

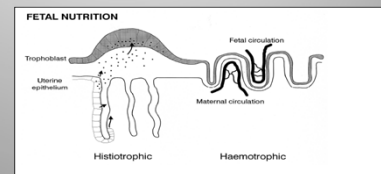
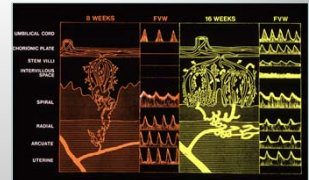
Does first trimester growth relate to birthweight?

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Why should first & second trimester growth differ?

<11 weeks, Histiotrophic nutrition:
 Dependent on nutrient & oxygen diffusion

>11 weeks, Haematotrophic nutrition:
 Dependent on spiral artery transformation and trophoblast invasion



Is there an association between pre and post 11 week fetal growth...not simply a continuum?

"All fetuses grow the same in the first trimester"

"first trimester CRL is the most accurate way of dating a pregnancy"

"first trimester growth problems translate into later growth problems"

Evidence of early first-trimester growth restriction in pregnancies that subsequently end in miscarriage

F Mukri,^a T Bourne,^{a,b,c} C Bottomley,^{a,b} C Schoeb,^b E Kirk,^a AT Papageorgiou^{a,b,d}

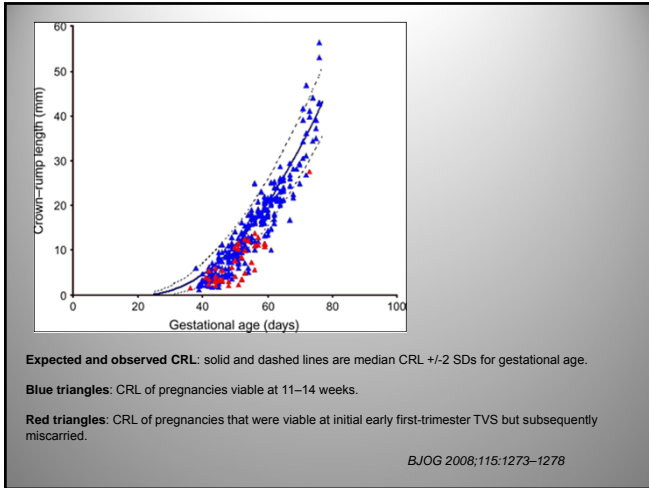
316 women; Twenty-four excluded.

Of 292, pregnancy remained viable in 251 (86%) and 41 (14%) miscarried.

At the first TV USS, z score of the mean CRL for pregnancies that remained viable was -0.82 , SD 1.46

z score in pregnancies that miscarried was -2.42 and the CRL was significantly smaller, SD 1.31 ($P < 0.0001$). Initial CRL was below the expected mean for gestational age in all women; in 61%, the CRL was at least 2 SDs below the expected mean.

BJOG 2008;115:1273-1278



What factors affect first trimester growth rate?

1828 singleton pregnancies before 12 weeks gestation. Maternal characteristics (ethnicity, maternal age, obstetric history, abdominal pain and vaginal bleeding), crown rump length (CRL).

Rate of increase in CRL was higher in women of black ethnic origin ($P = 0.0261$) compared with white, and increased with advancing maternal age ($P = 0.0046$).

Rate of increase in CRL was greater in fetuses of black versus white women and increased with advancing maternal age. As CRL is used to date pregnancies, and this influences further growth assessment, consideration should be given to the use of individualized growth charts which take account of maternal factors found to influence first trimester growth.

