

AGEING IN PRADER-WILLI SYNDROME

What do we know. What can we do to avoid too early aging

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2026

My wish, hope and goal for to day

- To tell that early physical ageing is not a rule for all with PWS
- To give information about medical facts and possible treatments (PWS.)
- To avoid too early ageing ,because of lack of knowledge about medical needs
- To secure a focus always on individual needs, also with changes and ageing

- We still need to learn more, more research is needed about PWS and ageing
- We must avoid false expectations, that can arise without documentation

- And you to day are the experts, so we look forward to learn from each other

What we know to day about PWS

- It is possible to have a long ,happy and healthy life with PWS
- More and more adults are living healthy , happy with normal weight

Special support is always needed, and individual realistic expectations

- Family, caregivers and health professionals must know PWS:
- And know about diseases in PWS and react when specific help is needed.

Adults to day with PWS becomming older

- They are different
- They have very different backgrounds
- Some have been healthy without diseases, for many years
- Some have had several illnesses and perhaps still have.

- Upbringing, family support before and now , varies a lot
- Childhood possibilities, school, social contacts and acceptance vary
- Actual situation: illnesses, living situation, occupation ?
- All this will influence on the ageing process

What is sometimes wrongly expected

- Adults with PWS cannot survive healthy until “old age”
- Early death is to be expected, as it is for many congenital syndromes
- People with intellectual disabilities like PWS will develop dementia (wrong!)
- We need published data on healthy ageing in PWS.
- But we know adults with PWS who are healthy and now “older”
- We have case reports, about people with diseases and dementia
- We need more information about the medical conditions of those who died



And when you are old: PWS and all others

- Looking older
 - Less muscle power.
 - Balance can be weak. More weak than before (PWS)
- More risks for diseases.
- Need for help can change, when you are not able to do as before
- Mentally : you are in many aspects the same... and have more experience
- But it can be difficult to manage the changes that come with age

Diseases in PWS- It can be difficult

- Symptoms can be different and unexpected in PWS compared to others
- Less pain with fractures, and abdominal diseases, no fever with infections
- People with PWS can not always explain their symptoms when if they are ill

A great risk that diseases are overlooked and diagnosed late, or even too late

Many know cases with too late diagnoses, too late medical intervention

What we know about PWS

- PWS is a very complex disease.
- Many physical problems and symptoms typical for PWS can arise.
- To day we know how to treat many of the well known medical problems in PWS
- It happens that the medical problems are not seen, and then not treated, which can cause early aging or even early death
- A recent Dutch investigation showed that among 115 adults 61% had one or more untreated health problems, and 25 % had multiple untreated health problems

The 115 adults with PWS (Netherland)

The journal of Clinical Endocrinology & Metabolism, 2020, Vol. 105, No. 12, e4671–e4687(Pellikan et al)

- Seventy patients (61%) had undiagnosed health problems
- 1 in every 4 patients had multiple undiagnosed health problems simultaneously.
- All males and 93% of females had hypogonadism
- 74% had scoliosis, 18% had hypertension,
- 19% had hypercholesterolemia,
- 17% had type 2 diabetes mellitus,
- 17% had hypothyroidism.
- Unfavorable lifestyles were common: 22% exercised too little
- 37% did not see a dietitian

CAUSES OF DEATHS IN PWS

- Overweight
- Respiratory problems: lung infections not treated, apnea
- Abdominal diseases: infections and stomach rupture
- Accidents: also in traffic
- Choking. Breathing is blocked by food in the throat.
- But often no information about the actual health status of those above who died
- Sudden unexpected death, and often no reason found and described

More research is needed

- Only one brain study:
- A MRI study finds that the brain ages in adults with PWS is advanced for age, but the participants in the study had different background and medical status.
- So is ageing different ? , also when correct medical treatment is given ?
- It makes research difficult when adults with PWS have different backgrounds

- Daily life:
- Individual evaluation and correct treatment in acute situations and daily
- To avoid too early ageing because of diseases

So what to be aware of: Weight....

