Observations from Camden

- Maternal growth, and the competition for nutrients
- Gestational weight gain
  - Leptin, insulin and other hormones

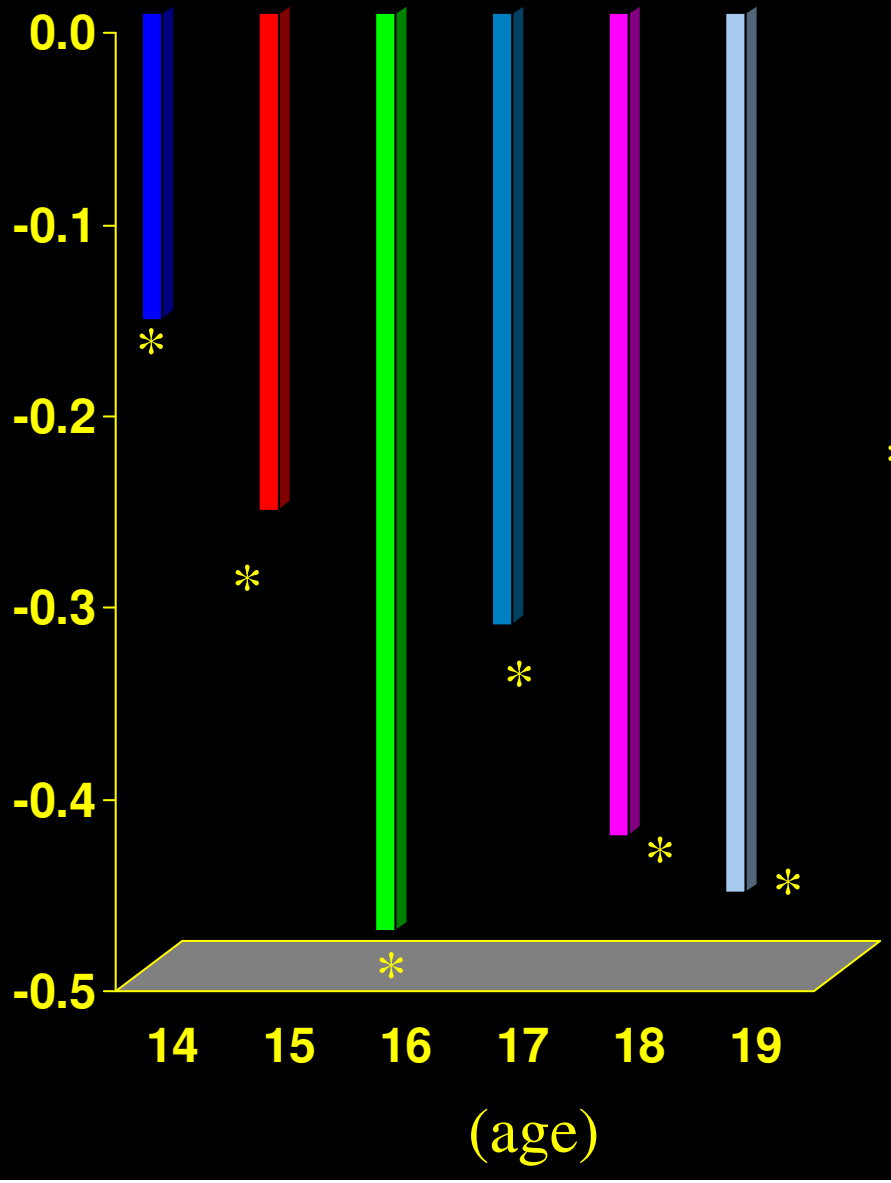
Adolescent Pregnancy

In 1981 Richard Naeye (Pediatrics 67, 1981) suggested that early childbearing might engender competion for nutrients between mother and fetus

The young mother was not mature enough for successful pregnancy

The infant was more likely to be “premature”

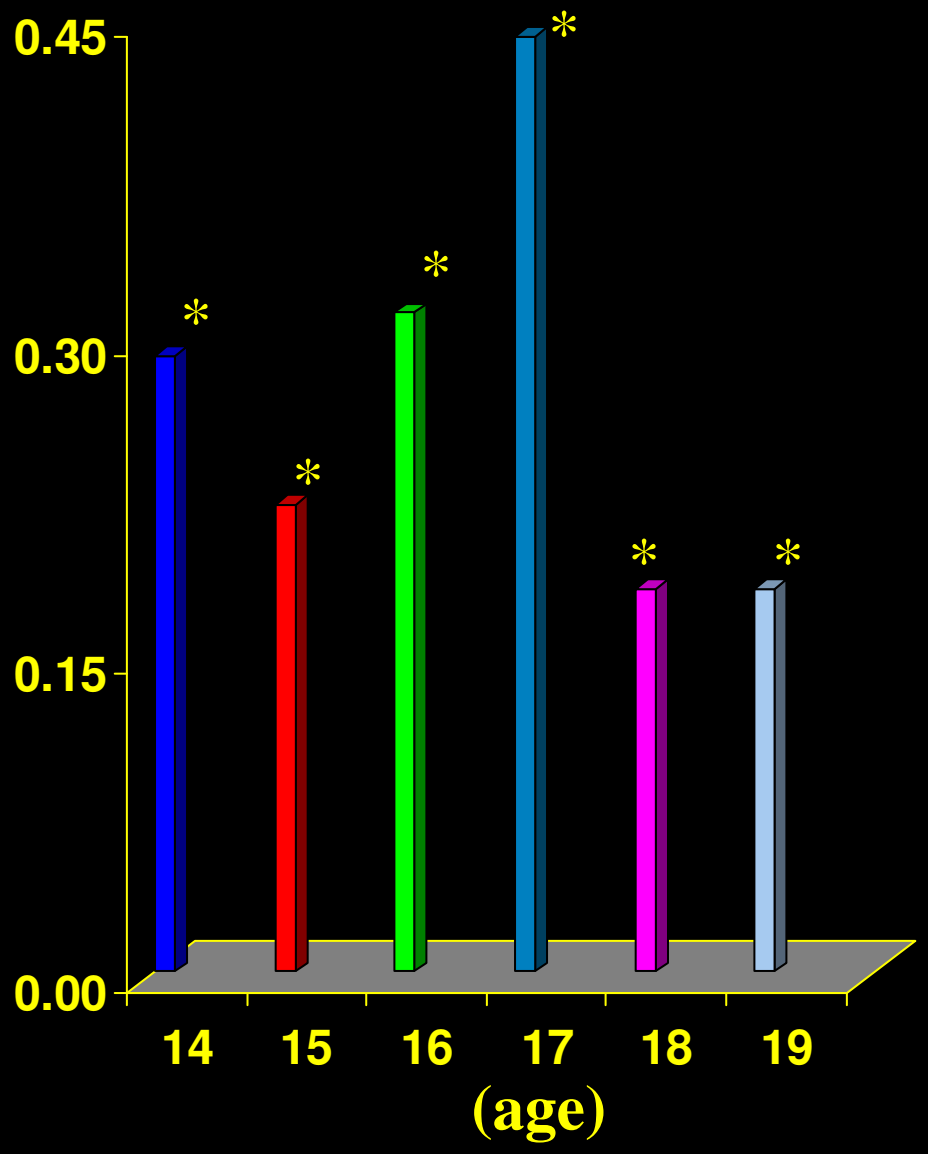
Stature Increments by Maternal Age



- **When stature is measured during pregnancy, there is "shrinkage" at every age**
- **Decrements are less for teenagers than mature women**
- **Tendency to "shrink" probably due to**
  - **lordosis**
  - **vertebral compression**
  - **weight gain**

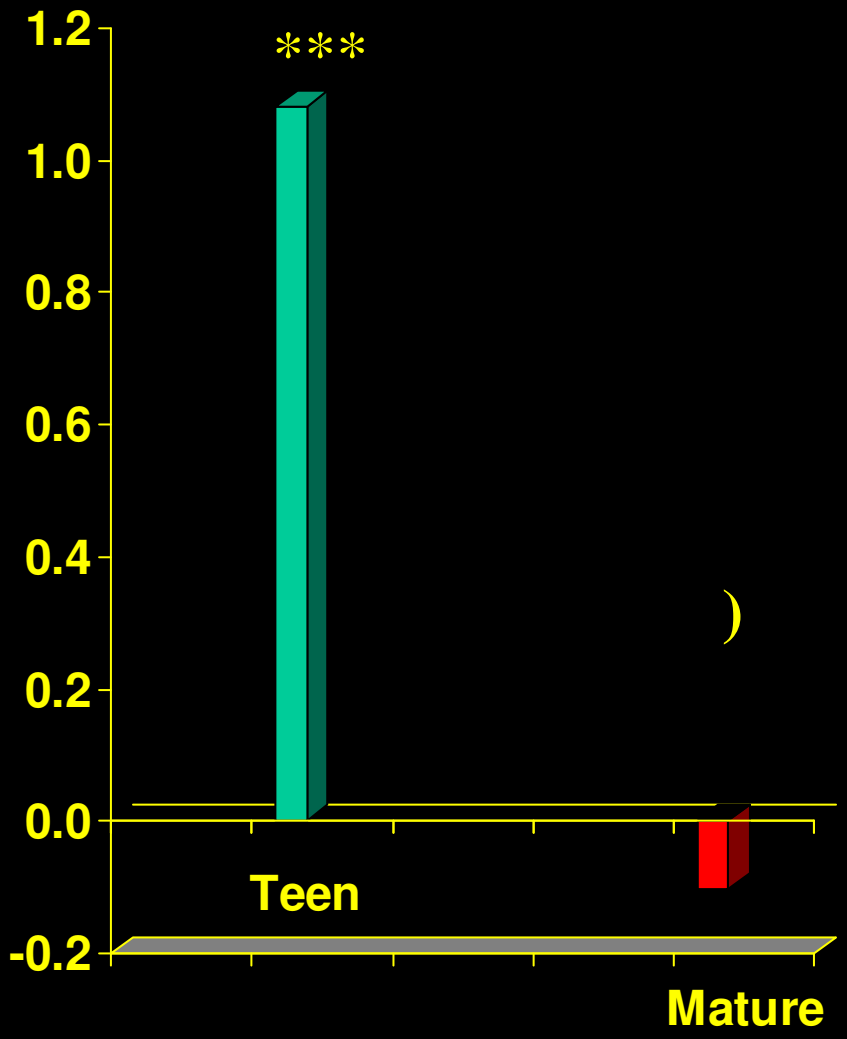
p<.05 * vs zero

Stature Rebound



- **Stature rebounds by 6 months postpartum but the amount is variable**
- **Regardless of age, some patients measure taller or shorter compared to entry stature**
- p<.05 * vs zero

