# Prader-Willi

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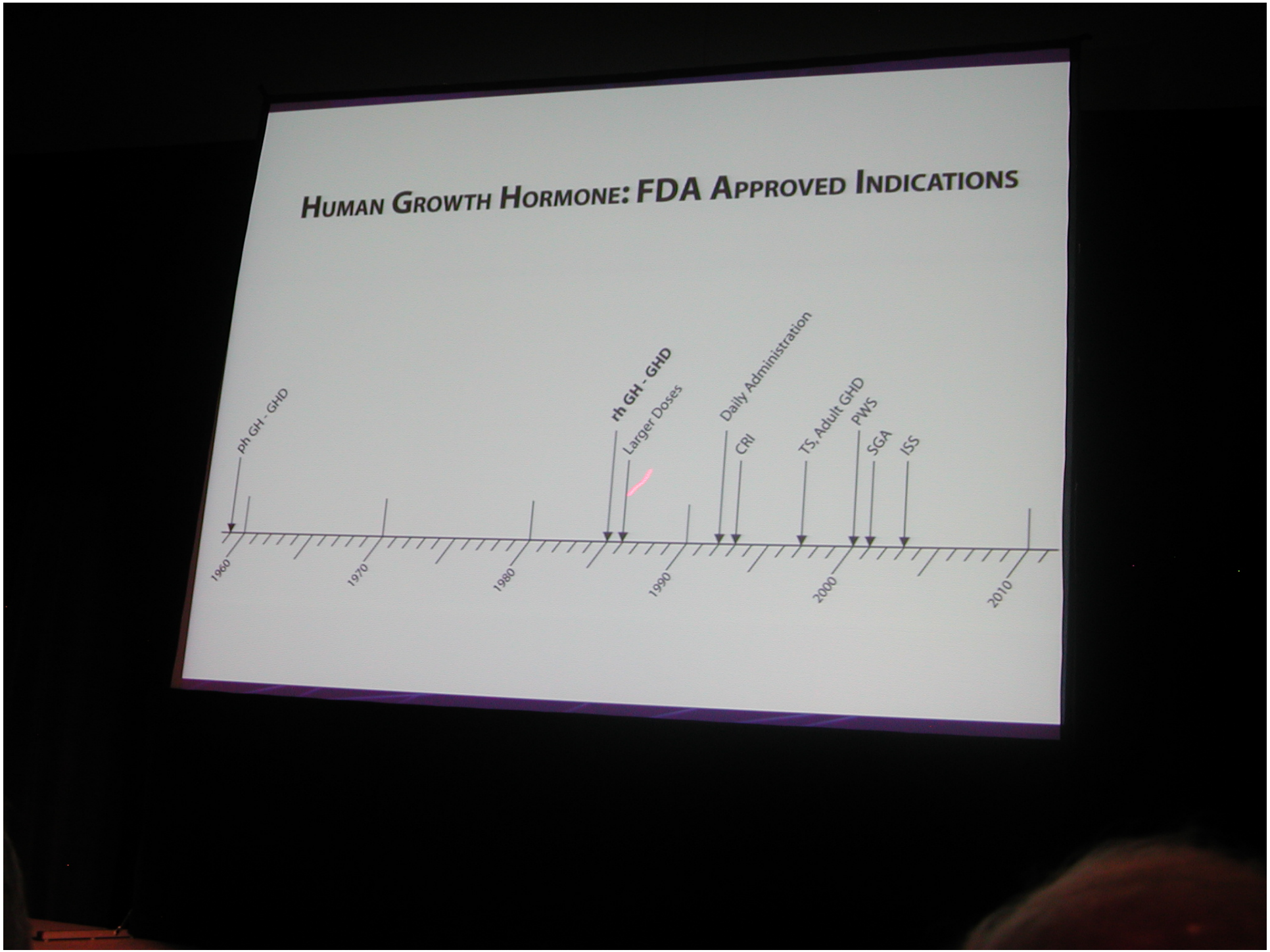
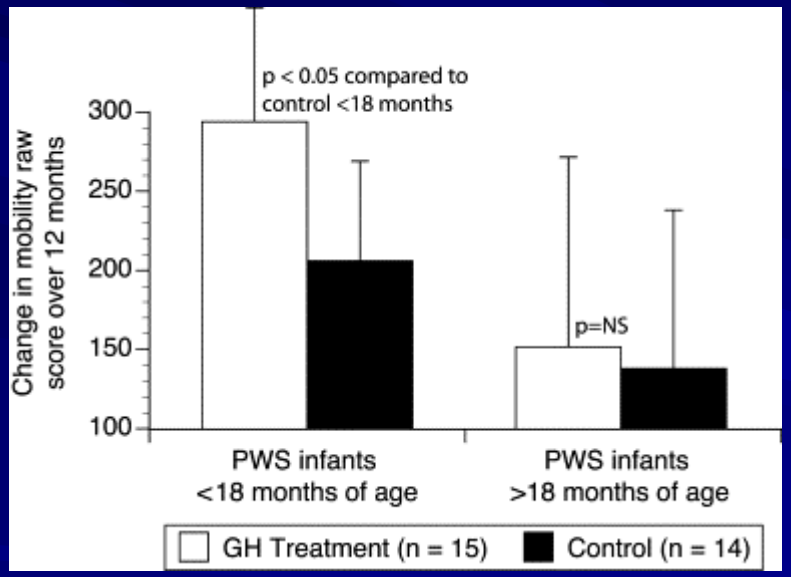
Tabarka 2006


HUMAN GROWTH HORMONE: FDA APPROVED INDICATIONS
ph GH - GHD
rh GH - GHD
Larger Doses
Daily Administration
CRI
TS, Adult GHD
PWS
SGA
ISS
1960
1970
1980
1990
2000
2010

# Growth hormone improves mobility and body composition in infants and toddlers with Prader-Willi syndrome

J. Carrel et al J. Pediatr.2004




Age-related comparisons of change in mobility scores over 12 months revealed a significant effect for GH for infants who began GH before 18 months of age, an effect that was not observed in toddlers who began GH after 18 months of age.