- Weight : Overweight can result in diseases in PWS:
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- 1. Diabetes that causes:
- circulation problems, edema, heart, kidney , eye diseases
- 2. Joint problems, difficult to walk
- 3. Breathing (lung) problems, low oxygen, poor general condition
- 5. Sleep problems with apnea, daytime sleeping
- 6. Bladder control and intestinal problems, obstipation
- 7. Infections, cancer (follow screenings for cancer)

And how to treat overweight in PWS

- Gradual weight loss based on “correct food” and moving
- Supported by a dietician who knows (or can learn) about PWS.
- To secure a correct diet plan : protein, carb, fat, vitamin D.
- And having a plan for structure of administration of food
- Daily program for moving:
 - walking is possible for all.
 - other activities that demands physical activity, plays etc

Hormonal diseases caused by hypothalamic dysfunction PWS

- Growth hormone deficiency (many adults need treatment ?)
- Hypogonadism (all men, most women)
- Hypothyreodism (15%-20%)
- Adrenal insufficiency (rare)

Growth hormone (GH) deficiency in PWS

- Many young adults have been treated with growth hormone during childhood some have stopped at age 18 some are still treated.
- GH is important for muscles and organs, also for adults. Does not affect appetite.
- There are different rules about GH treatment for adults in countries
- In some countries some special tests are needed before start
- We know that adults (not PWS) with GH deficiency, can have medical problems and earlier aging and earlier death if untreated is seen.
- GH is given as daily injections, and the dose is adjusted after regular blood tests

Hypogonadism (low testosterone) in men

- Small genitals since birth and no normal maturation of genitals in puberty:
- Insufficient testosterone in blood (produced in the testicles): results in:
- No growth spurt in puberty
- No normal muscle growth in puberty, smaller than normal muscles in adults
- High pitched voice as adults
- Small genitals as adults, little body hair
- Looks young in the first adult years, but early aging, looks old, seen around age 30
- Osteoporosis will arise , risk of fractures
- Anemia can arise

Early aging and weak muscles are seen in men with low testosterone (hypogonadism)

Testosterone treatment in PWS

- In puberty or later: blood tests will show if treatment is needed
- An individual assessment if treatment is to be given
- Can be given as daily gel(cream) on the skin
- Or as injections every 3 months
- Recommendation: start with low dose and follow with blood tests
- Testosterone deficiency in men was seen in all of the Dutch cases, many were not treated, and in 50% it was not diagnosed before

Hypogonadism in women, low estrogen

- Lack of female hormones (estrogen and progesterone) result in:
- No growth spurt in puberty.
- Not normal breast development.
- No or late or irregular menstruation periods.
- Early aging,
- Early osteoporosis

- Caution: a few women will have menstruations, often late and irregular and few (if no treatment is given)
- all women (PWS) are in theory at risk of becoming pregnant.

Treatment of women with hypogonadism

- Blood tests can be done to evaluate the degree of hypogonadism
- Estrogen supplement must be considered in women with no / few menstruations
- An individual assessment if medical treatment is needed,
- Evaluate possible side effects .
- Hormone treatment can be given as P pills
- Important to know and tell the possible risk of pregnancy
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- Gynecologist contact is to be recommended for all women with PWS

Hypothyroidism

- Hypothyroidism is seen in around 15% of persons with PWS.
- The hormone is normally produced in thyroid gland.
- Hypothyroidism can arise in childhood or later
- Hypothyroidism can result in
- Less muscle power.
- Loosing weight (muscles)
- Feeling cold
- Slow heart rate
- Being slow, no energy,
- Early aging, physically and mentally

