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Do In Utero Events Contribute to Current Health Disparities in Reproductive Medicine?

May-Tal Sauerbrun-Cutler, MD¹ and James H. Segars, MD¹

¹Department of Obstetrics and Gynecology, St. Luke's-Roosevelt Hospital, New York, New York

²Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland

Abstract

Health disparities exist in reproductive medicine as discussed in detail in the subsequent articles of this issue; however, in most cases, the exact cause of these differences is unknown. Some of these disparities can be linked to environmental exposures such as alcohol and other hazardous toxic exposures (polycarbonate, pesticides, nicotine) in adults. In addition, low socioeconomic status, behavioral risk factors, and lack of education have been linked to poor obstetric and reproductive outcomes in minority groups. Aside from these various environmental exposures later in life, there is evidence that adverse events in utero could contribute to poor reproductive outcome in specific minority groups. We will focus on the developmental origins of health and disease as a possible causal mechanism for health disparities in reproductive diseases, as this perspective may suggest tractable solutions of how to address and eliminate these health disparities.

Keywords

DOHaD; preterm labor; obesity; African Americans; preterm birth

Epigenetic Origins of Health and Disease

Evidence from many sources has firmly established the existence of reproductive health disparities. Some of these disparities may be linked to environmental exposures such as alcohol and other hazardous toxic exposures (polycarbonate, pesticides, nicotine) in adults.^{1,2} However, in most cases, the root cause for these health disparities is unknown. In this article, we examine the data, suggesting a possible etiologic role for epigenetics in reproductive health disparities.

The developmental origins of health and disease (DOHaD) perspective explains how adverse events occurring during early phases of human development may affect the pattern of health and disease throughout life. The DOHaD hypothesis was initially described by Dr.

Barker as an explanation for the response to the maternal exposure to nutritional deprivation during early gestation (also known as the fetal origins of adult disease). During the late period of the Dutch Hunger Winter of 1944 to 1945 when the population of Amsterdam was subjected to a severe and well-circumscribed famine, maternal deprivation to nutrients was noted to be associated with an increased risk of early onset cardiovascular disease, hypertension, increased body mass index (BMI), and glucose intolerance in the offspring.^{3,4} Mothers exposed to famine in early gestation had children with more atherogenic lipid profile and an elevated risk of coronary artery disease (CAD).⁵ The exposed fetuses adapted to malnutrition via mechanisms that permanently changed their physiology and metabolism.

Various population studies, along with animal models, have supported these findings. Studies in several countries have shown that children who were small at birth (using small birth weight as a marker for growth restriction) have elevated blood pressure and evidence of an abnormal response to an oral glucose challenge. For example, low-birth-weight children in Pune, India, showed a higher prevalence of hypertension, insulin resistance, and elevated serum lipids in children 8 years of age compared with children born at a normal weight.⁶ These adverse metabolic profiles present in young children are evidence that the associations detected in adults do not reflect confounding variables linked to lifestyle. The effects of maternal malnutrition on offspring from famine in China in 1959 and in Nigeria during civil war in 1968 to 1970 also support this concept. Individuals exposed in utero to the Nigerian civil war famine of 1968 to 1970 were at increased risk of hypertension, impaired glucose tolerance, and being overweight 40 years later.¹ Similarly, women exposed to the 1959 to 1961 famine in China during gestation are reported to have a greater risk of metabolic syndrome.

What happens in utero that causes this adverse metabolic profile and what are the genetic mechanisms that result in reprogramming of the fetus? The mechanisms are complex and involve epigenetic changes that can persist for generations. Epigenetic effects are heritable changes in gene expression that are not mediated by changes in primary DNA sequence. Available evidence supports the idea that such epigenetic changes could contribute to reproductive health disparities. When survival is threatened, a fetus will make adaptations to limit growth and prioritize development of essential tissues. The result is not only a low-birth-weight infant, but this is accompanied by a re-setting of endocrine and metabolic axes.⁵ Even prenatal normal birth weights that were exposed to stress, whether emotional or via toxic exposure, exhibited primary insulin resistance and a lipid profile consistent with the metabolic syndrome.⁷

Metabolic Syndrome

Metabolic syndrome is defined as the clinical abnormalities that include obesity, insulin resistance, glucose intolerance, hypertension, and dyslipidemia, which increase the risk of atherosclerotic cardiovascular disease and is the earliest predictor for type 2 diabetes mellitus and CAD. Although the prevalence of obesity has been increasing worldwide, there are striking differences between different groups. Based on the National Health and Nutrition Examination Survey data in 2009 to 2010, between 1988 to 1994 and 2009 to 2010, the prevalence of obesity among women increased in all ethnic groups (Fig. 1).⁸