Six Month Knee Height Velocity



Teenage gravidas have positive KHMD increments. Mature gravidas do not

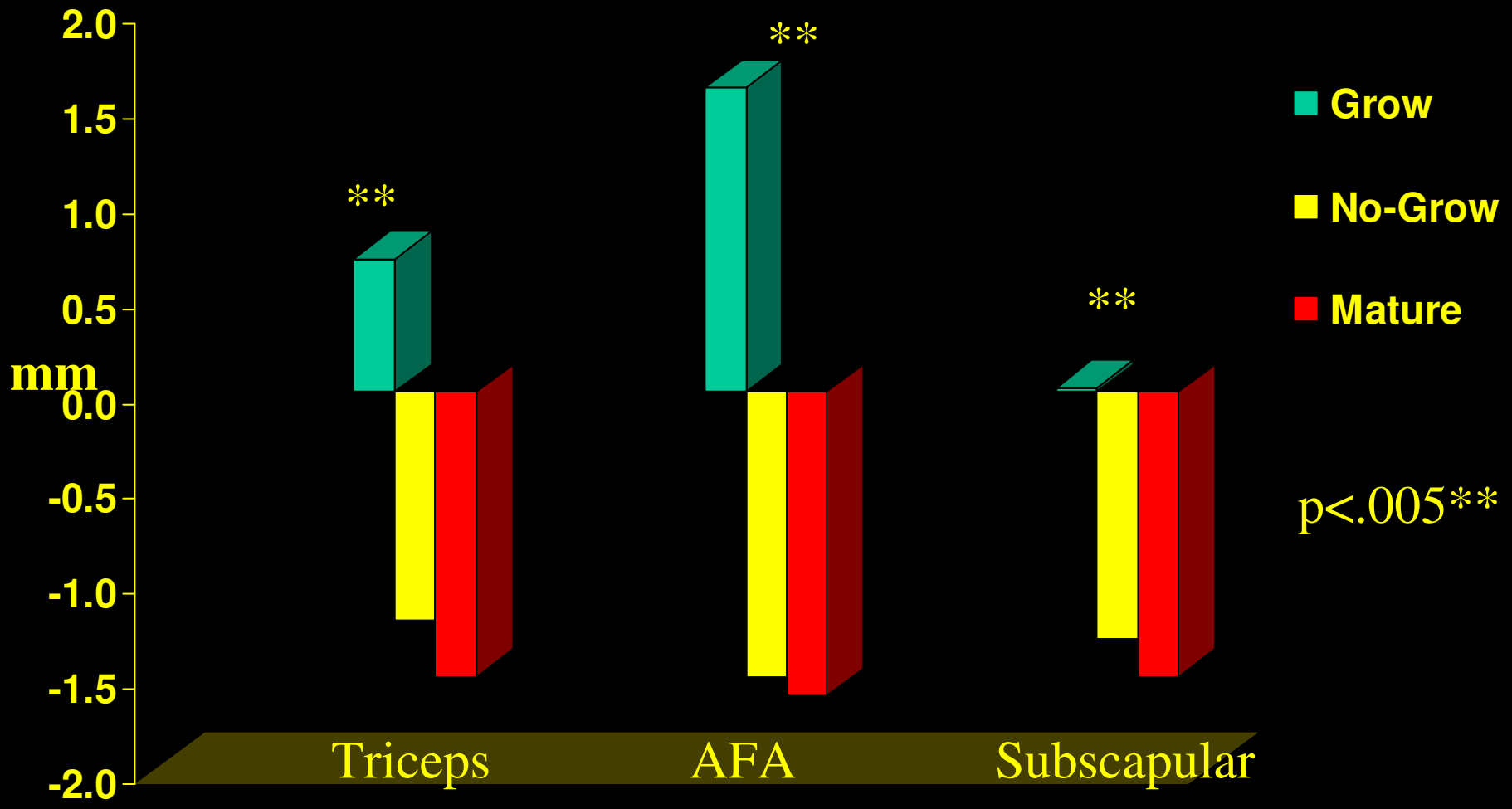
- **Maternal growth indexed by a six month knee height velocity ≥ 1 mm (2X error)**
- **30- 50% of teens grow during pregnancy**

p<.001 ***

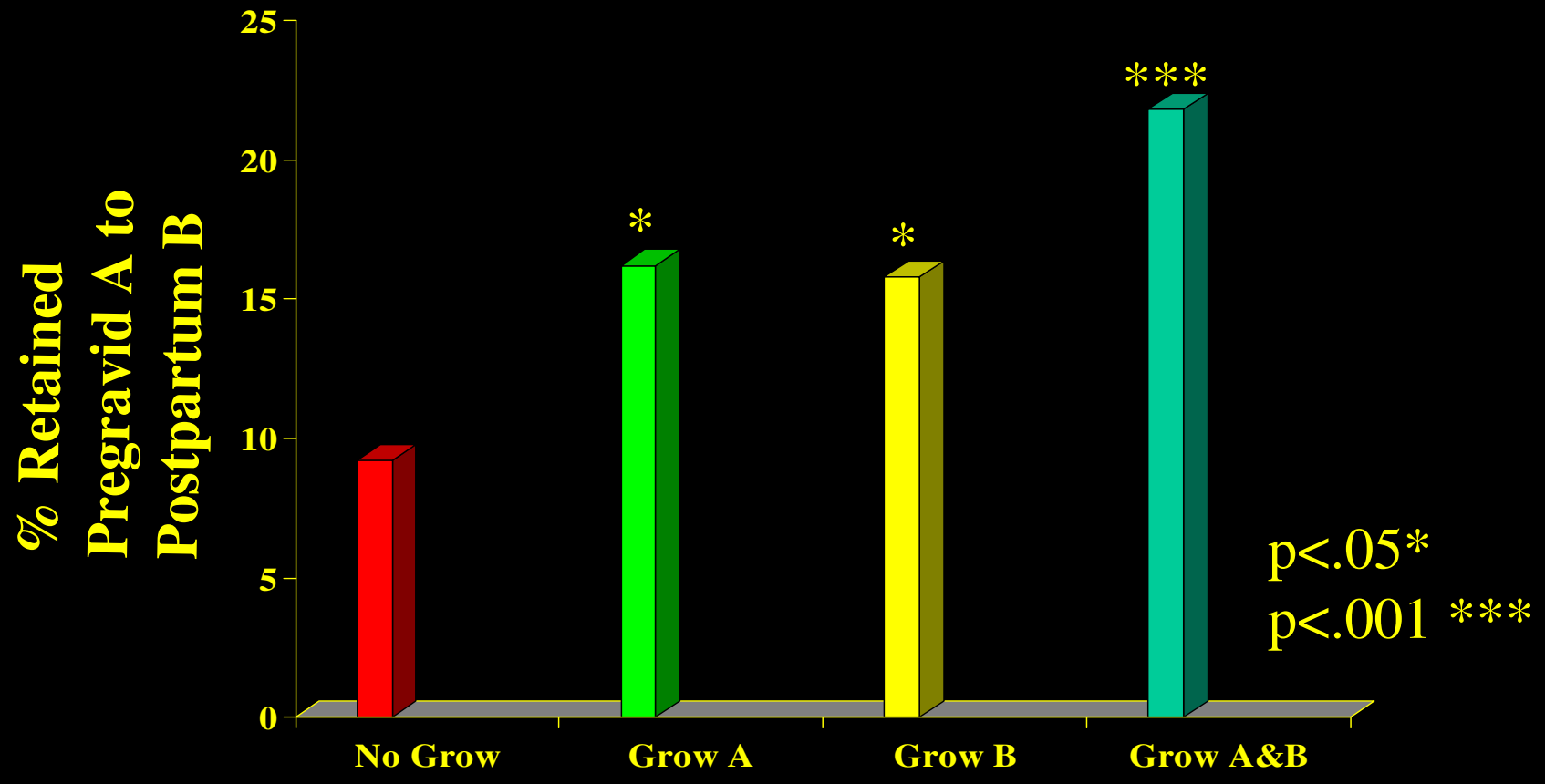
Maternal Anthropometry

- Anthropometric data are adjusted for the following potential confounding variables
  - maternal age
  - ethnicity
  - parity
  - gestation at measurement
- Data on gestational weight gain and weight retention are also adjusted for
  - gestation duration
  - pregravid BMI

Arm Fat Area, Triceps & Subscapular Skinfolds: Changes With Pregnancy



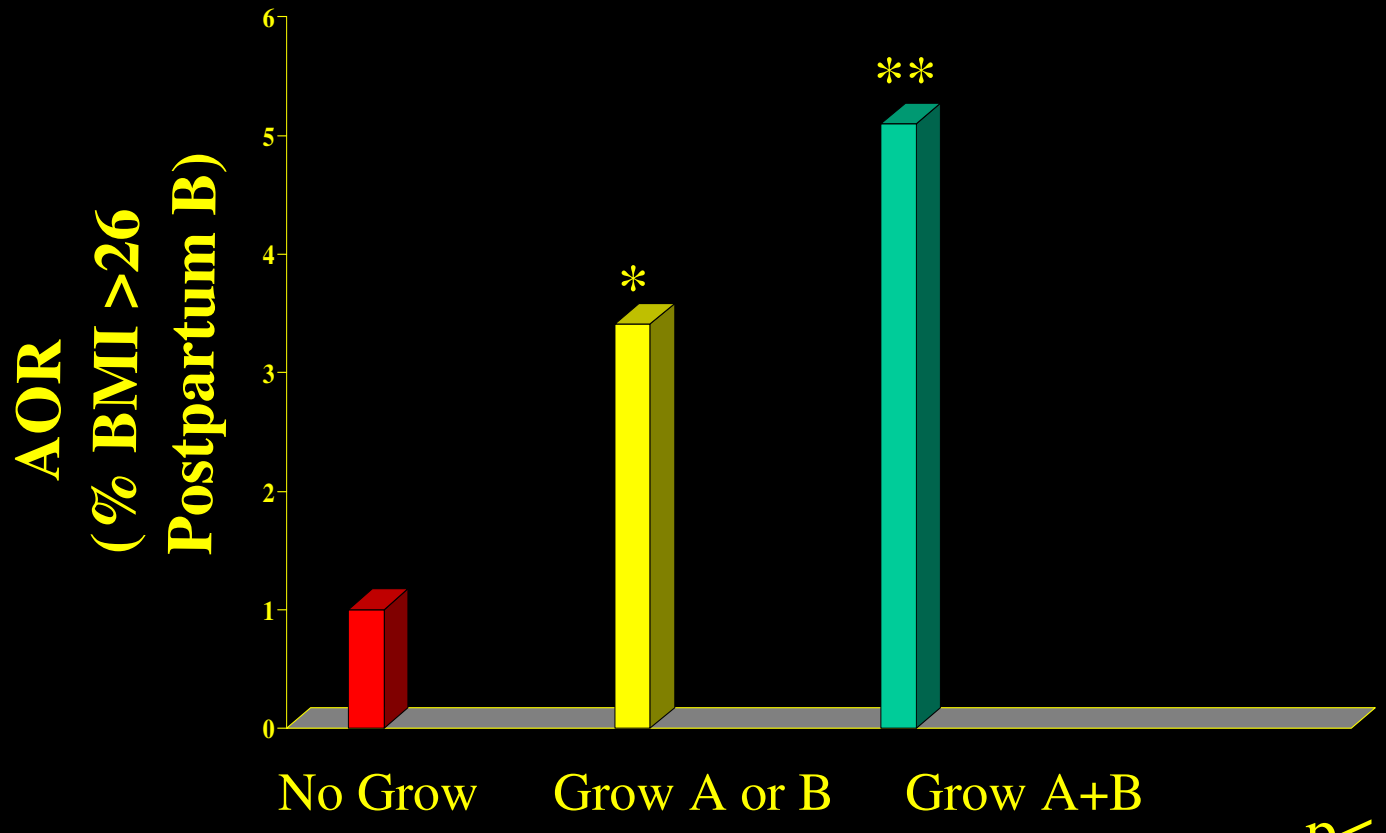
Growth During Two Pregnancies: Postpartum Weight Retention



