Intergenerational Transmission of the Effects of Acculturation on Health in Hispanic Americans: A Fetal Programming Perspective

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We propose a transdisciplinary, life span framework for examining the underlying cause of the observed intergenerational decline in health among Hispanic Americans. We focus on acculturation, and we posit that acculturation-related processes in first-generation Hispanic immigrant mothers may affect the intrauterine development of an unborn child, via the process of fetal programming, to produce phenotypic effects that may alter the susceptibility for noncommunicable chronic diseases. In this manner, an intergenerational cascade of perpetuation may become established. Our framework may shed light on the biological, behavioral, and social causes of intergenerational cycles of vulnerability among immigrant minority groups, with public health and policy implications for primary prevention and intervention. (*Am J Public Health*. 2015;105:S409–S423. doi:10.2105/AJPH.2015.302571)

The public health significance of addressing the issue of health and health disparities in Hispanics, the largest ethnic minority in the United States[1] and an especially disenfranchised segment of American society,[2] is well established. The fact that the majority of Hispanic Americans are immigrants or the children of immigrants,[3] coupled with the robust epidemiologic observation that Hispanic immigrants in the United States exhibit a progressive decline in health over time[4–11] and across generations,[5,12–20] has justified a particular focus on how postimmigration conditions affect health in this population. The negative consequences of acculturation have commonly been invoked to explain this phenomenon, and several studies in Hispanic Americans have established associations between measures of acculturation and adverse health outcomes.[21–24] The prevailing paradigm posits the deleterious effect of acculturation on health is a consequence of the biological embedding of its psychological and behavioral sequelae, such as excess psychological stress,[25–27] declining social ties,[28,29] and adoption of unhealthy diets and other behaviors.[30–36] This paradigm, as currently formulated, may account for the observed decline in first-generation immigrant health associated with length of residence in the United States. However, a major shortcoming is that it does not adequately explain the intergenerational aspect of the observed health decline. We sought to address this important limitation.

In this article, we articulate a novel framework that is grounded in principles from evolutionary and developmental biology, and we integrate the concepts of biological embedding of life experiences and fetal origins of health and disease risk. We propose that the origins of the observed intergenerational health decline among Hispanic Americans might be traced back to as early as the intrauterine period of life, at which time the effects of acculturation could be transmitted from a mother to her as-yet-unborn child via the process of fetal programming. This process might produce phenotypic alterations in the structure and function of cells, tissues, and organ systems that increase the offspring's susceptibility for developing many of the health disorders that are disproportionately prevalent among Hispanic Americans. In this manner, an intergenerational cascade of perpetuation of the deleterious consequences of acculturation on health might become established. Our framework also addresses the proximate causal pathway by highlighting the tripartite role of maternal–placental–fetal endocrine, immune, and oxidative-state–related biological processes, such as sensors, transducers, and effectors of acculturation-related states and conditions on the developing fetus. The plausibility of our formulation was supported by empirical evidence in the general population that the same psychological and behavioral processes associated with acculturation (e.g., stress, diet) are also known to affect biological processes implicated in fetal programming.[37] Moreover, studies in pregnant Hispanic women demonstrate that maternal acculturation is associated with the same psychological, behavioral, and biological processes during gestation that are implicated in the process of fetal programming.[30,33,38–41] In this way, we suggest that the fetal programming perspective potentially offers a parsimonious explanation for the observed intergenerational decline in Hispanic American health, and also reconciles the apparent contradiction between the observations in this population that disease risk increases across generations despite improvements in life conditions.

SIGNIFICANCE OF HISPANIC AMERICAN HEALTH

The importance of addressing the issue of health and health disparities in minority and underserved populations is well recognized[42,43] (Healthy People 2020[44]; NIH Health Disparities Strategic Plan 2009–2013[45]), and the need for investigating the social determinants of health disparities is well established.[46–50] In this context, a particular focus on the Hispanic population in the United States is warranted. Hispanic Americans exhibit disproportionately high rates of many of the noncommunicable chronic disorders (NCDs) that confer the major national burden of disease, including obesity,[51] diabetes,[52] the metabolic syndrome,[53] certain cancers,[54] and dementia.[55]

Hispanics currently represent the largest minority group in the United States, and it is projected that by 2030, Hispanics will constitute one third of the United States population.[1]

Moreover, Hispanics are the most rapidly growing population in the United States,[56] and the only ethnic group projected to maintain population growth above replacement level.[57] The majority (70%) of Hispanics in the United States are immigrants or the children of immigrants.[3] Hispanics exhibit the highest immigration rate to the United States of any ethnic group,[58] making up 36% of all immigrants in the United States.[58] Mexican Americans account for the majority (65%) of Hispanic Americans.[56] Hispanics represent a disadvantaged segment of American society. According to the Census Bureau's Supplemental Poverty Measure, Hispanics have the highest poverty rate (28.2%) of any ethnic group in the United States.[59] Mexican immigrants are exceptionally disenfranchised, with the highest poverty rate (29%) of any immigrant group in the United States.[60,61]

