Fetal growth, in contrast to postnatal growth, is largely regulated by fetal nutrition. However, fetal nutrition is not synonymous with maternal nutrition. During much of the first trimester, fetal nutrition is histiotrophic from the uterine glands. Once placentation has occurred and hematotrophic nutrition is established, the fetus lies at the end of a long supply line comprising maternal nutritional status, uterine blood supply, placental function, umbilical blood supply and the fetal hormonal milieu. Thus, it is not surprising that attempted manipulation of fetal growth by maternal nutritional supplementation after the first trimester has not been very successful. Nevertheless, experiments in a variety of species, and perhaps most notably in sheep where direct fetal instrumentation is possible, have shown that it is possible to restrict fetal growth by means of restricting maternal nutrition at various stages of pregnancy.

In contrast to the relatively limited evidence for maternal nutrient supplementation increasing fetal growth during pregnancy, there is good evidence that the uterine environment, determined by maternal factors, plays a substantial role in determining size at birth. Indeed, maternal factors relating to her nutritional status throughout her life course, including around the time of conception, appear to have a greater effect on offspring birthweight than nutritional factors during pregnancy.

A variety of factors operating in the periconceptional period now have been shown to impact on fetal growth, gestation length and fetal developmental trajectory; they include maternal nutritional status, artificial reproductive technology and twin conception. In the case of maternal nutrition (e.g. the Dutch Famine) and twin conception, these effects have been shown to result in physiological changes in adulthood consistent with an increased risk of non-communicable disease.

The mechanisms by which these factors signal to the developing embryo and determine growth and developmental trajectories throughout pregnancy is not known. Possibilities include nutritional, hormonal or other factors. These factors may influence fetal growth and development via epigenetic changes in the developing embryo. Offspring of women
who conceived during periods of relative famine in Gambia have been shown to have altered methylation profiles from those conceived during the harvest, and the methylation status of RXRA in the umbilical cord has been shown to correlate with the phenotype in childhood. In experimental studies, maternal periconceptional undernutrition and twin conception have both been shown to result in similar epigenetic changes (both methylation and histone acetylation) in the appetite regulatory pathways of the ventral hypothalamus in the late-gestation fetus. Some, but not all, of these epigenetic marks persist into postnatal life and adulthood and are associated with increased adult fat mass, suggesting that maternal environmental factors, including nutrition, around the time of conception may not only affect fetal growth and development, but may also affect lifelong risks of obesity and the metabolic syndrome.