Adjusted for maternal age,#pregnancies,ethnicity and cigarettes/day.

Women with pregravid BMI >26 at pregnancy A are excluded

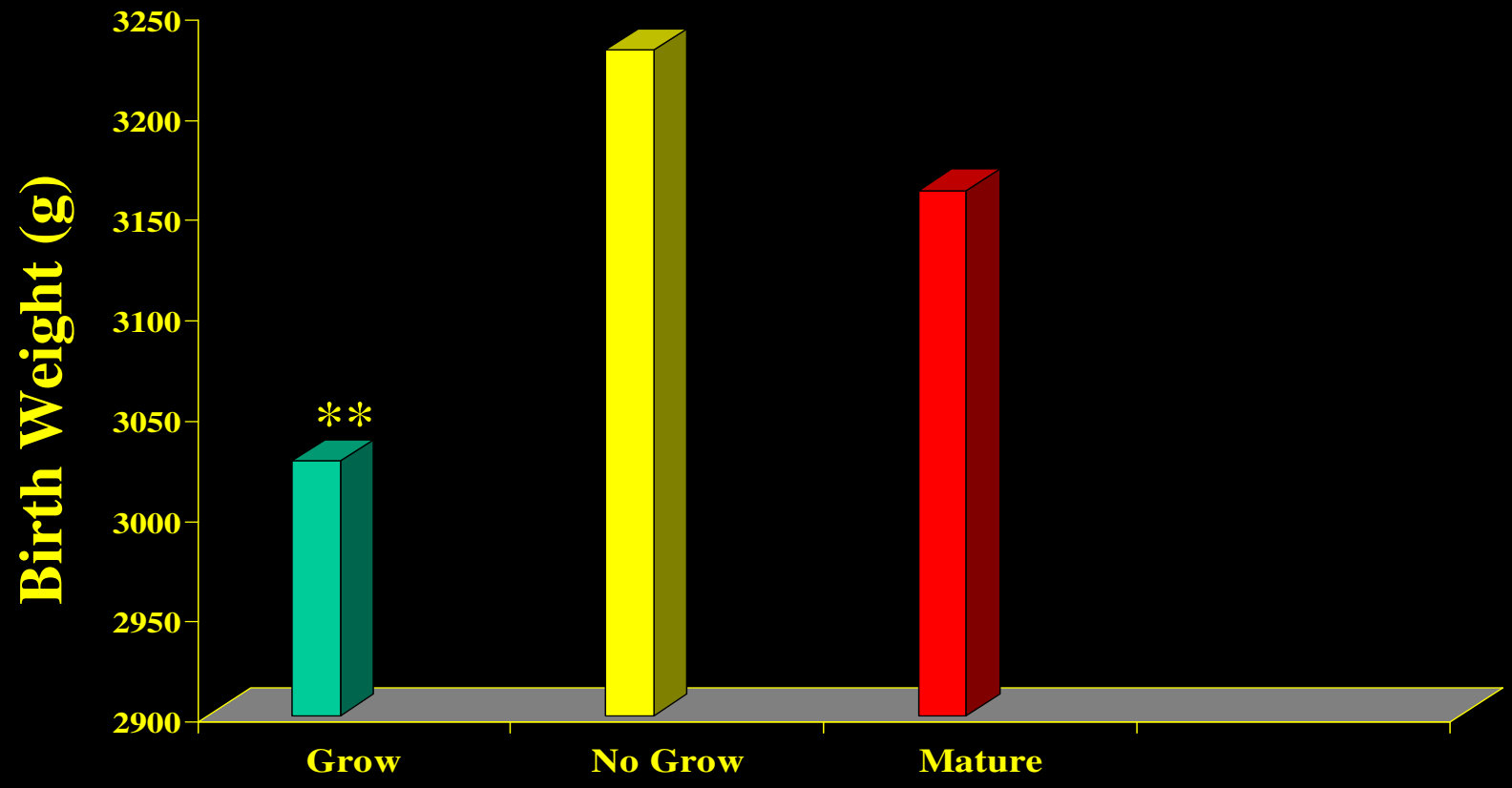
Risk of New Postpartum Overweight/Obesity with Maternal Growth in One or Two Pregnancies



Adjusted for maternal age,ethnicity, smoking ,#pregnancies

p<.001**
p<.05*

Maternal Growth by KHMD Birth Weight



Adjusted for age, parity, ethnicity,weight gain, prior poor outcome, pregravid BMI, cigarettes/day

p<.01 **

Summary

Teenagers who grow while pregnant

- have greater weight gain
- bear infants 150-200 grams smaller
- retain more of the weight they gain in pregnancy
- retain more subcutaneous fat
- diet is not different

Summary

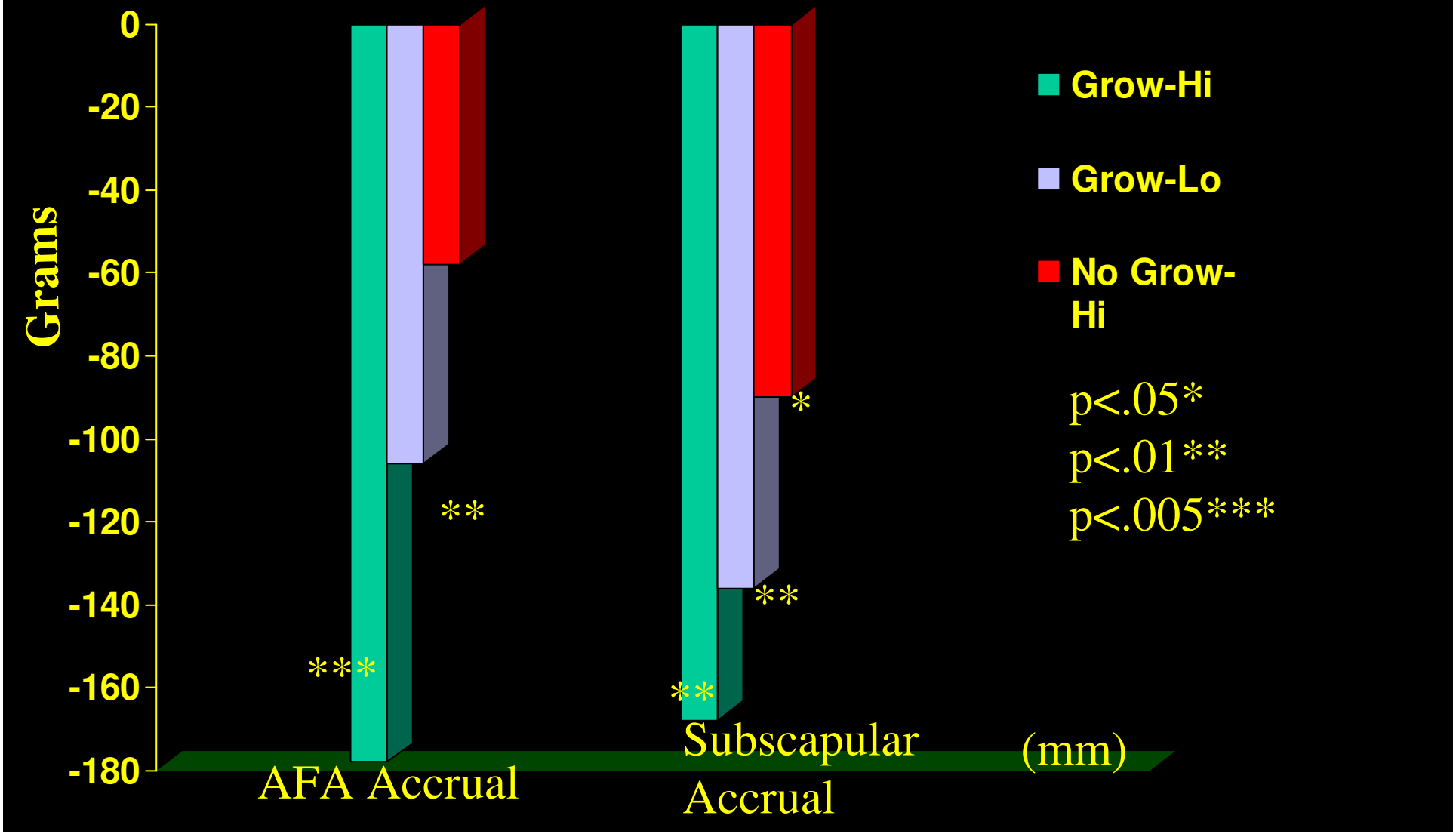
- Metabolic demands of the young mother appear to take precedence over nutrient demands for fetal growth

  - **Maternal stores not mobilized during 3rd trimester**
  - **Reserved for continued development of still-growing gravida**
  - **Additive effect when gravida grows in another pregnancy**
  - **Increased risk of "new" overweight (BMI >26)**
    - **3 fold increase with growth in one pregnancy**
    - **5 fold increase with growth in two pregnancies**