EPIDEMIOLOGICAL TRENDS IN HISPANIC AMERICAN HEALTH OUTCOMES

Two major epidemiological trends have consistently been described in terms of health outcomes in the Hispanic American population: a health paradox, and an acculturation paradox. The Hispanic health paradox[62] refers to the observation that despite lower socioeconomic status (SES) and less access to health care, Hispanic Americans appear to exhibit mortality rates[63–67] and health outcomes[68,69] that are similar to non-Hispanic White Americans, and are more favorable than those of other disadvantaged minorities, such as African Americans (although not all studies have demonstrated this effect[70–73]). This pattern does not appear to merely reflect data artifacts,[74–78] although healthy migrant (selective migration) and salmon biases (selective return migration because of poor health) may contribute.[77,79]

A more nuanced trend is revealed upon closer inspection: the acculturation paradox. After immigrating and while acculturating to the mainstream US lifestyle, Hispanics appear to exhibit a progressive decline in health, in many instances despite concurrent improvement in SES and greater access to health care.[8,17,18,69,80–91] First-generation (immigrant) Hispanics exhibit better physical[5,12,13] and mental[14–20] health outcomes, and lower mortality rates[67] than second-generation (US-born) Hispanics. Also, among first-generation Hispanics, longer residence in the United States has been associated with diminished mental[4] and physical health[5–11] and higher mortality rates.[67]

The Construct of Acculturation

Of the myriad factors that influence health, the effects of postmigration sociocultural conditions in the Hispanic population may warrant particular consideration because, as discussed previously, the majority of Hispanics in the United States are immigrants or the children of immigrants.[3] The rapid rate of Hispanic immigration is a major contributor to the growth of this population.[58,92] Migration necessitates adjustment to life in the adoptive-host country, which may be substantially different from life in the origin country. This adjustment may involve changes in identity, values, beliefs, and behaviors. The term "acculturation" is commonly used to describe this process of postmigration adjustment, which involves the acquisition of the host-country cultural orientation, the loss of origin-country cultural orientation, or both.[93–95] Some of the major aspects of cultural change measured in acculturation instruments are related to language, self-identification, attitudes, knowledge of customs and history, contact with media, and social interactions.[96,97]

The construct of acculturation was born more than 100 years ago in anthropology,[94] subsequently adopted by psychology,[95,98–100] and more recently, it has become a concept of interest in the biomedical community.[101,102] Along the way, a variety of changes have been proposed and made to its conceptualization and operationalization. Acculturation was initially conceptualized to be a unidimensional process, with adoption of host country culture necessarily characterized by loss of heritage country culture.[103–106] Thereafter, acculturation was considered a multidimensional process with cultural change occurring independently in various domains,[105,107,108] or as a bidimensional process[93,109] in which acquisition of the host culture and retention of the heritage culture represent independent, orthogonal processes.[105,109–111] The conceptualization and operationalization of the construct has been critiqued for various reasons.[112–114] For example, sociocultural changes occur at varying rates and time points, in multiple directions, with variation in the order and nature of these life changes,[115] which is not sufficiently captured in many of the existing instruments. One ideology with respect to intercultural relations, often adopted in the United States, is guided by an assumption of assimilation, in which the terms acculturation and assimilation are equated and used synonymously. However, this may not represent an accurate depiction because acculturation can take many different paths.[100,116] For example, certain acculturation strategies are more often associated than other strategies with health mediators (e.g., psychological distress). With regard to the widely used 4-category model of acculturation profiles by Berry,[100,117] research has demonstrated that individuals who abandon heritage cultural identity alongside acquisition of host cultural identity ("assimilation"), or who retain heritage cultural identity and do not acquire host cultural identity ("separation"), may be at greater risk for poor mental health than those who exhibit a bicultural orientation ("integration").[108,109,118–121] However, biculturalism has also been associated with higher levels of stress attributed to one's role as cultural translator in the family,[32,122] and has been associated with poor health in some studies.[111,123] Lastly, the effects of acculturation on health may be context-dependent and vary as a function of the underlying reason(s) for migration, relative changes between heritage and host cultures, the ethnic composition of the neighborhood of residence, and sociological features of the host country.[112,116,124,125] It is important to note that many studies of the relationship between acculturation and health do not adequately address these issues. Moreover, for lack of access or ease of operationalization, several studies have relied on acculturation proxy variables, such as nativity, length of stay in the United States, and language preference or use instead of assessing acculturation directly.[22,126–128]

Evidence of the Acculturation Paradox

The Hispanic acculturation paradox refers to the observed decline in mental and physical health that is concurrent with duration of residence in the United States,[5–11] and also occurs across generations in the United States.[5,12–20] For example, higher degrees of acculturation (typically defined as greater

adoption of Anglo cultural identity) and later generation status have been associated with overall more mental health problems,[14–16] including higher rates of psychopathology,[17,18] anxiety,[129–131] depression,[19,131,132] and fewer positive self-feelings.[133] Degree of acculturation has been associated in many studies with decline in physical health for a range of chronic conditions,[5,67,74] including poor overall physical health,[74] hypertension,[88] cardiovascular disease,[13] and diabetes.[12,134] It should be noted that some studies have failed to demonstrate a relationship between acculturation and health,[36,85,135–146] and that a few studies have reported health advantages.[80,84,86,147]

The acculturation paradox is particularly apparent when considering birth outcomes and obesity. For example, a greater degree of acculturation[33,82,148] and later generation status[82,90,149–155] have been associated with adverse birth outcomes, including low birth weight and premature birth, as well as lower infant survival[89,156–158] (see Lara et al.[159] for review). Among Hispanic immigrants, English language preference[160] and length of United States residence[6,67,161–166] have been positively associated with body mass index and the likelihood of being overweight or obese. Generation status has also been positively associated with body mass index and obesity, such that second-generation Hispanics have higher rates of obesity than first-generation Hispanic immigrants.[67,160,162,167–169] These trends have been observed among Hispanics across the entire age spectrum, including children and adolescents[161,170] (see Yeh et al.[171] for review).

