

Management of Pituitary Disorders in Pregnancy

Laurence Katznelson, MD

Professor of Medicine and Neurosurgery

Stanford University School of Medicine



Outline

- 1) Impact of hypopituitarism on pregnancy outcomes
- 2) Impact of hypopituitarism on fertility
- 3) Value of Growth Hormone on fertility
 - a. Normal pituitary subjects
 - b. Hypopit subjects
- 4) Management of other replacement regimen in pregnancy
 - a. GH replacement
 - b. Thyroid, glucocorticoid, desmopressin
- 5) Acromegaly, Prolactinoma

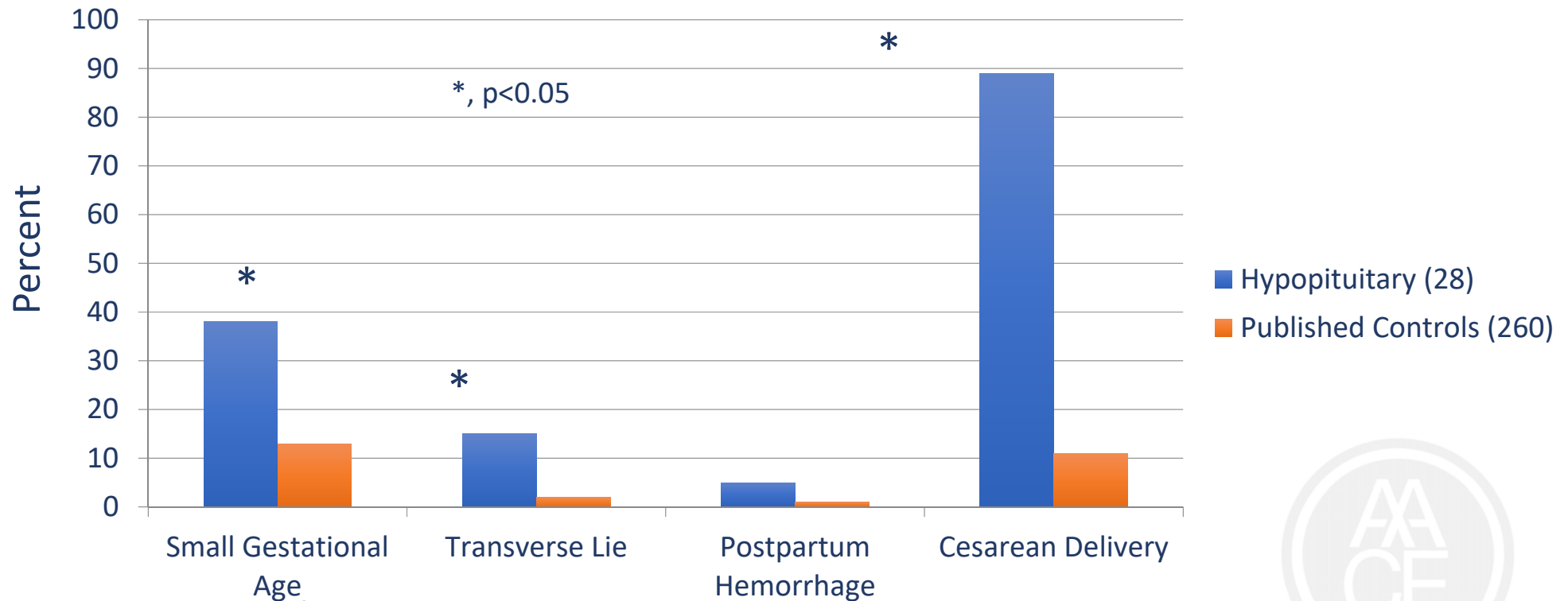


Case 1

- 29 yo female, 4 yr ago had excision of a nonfunctioning pituitary macroadenoma.
- Panhypopituitarism: on Synthroid 112 mcg, Hydrocortisone 15/10 mg, OCP, DDAVP 0.2 mg po tid.
- She is adequately replaced
- No diabetes insipidus
- Has mild fatigue and increase in abdominal girth, with low IGF-1
 - decided not to use GH replacement.
- Amenorrhea with undetectable gonadotropins
- She asks about fertility



Pregnancy outcomes in hypopituitarism



- Retrospective review of 31 pregnancies in 27 women
- Higher rates of C-xn: oxytocin deficiency?



