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Gravens By Design: Racial Disparities in Preterm Birth are Rooted in Environmental Exposures

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For decades, epidemiologic studies have shown persistent racial disparities in preterm birth. Compared with white infants, Black infants are 50% more likely to be born preterm and three times more likely to be born extremely preterm (<28 weeks of gestation). (1) Investigators have searched for the etiology of racial disparities in preterm birth, but the phenomenon remains poorly understood. The lack of meaningful progress in achieving equity with respect to preterm birth results from two major knowledge gaps. First, we lack a fundamental understanding of the pathophysiology of preterm birth (regardless of race). Second, we conflate race with genetics. As scientists work to delineate the biological processes that lead to preterm birth, we, as a society, must recognize that race is a social construct with biological implications. Given longstanding racial segregation in nearly all aspects of life in the U.S. (residential, occupational, recreational, etc.), environmental exposures differ by race and affect the chances of a healthy, long life.

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Spontaneous preterm birth occurs without any intervention by a provider, while the medically indicated preterm birth occurs after induction or cesarean birth. As neonatal providers, we use many of the same clinical tools to provide intensive care for extremely preterm infants regardless of why a particular infant was born early. There are a few exceptions. We might be more likely to use antibiotics if there had been spontaneous preterm labor or less likely to feed soon after birth if there had been severe preeclampsia with significant placental insufficiency and intrauterine growth restriction.

However, for the most part, we treat infants very similarly, given their gestational age and set of presenting signs. Yet, the maternal processes that occur in the setting of preterm labor or preeclampsia, for example, are different. The former might be triggered by ascending intrauterine infection (2) and the latter by events that remotely occurred during implantation. (3,4) These etiologies of these distinct processes remain poorly understood and very difficult to prevent, reducing racial disparities in these conditions nearly impossible for clinicians. However, clues from other complex, multifactorial, heterogeneous health conditions may provide some insights.

All health exists along a continuum from genetic in origin to environmental and most conditions exist in between (Figure 1). During medical training, we learn about monogenic disorders such as sickle cell disease and cystic fibrosis caused by single-gene mutations. (5,6) These mutations have varying population frequencies in different racial groups. Thus, the racial disparity in these disorders is attributable to genetics. The connection between genes and race can become entrenched in clinical medicine because of the strong association between race and those monogenic disorders. However, race and genetics are not synonymous. There are a few ways to demonstrate this. First, there is more genetic variation within racial groups than between. (7) To conceptualize this concept, let us consider height. Some groups of people are shorter than other groups. However, there is a larger variation within a population than between populations; the average heights of various populations are more similar than the range of heights within a population. Second, there has been so much sharing of genetic information between racial groups in the U.S. that race is not a reliable way to determine whether individuals are at risk for sickle cell disease or cystic fibrosis.

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Thus these conditions are now part of routine newborn screening for all infants since race is not a reliable screening tool for who should be tested. (8,9) Finally, even if we recognize that some genetic sequences are more common in one racial group from shared ancestry, (10) for complex, multifactorial, heterogeneous conditions, (11,12) the role of genetics is dwarfed by environmental determinants of health. Concerning preterm birth, the most compelling evidence regarding the critical role of the environment comes from studies of foreign-born and US-born Black birth outcomes. Foreign-born Black individuals have lower preterm birth rates (similar to rates among US-born white individuals) than US-born Black individuals, and this foreign-born advantage erodes after a single generation of living in the U.S. (13,14) Genetics do not change that quickly, and no single gene is going to be responsible for spontaneous rupture of membrane, preterm labor, preeclampsia, abruption, impaired fetal growth- all of which can lead to an infant being born preterm and all of which have large racial disparities.