Existing Paradigm Proposed to Explain the Acculturation Paradox

Change in an individual's health after migration could hypothetically be attributable to change in ecological–environmental conditions or change in sociobehavioral conditions.[172–174] Because the observed postmigration decline in Hispanic health has been shown to occur despite improvement in ecological–environmental conditions, such as higher SES, residence in neighborhoods with more health-promoting resources, and greater access to health care and education,[8,17,18,69,80–91] previous authors have suggested changes in other factors as the likely pathway. The prevailing paradigm to explain the Hispanic acculturation paradox (Figure 1) posits that the effects of acculturation on health are mediated via the behavioral and psychological sequelae of acculturation, including (1) unhealthy behaviors, (2) loss of social support, and (3) acculturative stress, that, in turn, have impact on biology and health (i.e., the concept of biological embedding of life experience[175,176]). These pathways are not mutually exclusive. Here, we briefly summarize these processes (for reviews, see[96,112,159]).

Unhealthy behaviors. Acculturation appears to be associated with the adoption of unhealthy behaviors and the abandonment of healthy behaviors. Traditional Hispanic cultural values are generally associated with healthier behaviors that have been shown to deteriorate with acculturation. Acculturation has been associated with poor nutrition diets,[81,161,177–181] fast food consumption,[182,183] and less fruit and vegetable consumption.[184,185] Acculturation has been positively associated with smoking,[186,187] alcohol consumption,[188,189] and illicit drug use,[14,15,135,137,190–193] especially marijuana and cocaine.[190,194,195] Subsequent-generation Hispanic immigrants are more likely to have insufficient sleep duration than first-generation Hispanics,[196–198] and acculturation has been associated with poor sleep quality[199,200] and insomnia.[201] Contrary to expectations, acculturation among Hispanics appears to be associated with increasing amounts of time engaged in physical activity.[202–206]

Loss of social support. The direct and indirect pathways linking social networks, relationships, and support with health are well established.[207–209] A distinctive feature of Hispanic cultures is the quality of "familism,"[28] which refers to strong attachment, identification, and loyalty toward one's family[132] and a high degree of social support.[210–212] Immigration erodes ties between immigrants and family remaining in the home country, causing loss of social support and psychological distress.[213] Maintaining contact with loved ones in the origin country can be more difficult with an increasing degree of acculturation because of linguistic and cultural barriers.[214] Social isolation may accompany improvements in SES, as wealthier communities may also be characterized by fewer coethnics and more racism.[215]

Acculturative stress. The direct and indirect pathways linking psychological stress with health are well established,[216–218] including elucidation of their endocrine,[219,220] immune,[221,222] and oxidative[223,224] pathways. Moreover, the effects of stress on health have been also demonstrated specifically in Mexican immigrants.[225,226] The psychological distress associated with acculturation has been referred to as "acculturative stress,"[26,227] and several authors have discussed the role of acculturative stress in negative health outcomes and as an important contributor to the acculturation paradox.[130,131,228–231] Learning a new

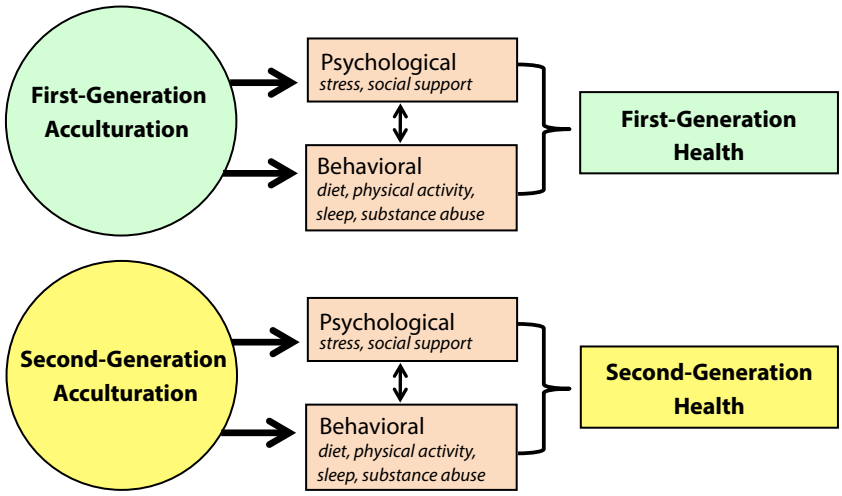


FIGURE 1—The prevailing paradigm, which suggests that the decline in health observed both within individuals and across generations of Hispanic Americans is explained by the degree of acculturation.