African Americans also have an increased rate of metabolic syndrome and type 2 diabetes mellitus. Considering the DOHaD hypothesis, a possible etiology for this racial difference and resultant obese phenotype dates back to American slavery from the 16th to the 19th centuries, which may have caused epigenetic changes that have persisted for many generations. Mothers who were indentured to slavery may have been malnourished which slowed down fetal growth. This condition could have resulted in reduced cell growth in utero and a lower birth weight. Nutrients needed to be shunted to vital organs such as the brain caused decreased production of pancreatic (β) cells with decreased ability to make insulin. As mentioned above, studies in the United Kingdom confirmed that thinness (birth weight/length) resulting from stunted cell growth was associated with insulin resistance and diabetes later in life.^{9,10} The thin neonate lacks muscle and fat which are the main sites of insulin action leading to reduced rates of glycolysis and an increased susceptibility to an insulin-resistant profile.

Today there are additional risk factors that may perpetuate obesity such as poor health behaviors related to lack of physical exercise, poor diet, and restricted access to health care in African Americans.¹¹ The Western World suffers more from over nutrition with high saturated fats than from under nutrition. It is not only malnutrition that increases the risk for metabolic syndrome but over nutrition along with maternal obesity and diabetes also increases the risk of metabolic syndrome in future generations.¹²⁻¹⁵

Another factor that is associated with obesity and that may perpetuate obesity is oxidative stress and high levels of reactive oxygen species (ROS) from high levels of maternal triglycerides. Oxidative stress may arise from intracellular accumulation of triglycerides that suppress mitochondrial efficiency and the electron transport chain. In humans, the placenta in obese patients has increased levels of proteins involved with oxidative stress, inflammation, and gene expression of proadipogenic proteins. These proteins were increased in placentas that nourished fetuses of rats fed with high-fat diets. The fetuses of rats whose mothers were fed high-fat diets had increased adiposity with impaired glucose tolerance.¹⁶ However, this inheritance pattern was able to be reversed when the maternal rats were given antioxidant supplements.

Yet another factor that promotes obesity is excess carbohydrate consumption. Methylation levels at a single CpG (regions of DNA where a cytosine nucleotide occurs next to a guanine nucleotide) occur in the *RXRA* gene in umbilical cord tissue and are inversely correlated with excess carbohydrate consumption during the first trimester of pregnancy. This methylation pattern was found to be associated with child's adiposity at age 6 suggesting an epigenetic link to obesity.¹ Therefore, it is possible that a vicious cycle arises: malnutrition predisposes to obesity, and obesity predisposes future generations to more obesity.

An important and relevant obesity-related complication is poor reproductive outcomes in minorities. Although obesity is likely to be linked to poor reproductive outcomes in all minority groups, most of the published literature pertains to African Americans. Two of the most common complications are lower fertility and increased pregnancy complications. In both spontaneous and in vitro fertilization (IVF) pregnancies, African American women had increased risk factors for miscarriage because this group has a greater BMI. Women with a

BMI > 25 kg/m² have a lower chance of pregnancy following IVF (odds ratio [OR], 0.71; 95% confidence interval [CI], 0.62, 0.81), require higher dose of gonadotropins (mean differences, 210.08; 95% CI, 149.12, 271.05), and have an increased miscarriage rate (OR, 1.33; 95% CI, 1.06, 1.68).¹⁷ In addition, African American women have increased rates of gestational diabetes mellitus, gestational hypertension, preeclampsia, placental abruption/infarction, and increased pre-term births (PTBs) and intrauterine growth restriction (IUGR). These reproductive consequences are discussed in detail in subsequent articles of this issue. The salient point is that obesity may contribute to reproductive health disparities. Thus, these conditions may be linked to in utero events and exposures.