Hypopituitarism and Pregnancy: High Risk Pregnancies

- In 18 pregnancies in 9 hypopit women,
 - live birth rate was 61%, miscarriage rate 28% and mid-trimester uterine death rate 11% with no survivors from four sets of twins.
 - Caesarian section rate was 100%
 - Half of the live births were on or below the 10th centile for weight.
 - Overton et al (2002) Hum Repro. 17:464



Hypopituitarism and Pregnancy

- Hypoprolactinemia may result in insufficient milk production to nurse
 - Overton et al (2002). Hum Reprod. 17:1464



Hypopituitarism and Fertility

- Will require gonadotropin therapy with hypogonadotropic hypogonadism
- Role of an intact GH/IGF-1 axis?
- GH:
 - Binds to granulosa, thecal and luteal cells
 - Enhances steroidogenesis
 - Affects maturation of the follicle and gamete
 - Recruitment of follicles
 - Inhibits follicle apoptosis



GHD and Fertility: Role of GH

- *Giampietro et al, Fer Ster (2009) 91:930.e7*
 - 6 successful pregnancies in 4 eugonal women with GHD
 - Followed for infertility
 - Pregnancies occurred after GH replacement
 - GH stopped after conception
 - *Routine role in such patients?*



GH and Fertility

- In hypogonadotropic hypogonadism, reasonable to consider GH replacement
- Impact on fertility?



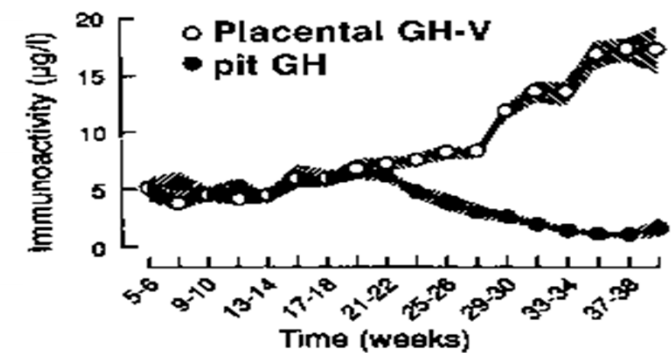
- If GH replacement is administered and the patient becomes pregnant, how long to continue it?



Growth Hormone Deficiency and Pregnancy

- There are few data
- Most recommend stopping GH replacement at conception
- Continue GH replacement through the 1st half of pregnancy only?
- No consensus on this

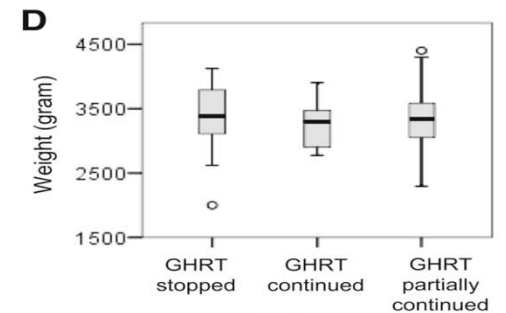
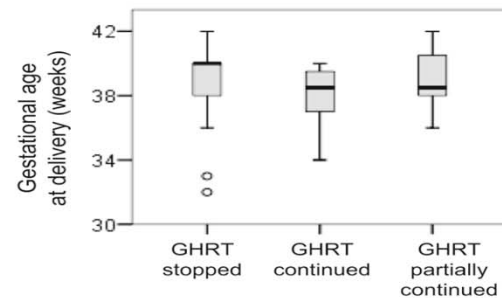
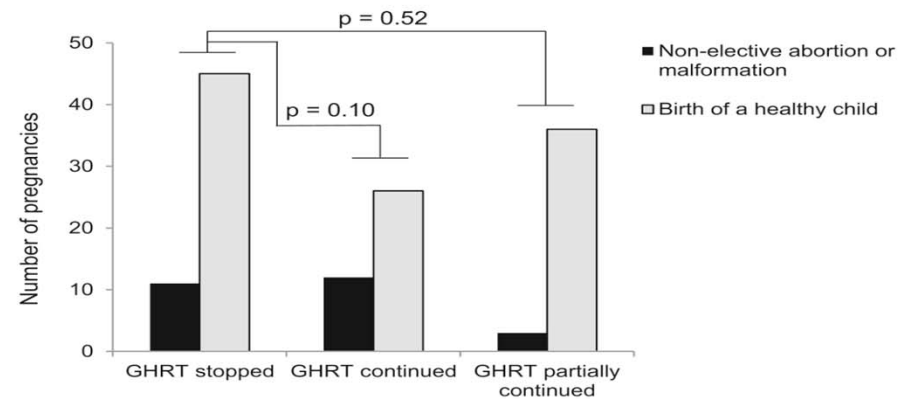
Frankenne et al, 1988, JCEM 66:1171



