schedule disruptions



Tips for Successful Research Visits

Common Behavior Issues

- Anxiety
 - Be clear, break things down into smaller steps
 - Use visual schedule
 - Be positive
 - Child Life
- Crying/meltdowns
 - Provide a break if appropriate
 - Minimize sensory input
 - Be firm and remind patient of expectations
 - Respect Assent
- Aggression
 - Remain calm, set the tone
 - Provide a break



Tips for Successful Research Visits

Common Behavior Issues

- Defiance/refusal to cooperate
 - Set the expectations right away
 - Create a "new routine" around research
 - Offer minimal choices if possible
 - Don't engage in power battle
- Withdrawal/"the silent treatment"
 - Try to engage patient with their interests
 - Don't withdraw in return
 - Keep schedule moving



Tips for Successful Research Visits

Developmental Delay

- Obtaining meaningful assent
- May not know developmental level prior to visit
- Send assent home prior to visit
- Don't assume participant understands routine requests
- Provide developmentally appropriate distractions, rewards, explanations



Tips for Successful Research Visits

Obesity

- May be too large for certain procedures
- May be a challenge to position for measurements
- Blood draws may be very difficult.
 - Have patient hydrate 1-2 days prior to visit
 - Warm venipuncture site if tolerated
 - Use longer needles/PIV needle
 - Explain multiple pokes may be needed.
 - Consider an IV if serial draws required.



Cortés, F. Revista Médica de Chile. 2005; 133: 33-41

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Tips for Successful Research Visits

Scoliosis

- Heights-may be difficult to obtain consistent heights
- Allow adequate time for positioning, triplicate collection
- Use at least two people
- Consider lying down



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Tips for Successful Research Visits

Questionnaires

- Parent or guardian completes questionnaires
- Provide activities to do with additional staff
- Participant may try to "negotiate" with you
- Move past repetitive questions
- Consistent caregiver/staff members



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Other Considerations

- No two PWS patients are the same
- Community engagement
 - Very well connected on social media and parent groups
 - Studies may have rules regarding social media
 - Community is dedicated
- Managing multiple studies
 - Maintain a participant prescreening log with key information
 - Set aside 30+ minutes for a new potential participant phone call



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Questions?

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