Epigenetic and Transgenerational Effects on Metabolic Syndrome

Precisely how obesity is programed in utero is not entirely clear. Nonetheless, persistence of metabolic syndrome in certain racial groups likely arises from epigenetic and trans-generational effects. Examples of epigenetic changes include DNA methylation of CpG dinucleotides, RNA-associated gene silencing, chromatin remodeling, and posttranslational adenosine triphosphate-dependent histone modification.¹⁴ DNA methylation acts with other enzymes to covalently modify histones to cause gene silencing or activation depending on the location.¹⁸ The transmission of epigenetic information between generations in the absence of any direct environmental exposures is defined as epigenetic transgenerational inheritance.¹⁹

Of note, epigenetic changes were shown to exist in offspring of mothers exposed to the Dutch famine who had increased prevalence of childhood adiposity and increased insulin resistance. Hypomethylation at the promoter of insulin-like growth factor 2 (IGF2) was noted in offspring of mothers exposed to famine periconceptionally.²⁰ Studies between same-sex adult siblings who were exposed to the famine in utero and who were not exposed showed that the exposed siblings have less DNA methylation at the imprinted IGF2 locus 60 years following the famine. IGF2 is a key factor in human growth and development and its hypomethylation leads to bi-allelic expression of IGF2 increasing its levels.²¹ Associations between DNA methylation at IGF2 differentially methylated regions and increased circulating IGF2 protein concentrations were found in umbilical cord blood of neonates of overweight mothers.²² Therefore, methylation at IGF2 regulatory regions appears to be one early marker for future obesity.

Epigenetic change that results in transgenerational change is best demonstrated by animal models of in utero exposure to toxins that are highly prevalent in low-income areas. In the event that the germ cell is affected by environmental exposure, the altered germ line has the ability to promote a transgenerational phenotype that is maintained in future generations.¹⁹ For example, reduced fertility and an increased incidence of PTB were noted in mice exposed in utero to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). TCDD is an endocrine disrupting toxin known to interfere with reproductive function in humans and is an unwanted by-product of industrial processes. This phenotype, decreased fertility and increased preterm delivery, was maintained for multiple generations despite no exposure to the toxin.²³ In addition, the Skinner laboratories showed that exposure to vinclozolin (fungicide) and methoxychlor (pesticide) by mothers showed a twofold increase in

spermatogenic apoptosis, reduced sperm numbers, and reduced sperm motility in their offspring. These phenotypes were transmitted specifically through the male germ cell line. Vinclozolin was shown to disrupt DNA methylation in rat testes. In later studies, the Skinner laboratory observed that the male rodent offspring had epithelial cell atrophy, glandular dysgenesis, prostatitis, and hyperplasia of the ventral prostate four generations later.^{24,25}

Poor Obstetrical Outcomes, Growth Restriction, and Preterm Birth

African Americans have an increased incidence of low birth weight (LBW) and growth restricted (IUGR) fetuses. The incidence of IUGR is below 7% in developed countries but as high as 16.5 to 18% in developing countries.^{26–28} LBW has been defined by the World Health Organization as weight at birth of less than 2,500 g and very low birth weight (VLBW) as weight less than 1,500 g. The risk factors for IUGR include maternal malnutrition, lifestyle (e.g., alcohol, tobacco, or drug abuse), infectious exposures (e.g., malaria, HIV, or syphilis), hypertension or preeclampsia, obesity, and diabetes. Many of these risks are associated with deprived socioeconomic conditions. In addition, it is difficult to determine whether the majority of these low-birth-weight infants are a result of early delivery (preterm labor) versus growth restriction. In a population study of 7,800 infants of LBW, Sparks²⁹ found an OR of 2.09 among non-Hispanic blacks compared with non-Hispanic whites. These large disparities between races have remained stable over years. LBW among white mothers was stable at 7.19% from 7.14% of the previous year. Non-Hispanic blacks had a significantly higher rate of 13.53% similar to the previous year and Hispanic women had a stable rate of 6.97%. In regard to the VLBW infants, those infants at the greatest risk of adverse outcomes were approximately 2½ times as high among non-Hispanic black infants in comparison with non-Hispanic whites. The VLBW rates for non-Hispanic blacks were 2.98%, compared with 1.16% for non-Hispanic whites and 1.20% for Hispanic infants (•Fig. 2).³⁰

Based on the concept of DOHaD, an IUGR fetus would be expected to have excess weight gain and metabolic disorders in adulthood, including diabetes and obesity.^{31,32} These neonates will need to “catch up” with growth during infancy, which has been shown to even further increase insulin resistance and visceral adiposity.^{33–35} After the Dutch famine, neonates who were starved in utero and were born IUGR were able to eat normal diets because the famine was over. The death rates from cardiovascular disease were highest among men who were thin at birth but had accelerated weight gain in childhood.^{5,36,37} In contrast, during the famine in Leningrad, the neonates continued to be nutritionally deprived after birth and the rates of coronary heart disease were not increased.