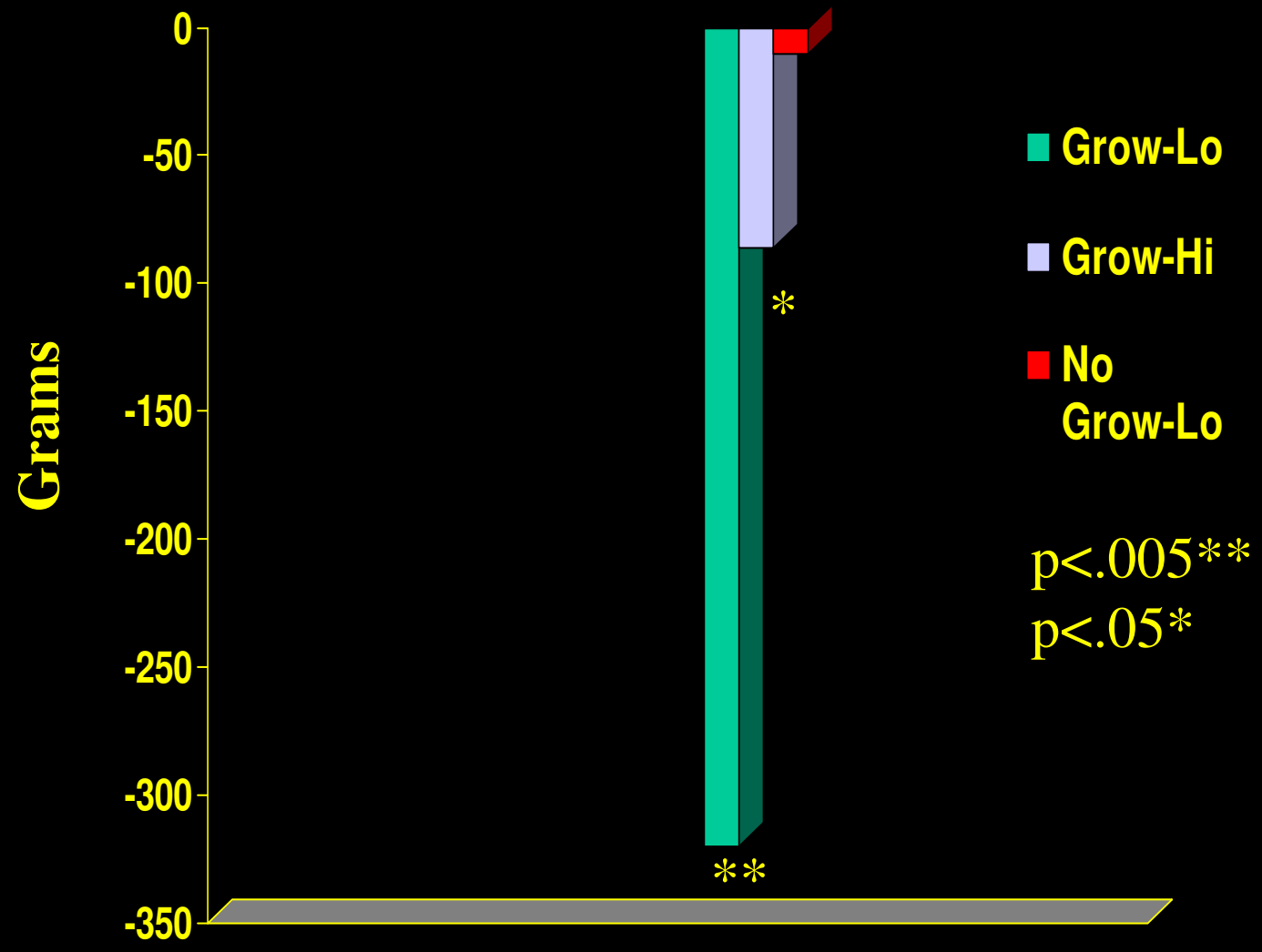
Influence of Maternal Growth, Fat Accrual and Energy Intake on Infant Birthweight

- Data are adjusted for the following variables:
  - maternal age
  - parity
  - ethnicity
  - gestation duration
  - pregravid BMI
  - gestational weight gain
  - prior poor outcome
  - cigarettes smoked daily

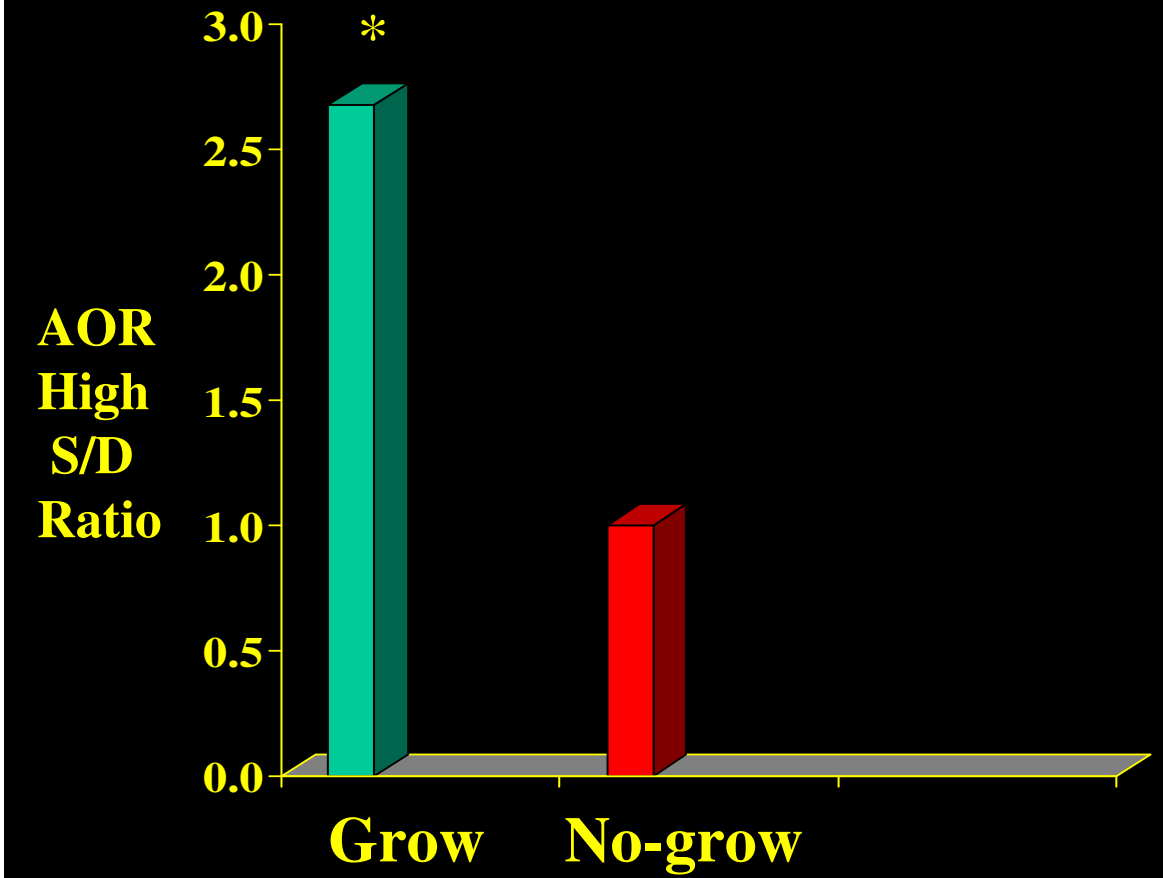
Influence of Maternal Growth &Fat Accrual on Infant Birth Weight



Influence of Energy Intake on Birth Weight by Growth



Maternal Growth and High Umbilical Artery S/D Ratio



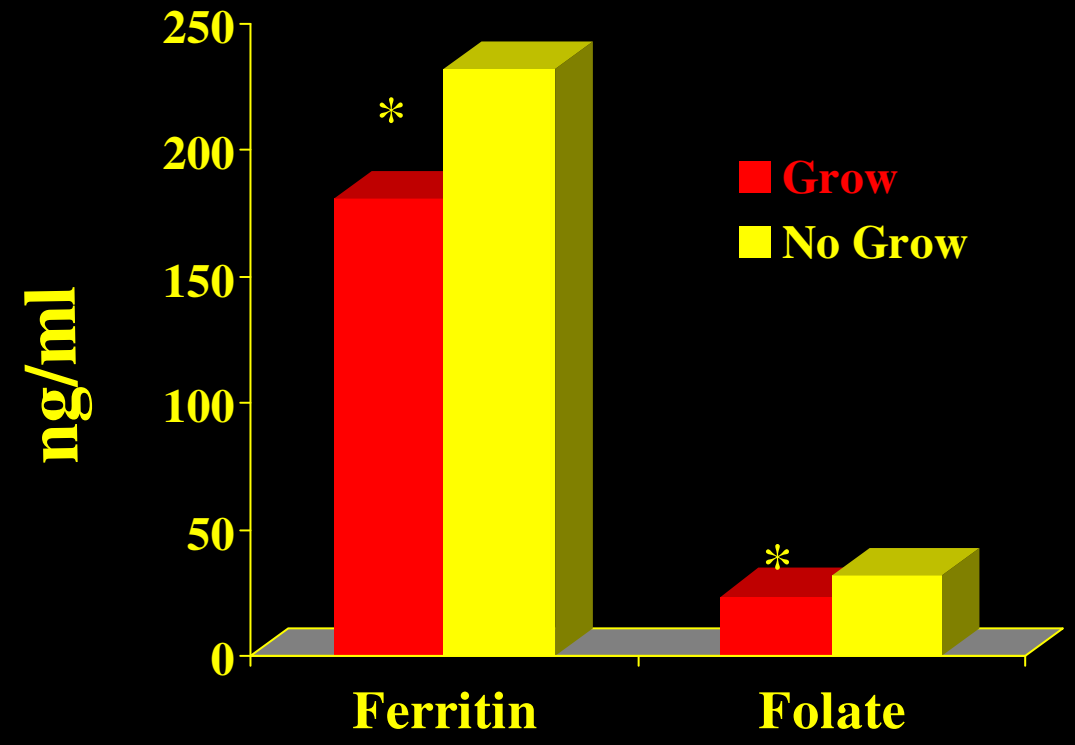
- **Growers had greater gains 16.3±0.7 vs 13.76± 0.5 kg * and**
- **Increased FGR AOR=3.41, 95% CI 1.09-10.66**

