United in Hope

FOR PWS

PWSA | USA 2023

NATIONAL CONVENTION

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Prader-Willi Syndrome Association | USA • www.pwsausa.org • (941) 312-0400

Aging in Prader Willi Syndrome

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Learning Objectives:

- Identify changing health with aging
- Identify specific medical concerns
- Identify ways to recognize need for intervention
- Identify how to include multi-disciplinary teams
- Identify ways to modify supports

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In The Beginning

1887, Langdon Down described an adolescent girl with mental impairment, short stature, hypogonadism and obesity

Although she was diagnosed with polysarcia she is now known to be the first reported case of PWS

1956, Drs. Andrea Prader, Alexis Labhart, and Heinrich Willi first described this as a syndrome based on the clinical characteristics of nine children.

Prader, A., Labhart, A., & Willi, H. (1956). [A syndrome characterized by obesity, short stature, cryptorchidism, and oligophrenia following a myotonia-like condition in infancy]. Schweizerische Medizinische Wochenschrift, 86, 1260.

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Where we are today

Life span has increased with some individuals living into their 60's and 70's

- Early diagnosis, evaluation and treatment by multidisciplinary teams
- Introduction of Growth hormone
- Early intervention programs – eg control of food environment
- Better understanding of behavior and psychiatric aspects of PWS
- Improved access to technology

We continue to experience challenges and our work continues

We remain United in Hope

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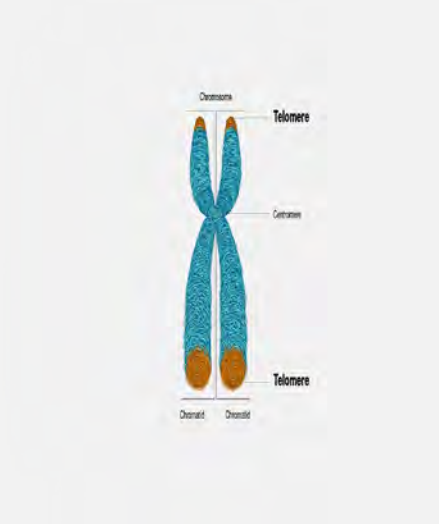
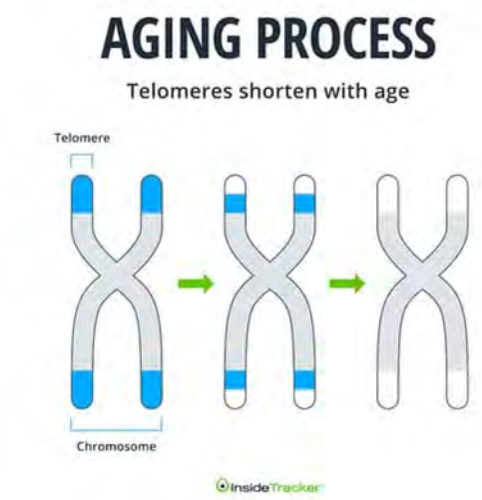
What is aging?



Aging is characterized by a progressive time-dependent functional decline of tissues & telomere shortening, which is considered to be involved in the process.

Individuals with shorter telomere length show increased mortality risk providing support for an association between telomere length & life span.



How is aging different in PWS?

- Premature aging occurs in PWS
- Early identification of dementia in individuals with intellectual delays is often challenging
- Missed diagnoses can occur due to lack of awareness and appropriate surveillance

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Accelerated Biological Aging in Young adults with PWS

Studies from adults with PWS, not treated with GH describe an increased risk of age-associated diseases early in life (T2D, CVD, **cognitive decline**)

Mortality is estimated at 3%/year across all ages rising to 7% in those over age 30.

Donze, Sh et al, J Clin Endocrinol Metab 2020
Janicki et al, J Intell Disabil Res 1996, 2002

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What Do We Know So Far?

