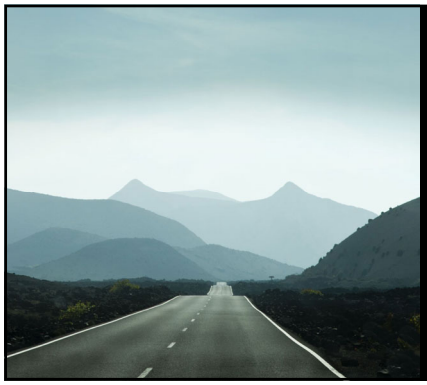

Use of GH in Silver-Russell Syndrome

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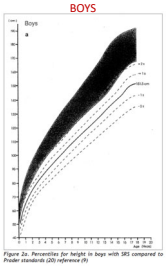
Conflict of Interest

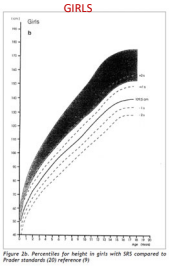
- None to declare

Post-Natal Growth

BOYS



GIRLS



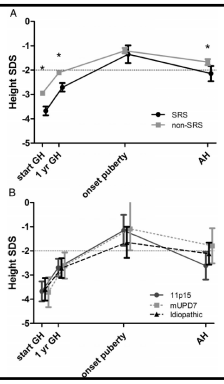
Wollmann and Ranke, Pediatric Endocinology Reviews 2017;15 (suppl 1): 85-91

Why should we treat SRS with rhGH?

- To improve final adult height?
- To enhance neurocognitive outcome?
- To improve quality of life?

Need to look at measured final adult height

- ❑ Accelerated tempo of puberty
- ❑ Decreased pubertal growth spurt



Smeets et al, JCEM 2016;101(5):2105-2112

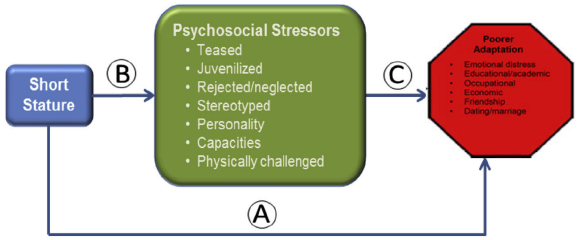
Why do we treat SRS? Facts about final adult height

- Average height of untreated patients are 151 cm for ♂♀ ♂ ♂ ♂ and 140 cm for ♀♀ ♀ ♀ .
- Based on 3 studies in patients with SRS
  - study 1: n= 26 with questionable dx
  - study 2: n= 37 treated vs 13 not treated with self reported FH
  - study 3: n= 26 with measured FH vs 159 non SRS controls

  Of note: 3 studies- average gain is 1 to 1.3 SDS.
- 3500 daily injections for an average increase of 4 to 10 cm

Wollmann et al, Eur J Pediatr 1995;154:958-968
Toumba et al, Horm Res Paediatric 2010;74:212-217
Binder et al, Horm Res Paediatric 2013;80:193-200
Smeets et al, JCEM 2016;101(5):2105-2112

Why do we treat? Behavioural and Cognitive Outcomes



Sandberg and Gardner, Pediatr Clin N Am 2015;62:963-982

Why do we treat? Behavioural and Cognitive Outcomes (SGA)

QoL/Behaviour

- 1997 (Dutch study) after 2 yrs TX: improvement behavior, and self-perception (went from below average to average)
- 2000 and 2005 (2 studies from same authors): GH improved QoL of SGA kids
- 2008: improved QoL after 2 years of TX
- 2011 study: QoL better in treated SGA

Of note:

- No consistent reliable standardized questionnaires and QoL still lower than AGA despite GH. Same cohort.
- High risk of bias on outcomes (particular lack of blinding, lack of concurrent control group, industry involvement sponsorship and positive publication bias)

IQ (COGNITIVE)

- 1997 (Dutch) : effect + on IQ
- 2008 (Belgium study) GH: no effect on IQ, Cognitive abilities, behavior.
- 2012 (Spain): no clinical effect of GH on IQ.

Of note:

Similar to kids born SGA IQ dependent on

- SES ($), Parental IQ ,severity of growth restriction

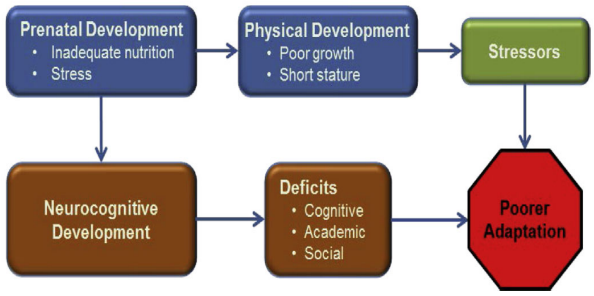
In sum: Probably non-conclusive evidence that GH affect IQ outcomes.