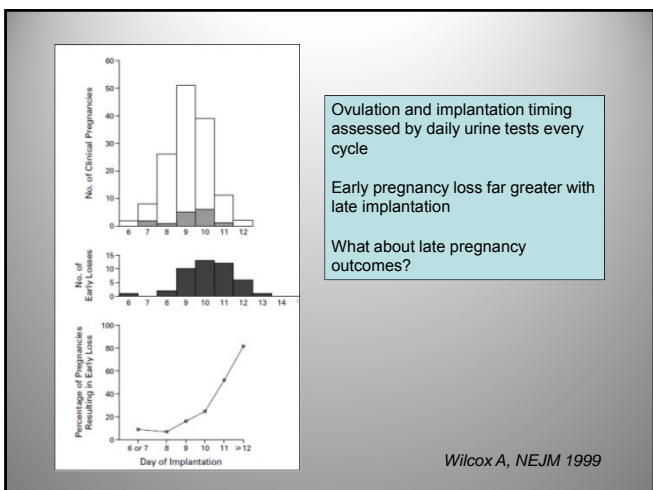
Bottomley et al Hum Reprod. 2009 Feb;24(2):284-90

The New England Journal of Medicine

TIME OF IMPLANTATION OF THE CONCEPTUS AND LOSS OF PREGNANCY

ALLEN J. WILCOX, M.D., PH.D., DONNA DAY BAIRD, PH.D., AND CLARICE R. WEINBERG, PH.D.

ABSTRACT
Background Implantation of the conceptus is a key step in pregnancy, but little is known about the time of implantation or the relation between the time of implantation and the outcome of pregnancy.
Methods We collected daily urine samples for up to six months from 221 women attempting to conceive after ceasing to use contraception. Ovulation was identified on the basis of the ratio of urinary estrogen metabolites to progesterone metabolites, which changes rapidly with luteinization of the ovarian follicle. The time of implantation was defined by the appearance of chorionic gonadotropin in maternal urine.
Results There were 199 conceptions, for 95 percent of which (199) we had sufficient data for analysis. Of these 199 pregnancies, 141 (70 percent) lasted at least six weeks past the last menstrual period, and the remaining 48 pregnancies (25 percent) ended in early loss. Among the pregnancies that lasted 6 weeks or more, the first appearance of chorionic gonadotropin occurred 6 to 12 days after ovulation; 118 women (84 percent) had implantation on day 8, 9, or 10. The risk of early pregnancy loss increased with later implantation ($P < 0.001$). Among the 102 conceptuses that implanted by the ninth day, 13 percent ended in early loss. This proportion rose to 26 percent with implantation on day 10, to 52 percent on day 11, and to 82 percent after day 11.
Conclusions In most successful human pregnancies, the conceptus implants 8 to 10 days after ovulation. The risk of early pregnancy loss increases with later implantation. (N Engl J Med 1999;340:1796-81) ©1999, Massachusetts Medical Society.



First trimester growth & growth rate is more complicated than it seems:

- Maternal ethnicity
• *Mukri et al 2008*
- Maternal age
• *Mukri et al 2008*
- Ovulation, fertilization, implantation timing
• *Wilcox et al 1999*
- Trisomy 18, triploidy
multiple authors
- Pregnancy outcome (miscarriage)
• *Bottomley et al 2009*

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BMJ RESEARCH

Fetal growth in early pregnancy and risk of delivering low birth weight infant: prospective cohort study

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976 women who conceived by IVF had first trimester CRL and delivered live singleton infants without evidence of chromosomal or congenital abnormalities.

First trimester growth was expressed as the difference between the observed and expected size of the fetus, expressed as equivalence to days of gestational age.

Results For each one day increase in the observed size of the fetus, birth weight increased by 28.2 (95% confidence interval 14.6 to 41.2) g.