- Cross-sectional MRI study in 20 YA with PWS showed that predicted brain age was on average 8.7 years higher than chronological age

- Brain structure in PWS resembles healthy older brains, indicative of premature neuronal loss and atrophy

Telomere are suggested to play a role in biological aging but had not been studied in PWS

Azor, AM et al, Increased brain age in adults with PWS, Neuroimag Clin 2019;21: 101664

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Accelerated Biological Aging in Young adults with PWS

- Cross-sectional study in 47 YA with PWS (median age 19.2 y) showed that median leukocyte telomere length is shorter in YA with PWS compared with 135 age matched healthy adults and 75 YA born SGA tx with GH because of short stature.
- **FINDINGS:** LTL is shorter in YA with PWS

  Tendency toward an association between a shorter LTL & lower total IQ which might imply a role of LTL in cognitive functioning in PWS.
- **CONCLUSIONS:** Findings suggest that a shorter LTL is involved in the reported accelerated aging process in adults in PWS

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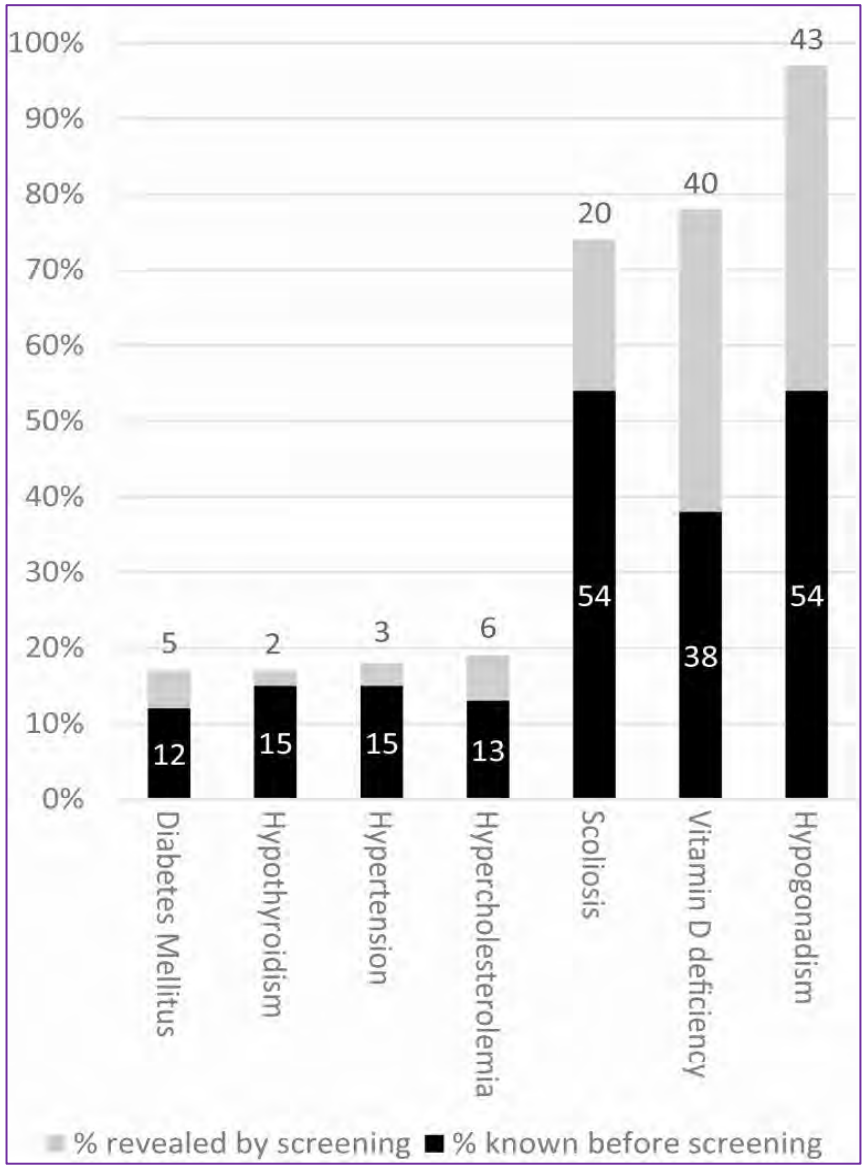
Avoiding misdiagnosis, missed diagnoses and inappropriate interventions: The Importance of Screening



Health Problems Before & After Screening

	Total, N = 115			
	Before Screening	**Detected by Screening**	**After Screening**	**Missing**
Hypogonadism				
Male (n = 56)	26 (48%)	**+52%**	54 (100%)	2
Female (n = 59)	26 (60%)	**+33%**	40 (93%)	16[a]
Scoliosis	61 (54%)	**+20%**	83 (74%)[b]	3
Hypercholesterolemia	14 (13%)	**+6%**	22 (19%)	2
Type 2 diabetes mellitus	13 (12%)	**+5%**	19 (17%)	2
Hypertension	17 (15%)[c]	**+3%**	20 (18%)	3[d]
Hypothyroidism	17 (15%)	**+2%**	19 (17%)	0
Vitamin D deficiency	26 (38%)	**+40%**	54 (78%)	46[e]
Severe vitamin D deficiency			8 (13%)	55
Total undiagnosed health problems				
At least 1		**70 (61%)**		
At least 2		**28 (24%)**		
3 or more		**10 (9%)**		