Adjusted for age, parity, ethnicity, pregravid BMI,weight gain, smoking

High S/D ratio associated with lower B weight (-285 grams)*

p<.05*

Cord Blood Nutrients & Maternal Growth



Growing adolescents had greater weight gain 17.1±1.0 vs 13.7 ± 1.1 kg *

Lower infant birth weight 3130 ±51 vs 3257 ±54 grams*

Adjusted for age, parity, ethnicity, smoking

p<.05*

Summary

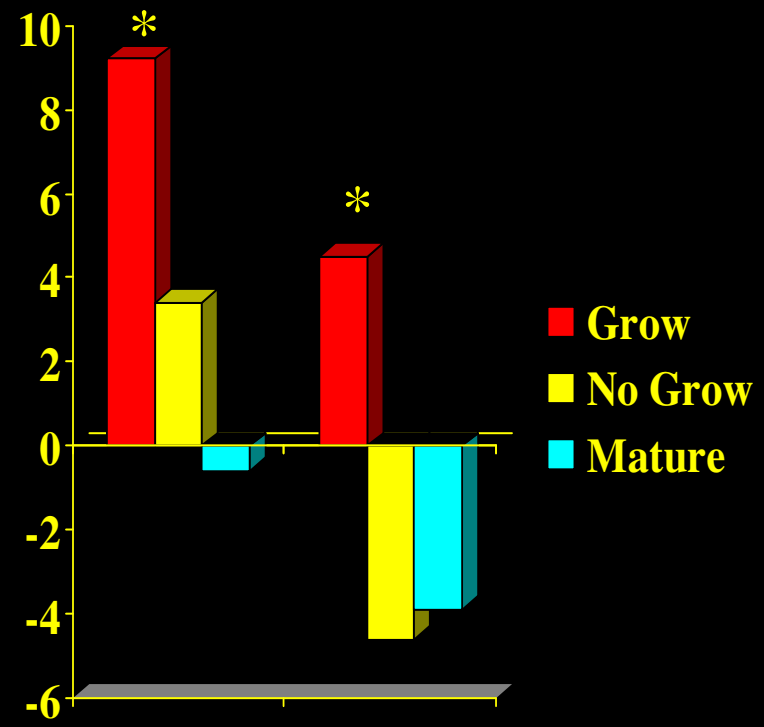
- Maternal growth by KHMD may interfere with normal physiology of pregnancy
  - Influence on fetal growth is greater in still-growing gravida with
    - high maternal fat accrual in 3rd trimester
    - maternal energy intake below the RDA for pregnancy (<100%)
  - Support for hypothesis of maternal-fetal competition with maternal growth
    - Evidence of decreased uterine blood flow
    - Reduced nutrient transmission to fetus

Other evidence of competition

- Evidence for competition apart from US adolescents:
  - Frisancho-Peru
- Animal model
  - Wallace
  - Hashizume

Leptin Surge (nmol/L) and Growth by KHMD

- **Baseline leptin is lower (-9.5%) among still-growing teenagers**
- **Greater leptin surge (Wk 28-entry) for growing teenagers (p<0.01) during pregnancy.**
- **At 6 wks postpartum, growing teenagers have leptin levels above entry (p<.01); leptin goes below entry levels in non-growing teens and mature women.**

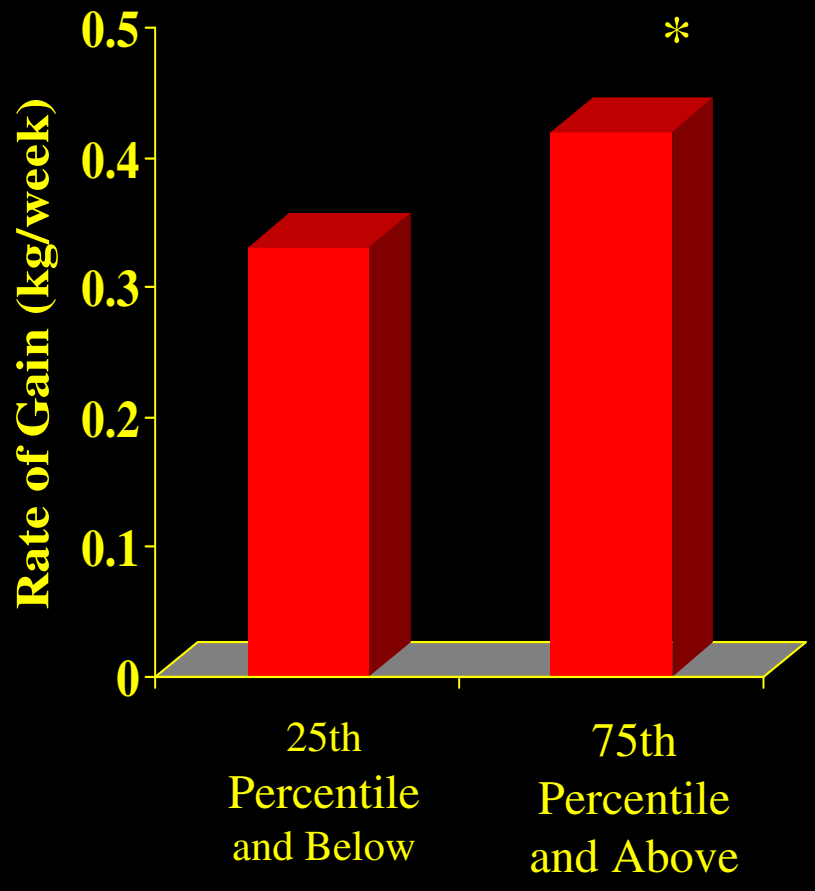


Model adjusted for age, parity, ethnicity, smoking, pregravid BMI, gestation at entry, energy adjusted protein intake

Leptin Surge Quartiles and Rate of Weight Gain During Pregnancy

- **Leptin surge is associated with**
  - **higher rates of gestational gain, (p<.05)**
  - **greater increases in triceps and subscapular skinfolds and arm fat area (p<.05)**

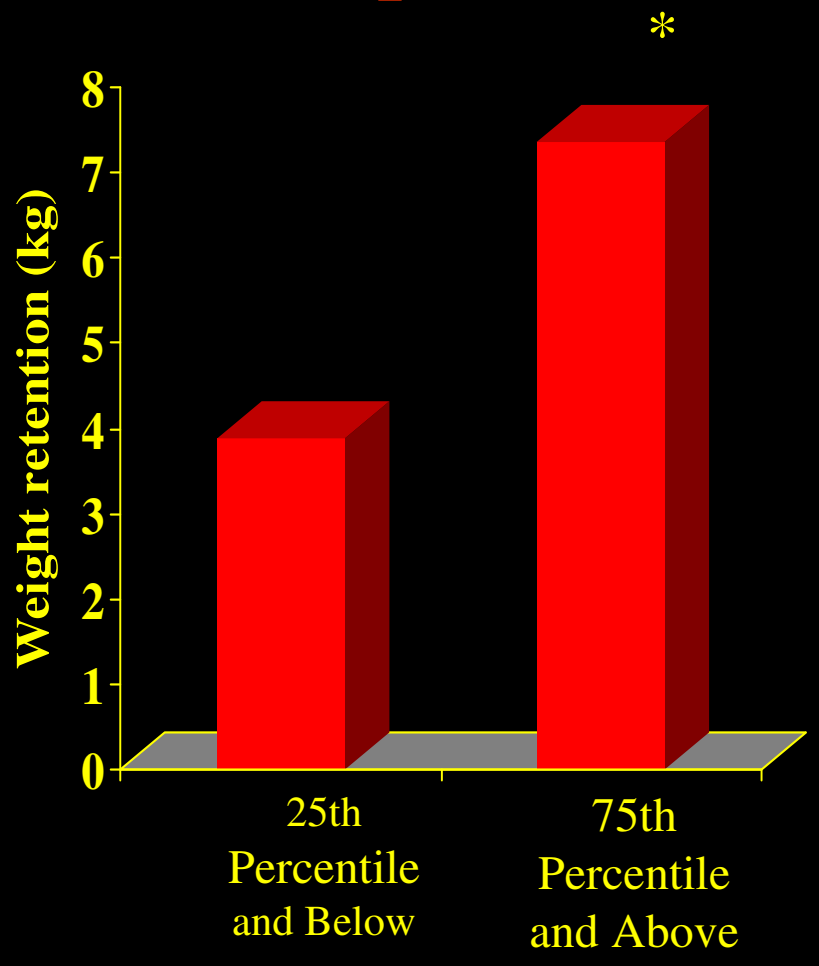
- Controlling for age, parity, ethnicity, smoking, pregravid BMI, and gestation at entry to care



Leptin Surge Quartiles and Weight Retention at Six Weeks Postpartum

- **Leptin surge is associated with greater postpartum weight retention at 4-6 wks pp, p<.05.**

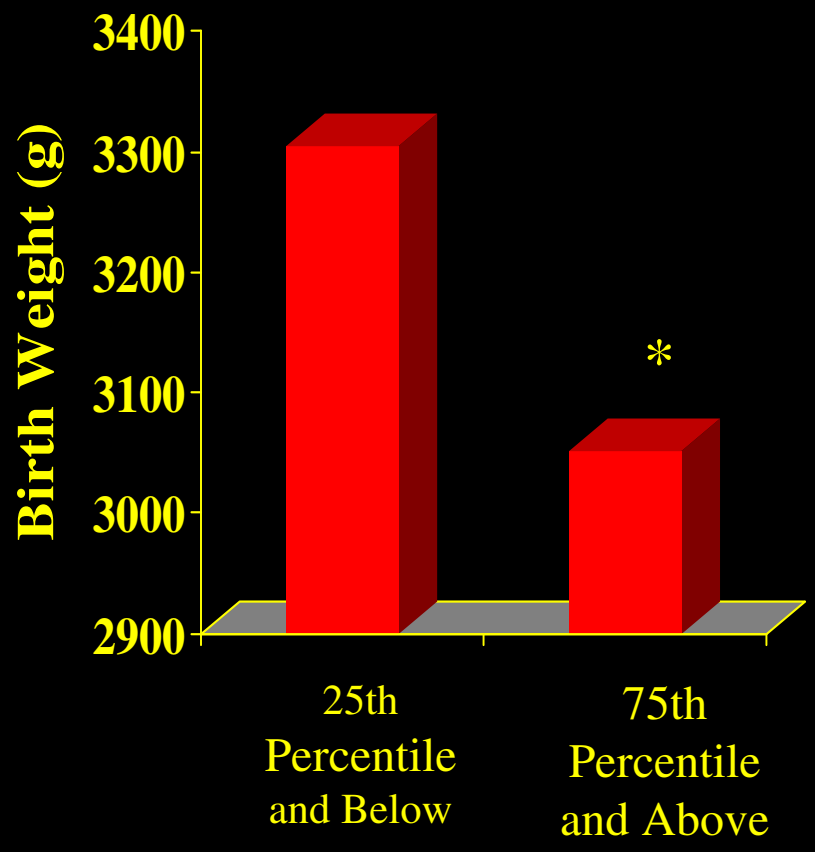
- Controlling for age, parity, ethnicity, smoking, pregravid BMI, and gestation at entry to care.