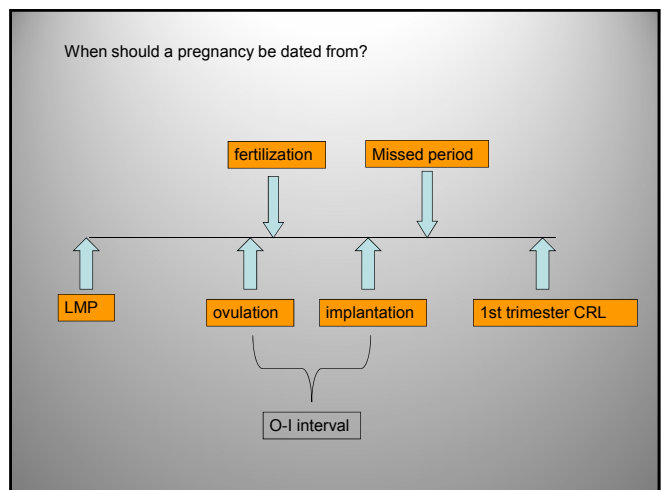
The risk of delivering a small for gestational age infant decreased with increasing size in the first trimester (odds ratio for a one day increase 0.87, 0.81 to 0.94).

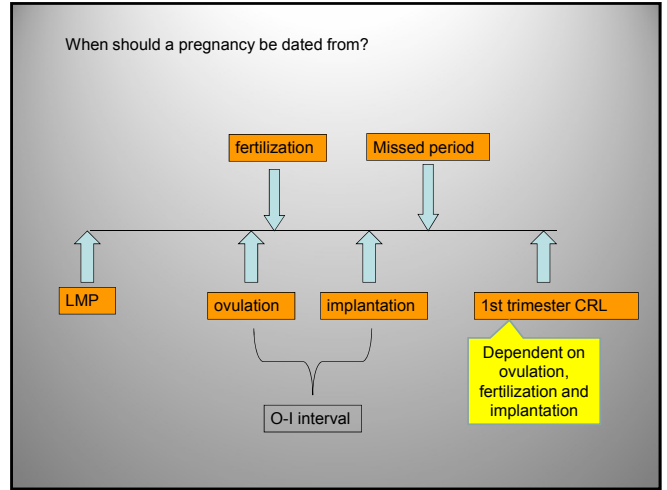
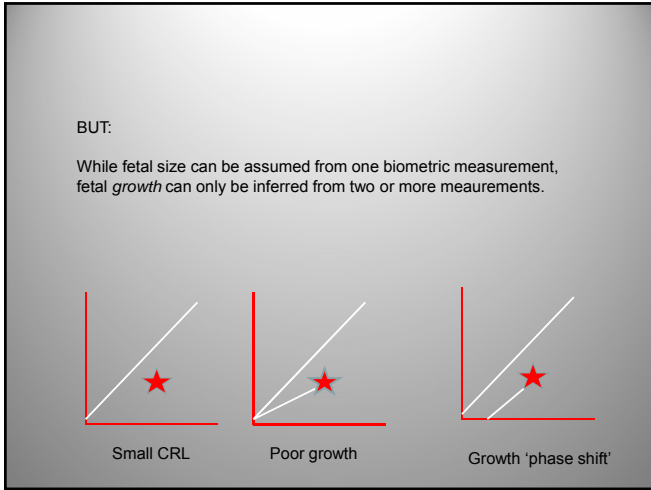
Conclusion Variation in birth weight may be determined, at least in part, by fetal growth in the first 12 weeks after conception through effects on timing of delivery and fetal growth velocity.

At the 'extreme' of gestational age difference, the proportion of SGA babies is far greater than predicted

In this study, first trimester CRL was taken from certain IVF embryo transfer date as a proxy for growth