Rat and primate models have been useful to assess models of IUGR and development of disease. The concept of catch-up growth can be seen in the Fernandez-Twinn et al³⁸ study where pregnant rats were fed reduced protein in comparison with normally fed controls. The levels of maternal serum leptin were increased in the malnourished group and the rat pups suffered from IUGR. However, in adulthood once they caught up with normal or above average weights, the rats were more likely to develop diabetes and hyperinsulinemia.³⁸ The transition from nutritional deprivation in early gestation to nutritional adequacy later on may have led to metabolic conflicts resulting in disease in later life.⁵ This conflict has to do with

“The Mismatch Concept”; when there is a “match” between the predicted and the actual environment, survival is maximized. Conversely, when the two environments are “mismatched,” a predisposition to disease may result.

Preterm Birth

African Americans have a higher rate of PTB (16–18%) than other racial/ethnic groups (11.4% in white and 12.2% in Hispanic women).³⁹ It is hypothesized that this difference is related to the poorer overall preconception health with higher median health burden scores, 3.0, compared with white or Mexican American women who had a median of 2.0.³⁹ This high rate of PTB is also observed in pregnancies conceived by assisted reproductive technology (ART). Early PTB and very early PTB ORs were 1.79 and 4.25, respectively ($p < 0.0001$) in African American compared with white populations in pregnancies conceived by ART.⁴⁰

Poor health conditions such as diabetes, hypertension, iron-deficiency anemia, obesity, and infections are contributing factors to the increased rate of preterm delivery among African Americans.^{41–43} Multiple studies have confirmed the link between maternal obesity and PTB.^{44,45} An increased risk of PTB was found in women with BMI > 25 (OR, 1.662; 95% CI, 1.033–2.676; $p = 0.0365$) in a retrospective study.⁴⁵ The increased rates of obesity in African American population contribute to their increased rates of preterm labor; however, even when these poor health conditions were taken into consideration, African Americans continued to have higher rates of PTBs compared with whites. Among low-risk women, (defined risk status using maternal age, education, marital status at delivery, parity, interpregnancy interval, tobacco or alcohol use, source and amount of income, and pre-pregnancy BMI), multiparous African American women still had more PTBs than white women (OR, 1.3; 95% CI, 1.0, 1.6).⁴⁶ Therefore, there may be an inherent link between race and predisposition to preterm labor that cannot be explained by traditional risk factors.⁴⁶

Collins et al⁴⁷ undertook an analysis of Illinois vital records and US Census income data to determine the extent to which former LBW and non-LBW African American women's upward economic mobility across the life course was associated with the PTB of their children. The upward economic mobility in African American from early life impoverishment was associated with a decreased risk of PTB. However, consistent with fetal reprogramming, this phenomenon failed to occur among mothers born at LBW.⁴⁷ This finding suggests that the epigenetic changes that passed down from previous generations were unable to be modified by improved socioeconomic status.

In addition to in utero stress, environmental exposures can alter the epigenome and cause disease that is passed from generation to generation (transgenerational effect). In an animal model, this effect includes susceptibility to preterm labor. In utero exposure to TCDD led to alterations in normal adult rat reproductive function and negatively influences maintenance of pregnancy in their offspring.⁴⁸ Bruner-Tran and Osteen²³ developed a murine model of TCDD exposure during pregnancy to examine the potential developmental effects of this toxicant on reproductive function. The investigators observed that female mice exposed to TCDD in utero exhibited a dose-dependent reduction in uterine progesterone receptor (*Pgr*)

messenger RNA (mRNA) and protein expression as adults. The link between reduced levels of progesterone and preterm labor is a well-known phenomenon. Female mice frequently exhibited infertility and PTB was common in mice achieving pregnancy. In addition, PTB in offspring of exposed female mice was associated with a heightened sensitivity to inflammatory challenge when these mice were injected with a lipopolysaccharide inflammatory trigger. These phenotypic changes persisted for three generations among female offspring in the absence of additional toxicant exposure.

