

Providing care to the unborn

UPDATES ON PERINATAL ISSUES AND NEWS ABOUT KOFINAS PERINATAL

Fetal Nutrition and Adult Health

Part I: the physiology

How nutrition during intrauterine life defines the health of the future adult

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*Kofinas Perinatal baby of
the month*

Avery Sophia was born October 9, 2009. She is the most precious little person and the absolute light of our lives. We waited a long time for our little miracle, and she brings us more joy and happiness than we ever could have imagined. The best part of the day is watching her EXPLODE with smiles and coos as she wakes up!

Proud Parents



The subject of fetal nutrition and adult health has evaded for the most part the obstetrical literature over the last 15 years. Most of the work on the subject has been done primarily by scientists other than physicians, as well as physicians other than obstetricians. Most of the physicians involved are physicians trained in pediatric specialties as well as nutritional and epidemiological scientists. It is really sad when one thinks that most of the advances in obstetrical care had come out of other specialties rather than obstetrics, such as improved blood banking techniques that saved many mothers from obstetrical hemorrhage, the use of antibiotics that saved mothers from infectious deaths, the establishment of NICU units which saved countless premature babies; even the use of steroids has been pioneered by the pediatrician Dr. Graham Liggins. In the last 15 years, quite a significant amount of literature has been devoted to the elucidation of the relationships between fetal development and adult disease. The concept of “fetal origin of adult disease” has been very well established not only with epidemiological studies over the last 15 years, but also experimental animal as well as human studies. The first time that the concept of the “fetal origin of adult disease” was suspected, was when



Professor Graham Liggins

men in Netherlands who were dying from premature cardiovascular deaths, were found to have something in common; they were in the mother's uterus at the time of the Dutch famine which was brought about by the German blockade of the Netherlands.

Later on, additional studies from the United Kingdom revealed that indeed, deprivation of nutrition during intrauterine life is associated with substantial morbidity from cardiovascular disease as well as mortality in both men and women. A baby born at close to 9 lbs. and 6 oz. (4 Kg) has the lowest chance when he gets to his middle age to suffer a fatal heart attack or a stroke. In contrast, babies born at less than 5 lbs. 8 oz (2.5 Kg) are almost twice more likely to experience such fatal heart attack. For women, there is a similar association but the less severe than in men. Most likely this is due to the beneficial effect of estrogen. However, after menopause, the beneficial effect of estrogen is gone and the women's cardiovascular risk is the same as men's. Maternal weight at birth is a strong determinant of neonatal birth weight. When maternal birth weight is less than 5lbs. 8 oz or 2.5 kg, there is a significant risk that her babies will be small for gestation and even suffer significant growth restriction. This means that the babies of women born small for gestation, do not realize the nutritional advantage of their expected genetic potential and of course, this leads to bad health consequences later on. In contrast, the father's birth weight does not really influence the birth weight of the offspring.

Pregnancy is a wonderful, natural phenomenon. It transforms the female body to a life generator. For this to be achieved, the maternal body must undergo certain changes in order to support the development of the fetus from a tiny, single cell to a complete human being. This includes, gastrointestinal, renal and cardiovascular changes. Below is a list of such changes that are important for normal fetal development.

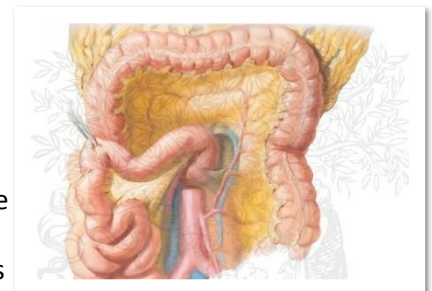


1. Physiological changes in energy and weight requirements

- a. Food intake in the first trimester remains at prepregnancy levels or it may even decrease due to nausea and vomiting.
- b. Food intake increases during the second, and in the third trimester food intake varies according to different studies. Some studies indicate increase and some studies indicate decrease in consumption of calories.
 - i. The average daily increase in the caloric consumption during pregnancy is 60-70 Kcal/ day or 20,000 Kcal for the entire pregnancy.
 - ii. The average weight gain in pregnancy is 12.5 Kg (25 lb.). Of course, this should be applied to the particular patient's body composition. Some patients should gain more and some less. Patients who are below ideal body weight prior to pregnancy should make up the deficit and then add 25 more pounds. Overweight patients need to gain less (10-15 lb.) and obese patients do not need to gain any weight.
- c. It is not clear what causes women to increase their intake. Progesterone is believed to increase the appetite and estrogen to decrease it. The rapid rise of progesterone in the first half of pregnancy may at least in part be responsible for the increased appetite and the anabolic state of the pregnant woman's body. During the first 20 weeks of pregnancy, the maternal body is in a metabolic mode of increased storage for future use. Fetal growth accelerates and fetal demands increase exponentially after 28 weeks. Without such storage of energy during the first half of the pregnancy, fetal growth will be decreased during the last 12 weeks and this can lead to serious problems.