Bukowski *BMJ* 2007



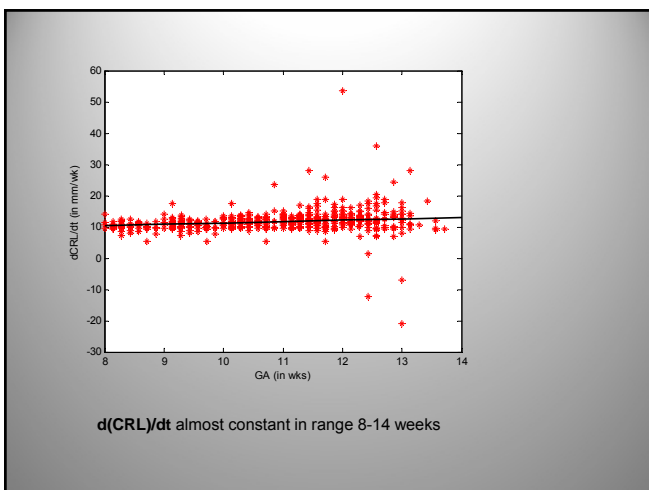
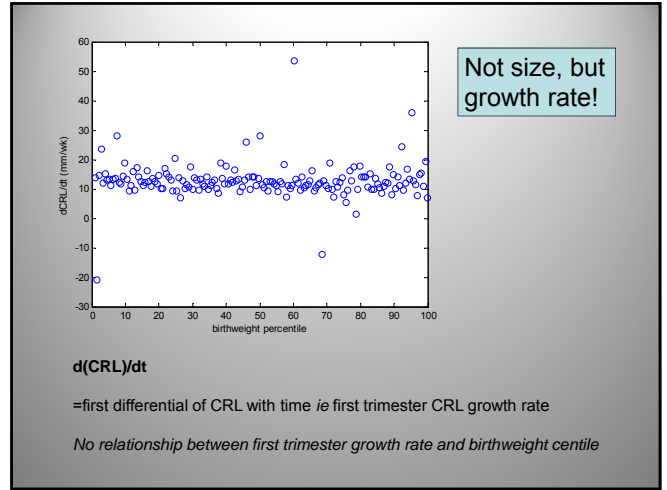
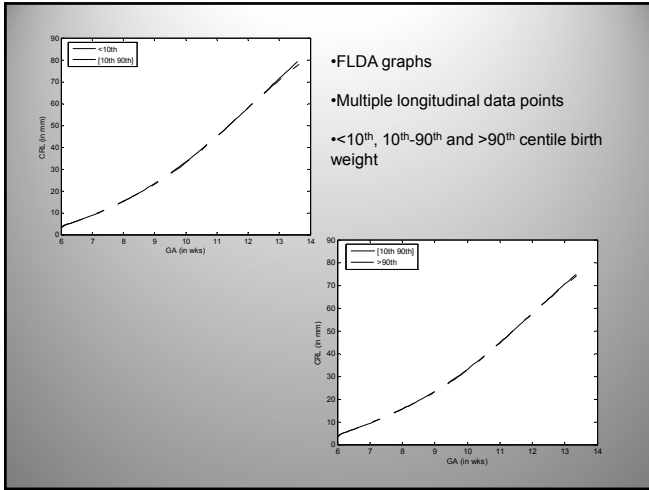


Methods:

201 women attending a combined first and second trimester Down's screening service were included in the analysis.

Fetal growth curves were derived using functional linear discriminant analysis (FLDA), and relationship with birthweight percentile investigated.

functional linear discriminant analysis (FLDA) is a statistical technique that allows multiple longitudinal data points from several pregnancies to be combined in a single curve, taking out the effect of co-dependence



Results:

Median maternal age 35 years
 Median gestation at delivery 40 weeks and birthweight 3425 grams

No association between first trimester fetal growth rate and birthweight percentile.

Conclusions:

First trimester fetal growth rate is not related to birthweight percentile

Points of controversy...

First trimester CRL ≠ growth

Growth rate can only be assessed using at least two first trimester CRL measurements

Though normal fetuses grow at broadly similar rates, all fetuses dated from a given ovulation date are not the same size in the first trimester

First trimester dating is only as accurate as knowledge of implantation date



Conclusions

Does first trimester CRL relate to birth weight because of first trimester growth rate, or differences in implantation timing?

Studies don't take into account timing of implantation

Where timing of implantation is controlled for, much higher rate of early pregnancy loss in late implantation

There is no evidence that first trimester fetal growth rate is related to birthweight, though first trimester CRL may be related to birth weight