language, customs, dress, cuisine, and interpersonal relationship styles can induce a high degree of psychosocial stress.[214,232] The loss of heritage identity may be its own source of psychological stress.[18,233,234] Poor English language ability and the challenges of finding living arrangements and employment have been associated with a greater degree of acculturative stress.[214,235] Fear of deportation can induce acculturative stress,[236–238] and legal status can affect immigrants' ability to incorporate into the mainstream culture.[239] Documented and undocumented Hispanic immigrants have been shown to exhibit similar degrees of fear of deportation[240] and no differences in health outcomes.[155] Hispanics generally face considerable racism or discrimination,[241] with studies suggesting that US-born Americans tend to regard Hispanic immigrants the most negatively of any migrant group in the United States.[242] Immigrants may experience stress resulting from discrimination by Whites, other minorities, and later-generation Hispanic Americans.[243,244]

Acculturation and Biological Processes

A relatively small number of studies have examined the relationship of acculturation with biological pathways. In studies that used proxy measures of acculturation, nativity status (US-born Hispanics compared with foreign-born Hispanic immigrants) and longer duration of residence in the United States among Hispanic immigrants have been associated with higher blood pressure, metabolic risk biomarkers such as higher total cholesterol, low high-density lipoprotein to total cholesterol ratio, and glycosylated hemoglobin, inflammatory risk biomarkers such as circulating concentrations of proinflammatory cytokines, and higher levels of the stress hormone cortisol.[78,245] In a study that used a multidimensional acculturation rating scale for Mexican Americans, greater Anglo cultural orientation was associated with an attenuated cortisol awakening response.[246]

Shortcomings of the Existing Paradigm and Unresolved Issues

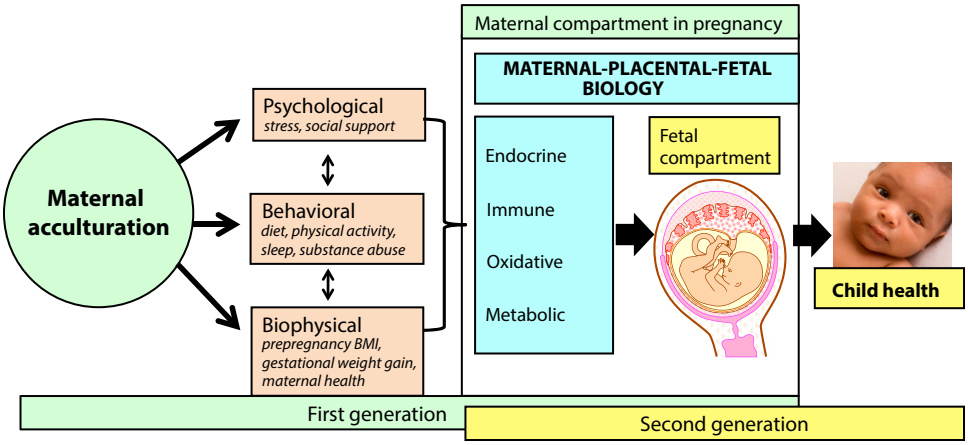
The current paradigm linking acculturation with health in Hispanic Americans provides a plausible explanation, supported by empirical findings, for the within-individual health decline that is associated with length of residence in the United States. Previous authors have suggested that the intergenerational aspect of the observed health decline can also be explained using the same formulation (Figure 1), simply because US-born individuals are also likely to be more acculturated than foreign-born individuals.[15,151,168,247] We, however, suggest that this explanation is not sufficient, and argue that its major shortcoming is its inability to adequately account for the observed intergenerational aspect of the health decline. Specifically, the existing paradigm (1) does not consider the biological continuity between generations, (2) fails to explain the observed decline in health outcomes between first-generation immigrants (foreign-born) and second- and subsequent generation native (US-born) individuals, and (3) does not appear to fully appreciate the potential implications of adverse birth outcomes in lifelong health.

Biological continuity between generations. The acculturation paradox has been the subject of considerable interest in the academic, public health, and public policy sectors.[68,69,150,248–250] However, until now, research has overlooked a crucial feature of the acculturation paradox: it includes an intergenerational component, and yet intergenerational transmission is unaddressed. It remains unknown whether effects associated with acculturation are biologically transmitted from one generation to the next. Rather, each generation has been considered as a biologically isolated entity, despite the fact that the generations are biologically linked. In other words, second-generation individuals are, by definition, the offspring of first-generation individuals, and yet the health effects of acculturation in first-generation Hispanics have not been included in previous efforts to understand health in second-generation Hispanics. The biological link between generations provides a basis for the possibility of intergenerational transmission, with pregnancy and fetal development representing an especially vulnerable period of time for the intergenerational transmission of the deleterious biobehavioral effects of acculturation from mothers to their children.