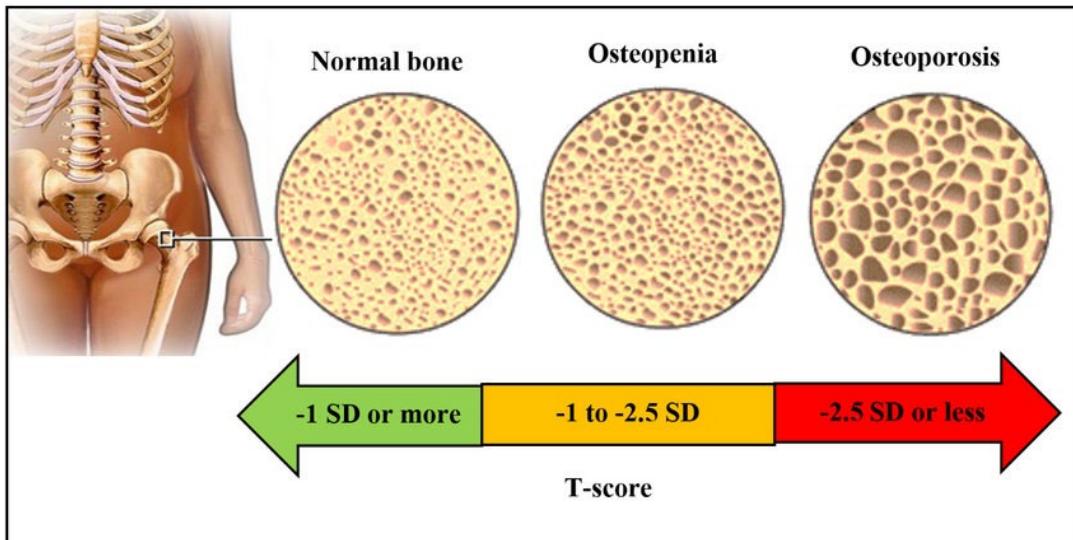
Hypothyroidism diagnoses and treatment

- Regular blood tests for hypothyroidism , measuring hormones in blood
- Blood test will show if hormone treatment is needed.
- Treatment is easy:
- a daily tablet, taken $\frac{1}{2}$ hour before breakfast
- Regular blood test is needed to regulate the tablet doses

ADRENAL INSUFFICIENCY

- Adrenal insufficiency in PWS seems to be rare.
- Adrenal hormones are important for the body to react normally when we are ill, having severe infections
- Is recommended to measure adrenal hormone cortisol, with blood tests in acute situations with severe physical illness, to know if supplement is needed.

Bones and osteoporoses.



- Osteoporoses often seen with age in PWS
- Causes: hypogonadism, reduced activity, (a family thing)
- Both men and women in PWS
- Risk. :
- Bone fractures. Vertebra. hips
- DEXA scan recommended for all to evaluate bone structure

Autonomic dysfunction

- Our inner nervous system. We cannot control-
- Works by itself: Sympathetic and parasympathetic nerve system.

- Stimulates and regulates.:
- Bowel and urinary system
- Blood pressure
- Sweat, blood circulation in organs and skin
- Sleep

Temperature with diseases: fever or not

- Nervous Vagus is important for the autonomic nerve system

More Symptoms to be aware of in PWS

IMPORTANT for all ages also when aging

Chewing and swallowing and teeth

- Mouth pharynx and upper esophagus: muscles are weak:
- Some are not chewing the food sufficiently: risk of choking
- Food is often not swallowed normally: Saliva is sticky
- After a meal some has food in mouth, pharynx and upper esophagus
- Advice: drink $\frac{1}{2}$ glass of water when the meal is finished:
- Teeth:
- gastro-intestinal reflux is common in PWS: Teeth can be acid-destroyed

Constipation

- One of the most common problems in adults with PWS
- Because of slow intestinal passage, which is the case for many adults, the result can be severe constipation, sometimes so extreme, so it causes vomiting.
- The cause is slow movement of muscles in the intestines.
- Laxantia can help, and the dietician can prescribe the best diet.
- Constipation can affect mood, alertness and general welbeing

Bristol Stool Chart

| | | |
|--------|---|--|
| Type 1 |  | Separate hard lumps, like nuts (hard to pass) |
| Type 2 |  | Sausage-shaped but lumpy |
| Type 3 |  | Like a sausage but with cracks on the surface |
| Type 4 |  | Like a sausage or snake, smooth and soft |
| Type 5 |  | Soft blobs with clear-cut edges |
| Type 6 |  | Fluffy pieces with ragged edges, a mushy stool |
| Type 7 |  | Watery, no solid pieces. Entirely Liquid |

Sleep and sleep apnea

- Sleep investigations have shown that sleep pattern can differ from normal (the different sleep phases, deep sleep and dream phases)
- Sleep apnea (breath holding during sleep) can be central or obstructive:
- Central sleep apnea: abnormal regulation from the brain
- Obstructive sleep apnea: caused by enlarged tonsils or adenoids.
- If snoring or sleep apnea is noted : sleep investigation is recommended and
- Evaluation by an ear-nose-throat doctor
- Some will need CPAP treatment.
- Narcolepsy and cataplexia(sudden sleep attacks)

Sleep disorders in 60 adults with PWS

Sleep. 2017 Ghergan et al

- Many adults are reported to be more sleepy than others
- A detailed investigation about sleep and sleep disorders:
- 60 adults with PWS , men and women 15-35 years old
- Most were overweight and obese