Leptin Surge and Reduced Infant Birth Weight

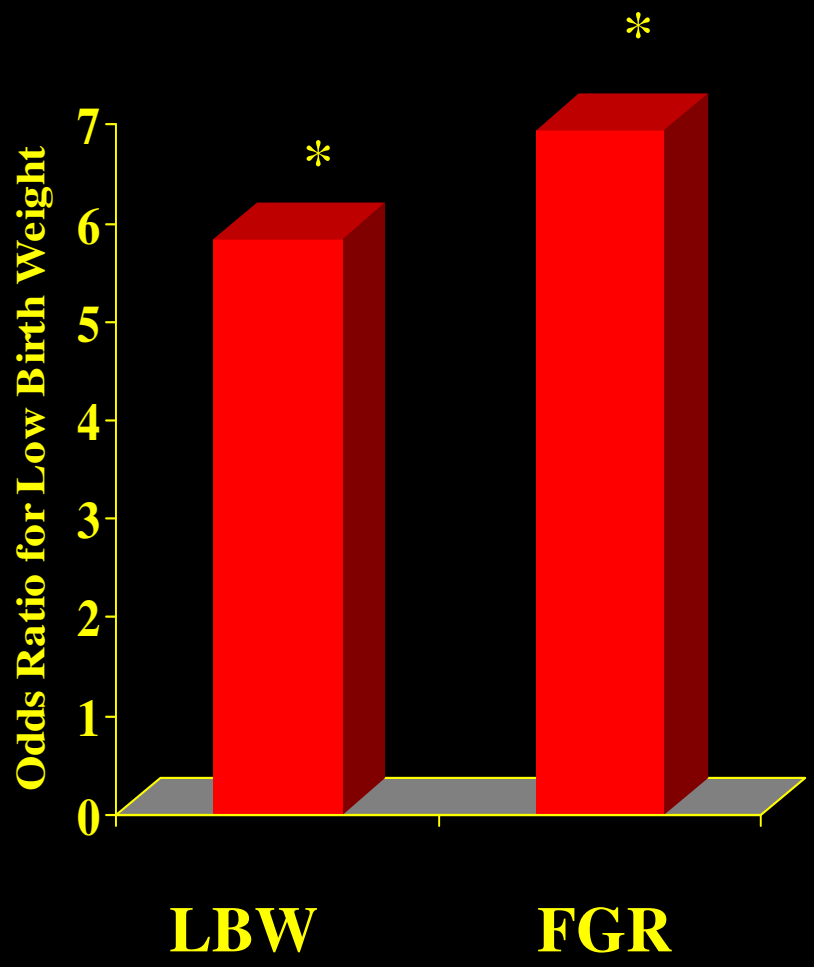
- Leptin surge is associated with lower infant birth weight ($p<.03$)

- Controlling for age, parity, ethnicity, smoking, gestation at blood draw, BMI, inadequate weight gain, energy-adjusted protein intake, and gestation duration



Leptin Surge, Low Birth Weight and Fetal Growth Retardation

- **Leptin surge associated with an increased risk of**
  - **low birth weight (AOR=5.84, 95% CI 1.24-27.63) for highest quartile**
  - **fetal growth restriction (AOR=6.94, 95% CI 1.04-46.44) for highest quartile**
- Controlling for age, parity, ethnicity, smoking, pregravid BMI, inadequate weight gain, gestation at blood draw, protein intake



Summary

- **Leptin surge is a biomarker for maternal growth**
- **Like maternal growth by KHMD, the leptin surge between entry and week 28 associated with**
  - Increased risks of fetal growth restriction and low birth weight
  - Decreased infant birth weight
- **Leptin surge associated with anthropometric changes in mother**
  - Increased weight gain and retained postpartum weight
  - Increased skinfolds and arm fat area

Gestational weight gain: Leptin, insulin and other hormones

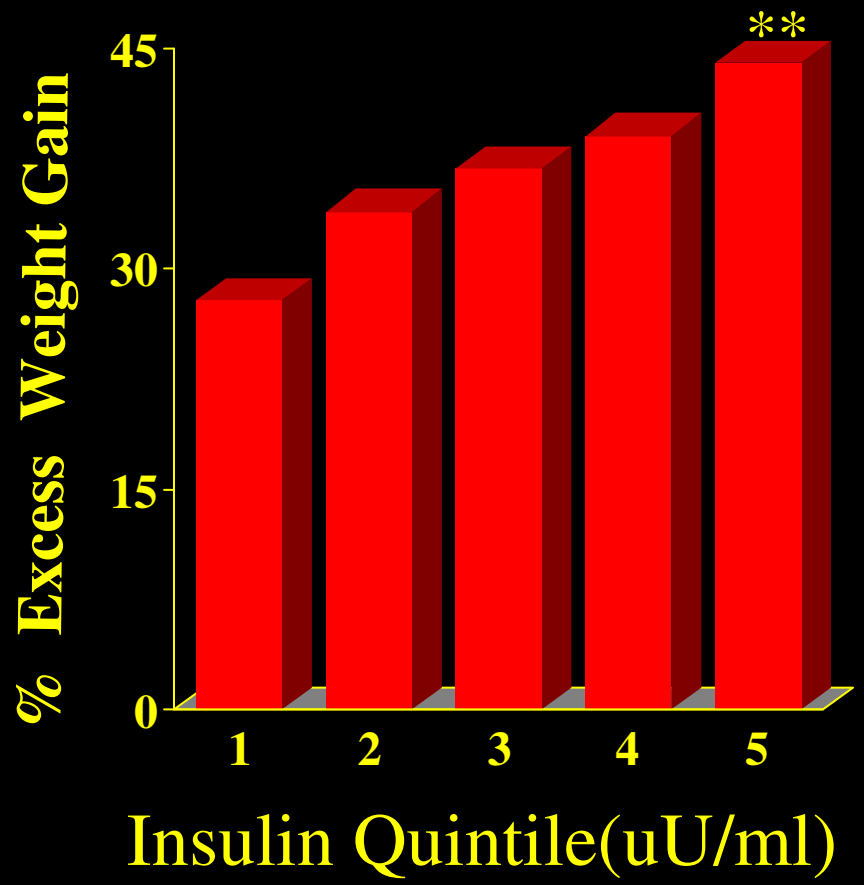
Leptin, weight gain and weight retention : a replication

- In gravidas with a BMI in the normal range (19.8-26.0) entry leptin linearly related to:

- Increased rate of gestational gain (0.25 kg/wk/ug/L leptin at entry)
  - 10^{th} percentile entry leptin 0.31 kg/wk
  - 90^{th} percentile 0.45 kg/wk

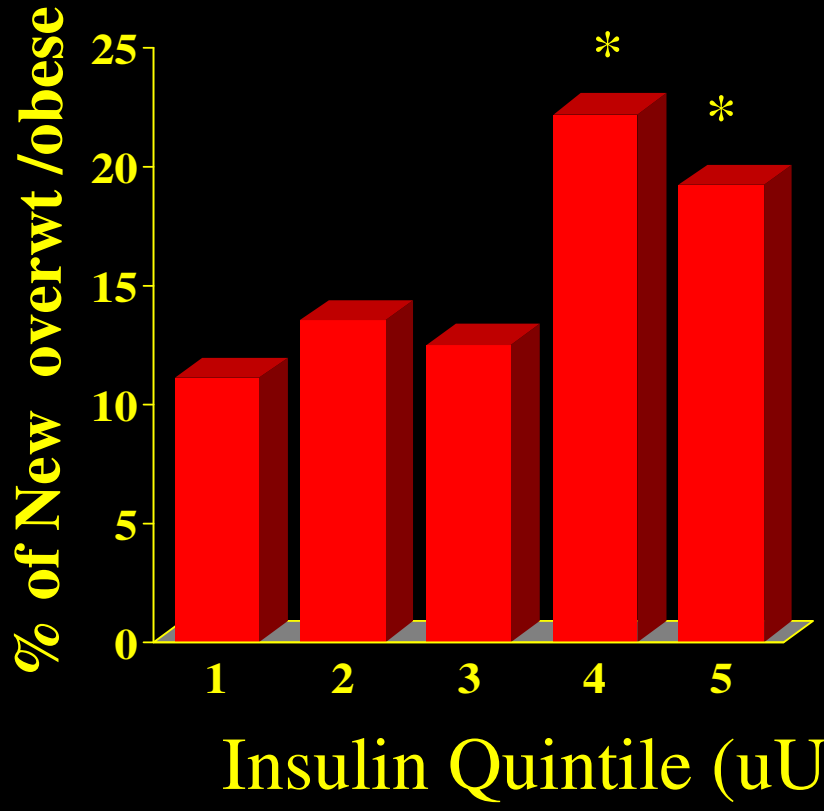
- Increased weight retention-6 mos pp (7.29 kg/ug/L leptin at entry)
  - 10^{th} percentile entry leptin + 2.7 kg
  - 90^{th} percentile + 13.9 kg

Women with high fasting insulin at entry are more likely to have an excessive gestational weight gain - Camden Study



- **Excess weight gain (IOM Criteria) for gravidas in the highest quintile of insulin is AOR= 1.56 X higher**
- **(95% CI 1.05, 2.33)**
- **Adjusted for age, parity , ethnicity, pregravid BMI**