Nativity. Among first-generation immigrants, acculturation status represents the change in cultural orientation that has occurred since immigration. Therefore, previous authors are justified in suggesting that acculturation may induce poor health both through adoption of unhealthy behaviors and through the psychosocial difficulties of cultural change. However, among subsequent-generation (US-born) individuals, acculturation status is not necessarily reflective of sociocultural change. US-born persons' health status cannot be attributed to the experience or extent of the sociocultural adjustment associated with migration. Acculturation status may reflect a different construct for foreign-born and US-born individuals, and previous authors' suggestions that acculturation's relationship to health is similarly interpreted for foreign-born and native-born individuals[15,151,168,247] may be unjustified (Figure 1). In accordance with this line of reasoning, several findings suggest that the acculturation status of first-generation and later-generation Hispanic individuals may not account for health differences between these 2 groups. For example, language preference did not explain the effect of nativity on birth outcomes in Mexican Americans.[143] A multidimensional assessment of acculturation[251] did not explain the effect of nativity on biological risk profiles.[245] An acculturation variable encompassing language spoken at home and the proportion of foreign-born neighbors did not explain the effect of nativity on adolescent obesity.[161]

Existing frameworks are based on the premise that the health benefits of improvements in socioeconomic conditions that accompany longer duration of residence in the United States and acculturation are overshadowed by the more potent health detriments of the deleterious psychological and behavioral factors associated with acculturation. However, these deleterious psychological and behavioral factors, especially acculturative stress and loss of social support, may be less relevant for subsequent-generation individuals because they have not migrated. Also, Hispanic immigrants of different generational status do not experience different degrees of discrimination, which is an important contributor to acculturative stress.[214,241,243]

Birth outcomes. Greater degree of acculturation[33,82,148] and later generation status[82,90,149–155] are associated with higher rates of adverse birth outcomes, including low birth weight, preterm birth, and lower infant survival.[89,156–158] Existing frameworks suggest that acculturation's



Note. BMI = body mass index.

FIGURE 2—New, proposed framework suggesting that maternal acculturation may influence fetal programming in ways that affect the offspring's lifelong health, potentially accounting for the intergenerational decline in health observed in Hispanic Americans.

deleterious health consequences may result in poor maternal condition during pregnancy, and thereby, contribute to adverse birth outcomes. However, these frameworks have not extended the logic of this phenomenon to consider whether maternal acculturation may affect the health of the offspring. We suggest that this effect of maternal acculturation on adverse birth outcomes should be considered in addressing the question of why subsequent-generation Hispanic individuals exhibit worse lifelong health than first-generation immigrants. The observation that maternal acculturation is associated with her child's condition from as early as at the time of birth may be particularly relevant for interpreting intergenerational health patterns, because adverse birth outcomes are well-established predictors of increased risk for other adverse health conditions over the life course.[252] In addition, many of the long-term health effects of intrauterine perturbations may not be evident at the time of birth, but may become apparent later in the life course.[253–255] For example, even in the absence of adverse birth outcomes, the adult children of mothers who experience excessive psychological stress during pregnancy exhibit impaired endocrine stress reactivity,[256] compromised immune function,[257] insulin resistance,[258] cognitive decline,[259,260] and accelerated aging.[261,262]

A NEW PERSPECTIVE ON HISPANIC HEALTH DECLINE ACROSS GENERATIONS

What, then, may account for the observed intergenerational decline in Hispanic health? There are 2 broad possibilities. First, the same exposures and processes whereby acculturation affects the health of first-generation individuals may operate independently in subsequent-generational individuals, somehow exerting a stronger effect on health status in subsequent generations (to account for escalation of poor health outcomes; Figure 1). Second, the health-related effects of acculturation that already have occurred in first-generation individuals may be transmitted to the next generation individuals in a way that perpetuates and possibly amplifies these effects (Figure 2). We argue in support of the latter possibility, because the former explanation has proven inadequate (see shortcomings of the existing paradigm, as previously described), and unfavorable health outcomes or their antecedent risk phenotypes in later-generation Hispanics may be already apparent during early stages of the life course, as indicated by patterns of adverse birth outcomes[33,82,148] and childhood obesity.[161,170]

Our framework integrates the concepts of biological embedding of life experiences and fetal origins of health and disease risk (Figure 2) to posit that the effects of acculturation can be transmitted across generations from mothers to their offspring. We suggest that intrauterine life represents a key time period when the effects of maternal acculturation may be transmitted to offspring, that the principal mode of transmission is biological, and that transmission occurs via the psychological and behavioral consequences of maternal acculturation on aspects of maternal–placental–fetal gestational biology that participate in the process of fetal programming of health and disease risk. There is extensive empirical evidence from human and animal-model studies that the same processes that have been associated in Hispanics with maternal acculturation (i.e., unfavorable psychological and behavioral states) exert pervasive effects on gestational processes implicated in fetal programming.[37,253,263–265] There is also some evidence specifically in pregnant Hispanic women that links acculturation and acculturation-related processes with gestational biology,[38,40,41,148,266,267] and with maternal psychological[36,38,268,269] and behavioral[30–36,161] states that are linked to gestational biology. Through the pathway of fetal programming, the acculturation experience of one generation may influence the health of subsequent generations. This pattern can account for and also

reconcile unresolved issues in the acculturation paradox.