Pellikaan 2020

MISSED DIAGNOSIS BY RESIDENCE

	Missing	PWS Home[a], N = 23	Non-PWS home[b], N = 61	Family[c], N = 28	*P*-value
Age, median [IQR]	0	26 [21–32]	36 [28–50]	19 [19–22]	<0.001
BMI, median [IQR]	0	27 [22–30]	30 [27–40]	28 [26–36]	0.004
Undiagnosed health problems[d]					
At least one		9 (39%)	44 (72%)	15 (54%)	0.16
At least two		2 (9%)	19 (31%)	5 (18%)	
Three or more		2 (9%)	4 (7%)	4 (14%)	
Hypogonadism					
Male (n = 56)	2	9 (100%)	28 (100%)	15 (100%)	NA[e]
Female (n = 59)	16[f]	10 (100%)	20 (87%)	10 (100%)	0.2
Hypothyroidism	0	4 (17%)	12 (20%)	3 (11%)	0.6
Type 2 diabetes mellitus	2	2 (9%)	13 (22%)	3 (11%)	0.2
Hypertension	3	0 (0%)	17 (29%)	2 (7%)	0.002
Hypercholesterolemia	2	4 (17%)	15 (25%)	2 (7%)	0.1
Scoliosis	3	18 (78%)	44 (76%)	19 (68%)	0.6
Vitamin D deficiency	46[g]	14 (88%)	22 (85%)	16 (64%)	NA[h]

Syndrome Specific Health Risks in Adults with PWS

- **Cardiovascular** – hypertension, stoke, **diabetes**
- **Respiratory & Sleep** – pneumonia, **excessive daytime sleepiness**
- **Gastrointestinal** – constipation, GER, Anemia of unknown origin
- **Genitourinary** – kidney problems
- **Endocrine** – osteoporosis, **hx of any fracture**, primary amenorrhea
- **Neurologic** – epilepsy
- **Orthopedic** - scoliosis, **foot problems**, hip problems
- **Dermatologic** – **edema, erysipelas**, varices

Bolded risk were present in at least 50%

Sinnema et al 2012

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SAMPLE EVALUATION AND TREATMENT TEMPLATE

New patients & yearly controls
Interview
Physical examination
Biochemical measurements

- If creatinine > 93 µmol/L (males), > 76 µmol/L (females) or eGFR > 93 ml/min/1.73m^2 (males), eGFR > 98 ml/min/1.73m^2 (females): perform nephrologic analysis

↓

Vitamin D / calcium

- Start vitamin D supplementation if vitamin D level < 50 nmol/L
- Add calcium supplementation if dairy intake < 3 units per day
- Start vitamin D + calcium in case of known osteopenia/osteoporosis

↓

Start hormone replacement therapy

if

Females
- Amenorrhea or oligomenorrhea (do not rely on estradiol levels)

Males
- Sparse body hair ***or***
- Underdeveloped genitals ***or***
- Daytime sleepiness and testosterone < 10 nmol/L

↓

Perform poly(somno)graphy

if
- Daytime sleepiness ***or***
- Reported apneas ***or***
- BMI > 25 kg/m^2 ***or***
- Hypertension ***or***
- Plan to start GH treatment