# GH therapy and mortality

Approval of GH treatment was obtained in 2000 by P&U, and the safety surveillance database registered 675 PWS patients treated with GH up until 2003.
However, fatal events after the start of GH therapy have been recently reported (within 6 months).

# GH therapy and mortality

| | n | sex | age (yr) | obesity |
|---|---|---|---|---|
| Nordmann, 2002 | 1 | m | 0.7 | no |
| Eiholzer, 2002 | 1 | m | 6.5 | yes |
| Pharmacia, 2003 | 4 | m | 6.2±4.9 | yes |

# GH therapy and mortality

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| Nordmann, 2002 | 1 | m | 0.7 | no |
| Eiholzer, 2002 | 1 | m | 6.5 | yes |
| Pharmacia, 2003 | 4 | m | 6.2±4.9 | yes |
| Van Vliet, 2004 | 1 | m | 4.5 | yes |
| Sacco, 2005 | 1 | m | 3.9 | yes |
| Grugni, 2005 | 2 | m/f | 6.3/3.8 | yes |
| Riedl, 2005 | 2 | f | 4.7/9.3 | yes |

J. Endocrinol. Invest. 28: 554-557, 2005


CASE REPORT

# Death during GH therapy in children with Prader-Willi syndrome: Description of two new cases

G. Grugni[1], C. Livieri[2], A. Corrias[3], A. Sartorio[1], and A. Crinò[4] on behalf of the Genetic Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology

[1]Division of Auxology, IRCCS "S. Giuseppe" Hospital, Italian Auxological Institute Foundation, Verbania; [2]Department of Health Sciences, University of Pavia, Pavia; [3]Department of Pediatric Endocrinology, University of Torino, Torino; [4]Unit of Autoimmune Endocrine Diseases, IRCCS "Bambino Gesù" Hospital, Roma, Italy

**ABSTRACT. A few cases of death worldwide during GH treatment in pediatric patients with Prader-Willi syndrome (PWS) have been recently described. The evaluation of further cases is needed to better identify possible causal mechanism(s), as well as to suggest some additional guidelines for prevention. We report the death of 2 additional children with genetically confirmed PWS in the first months of GH therapy. Case 1: This 3.9-yr-old girl was born at 39 weeks gestation. Low GH response to two stimulation tests was observed. GH administration was started at the age of 3.5 yr (0.33 mg/kg per week), when the patient was at 130% of her ideal body weight (ibw). Hypertrophy of adenoids was previously demonstrated. Snoring and sleep apnea were present before GH treatment, and did not increase during therapy. Four months later she died at home suddenly in the morning. Case 2: This patient was a 6.3-yr-old boy. He was born at term after an uneventful pregnancy. At the age of 6 yr, his weight was at 144% of his ibw. He showed reduced GH secretion during provocation tests, and GH therapy was started (0.20 mg/kg per week). The previously reported nocturnal respiratory impairment had worsened after beginning GH administration. Tonsils and adenoids hypertrophy were noted. At the age of 6.3 yr he died at home in the morning following an acute crisis of apnea. These additional cases seem to confirm that some children with PWS may be at risk of sudden death at the beginning of GH therapy.**
**(J. Endocrinol. Invest. 28: 554-557, 2005)**

# GH therapy and mortality

**Possible mechanism(s) by which GH treatment might contribute to this outcome in at-risk children include:**

- **Promotion of fluid retention leading to right heart failure;**
- **Promotion of growth of lymphoid tissue in the posterior pharynx resulting in airway obstruction.**

# GH therapy and mortality

**RISK FACTORS**

- Severe obesity
- History of respiratory impairment
- Sleep apnea
- Respiratory infection
- Gender (M:F= 3:1)

# GH therapy and mortality

According to these data, it has been recommended:

→ to perform polysomnography and ENT examination before and 6-8 weeks after starting of GH therapy;

→ in the case of hyperplasia of lymphoid tissue, adenoidectomy + tonsillectomy should be taken into consideration, either before or during GH administration;

# GH therapy and mortality

→ GH therapy might start with a lower dose, and dosage could be increased gradually on the basis of clinical response and instrumental assessment;

→ in the case of respiratory infection, GH treatment should be interrupted and aggressive therapy of the infection is mandatory;

→ a close cardiologic evaluation should be performed before and during GH therapy.

# PRADER-WILLI SYNDROME

~17 obese PWS children receiving rhGH have been died : however mortality in PWS treated with rhGH (0,4%) is likely no more and may even be less frequent than in an untreated PWS population (~ 2,6%)

Lee P GGH 22-17-2006

# Short-Term Effects of Growth Hormone on Sleep Abnormalities in Prader-Willi Syndrome

J Miller, J Silversein, J Shuster, DJ. Driscoll, M Wagner

J Clin Endocrinol Metab .2006

**Conclusions:** Most of our PWS patients had improvement after short-term GH treatment, but 32% had worsening of sleep disturbance. A subset of PWS patients are at risk during this window of vulnerability shortly after initiation of GH.

Because it is difficult to predict who will worsen with GH, patients with PWS should have PSA before and after starting GH and should be monitored for sleep apnea with upper respiratory tract infections. Otorhinolaryngological evaluation is warranted if sleep apnea worsens on GH.

IGF-I levels should be monitored, with the goal being physiological levels.