Fetal Programming and Lifelong Health

In the context of the intergenerational transmission of the effects of acculturation, our focus on fetal programming as the principal candidate mechanism of interest is justified by the fact that the origins of many health outcomes whose prevalence differs by generation status in Hispanics can be traced back to developmental processes in the fetal period of life. As described previously, the adult health outcomes most robustly implicated in the Hispanic acculturation paradox are obesity, diabetes, cardiovascular disease, and depression.[159] Each of these conditions is a noncommunicable chronic disease or disorder. For any given individual, the likelihood of developing an NCD is a joint function of both cumulative exposures to risk factors (e.g., excess caloric intake, hyperglycemia, hyperlipidemia, antigen exposure, stressful life events) and susceptibility to these exposures, as reflected in the wide interindividual variation in the magnitude and duration of biological responses to these and other health-risk exposures in question.[37,255,263] Contrary to the assertion that susceptibility is determined solely by genetic (DNA base-pair) variation,[45] a growing and converging body of epidemiological, clinical, experimental, cellular, and molecular evidence supports the concept that susceptibility for NCDs is determined by the dynamic interplay between genetic makeup and environment, particularly during the embryonic and fetal periods of development.[253,263,270,271] Development is a plastic process in which a range of different phenotypes can be expressed from a given genotype. The unfolding of developmental processes across the multicontoured landscape from genotype to phenotype is context-dependent, in which the developing embryo or fetus seeks, receives, and responds to, or is acted upon by, the intrauterine environment during sensitive periods of cellular proliferation, differentiation, and maturation, which results in structural and functional changes in cells, tissues, organ systems, and homeostatic set points (the process of phenotypic specification). These changes may, either independently or through interactions with subsequent developmental processes and environments, have short- or long-term consequences for health and disease susceptibility.[253,263] These concepts have variously been referred to as the fetal or developmental origins of health and disease risk.[270,272,273] It is important to emphasize that, except in extreme cases, this process of phenotypic specification does not, per se, cause disease, but, instead, determines propensity or susceptibility for the development of disease(s) in later life by shaping the individual's responses to subsequent endogenous and exogenous conditions.[273]

Our framework also addresses the proximate causal pathway by emphasizing the tripartite role of metabolism- and stress-related maternal–placental–fetal biological processes as key sensors, transducers, and effectors of acculturation-related states and conditions on the developing fetus. Extrinsic (environmental) conditions related to energy availability and mortality risk represent key factors that determine the evolutionary adaptiveness of traits. We, therefore, propose that the biological systems most sensitive to these 2 classes of conditions would be expected to directly mediate phenotypic specification during development. Metabolism- and stress-related processes constitute an attractive underlying common candidate mechanism because of their sensitivity to these 2 types of environmental conditions. Metabolism- and stress-related maternal–placental–fetal endocrine, immune, and oxidative processes in gestation represent a plausible mediating pathway during fetal development because they are responsive to all classes of intrauterine perturbations (sensors), they mediate all communication between maternal and fetal compartments (transducers), and they play an essential and obligatory role in orchestrating key events and variations underlying cellular growth, replication, and differentiation in the brain and peripheral tissues (effectors).[264,265,274–277]

Maternal Acculturation and Fetal Programming of Health

The predominant, proximate pathway by which maternal environmental, psychological, behavioral, or other conditions influence offspring development in utero is ultimately biological in nature and involves maternal–placental–fetal gestational physiology. It follows, then, that a crucial component of our framework of intergenerational transmission of the effects of maternal acculturation on offspring health and disease risk (Figure 2) is the question of whether maternal acculturation can influence maternal–placental–fetal gestational biology, particularly those aspects of gestation biology that have been implicated in fetal programming of health and disease risk. Our model proposes that the effects of maternal acculturation on maternal–placental–fetal gestational biology are mediated by the same behavioral, psychosocial, and biophysical sequelae of acculturation that are linked to health and disease risk within the individual life span (Figure 1), because in the context of pregnancy, each of these domains has previously been shown to affect gestational biology.[263,278–280] The plausibility of our model is supported by empirical evidence in the general population, and is also supported more specifically by study findings in pregnant Hispanic women that describe the effects of maternal acculturation on the same psychological, behavioral, and biological processes that have been implicated in the process of fetal programming.

Maternal acculturation and gestational biology. The small number of studies that have addressed maternal acculturation's effect on maternal–placental–fetal gestational biology have consistently reported that among pregnant Mexican American women, a greater degree of acculturation is associated with several indicators of gestational biology that are implicated in the process of fetal programming. These include higher concentrations of the stress hormones cortisol[266] and placental corticotrophin-releasing factor,[148] hypothalamic–pituitary–adrenal axis feedback dysregulation (blunted diurnal cortisol slope),[267] a higher estriol-to-progesterone ratio,[40,41] and higher concentrations of proinflammatory cytokines.[38] Later generation status was associated with lower concentrations of the stress hormones cortisol and corticotropin-releasing hormone and a higher estriol-to-progesterone ratio in Mexican American pregnant women.[39] Also, the evidence, reviewed in a preceding section,[78,245] that acculturation is associated with biomarkers of health in nonpregnant Hispanic individuals provides further, but more tentative, support of the likelihood that acculturation may influence gestational biology.