(SRS not always similar as SGA)

Why do we treat? Quality of Life

- Strong societal belief that short stature is detrimental to QoL (includes physicians)
- Studies supporting this mostly come from clinic samples
- Two large population-based studies:
  - SS not linked to psychosocial or academic disadvantage
  - Bullying not necessarily linked to negative effect of self-esteem or school performance
  - Marked SS not more likely to be picked on or socially isolated
  - Marked tall stature not related to any social advantage

Sandberg and Gardner, Pediatr Clin N Am 2015;62:963-982



Sandberg and Gardner, Pediatr Clin N Am 2015;62:963-982

Why do we treat? Impact of rhGH on Quality of Life for SGA

After 2 years of randomized trial:

- **50%** of parents of GH treated children report improved well-being

VS

- **50%** of parents of non-GH treated children report improved well-being

Legrou et al, Horm Res 2008;69:334-42

rhGH therapy economic evaluation

- Cost effectiveness usually set at a maximum of 35,000 to 50,000 CDN$

	Cost per QALY (CDN $)	Cost-effective at 50,000$
GH deficient children	39,400.00	95%
PWS	230,000.00	1%
TS children	67,000.00	19%
SHOX	69,000.00	15%
SGA children	56,200.00	38%

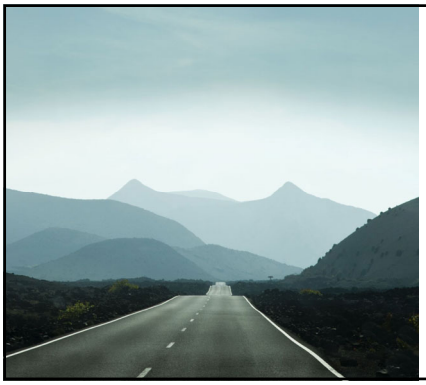
Takeda et al, Health Technol Assess 2010;14(42):1-209

What about unanswered potential risks of rhGH therapy?

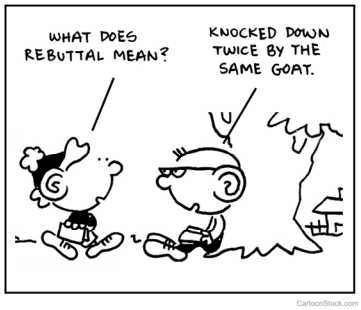
- These children may be at increased risk of sleep related breathing disorder — 87% of SRS with abnormal sleep studies and 5/12 worsened with rhGH initiation *
- Will the longterm exposure to increase levels of IGF-1 increased the risk of certain cancer later on in life?
- Potential increased risk of stroke?
- Could the longterm exposure to rhGH increase the risk of glucose intolerance/diabetes later in life?

* Giabicani et al, Sleep Medicine 2019;64:23-29

Evidence

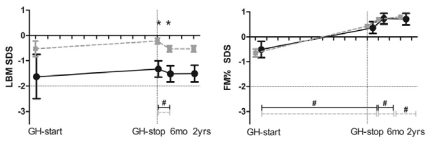


Think about it for a few seconds



Metabolic Health after rhGH discontinuation in SRS

Why do we treat? Metabolic outcomes



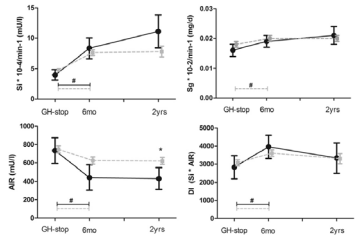
- **Compared SRS (n=29 black) to non-SRS SGA (n=171 gray)**
- **Average rhGH treatment duration 10 yrs**
- **Assessed at rhGH start, end, 6 months and 2 years after**

Smeets et al JCEM 2017;102(3): 983-991

Metabolic Health after rhGH discontinuation in SRS

- In both groups, none classified as metabolic syndrome
- Changes reported in BP, lipids, glucose homeostasis and renal function in SRS all within the norms

Glucose Homeostasis



Smeets et al JCEM 2017;102(3): 983-991

rhGH in childhood will likely not have any major impact on longterm metabolic health

Why should we treat SRS with rhGH?

- To improve final adult height? ? ✓
- To enhance neurocognitive outcome? ✗
- To improve quality of life? ✗
- To improve metabolic outcomes? ✗

Hormones to make a medically healthy short kid taller: Confidence booster or 'child abuse'

"That becomes the ethical dilemma," he said. "We have in our hospital spectacular plastic surgeons who do surgery that changes the appearance of kids who have serious malformations. You wouldn't call that cosmetic. So if somebody is going to be … 4'8" versus 5 ft., I don't think you can call that simply cosmetic."

"Is that any different than taking a three-year old child and injecting growth hormone daily?" he asked. "That's child abuse, in my opinion, if the child doesn't really need it."

National Post September 7, 2012


I'm now going to open the floor to questions.