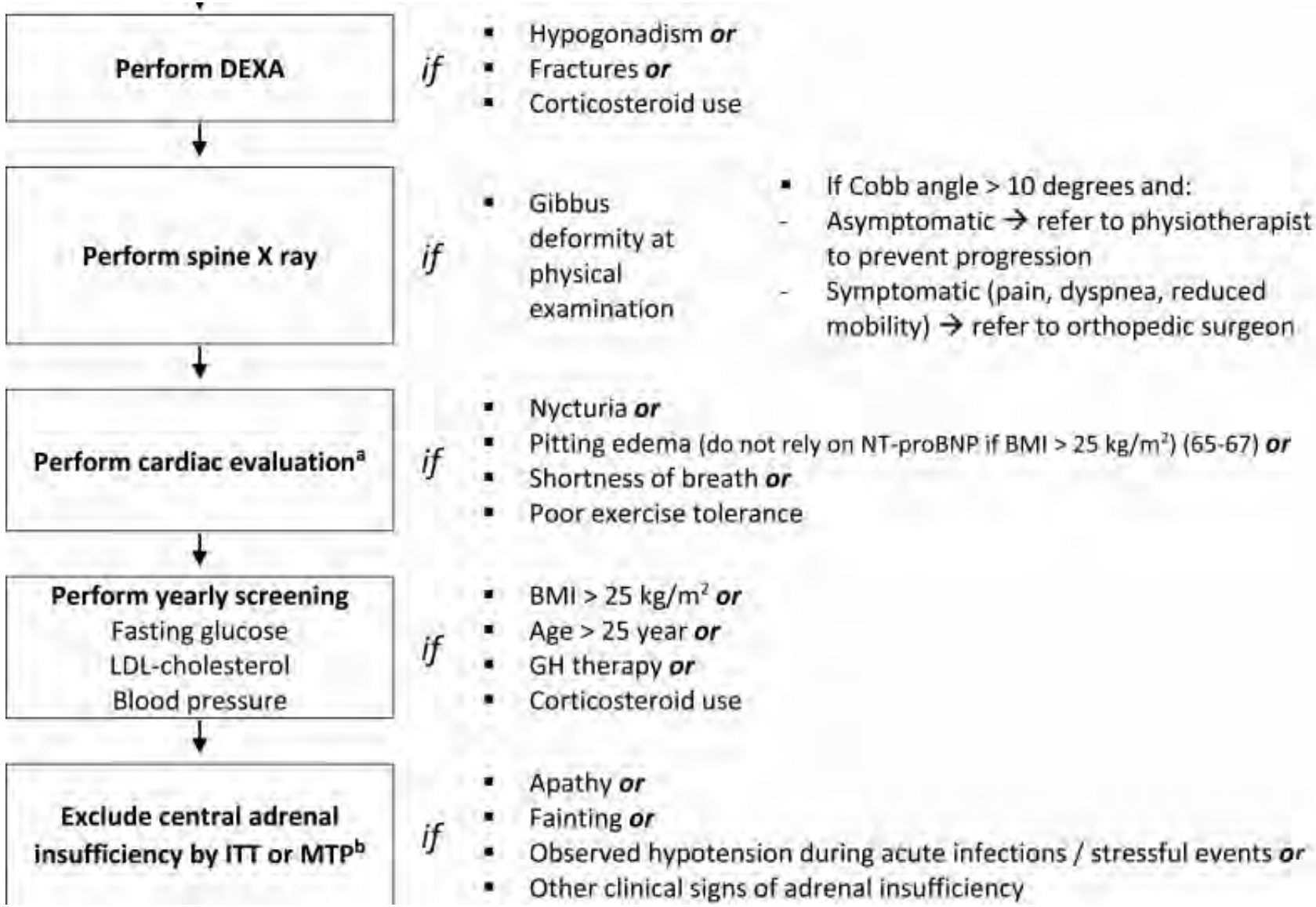
↓

Perform neuropsychological assessment[a]

if
- High blood pressure ***or***
- Temper tantrums ***or***
- Fatigue / daytime sleepiness

Pelikaan et al, 2020

SAMPLE EVALUATION AND TREATMENT TEMPLATE



Pellikaan et al 2020

Annual Physicals are Essential

Some frequent blood tests include

- TSH, free T3, free T4
- Hemoglobin A1c or fasting glucose
- Vitamin D
- Hemoglobin
- Sodium, potassium, creatinine
- Lipids, cholesterol, liver enzymes
- Men: testosterone, Luteinizing hormone
- Women: Estradiol, FSH
- IGF-1- for those on GH

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Benefits of an Interdisciplinary Team

- Motivates collaboration to provide evidence- based new standards of care
- Increase the knowledge base including through randomized controlled trials
- Offers an additional resource for the community
- Plays a role in global telemedicine, including to rural areas with few resources
- Create opportunities for clinical work to inform basic and translational research

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Multidisciplinary Teams Can Include

Neurology

Psychiatry

Genetics

Endocrinology

Pulmonology & Sleep Medicine

Gastroenterology

Nutrition

Orthopedics

Physical Therapy

Social Services

Nursing

Dentistry

Opthalmology

Collaboration and Communication Between Disciplines

- Gatekeeper
- Regular follow up
- Electronic medical records
- Ongoing updates to MH & medications