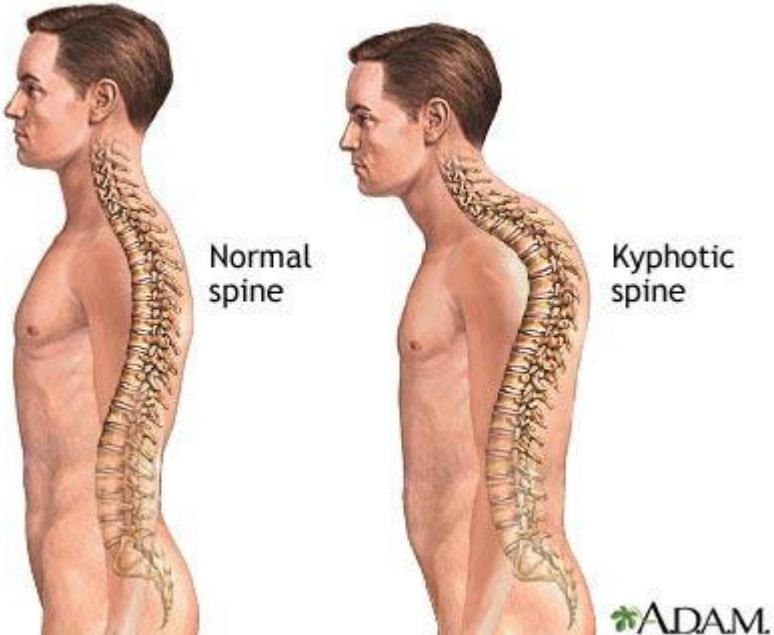
- 67% excessive sleepiness: some with narcolepsy (sudden sleep)
- 15% had sleep breathing disorders
- 14 had obstructive sleep apnea
- Some will benefit from CPAP or special medication for Narcolepsy

Not to forget the back and the muscles

- Many with PWS have scoliosis and /or kyphoses.
- Children are often treated with bracing or operation in teenage years.
- Many of the adults to day are not treated as children and can have back problems that causes, with age, more and more stiffness and pain:
- Treatment:
- contact to physiotherapist that prescribe excercises to be done daily at home, superwised by staff !

Kyphoses und Scoliose

- Kyphoses



- Scolioses



Edema and skin infections in PWS

- Leg edema is often seen, also with normal weight:
- Caused by insufficient lymph drainage, poor circulation:
- Treatment: supporting stockings, walking, avoid long hours of sitting
- Diuretics are only indicated for leg edema caused by heart or lung problems
- Risk of skin infection with swollen legs, and potentially life threatening

- With severe overweight edema can be seen in the whole body and lungs
- Diuretics given if there are heart and lung problems
- Treatment: weight loss and walking, moving

Behaviour , difficulties

- Arise with changes : family relations or loss , changing of staff , and more
- Misunderstandings
- Too high expectations from family or staff.
- Grief can come late
- Difficult behaviour demands personal support, often extra support
- Difficult behaviour is not a wish from the one with PWS.
- Difficult behaviour is painful for the one with PWS
- Difficult behaviour can not be cured with medication alone
- Analyse: when and why it happened, which changes were there

Psychiatric diseases

- Can arise in all. Can arise in all ages
- Be aware of changes in mood and behavior
- Can be because of physical illness or because of psychiatric diseases
- Depression can be seen: symptoms: loss of energy
- Dementia: symptoms : loss of skills..... Important difference to depression
- Psychoses can arise
- Psychiatric diseases can be treated with medication, must be diagnosed
- Medication must be started with low dose, to avoid side effects

DEMENTIA?

Definition: Changes that are persistent and interfere with activities of daily living and social interaction in:

- Memory- impaired or loss
- Cognition- loss or reduced abilities in doing tasks that they are normally capable of doing.
- Personality- change from the usual

DEPRESSION?

