PEDIATRICS

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Agenda

- Nutritional phases
- Diet
- GH
- Other endocrine issues
- Scoliosis
- Behavioral issues
- Supplements
- Questions

Syndroom treft één baby op 20.000

KORTRIJK – Veronique Denhaerinck (32) reist straks met haar eenjarige zoontje MaxMilan naar Amerika om groeihormonen. MaxMilan lijdt aan het weinig bekende Prader Willi syndroom, een afwijking in de chromosomen. Hoewel hij nu al veertien maanden is, heeft hij nog steeds de grootte van een baby van vier maanden. Zijn fysieke en mentale ontwikkeling is sterk vertraagd. Enkel groeihormonen kunnen die ontwikkeling vooruit helpen. Om de behandeling te financieren, organiseert mama Veronique allerlei benefietacties. © pagina 12

Baby MaxMilan moet naar Amerika voor behandeling met groeihormonen

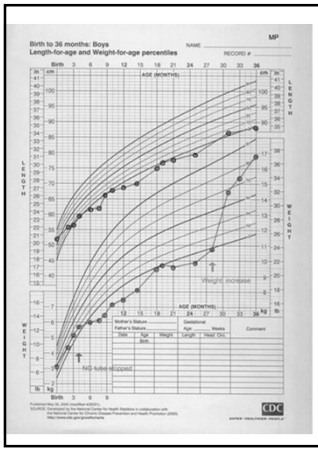
Nutritional Phases:

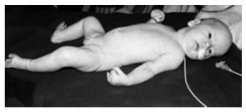
1a) Hyptonia with difficulty feeding *(0-6 mos.)*
- may also have FTT despite adequate calories
1b) No difficulty feeding, growing on curve *(3-24 mos.)*

2a) Weight ↑ without ↑ in cal.s *(1.5 - 3 yrs.)*
2b) Weight ↑ with ↑ in calories *(2 - 12 yrs.)*

3) Hyperphagic, rarely feels full *(3 yrs - adulthood)*

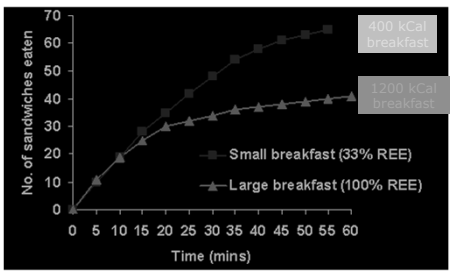
4) Prev. 3), but appetite is less now *(adulthood)*





Relative Resistance to Peripheral Satiety Signals in PWS IN nutritional Phase 3

Food intake during test lunch
3hrs after breakfast



19 yo PWS male, 52% body fat

Goldstone et al. *pilot studies*

Dietary Recommendations

- Beginning in Phase 2a we change the diet to be 30% fat, 45% carbohydrates, 25% protein with 20 grams/day of fiber
- This controls weight while requiring less caloric restriction.
- Also helps decrease body fat better than calorie restriction alone

Growth Hormone

History of Growth Hormone and PWS

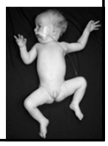
- First studies of GH in PWS were done in 1990's by Moris Angulo in the US and Martin Ritzen in Sweden.
- Both showed improvements in growth velocity and body composition with GH treatment.
- GH approved for use in children with PWS with "growth failure" in 2000.

History of Growth Hormone in PWS

- Many physicians quickly realized that not only children with growth failure could benefit from GH treatment, but that almost everyone with PWS could benefit, so it became widely accepted to start individuals with PWS on GH regardless of their growth pattern.
- Has been used off-label for infants, children without growth failure, and adults with PWS and has been shown to have multiple benefits aside from growth.
- GH improves body composition (decreases fat mass, increases muscle mass), increases bone mineral density, and improves respiratory parameters.

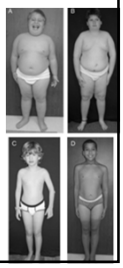
is it beneficial for infants to start GH treatment despite adequate growth?

- GH decreases ghrelin which is high even in infants with PWS, so may alter the natural course of the appetite progression in PWS.
- Data in PWS mice shows hypoglycemia and deficits in insulin secretion in infancy – GH increases insulin and glucose levels, which may be why it is beneficial for infants in terms of cognitive development.
- GH treatment shortens the initial failure-to-thrive phase of PWS



Other Benefits of GH for infants/young children

- Data from Carrel et al and Hokken-Koelega et al, shows that GH treatment for infants improves IQ and psychomotor development.
- We found that individuals treated with GH before age 1 had decreased fat mass, lower BMI, and higher resting energy expenditure as they age, compared to those treated after age 1, indicating that early treatment with GH may help prevent or ameliorate the obesity associated with PWS.