Developmental TCDD exposure was also found to negatively impact placental development in offspring, resulting in alterations in inflammatory signaling at the maternal–fetal interface, which compromised pregnancy maintenance. Fish oil supplementation of toxicant-exposed males led to normalization of placental expression of both *Pgr* and *Tlr4* mRNA and a marked increase in 15-hydroxyprostaglandin dehydrogenase (15-PGDH) expression. PGDH catabolizes the inflammatory prostaglandin E₂ (PGE₂) to an inactive form; thus, reduced expression of this enzyme would promote tissue inflammation. These studies suggest that a paternal preconception diet that includes omega-3 fatty acids prevents the toxicant-associated increase in the placental inflammatory response at late gestation, preventing PTB.⁴⁸

Omega-3 fatty acids play an important role in regulating inflammation via multiple mechanisms.⁴⁹ A recent human study has demonstrated incorporation of omega-3 fatty acids into leukocyte phospholipids and plasma within as short as 1 week of nutritional supplementation with fish oil.⁵⁰ These studies further revealed that fish oil supplementation or eicosapentaenoic acid (EPA) led to displacement of omega-6, a more inflammatory fatty acid from the cell membranes. Animal studies clearly support a role of dietary fish oil supplementation in rapidly modulating cell membrane composition and potentially influencing local tissue inflammation. However, reduction of preterm labor with omega-3 fatty acids in humans has shown mixed results with a significantly reduced risk of PTB < 34 weeks (relative risk (RR), 0.7; 95% CI, 0.5–0.9), but no reduction in high risk women for preterm labor < 37 weeks in randomized control trials.^{48,51–53}

Ethnic Differences in Assisted Reproductive Technology Outcomes

It is unclear how stress in utero affects an offspring's fertility potential. Based on studies on the offspring of mothers exposed to the Dutch famine, there was increase in fertility.³ However, data from animal models in mice show that maternal food deprivation induced a decrease in litter size of their daughters.⁵⁴ In cattle that were nutrient deprived, their offspring had fewer primordial and primary follicles and less healthy antral follicles along with a reduced number of ovulations in adult life.⁵⁵ Therefore, although animal models predict lower levels of fertility, there is no evidence in humans to corroborate this observation.

The SART database reveals lower pregnancy rates and higher miscarriage rates among blacks as compared with white women after controlling for age.^{40,56,57} Compared with white women, Hispanics and Asians had a significantly greater risk of pregnancy loss in the second and third trimesters, and African Americans had a significantly greater risk of

pregnancy loss in all trimesters.⁵⁷ Asian women had lower odds of clinical pregnancy and a live birth than white women.⁵⁸

The increase in poor prognostic factors of older age, diminished ovarian reserve, uterine factor, and suspected untreated tubal factor among black women may in part have contributed to the widening disparity of clinical outcomes between black and white women for clinical intrauterine gestations, and live births per cycle of initial ART started in 2004 to 2006 (22.2 vs. 32.3%, a 31% difference) in contrast to 1999 and 2000 (20.7 vs. 28.4%, a 27% difference). However, black women were still less likely to experience live birth per cycle of ART when controlling for age, parity, diagnosis.⁵⁶ African Americans have fewer embryos than Caucasian women and need more gonadotropin stimulation possibly related to their higher BMIs and, therefore, higher estrogen levels.⁵⁹ The higher prevalence of obesity and other cardiometabolic disorders in African Americans may be a factor in their worsened ART outcomes.

The *in vitro* environment in which the embryo develops in ART can cause widespread epigenetic modifications that can be linked to adipocyte development and differentiation, insulin signaling, and obesity.^{60,61} Changing culture conditions in mouse models with higher levels of oxygen tension causing increased ROS was shown to alter the normal epigenetic pattern and gene expression in the embryo and the placenta. However, there is no evidence that these epigenetic changes are race dependent, aside from the link to the epigenetic changes with obesity described in previous sections.

Racial and Ethnic Differences in the Physiology and Clinical Manifestations of Polycystic Ovarian Syndrome

The prevalence rates of polycystic ovarian syndrome (PCOS) for black and white women are not significantly different.⁶² Most of the differences in biometric and reproductive profiles of PCOS patients are linked to obesity. Overweight and obesity prevalence rates for black and white women with PCOS were statistically significant (25 and 42% vs. 21 and 19%). However, African American and white women with PCOS have a similar prevalence of metabolic syndrome when controlling for obesity, suggesting that the diagnosis may not be associated with inherent racial differences in cardiovascular risk factors.⁶³ Published reports consistently show that African American women with and without PCOS are more likely to be obese when compared with other racial groups and to have a higher odds of hypertension.