Maternal acculturation and health-related behaviors in pregnancy. Maternal health-related

behaviors before or during pregnancy are known to influence maternal–placental–fetal biology directly via biological pathways or indirectly via psychological pathways.[278,279,281] A greater degree of acculturation among Hispanic women has been associated during pregnancy with poorer diet,[30,33] more alcohol,[31,36] cigarette smoking,[30–34] marijuana[31] and other substance abuse,[34–36] and inactivity.[161] Another finding of note is that the effect of acculturation on health-related behaviors is strongest and most consistent for women (e.g., smoking,[282,283] alcohol,[179,180,189,284,285] drug use[193,195]) compared with men. Mexican American women with lower acculturation scores (as assessed by a combination of nativity, length of stay, and language preference) exhibited lower folic acid dietary intakes than more acculturated Mexican American women.[286,287]

Maternal acculturation and psychosocial processes in pregnancy. Maternal psychosocial conditions before or during pregnancy are known to influence maternal–placental–fetal biology directly via endocrine, immune, and oxidative state-related pathways, and indirectly via effects on health-related behaviors.[278,279,281,288,289] During pregnancy, second-generation Mexican American women are more likely than Mexican immigrant women to experience depression,[38,39] anxiety,[39,268] and prenatal stress.[36,39] More acculturated Mexican American women compared with those less acculturated (as measured by language preference) exhibited higher rates of depression during pregnancy.[269] With acculturation, women may lose an important source of social support during pregnancy.[290] In traditional Hispanic cultures, women within a community are close-knit, receiving support not only from their own female relatives but also from other women in the community and "comadres" or godmothers.[291] As acculturation progresses, the degree of community and family support may diminish. Hispanic immigrants to the United States who retain more traditional Hispanic values have been shown to benefit from more family support during pregnancy,[30,292] have higher degrees of pregnancy wantedness,[36,293] are more likely to be married or living with a partner,[31] and have more family-centered views with regard to reproduction and parenting.[293–295]

Interaction between the effects of maternal acculturation during gestation and child acculturation after birth on subsequent child health outcomes. As discussed previously, the likelihood of developing a complex, common NCD is a joint function of exposure to risk factors and the individual's predisposition or susceptibility. Fetal programming plays a major role in shaping predisposition or susceptibility. Thus, maternal acculturation may affect fetal developmental processes that alter her child's physiological or psychological susceptibility to potentially deleterious conditions encountered subsequently over the course of the child's life. Some of these conditions may themselves be causally related to the child's own acculturation status, such as an unhealthy diet. In this way, maternal acculturation during pregnancy could additionally affect child health by influencing the child's susceptibility to environmental risk factors associated with the child's own subsequent cultural orientation. For example, maternal acculturation may be associated with excess maternal stress or poor diet, which may alter maternal–placental–fetal glucocorticoid physiology during pregnancy. Exposure to inappropriate concentrations of glucocorticoids during sensitive periods of intrauterine development is known to produce alterations in the fetal brain and peripheral systems that have long-term consequences and can alter the offspring's propensity for developing excessive adiposity and metabolic disorders in the face of obesogenic exposures. These changes include altered set points in hypothalamic circuits that regulate appetite and satiety,[296,297] reduced β-cell mass,[298] impaired adipocyte (peroxisome proliferator-activated receptor-γ) function,[299,300] and decreased insulin sensitivity.[301] Through this pathway, a mother's acculturation could alter her offspring's degree of susceptibility to obesity and metabolic disorders in the context of her offspring's exposure to a typical US (as opposed to traditional Hispanic) diet. Similar suites of phenotypic changes in association with alterations in maternal–placental–fetal gestational biology have been described with respect to the propensity for developing the various other adverse health outcomes implicated in the Hispanic acculturation paradox.

Postnatal transmission of effects of maternal acculturation on child health. Only a small number of studies have examined the link between maternal acculturation and children's health (e.g., physical illness,[302] such as asthma,[303,304] and risk of psychological disorders, such as internalizing behaviors[305]). These authors postulated postnatal pathways of transmission, but they did not investigate the underlying mechanisms. Although it is quite plausible that the process of fetal programming may account for these findings (in the manner discussed previously), we recognize and note that intrauterine life is not the only time period when acculturation may exert an intergenerational effect on health. Another time window and mode of parent-to-child transmission of the effects of acculturation may be during postnatal life, potentially through the effects of maternal acculturation on infant feeding practices (including duration of breast feeding and breast milk composition),[306–308] parent–child interaction and parenting behaviors,[309,310] or health care utilization.[311,312] Further discussion of these postnatal pathways is beyond the scope of this article.

Reconciliation

We suggest that the fetal programming perspective potentially offers a parsimonious explanation to account for the observed intergenerational decline in Hispanic American health, and also to reconcile the apparent contradiction among the observations in this population that disease risk increases across generations despite improvements in life conditions.[8,17,18,69,80–91]

If the unfavorable psychological, behavioral, and biological sequelae of acculturation established in one generation of women are transmitted to the next generation particularly during the sensitive period of fetal life, the resulting consequences in the subsequent generation can include long-term alterations in the physiological sensitivity of endocrine, immune, vascular, metabolic, cognitive, and affective systems.[253,313,314] These alterations may not only perpetuate the intergenerational cycle of poor health but may amplify it. The same conditions that produced poor health in the prior generation may persist and act on the second generation and produce even larger adverse effects because the second-generation individual is physiologically more reactive to these exposures than the parent-generation

individual.[313,315,316] If the magnitude of this amplification is greater than the salutary effects of improvements in socioeconomic conditions, the net effect is worse health in the second-generation individuals compared with the first-generation individuals despite improvements in SES. Exposure to unfavorable conditions during the prenatal period of life is known to have greater and longer term effects compared with exposure to the same or equivalent unfavorable conditions encountered later in the life course.[253,263] Therefore, fetal exposure to the mother's stresses and unhealthy behaviors associated with acculturation may have lifelong health consequences for the US-born child, regardless of the postnatal improvements in the child's life conditions. This pattern may then enhance the likelihood of poor health among third-generation individuals, and so forth, across generations.