Cognitive function and growth hormone in pws – All ages

- IQ improved with growth hormone therapy (GHT) – those with most severe cognitive delays have the most improvement with therapy.
- GHT can attenuate the cognitive damage caused by hypoxia in animal models – unknown if this effect is present in humans.

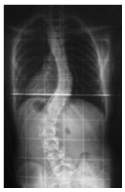
GH is NOT a cure for weight issues: ONLY diet and exercise work to control weight

Risks of GH treatment in PWS

- There are no difference in the causes of death between those who are treated with GH vs. those who are not.
- Major causes of mortality in PWS include: respiratory insufficiency or infection (61% of children), cardiac arrest, sudden unexplained death, infections, choking (5-8%), ruptured/necrotic stomach.
- Premature mortality peaks in newborn/early infancy and adulthood, increased in males – obesity is a factor in most.
- Therefore, we do need to be cautious when starting GH in infants and adults, to monitor closely especially during respiratory infections.

Other Issues with GH therapy

- **Scoliosis:** No evidence that GH treatment causes or exacerbates scoliosis, no matter what the age of treatment initiation.
- **Diabetes:** Massively obese or patients with a family history of diabetes should be monitored closely, but can be easily treated with an oral medication if occurs.



Other Concerns: GH

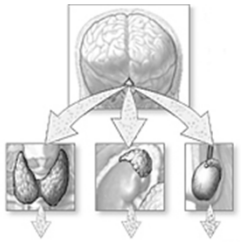
- **Respiratory Problems:** Individuals with sleep apnea prior to starting GH therapy should be seen by pulmonologist, GI, and ENT to determine confounding co-existing conditions. None of these conditions should cause endocrinologist to withhold GH treatment – just treat co-existing condition before starting GH.
- **Sudden Death:** Considerable evidence indicates that the risk of sudden death in PWS is the same with or without GH therapy.

IGF-1 Levels in pws

- Once individuals with PWS enter nutritional phase 2a, IGF-1 levels increase without a change in dose.
- Recent GRS meeting consensus: must tolerate IGF-1 levels 2 SDS above NL range for age to get maximum benefits of GH therapy.
- Decreasing GH dose to bring down IGF-1 levels decreases positive effects of treatment.
- IGF-I levels correlate with self-assessment of quality of life, IQ scores, and appetite assessment in adults with PWS.

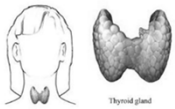
Van Nieuwpoort et al, 2011; Sode-Carlsen et al, 2010

Other Endocrine Issues



Hypothyroidism

- Central hypothyroidism is present in 15-25% of those with PWS.
- Primary hypothyroidism can also exist.
- Most often presents between ages 18-36 months of age.



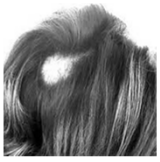
Adrenal insufficiency

- Investigated in PWS beginning in 2006 due to a high incidence of sudden death.
- Initial studies found evidence of central adrenal insufficiency (CAI) in 60% of children with PWS.
- Subsequent studies have found a lower prevalence.
- We have found 10% have CAI in our population. Similar numbers from France and the UK.

Hypogonadism

- Hypogonadism present in 87% of individuals with PWS.
- Can be due to hypogonadotropic hypogonadism, hypergonadotropic hypogonadism, or a combination.
- 4 women with PWS have had children.
- Thus far, no men have fathered children that we are aware of, but sperm counts have not been done on all adult patients.

Behavioral Issues

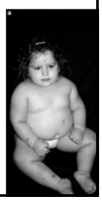


Temper Tantrums

- Common in toddlers with PWS just as in the general population.
- We recommend dealing with these issues the same way you would with any other child
- As children get older tantrums may become more related to food or anxiety
- Recommend speaking with psychologists/behavioral therapists who have experience with PWS to help stop these behaviors when children are older.

Obsessive-Compulsive Disorders

- Many individuals with PWS have compulsive and rigid behaviors.
- Over 60% of individuals with PWS collect, organize and arrange items compulsively, often spending over 1 hr per day engaging in these behaviors.
- Some question whether some of the eating issues in PWS are compulsive eating
- Skin-picking and nail biting are issues in PWS which may be compulsive as well.



Supplements

- N-acetylcysteine may help with OCD behaviors, specifically skin-picking
- Carnitine may help with energy level, alertness, and strength
- CoQ10 may help with daytime energy level
- Vitamin B12 – may help with daytime energy level and, anecdotally, speech
- Vitamin D – many kids with PWS are deficient – needs to be checked annually during winter to determine if supplementation is needed.

Lots done, more to do.

Famous Irish Political Slogan

Questions?