- PWS Medical Alert Book
- PWS resources

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Health and Medical

Dental

What we know

- Thick saliva, poor oral hygiene, dysphagia, aspiration, bruxism
- Abnormal ventilatory responses to hypoxia & hypercarbia
- (CAUTION WITH SEDATION & ANESTHESIA)

What we can do

- Regular dental exams and follow up
- Supervise brushing and flossing
- Use of special toothpaste & mouthwash
- Sugarless gum
- Limit fermentable carbohydrates & sugar containing acidic beverages

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Health and Medical

Pulmonary and Sleep Medicine

What we know

- Obesity, low tone, craniofacial anatomy, dysphagia and other comorbid conditions as well as some medications can increase risk of aspiration, respiratory infections and sleep apnea

What we can do

- Treat comorbid conditions such as sleep apnea
- Manage weight
- Regular exercise
- Preventive care including immunizations

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Health and Medical

Respiratory co-morbidities: aspiration

- Previously thought to occur mostly in infants due to hypotonia & swallowing incoordination
- Symptoms can be subtle
- HAVE A LOW THRESHOUT FOR EVALUATION with speech and language therapist specializing in dysphagia
- Consider videofluoroscopy
- **Complications:** recurrent aspiration can result in inflammation of the lungs, leading to bronchiectasis, pulmonary fibrosis and worsening restrictive lung disease

Health and Medical

CHOKING: RISK FACTORS IN PWS

- Hyperphagia/ Eating too much too fast
- Decreased chewing before swallowing
- Hypotonia
- Poor oromotor coordination
- Poor gag reflex
- Certain medications such as:
- SSRIs (eg Prozac, Zoloft), antipsychotics/neuroleptics (eg Respiridone), anti anxiety medications & anti epileptic drugs

Health and Medical

Choking: First Aid

https://www.mayoclinic.org/first-aid/first-aid-choking/basics/art-20056637

Health and Medical

Sleep and Breathing

What we know

- Sleep disordered breathing, especially obstructive sleep apnea is common in PWS adults. Multiple factors contribute to presence and severity of OSA including obesity, craniofacial anatomy, hypotonia, GER. Medications may also contribute to severity.

What we can do

- Be proactive. Monitor for habitual snoring, snorting breathing in sleep or in wakefulness, obstructive sleeping pattern, excessive daytime sleepiness; manage obesity when it exists
- Low threshold for sleep medicine consultation & polysomnogram
- If individual has been treated for OSA & remains very sleepy consider type 2 narcolepsy

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Health and Medical
Sleep apnea

OSA (obstructive sleep apnea)

- Habitual snoring
- Snorting
- Obstructive breathing pattern
- Witnessed apneas
- Hypersomnolence
- Poor focus/attention

CSA (central sleep apnea)

- Neurologic disorders are a common cause of CSA in non preterm
- Presentation varies from an incidental finding in an asymptomatic individual to frank apneas & hypersomnolence

Health and Medical

Gastrointestinal

What we know

Constipation and GER are both common in PWS

What we can do

- Avoid overconsumption
- Regulate diet. Input from nutritionist is important
- Routine exercise
- Use GI algorithm

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Health and Medical

Cardiac

What we know

- The most common heart condition in PWS is right heart failure due to significant obesity

What we can do

- Maintain healthy weight, routine exams, keep record of vital signs, monitor for edema, routine exercise,

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Health and Medical

Genitourinary

What we know

- Urinary incontinence, infection, low tone and retention can all be issues in PWS

What we can do

- Maintain healthy weight
- Routine exams
- Know medication side effects
- Avoid fad diets

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Health and Medical

Neurology

What we know

- Epilepsy
- Premature aging/ may occur with early dementia
- Narcolepsy type 2

What we can do

- Monitor for changes in mental status, behavior changes, cataplexy
- Neurology and Sleep Medicine evaluations are necessary to evaluate for Type 2 Narcolepsy with NPSG & MSLT

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Health and Medical

Neurology

What we know

Excessive Daytime Sleepiness (Hypersomnolence) is very common in adults with PWS often limiting exercise, social activities and quality of life. It is usually attributed to a lack of hypothalamic arousal. However treatable underlying problems such as sleep apnea, narcolepsy, nycturia, vitamin D deficiency, untreated male hypogonadism or use of medications that can cause sleepiness

What we can do

Do not assume that this clinical finding cannot be modified. Evaluate for other causes and treat where indicated.