The genetics of PCOS is complicated by complexity of the disease and several metabolic and biochemical pathways are implicated. Multiple candidate genes have been found; however, the genetic reproducibility has been limited. There is a possibility that epigenetic factors may contribute to the PCOS phenotype because an elevated BMI and insulin resistance has clearly shown epigenetic inheritance.⁶⁴ Hickey et al⁶⁵ studied epigenetic changes between sisters and found a statistical odds on a different clinical presentation (one sister with PCOS and one without) between sisters to be approximately 29 times higher in sister pairs with different patterns of X-chromosome inactivation (XCI), compared with sister pairs with the same pattern of XCI (OR, 28.9; 95% CI, 4.0–206; $p = 0.0008$). It is also possible that the environmental exposure to excess androgens during fetal organogenesis

may also cause PCOS, as animal studies have shown changes in XCI of androgen receptor with exposure to androgens in utero and production of PCO phenotype.⁶⁶ However, there is no evidence that certain racial groups are exposed to excess androgens in utero and carry this specific epigenetic XCI. Therefore, although epigenetics is a possible factor in PCOS, given current research it is unlikely to contribute to racial differences of PCOS.

Conclusion

There are an abundance of animal models to support the DOHaD hypothesis and the concept that the early life environment has widespread consequences for later health. Studies in animal models have shown abnormalities of insulin secretion and action, appetite regulation, obesity, nonalcoholic fatty liver disease, hypertension, and cardiovascular parameters following a variety of dietary challenges and toxic exposures during pregnancy.¹⁸ Given the historical nutritional deprivations that are linked to race and ethnicity, it is possible, even likely, that such stresses contributed to reproductive health disparities.

How might we reverse transgenerational effects that are rooted in utero exposure?

Animal models suggest solutions. For example, antioxidant and folic acid administration may be able to reverse the deleterious effects of generations of poor environmental exposures. The agouti mice have also been used to study the transgenerational inheritance of obesity because they have a propensity toward obesity and diabetes. Methyl supplementation of the maternal diet prevented the inheritance of obesity in the agouti mouse. This treatment may be one mechanism to improve outcomes in humans; by supplementing pregnant women with folic acid during the periconceptional period, specifically for certain racial groups, deficiencies can be modified. According to 2001–2002 NHANES data, African American women have lower folate intake (from both food and supplement sources) and while approximately 40% of Caucasian women consume 400 µg of folic daily, only 5% of African Americans achieve 400 µg of folic acid daily from fortified foods and supplements.⁶⁷ In addition, Bogdarina et al⁶⁸ showed that rats which received a low-protein diet during pregnancy had decreased DNA methylation of the angiotensin receptor gene in the adrenal gland (Agtr1b), which was upregulated by the first week of life in offspring, explaining the increase in blood pressure among these animals. When angiotensin receptor blockers were administered to mothers, in utero rates of hypertension were decreased. Mentioned previously, omega-3 (EPA and docosahexaenoic acid) antioxidants were also helpful in reversing the deleterious effects of TCCD exposure reducing preterm labor in generations of mice and have shown some benefit in randomized trials in humans.

In summary, more work needs to be done in this area specific to therapeutic benefits of interventions for different racial groups. Minority groups suffer from poor education and access to health resources, along with poor nutrition.⁵² Instituting public policies encouraging more preconception education and health literacy,³⁶ weight loss and improved diet are important especially preceding and during pregnancy. Importantly, reproduction, in general, and pregnancy, specifically, provide a unique opportunity to break the repeating cycle of health disparities fomented by historical nutritional deprivation (and current poor

nutrition), which may contribute, in part, to health disparities in many diseases involving many organ systems.

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Figure 1.

Prevalence of obesity by race and ethnicity in the United States. Y-axis, percentage of obese individuals in the respective groups. The prevalence of obesity among women increased in all ethnic groups in the United States between 1988–1994 and 2009–2010 according to the National Health and Nutrition Examination Survey data in 2009–2010.⁸

Figure 2.

Percentage of infants with low birth weight (LBW) and very low birth weight (VLBW) by race and ethnicity in the United States according to vital statistics records.³⁰ LBW, birth weight < 2,500 g; VLBW, birth weight < 1,500 g. There were large disparities between races in rates of LBW/VLBW. Non-Hispanic blacks had a significantly higher rate of LBW/VLBW in 2009 in comparison with whites and Hispanic women.