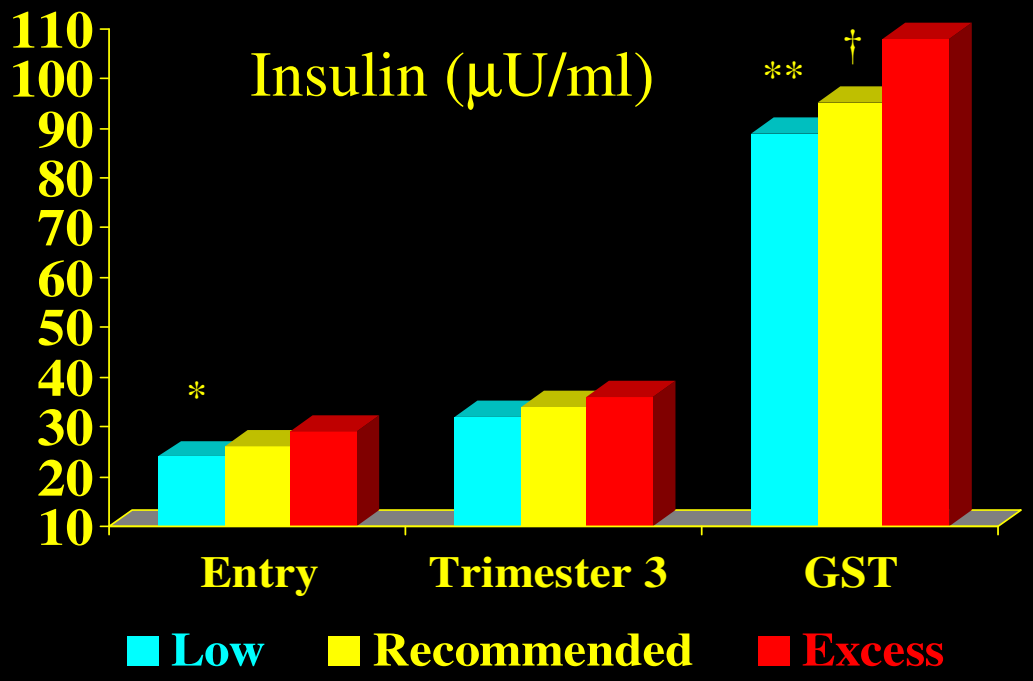
Women with high fasting insulin at entry are more likely to become newly overweight/obese



Gravidas in the two highest insulin quintiles are 2X more likely to become newly overweight /obese at 4-6 weeks postpartum. For the highest quintile AOR= 2.55, (95% CI 1.3-5.0)

Data are adjusted for age, parity, ethnicity and pregravid BMI

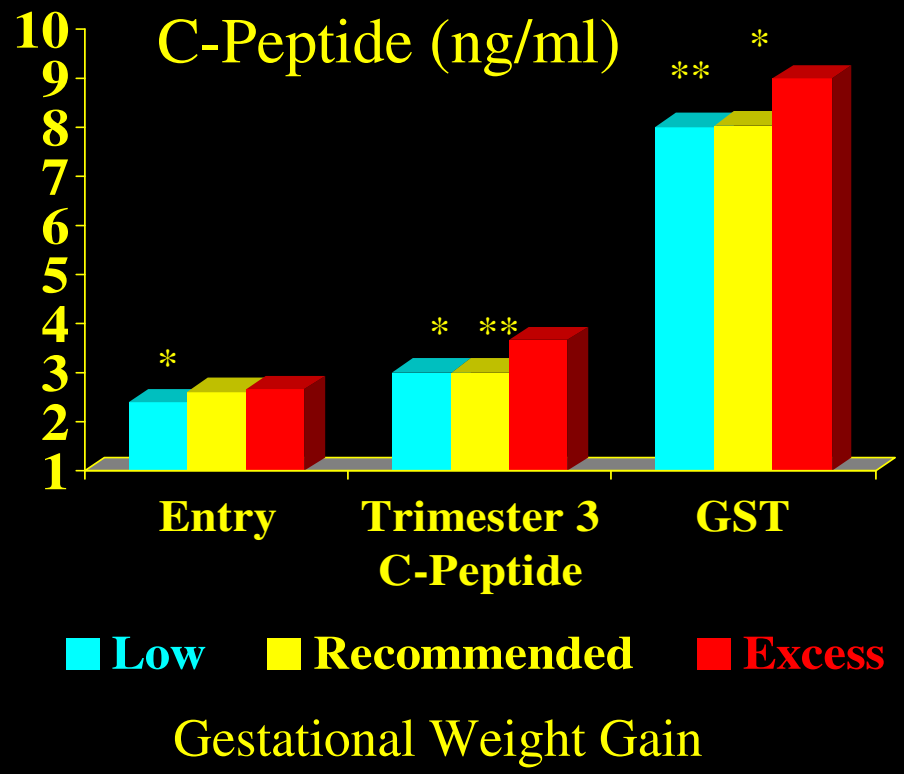
Women with excess weight gain have higher levels of fasting and post-load insulin: A replication



Adjusted for age, parity, ethnicity, BMI, gestation at testing ** p <0.01,* p<.05 , † p <0.1 vs excess gain

- Gravidae with excessive weight gain per IOM Guidelines
- Higher fasting insulin at entry (vs low gain)
- Higher insulin following a 50 g glucose load

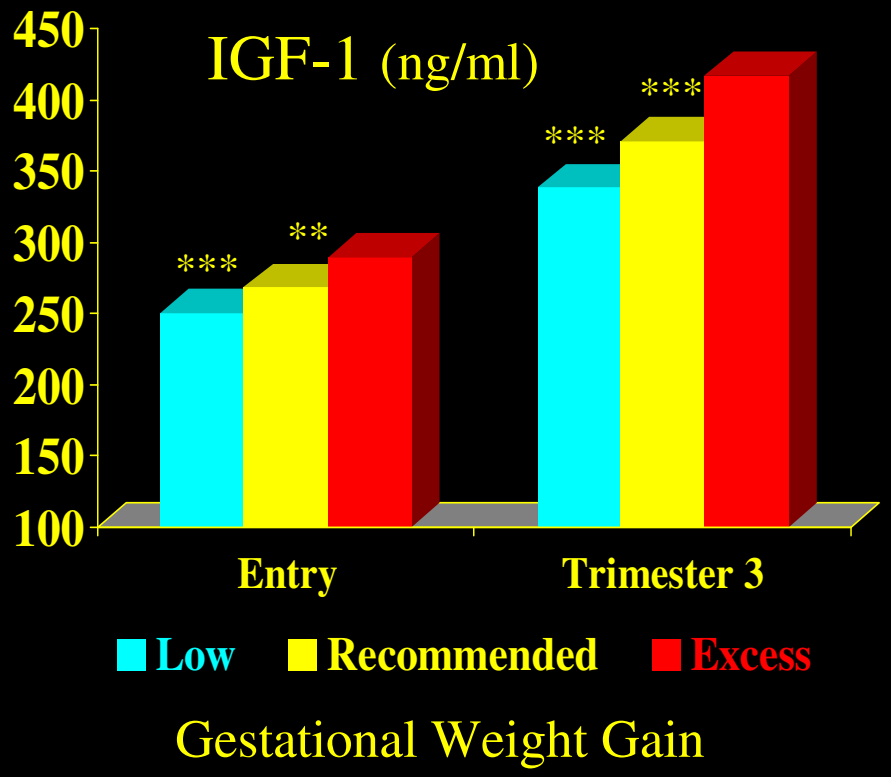
Women with excess weight gain have higher levels of fasting and post-load C-Peptide



Adjusted for age, parity, ethnicity, BMI, gestation at testing * p < .05 ** p <.01

- Gravidae with excessive weight gain per IOM Guidelines
- Increased fasting C-Peptide (entry and trimester 3)
- Increased C-Peptide following a 50 g glucose load

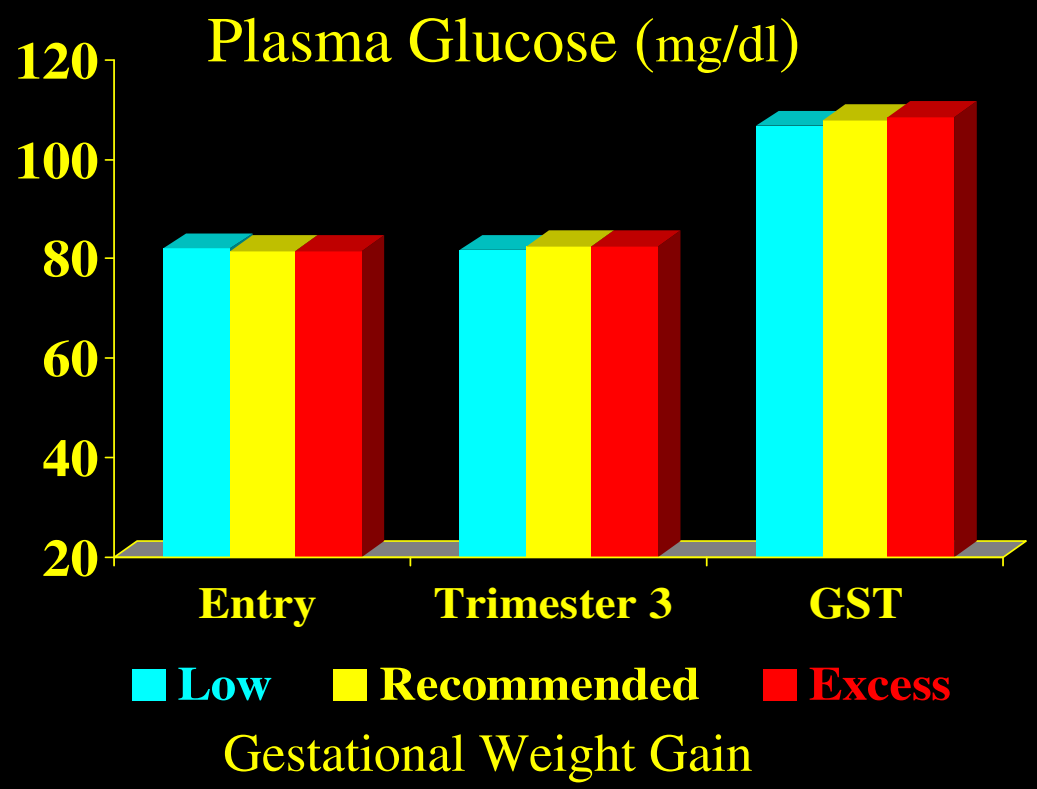
Women with excess weight gain have higher levels of IGF-1



- Gravidae with excessive weight gain per IOM Guidelines
- Increased IGF-1 at entry and trimester 3

Adjusted for age, parity, ethnicity, BMI, gestation at testing *** p<.001, ** p <0.01