Do patterns of GH replacement impact pregnancy outcomes?

Vila et al, Fert Ster (2015)

- Outcome data in 139 pregnancies with GHD
- No relationship between GH regimen and pregnancy outcomes



GH replacement in pregnancy?

- Fleseriu et al (2016) JCEM. 101:3888
- Endocrine Society Guidelines
- **We suggest discontinuing GH replacement during pregnancy because there is no clear evidence yet for efficacy or safety, and the placenta produces GH.**
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- **Changes in other hormones**



Thyroid Hormone replacement in Pregnancy

- Increase LT4 per standard thyroid/pregnancy management
 - Increase by 30% (2 tabs per week)
- Monitor every 4 weeks until mid-gestation and at least once near 30wk GA



Treatment of Central AI in Pregnancy

- GC doses usually stay the same during pregnancy
- Some authors suggest an increased dose of HC (by approximately 20–40%, i.e. 5–10 mg) during the third trimester because of the natural increase in free cortisol
 - *Lebbe and Arlt. Clin Endo 2013 78: 497*
- In contrast to HC, dexamethasone is not degraded by placental 11 β -HSD 2: use HC
- During labor, stress GC doses and then tapered over 48h
 - *Lindsay JR, Nieman LK, Endocr Rev. 2005;26(6):775.*



Diabetes Insipidus Management

- Between week 8 and midpregnancy, placental vasopressinase increases ADH clearance.
 - Enzyme activity peaks in the third trimester, and then falls to undetectable levels 2-4 wks postpartum.
 - In most pregnant women, plasma concentrations of ADH remain in the normal range because of a compensatory increase in ADH production by the pituitary gland.
 - May need higher DDAVP doses
 - No evidence of DDAVP induced stimulation of blood pressure or uterine contractions



Back to case

- The patient discontinued the OCPs and underwent ovulation induction with gonadotropin therapy
 - Unsuccessful first cycle
- She initiated GH at replacement doses and achieved a mid-normal IGF-1 level over 3 mos
- She underwent repeat ovulation induction
 - 3rd cycle was successful



Back to case

- She continued GH through 12 weeks, then stopped.
- Synthroid dose increased by 30% at conception
- HC maintained on same dose
- DDAVP dose increased to manage polyuria
- Pregnancy and delivery uncomplicated



Prolactinoma and Pregnancy

- Discontinue the DA with conception
 - Unless the tumor is invasive or is abutting the optic chiasm
 - Bcrt, not CBG, approved by FDA for conception
- No value for measuring serum prolactin
- Serial visual field testing
 - Normal gland expands in pregnancy
 - Risk of symptomatic enlargement of macroadenoma 31%
 - Gillam et al (2006) Endo Rev. 27:485
- Recc bcrt if there is symptomatic growth during pregnancy
 - Melmed et al (2011). JCEM 96:273



Acromegaly and Pregnancy

- Discontinue long-acting SRL formulations and pegvisomant approximately 2 months before attempts to conceive, with use of short-acting octreotide as necessary until conception.
- During pregnancy, withhold acromegaly medical therapy and administer only for tumor and headache control.
 - Short-acting octreotide
 - Cabergoline
- Serial visual field testing in patients with macroadenomas.
- No use for monitoring GH and/or IGF-1 levels during pregnancy.