2. Gastrointestinal system changes

- a. Pregnancy causes decreased stomach motility and increases the time it takes for the stomach to empty.
- b. The lower esophageal sphincter becomes relaxed and reflux is one of the most common symptoms of pregnancy.
- c. Intestinal motility decreases and transit time increases as much as

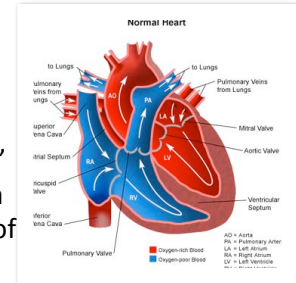


100%.

- d. The above changes should be taken into account when counseling pregnant women. Meals should be smaller in quantity and more frequent to reduce gastric overload symptoms, and to maintain adequate food intake. Women should avoid all foods that are difficult to digest under normal circumstances and might provoke nausea and vomiting during pregnancy.
- e. The ability of the human intestine to absorb nutrients is increased during pregnancy for specific nutrients such as iron, calcium and vitamin B12 but remains unchanged for most other nutrients.
- f. Colonic absorption of water and sodium but not potassium increases during pregnancy and this indicates that the colon plays an active role in maternal blood volume expansion (Parry et al., 1970b). From animal studies it appears that the hormones angiotensin and aldosterone are responsible for this colonic activity.

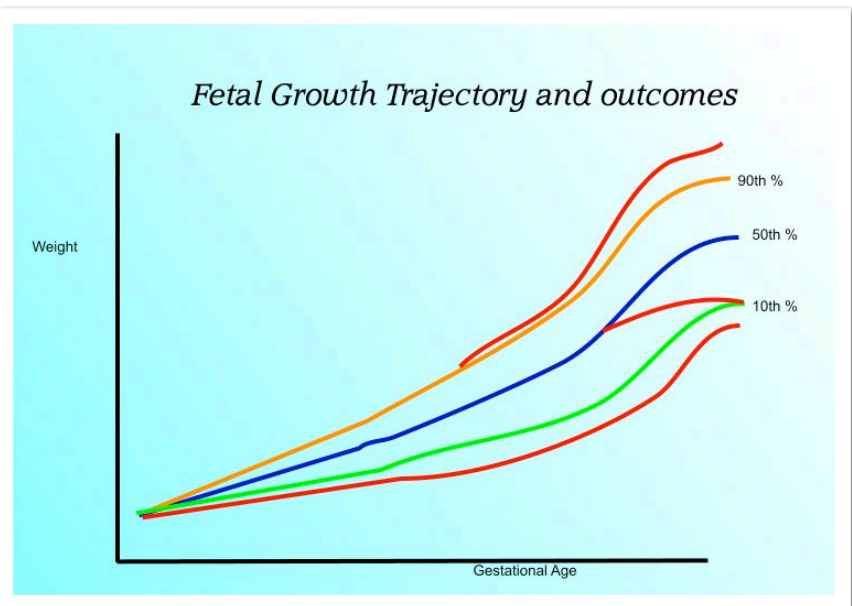
3. Cardiovascular changes

- a. Maternal blood volume expands by as much as 50% for singleton pregnancies and as much as 70% for multiple gestations. This is primarily achieved by means of plasma expansion and to a lesser degree by red cell production. This leads to the “physiological anemia” of pregnancy. The angiotensin-renin system (hormonal system) plays a central role in these changes; atrial natriuretic factor as well as many of the pregnancy related hormonal changes contribute to the cardiovascular and renal changes that cause increased blood volume and cardiac output during pregnancy.
- b. Uterine circulation undergoes significant changes to accommodate the increasing demands of the placenta and developing fetus. Uterine blood flow increases almost by 20 times from 50 ml / min to as high as 1000 ml / min.