Definition: A mood disorder that causes persistent feelings of sadness or loss of interest

- Memory- may be impaired
- Cognition- slow thinking but typically are still able to perform tasks correctly
- Personality- may see low energy, sadness or fluctuation in mood – anger, anxiety

PWS Aging Signs Checklist for Residential Care Providers

Monthly / Quarterly Observation Tool

Cognitive & Mental Health Changes

| | |
|--|-------------------------|
| Increased confusion or forgetfulness | Neuropsych eval |
| Decline in problem-solving or planning | Track cognitive tasks |
| Changes in language or word finding | Speech therapy referral |
| New or worsening anxiety or fears | Psychiatry consult |
| Withdrawal from preferred activities | Behavioral health |
| New or worsening OCD behaviors | Medication/CBT review |

Mobility & Physical Function

| | |
|--|--------------------------|
| Decrease in walking speed or endurance | PT referral |
| Increased falls or unsteadiness | Fall risk assessment |
| Loss of muscle tone/strength | Review GH, PT plan |
| Difficulty with stairs, rising from chairs | Functional mobility plan |
| Worsening scoliosis/postural changes | Ortho review |

Cardiovascular and Metabolic Health

| | |
|--------------------------------|-----------------------|
| Fatigue or shortness of breath | Cardiology workup |
| Swelling in legs or ankles | Check cardiac/kidney |
| New/worsening hypertension | Medication review |
| Changes in cholesterol/glucose | Lab monitoring |
| Unexplained weight loss | Nutritionist referral |

Bone Health & Endocrine Signs

| | |
|---------------------------------|------------------------|
| Frequent fractures or bone pain | DEXA scan |
| Shortened height/spine changes | Endocrine consult |
| Loss of GH therapy benefits | GH dosing review |
| Signs of menopause/andropause | Hormone panel |
| GI slowdown or constipation | GI consult/diet review |

Sleep & Breathing

| | |
|----------------------------------|---------------------------|
| Increased daytime sleepiness | Sleep study |
| Snoring or apnea symptoms | BiPAP/CPAP review |
| Resistance to sleep equipment | Re-education/device check |
| Frequent waking during the night | Sleep hygiene adjustment |
| Morning grogginess | Adjust sleep schedule |

Sensory & Neurological Health

| | |
|---------------------------------|---------------------|
| Vision changes | Eye exam |
| Hearing issues | Audiology referral |
| New tremors/coordination issues | Neuro consult |
| Headaches, dizziness, seizures | Urgent medical eval |

Social, Emotional, and Behavioral

| | |
|--------------------------------|---------------------------|
| Reduced social interaction | Increase engagement |
| More rigid/resistant to change | Behavioral support |
| Regression in self-care | OT reassessment |
| Increased emotional outbursts | Medication/therapy review |
| Paranoia or psychosis symptoms | Urgent psych referral |

What to do:

Yearly medical visits and blood tests

- Secure regular medical evaluation and treatment when needed.
- Yearly evaluation of the diet, must be individualized
- Blood tests yearly for:
 - Blood sugar level (diabetes?)
 - Hormones : testosterone(men) estrogen (women), thyroids (both)
 - Vitamin D, calcium
- Other investigations
 - Sleep studies
 - DEXA scan if obese in some cases

And not to forget

- Dentist every $\frac{1}{2}$ year, or more often if needed
- Vision:
 - need of glasses , test every 2-3 year after age 40
- Hearing:
 - test hearing after age 40 and then every 2-3 year, especially if there is a family history of hearing problems

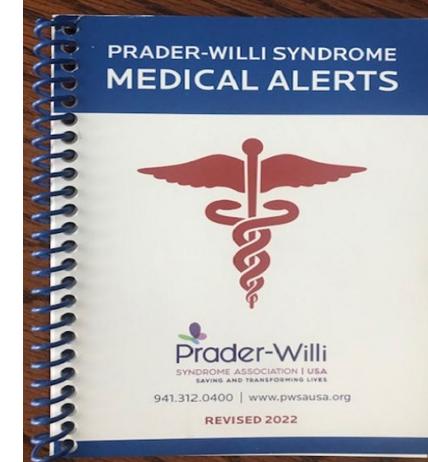
In difficult situations

- Insist for medical evaluation :
- When no wish to eat, vomiting
- Being ill, is behavior suddenly different. ?
- Swollen bones: fractures ? : insist for X ray
- Have the one page with you, in all languages:
[Important Medical Facts about Prader-Willi Syndrome - IPWSO](#)

Have written information ready

www.ipwso.org

- The one page for acute situations
- [Important Medical Facts about Prader-Willi Syndrome – IPWSO](#)
- Alerts booklets: in many languages, bring when you travel
- [Medical Alerts Booklet – IPWSO](#)
- www.ipwso.org:
- Here you can have the documents translated into to your own language



Always remember

- Write a yearly report: the year book with printed photos
- What has happened during the year.
- How was the physical and mental function
- Family contact ?
- Any loss of skills, any diseases
- What did you enjoy ? What do you want to do ?