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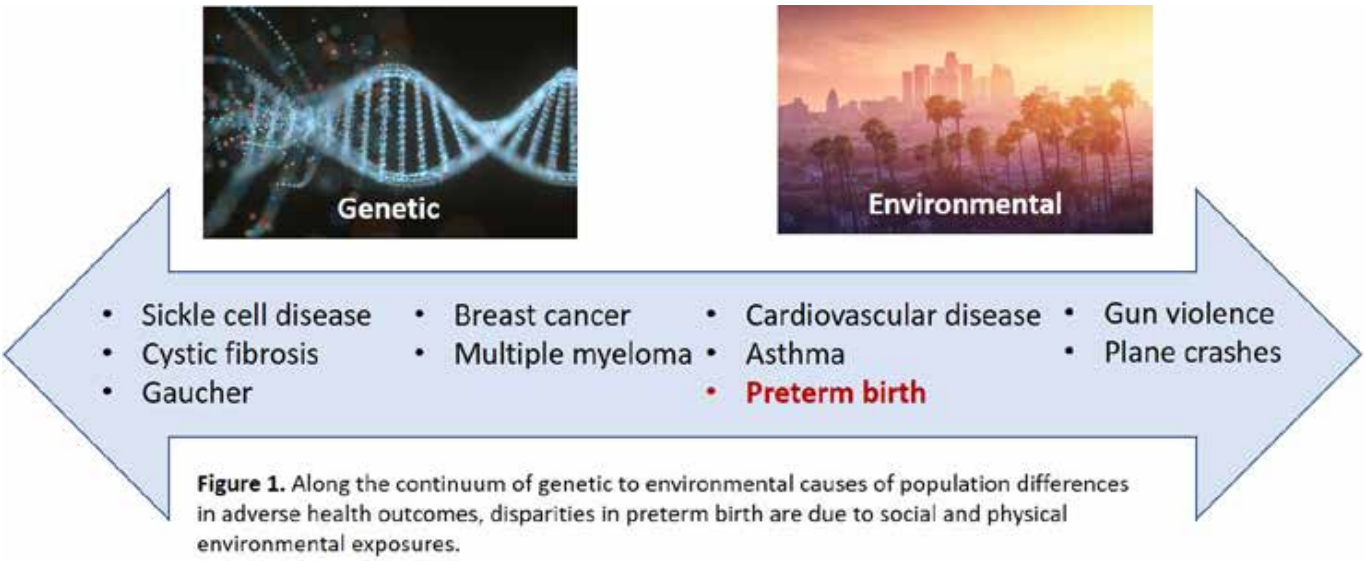

Figure 1. Along the continuum of genetic to environmental causes of population differences in adverse health outcomes, disparities in preterm birth are due to social and physical environmental exposures.

Clinicians alone will not be able to solve racial disparities in preterm birth. We must turn to our colleagues in public health, anthropology, and sociology. The critical question is why so many heterogeneous, multifactorial health conditions are more common among Black individuals in the U.S. There are two possibilities, differential susceptibility to, or differential doses of, harmful and beneficial exposures. Given the vastly different exposures to stressors (e.g., racism, poverty) (15) and toxicants (e.g., air pollution, heavy metals), (16) the differential doses of exposures are more likely to contribute to disparities in complex conditions. The mechanisms by which these exposures lead to complex disorders are an active area of investigation using "omic" technologies. Exposures can lead to differences in the microbiome, metabolome, epigenome, etc. These mechanisms change cellular and, ultimately, organ function leading to disease.

"However, simply because one can study these mechanisms does not mean the medical interventions will resolve disparities in health. It is possible, and even likely, that differences in omic signatures by race may be the result of environmental exposures. A societal movement to addresses the upstream structures of inequity resulting from historic and ongoing racism will be required to equalize the opportunity to lead healthy, long lives."

However, simply because one can study these mechanisms does not mean the medical interventions will resolve disparities in health. It is possible, and even likely, that differences in omic signatures by race may be the result of environmental exposures. A societal movement to addresses the upstream structures of inequity resulting from historic and ongoing racism will be required to equalize the opportunity to lead healthy, long lives. Potential interventions include providing a universal basic income, (17) expanding Medicaid, (18) greening vacant lots in urban settings, (19) and investing in Black neighborhoods. (20) Nothing short of a comprehensive effort to improve social and physical environmental exposures will achieve perinatal health equity.

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