There is already evidence for this kind of intergenerational trend among underprivileged US minority groups. Among African Americans, low-birth weight and preterm birth persist across generations despite improvement in socioeconomic conditions.[317–319] The authors of these studies have suggested that unfavorable life conditions in an initial generation of individuals could instigate a transgenerational cascade of adverse birth outcomes, regardless of the life conditions of subsequent generations.[318]

PUBLIC HEALTH RELEVANCE

The perspective that the effects of acculturation can be biologically transmitted across generations via the process of fetal programming to perpetuate intergenerational cycles of social disadvantage and poor health may have broad implications for public health and policy in the United States and elsewhere. The approach articulated in this article has implications for risk identification and the subsequent development of interventions directed toward primary prevention in not only the Hispanic American population but perhaps also has implications in other national and global minority, immigrant populations, and populations in transition.

Women's Health

The fetal origins perspective places a particular emphasis on the health and well-being of girls and women of reproductive age. Attending to the health of Hispanic women could be of vital importance for stemming transgenerational cascades of poor health.

Although child- and adult-intervention approaches have dominated national and global efforts to diminish NCD incidence and health disparities,[312,320,321] our framework points to the importance of interventions focused on the prenatal phase of life. Because of the abundance of evidence for NCD propensity being strongly influenced by prenatal conditions, along with the substantial and growing national and global threat of the NCD burden, primary prevention strategies aimed at girls and women are warranted.

Future Hispanic Demographics and Public Health

The fetal origins perspective is especially relevant for shedding light on the determinants of health in the offspring of individuals who experience adversity. Therefore, in the case of immigrants, this perspective offers specific insight into the determinants of health in second-generation individuals.

In terms of national disease burden, health in second-generation Hispanics is especially important to consider, because Hispanic demographic characteristic trends predict that over the next 20 years, the second generation is projected to emerge as the largest subset of Hispanic Americans, compared with the first-generation (immigrants) and subsequent generations.[3] Thus, health decline in second-generation Hispanics poses a particularly urgent and growing threat. In addition, the health status of second-generation individuals would affect fetal development of third-generation individuals and thereby affect third-generation health, and so forth; therefore, these adverse health conditions may perpetuate across generations.

Public Policy and Global Health

Understanding the health consequences of the integration of Hispanic immigrants into American society has profound implications for public policy. There is a need to understand the potential downstream health effects of policies that influence postmigration life, such as immigration reform, child education, and neighborhood integration. In addition, a better understanding of acculturation's transgenerational effects in Hispanic Americans could inform epidemiological and biomedical studies in other immigrant populations, especially because acculturation paradoxes have been observed in other immigrant groups, including African,[322] Chinese,[323,324] and Korean[325] immigrants in the United States, as well as ethnic-minority immigrants in the United Kingdom,[326,327] Canada,[328,329] Sweden, Finland,[330] and Israel.[233]

A better understanding of acculturation's transgenerational effects would also inform issues of public health in rapidly developing countries, where dramatic environmental and cultural change may occur within an individual's lifetime. In these populations in transition, the process of acculturation may be relevant for health among nonmigrant individuals who experience the change of sociocultural context that occurs with industrialization, urbanization, and globalization. Deciphering the mechanisms through which chronic disease risk varies by generation status in the United States will help in preparing for national disease and disability burden, and forecasting worldwide changes in health-related conditions as global migration continues to accelerate.

CONCLUSIONS

Existing frameworks on the effects of acculturation and acculturation-related processes in Hispanic Americans on health over time and across generations have not satisfactorily addressed important issues related to intergenerational transmission and nativity. In this context, we propose the adoption of a fetal programming perspective that takes into account the biological continuity between generations and considers each subsequent generation with regard to the cumulative effects of previous generations' acculturation experiences. This perspective provides the opportunity to arrive at a parsimonious explanation that accounts for the observed intergenerational decline in Hispanic American health and also reconciles the apparent contradiction of disease risk increases across generations despite improvements in life conditions. This understanding has important implications for risk identification and the development of interventions aimed at primary prevention to

break the cycle of perpetuation of suboptimal health in the disenfranchised and rapidly growing minority population of Hispanic Americans. ■

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This article was accepted January 11, 2015.

Contributors

M. Fox co-developed the conceptualization of the article, conducted the literature review, wrote major portions, edited all components, and organized the references. S. Entringer, C. Buss, and J. DeHaene contributed to the conceptualization and edited components of the article. All authors critiqued the article and approved the final version. P. D. Wadhwa initiated conceptualization of the article, developed the outline, wrote major portions, coordinated writing, and edited all components of the article.

Acknowledgments

The preparation of the article was supported, in part, by United States Public Health Service (National Institutes of Health; grants RO1 HD-060628 to P. D. W., RO1 HD-065825 to S. E., and RO1 MH-091351 to C. B.).

Human Participant Protection

Institutional review board approval was not needed because no research with human participants was conducted.

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