Several studies in animals and humans have shown that periconceptional (time before pregnancy until the postpartum period) maternal nutritional state plays a very important role in the subsequent development of the fetus. Nutritional imbalances prior to conception exert a significant effect on the quality of placental development and subsequent fetal growth. Balanced nutrition prior to conception in contrast,

leads to a healthy and well-grown neonate. Nutrition during pregnancy affects fetal growth differently in different stages of the development. Nutritional insufficiency in the first trimester, limits fetal growth and the neonate will be proportionately small giving the appearance of a normal small neonate. In contrast, third trimester nutritional deficiency leads to neonates with significant weight/length disproportions. The newborn is likely to be skinny and long suggestive of a genetic potential that was not fulfilled due to the insufficient nutritional supplies at a critical time that the baby was determined to grow faster according to its own growth trajectory (short red line between the blue and green lines). It is evident then, that



Normal and abnormal fetal growth trajectories according to the time of deprivation insult (red lines indicate abnormal growth trajectories)

early nutritional deprivation changes the baby's growth trajectory; the new trajectory expects the baby to grow

smaller but consistently throughout gestation (bottom red line in the above graph). The baby by means of metabolic alterations is able to survive and grow according to the new growth pattern (trajectory). This new pattern was created as a response to the nutritional deprivation in early pregnancy. When fetuses are deprived, they have the capacity to change their genes in order to change their metabolism. By doing so, they decrease their needs for nutrients and thus become able to survive a limited supply and a hostile environment. In terms of fetal risks, the early deficiency poses less of a risk than late deprivation. Fetuses genetically determined to be large at birth can suffer severe growth restriction and even death due to even minor nutritional insufficiency if it happens at the time of their maximal growth rate in the last few weeks of pregnancy. This is quite apparent on the demographics of fetal demise. Most stillbirths happen to fetuses that are at the low normal birth weight centiles for gestational age (between 10 and 25%) as opposed to babies who are below the 5th% and 10th%. Such babies were deprived early in pregnancy and had the time to change their genetic code and adapt to the hostile intrauterine environment and thus managed to survive.

Proportionately small babies are at increased risk of high blood pressure in adulthood but do not have an increased risk of coronary heart disease. By down-regulating growth (reduced growth demands) in response to under-nutrition early in development, the fetus adapts to the hostile environment; the fetus then reduces its demand for nutrients, and thus protects itself from relative under-nutrition in late gestation. As adults, individuals who were disproportionately short at birth tend to have abnormalities of systems controlled by the liver, and have increased rates of coronary heart disease. These may reflect adverse effects on liver development associated with cranial redistribution of blood flow later in gestation (brain sparing phenomenon). When oxygen and energy supplies are inadequate due to placental insufficiency, the cardiovascular system distributes most of the available oxygen and nutrients to the brain, the heart and the adrenals (the glands that produce the stress hormones). The rest of the body suffers the consequences. Thin babies with a low ponderal index (low birth weight in relation to length-skinny babies) at birth are thought to be at increased risk to develop insulin resistance syndrome and coronary heart disease in adulthood as a result of fetal under-nutrition in the weeks leading up to delivery (after 28 weeks gestation). Consistent with this, a recent follow-up study of men and women whose mothers were exposed to famine in pregnancy showed that third-trimester famine exposure resulted in impaired glucose tolerance (insulin resistance) in the offspring in later adult life. As might be expected, the predominant type of fetal growth retardation and the mix of babies with different types vary greatly in different populations. These variations may contribute to geographic differences in the prevalence of coronary heart disease. With respect to timing, it is important to appreciate that effects that are manifest late in pregnancy may commonly originate much earlier in gestation. For example, studies of the famine of 1944–1945 in the Netherlands led to the rigid concept that thinness at birth results from influences operating in the last trimester of pregnancy. Outside the setting of famine, both animal and human studies indicate that fetal under-nutrition late in pregnancy is, however, more commonly a consequence of a maternal-placental supply deficit determined earlier in gestation. This for the most part is not the result of poor nutritional supply in early pregnancy, but it is due to early placental damage from coagulation imbalances, immune system problems, anti-phospholipid antibody syndrome etc. It has been apparent to us over the last 25 years of placental research that most of the fetal nutritional problems are the result not of maternal nutritional deficiencies but due to defective placental development. (For more details on this subject please review the October issue of our newsletter about coagulation placental problems). It is therefore of paramount importance to pay close attention to placental development from the earliest stages in pregnancy when we can still act proactively and improve placental development. Knowing that the quality of fetal development is one of the most crucial factors in determining health and quality of life in adulthood, it is our moral and professional obligation to do everything in our power to provide the most optimal intrauterine life experience for *each and every one of the unborn*.