Health and Medical

Neurology: Risk of Early Onset Alzheimer's disease in PWS

Background:

- Autopsy findings in brains of 3 adults (> age 40y) with PWS
- showed signs of AD (severity increased with age)
- Life expectancy in PWS is increasing
- Early diagnosis of AD has the potential to prolong the non- dependent life of people with PWS by the use of suitable medication

Risk assessment for early onset AD in PWS

Research Outcomes: Project Summary

- Recruitment was problematic & evidence inconclusive
- However only those with a hx of psychosis were at risk of decline **AND**
- In all 4 cases carers described deterioration in functioning over & above that seen during acute psychotic episodes

Source: Foundation for Prader Willi Research

Health and Medical

Dementia in Adults With Intellectual Disability

- Most often will be the result of Alzheimer's
- UK studies in general population of adults (40-69 y) showed that adults who performed badly on problem solving & memory tests 9 years earlier were more likely to get diseases including Alzheimer's

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Health and Medical

Dementia Symptoms in Persons with ID

- Increased inability to stay focused
- Exaggeration of longstanding behavioral traits (most often stubbornness)
- Change in prior daily routine, sleeping or eating habits
- Inability to make clothing decisions
- Getting lost in familiar environments
- Not remembering the names of people previously known
- Increased aggression, unjustified fears, sleep problems
- Increased difficulty with visual/motor coordination
- Increased accidents and falls
- Difficulty learning new tasks
- Loss of language and other communication & social skills
- Progressive loss of prior activities of daily living
- Late onset seizures
- Frequent choking incidents
- Changes in hearing and vision

AA Caregiver Tips & Tools – accessed 5/7/2023

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Health and Medical

Orthopedic

What we know

There is a higher prevalence of scoliosis in PWS. Having PWS increases the risk of osteoporosis, certain medications can add to osteoporosis risk

What we can do

Know scoliosis and surgical history, routine weight bearing exercises, maintain healthy weight, routine exams (DEXA), medications

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Health and Medical

Endocrine

What we know

- Common endocrine issues in PWS are Growth hormone deficiency, Type 2 diabetes, hypothyroidism, and hypogonadism

What we can do

- Keep health records, routine follow up, monitor menstrual cycles, keep record of blood sugars if diabetic, maintain healthy weight

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Health and Medical

Dermatology

What we know

- There is an increased risk for skin picking, skin folds lead to skin breakdown and infections

What can we do

- Check skin on a routine basis
- Good hygiene; Keep nails short
- Sensory activities & distraction

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Health and Medical

Mental Health

What we know

- Mental health issues are prevalent in PWS, medications can mask or add to existing issues, sleep effects mental health, co-occurring health diagnosis can have effects on mental health, changes in structure and routine can change mental health and the list goes on

What can we do

- Behavior management, tracking behaviors, monitoring for side effects, consistency, security, communication, observation

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Health and Medical
Transitioning & Mental Health

What we know

Serious mental illness in PWS usually presents in teens & young adulthood and is characterized by sudden changes in mood, the onset of delusions &/or hallucinations & other manifestations associated with atypical psychotic illness. They usually have an acute onset and may be triggered by an infection or life stress.

What can we do

This increased risk of mental illness is around the age of transition & it may be unrecognized as changes in mental status or behavior may be attributed to transition. The cause may be the onset of illness requiring diagnosis & effective treatment.

Health and Medical
Suicidality

General population risk factors

- Depression/Substance Abuse
- Psychosis
- Anxiety
- Personality, Eating & Trauma related disorders

Peleggi et al 2021

PWS has a higher prevalence with

- Aggressive behaviors/ tantrums
- Higher rate & number of psychiatric hospitalizations
- Greater rates of treatments with behavioral therapies, psychotherapy & all medication categories except stimulants and atomoxetine

Health and Medical

End of life

What we know

- Individuals with PWS are living longer, end of life care is a difficult discussion

What can we do

- Provide support & choice
- Advanced directives
- Staff training

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Health and Medical
End-of-life care (cont)

4 major categories of EOL care

- Physical comfort
- Mental & Emotional Needs
- Support for Physical tasks
- Spiritual needs

NIH (NIA) - accessed 4/7/2023

Common concerns for end-of-life care

- Pain
- Breathing problems
- Digestive problems incl. constipation
- Temperature sensitivity
- Fatigue

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Teams, Coordination, and Communication

Communicate

Be proactive

Coordinate care

Research

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