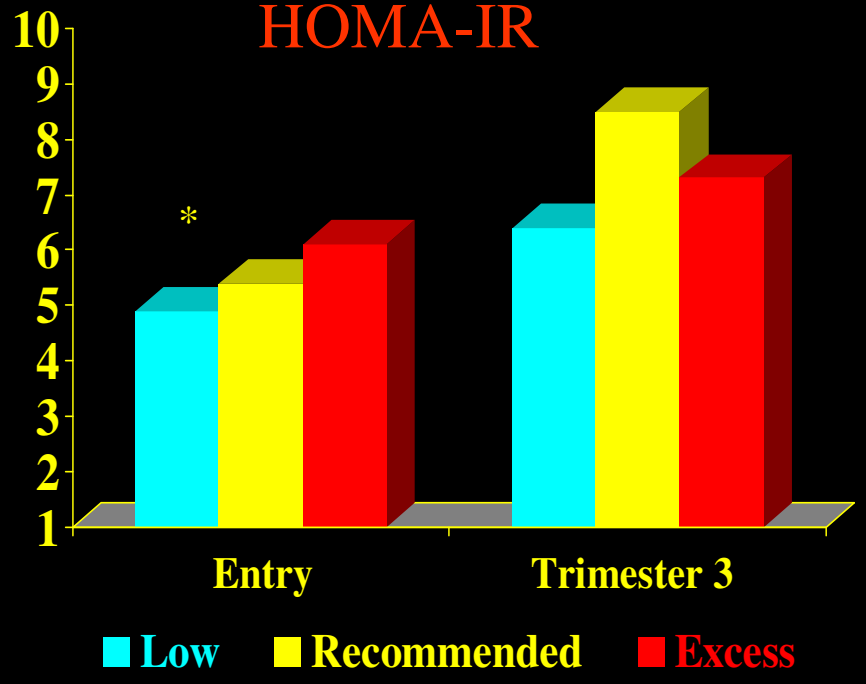
Women with excess weight gain have similar levels of Glucose



Adjusted for age, parity, ethnicity, BMI, gestation at testing

- Gravidae with excessive weight gain per IOM Guidelines
- No difference in fasting or post-load glucose

Women with excess weight gain have increased entry HOMA-IR

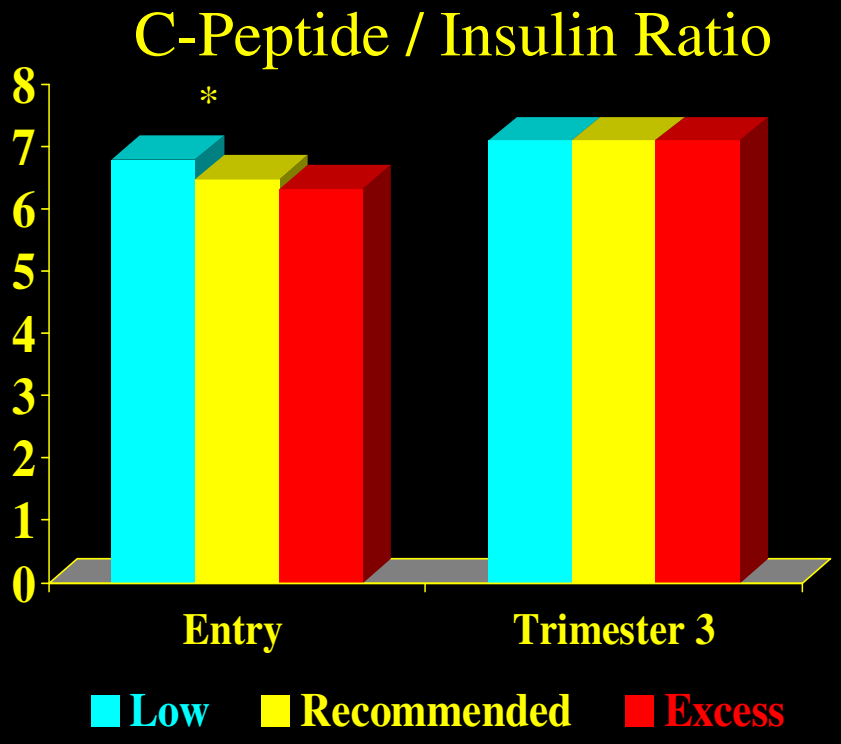


Gestational Weight Gain

Adjusted for age, parity, ethnicity, BMI, gestation at testing * $p < .05$

- Gravidae with excessive weight gain per IOM Guidelines
- Higher insulin resistance (estimated by HOMA-IR) at entry
- No difference during 3rd trimester

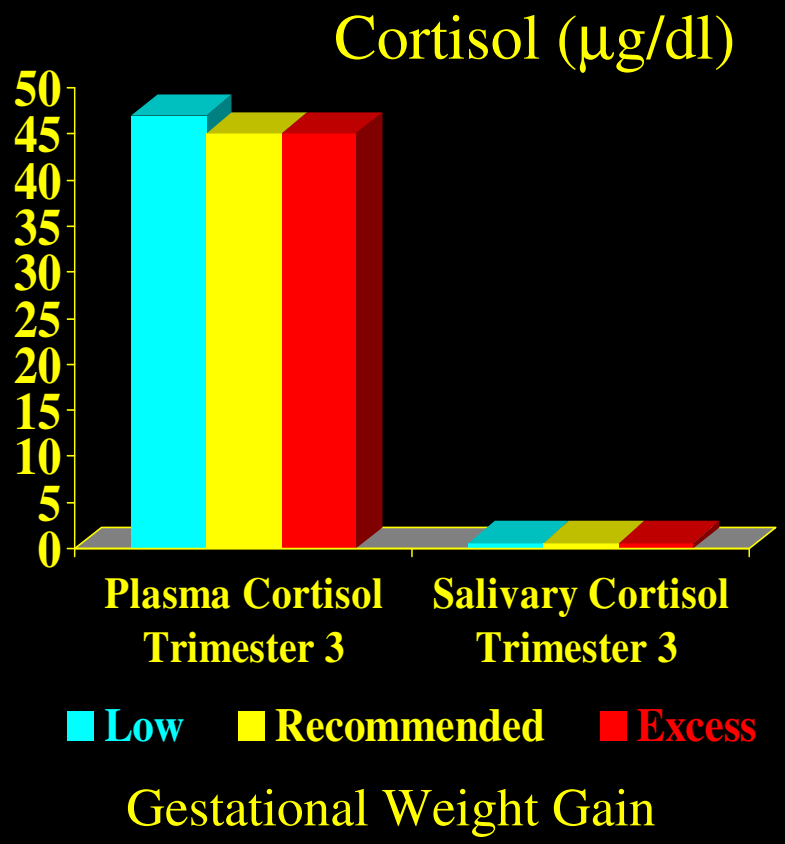
Women with excess weight gain have lower entry C-Peptide/Insulin Ratio



- Gravidae with excessive weight gain per IOM Guidelines
- Lower C-Peptide/ insulin ratio at entry, an index of insulin clearance
- No difference during 3rd trimester

Adjusted for age, parity, ethnicity, BMI, gestation at draw * $p < .05$

3rd trimester cortisol unrelated to weight gain



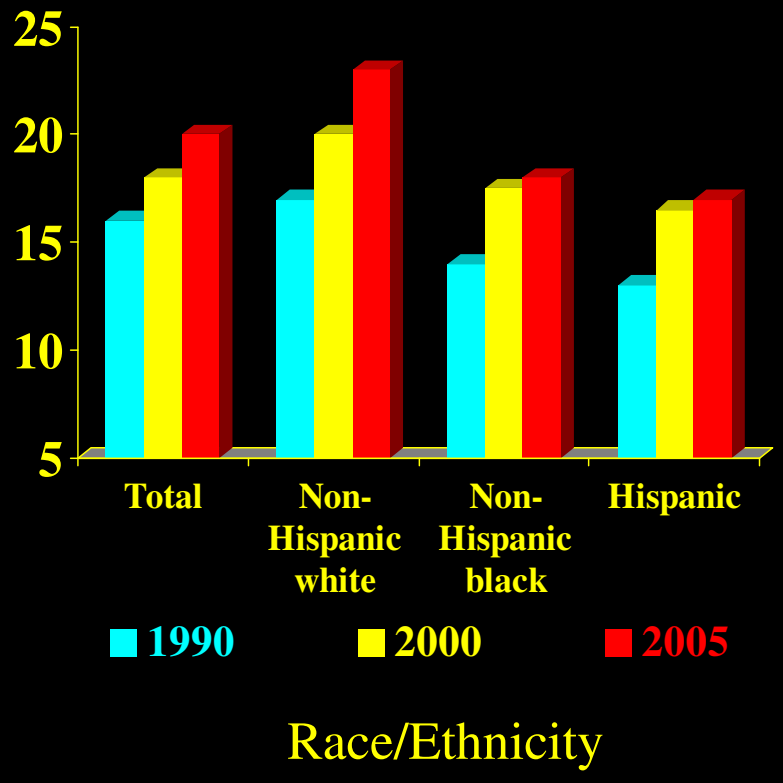
- Gravidae with excessive weight gain per IOM Guidelines
- No difference in 3rd trimester plasma or salivary cortisol

Adjusted for age, parity, ethnicity, diurnal variation, gestation at testing * $p < .05$

SUMMARY

- **Pregnant women with higher levels of leptin, IGF-1, insulin, C-Peptide at entry to care gain more weight or gain weight excessively during pregnancy.**
- **Higher levels of these hormones also observed at week 28 or following a 50 g GST at weeks 24-28**
- **Higher levels of insulin and leptin at entry also are associated with greater post-partum weight retention and new onset overweight/obesity in the postpartum**
- **Prior studies have documented that greater weight gain is associated with increased post-partum weight retention, and overweight/obesity in some populations.**

Percentage of US women gaining >40 pounds in pregnancy 1990-2005



- From 1990 to 2005 the percent of women gaining >40 pounds (excess weight gain for any BMI group) increased from 15% to 20%.

MMWR 57: 127,2008.

Neel's hypothesis

- **Neel proposed that high insulin levels**
  - **Adaptation to feast or famine**
  - **Thrifty individuals store calories**
  - **With "progress" thrift may increase risk of**
    - **Type 2 Diabetes**
    - **Weight Gain**
    - **Overweight**
    - **Obesity**

Data on maternal anabolic hormones and gestational weight gain support Neel's hypothesis

Higher anabolic hormone levels have benefits

- **Increased weight gain during pregnancy**
  - **Caloric store for the future**
  - **Prevent nutritional depletion**
  - **Reduce famine-related infertility**

- **There are also risks with excess gain**
  - **Overweight and obesity**
  - **Future Type 2 diabetes, CVD, breast cancer**