

# Structural racism and its pathways to asthma and atopic dermatitis



Adali Martinez, MD, MPH,<sup>a</sup> Rosemarie de la Rosa, PhD,<sup>b</sup> Mahasin Mujahid, PhD, MS,<sup>b</sup> and Neeta Thakur, MD, MPH<sup>a</sup>  
San Francisco and Berkeley, Calif

Black, Latinx, and Indigenous people in the United States experience a disproportionate burden of asthma and atopic dermatitis. The study of these disease disparities has focused on proximal socioenvironmental exposures and on the biomechanistic (including genetic) differences between racial and ethnic groups. Although biomedical research in allergy and immunology stands to benefit from the inclusion of diverse study populations, the narrow focus on biologic mechanisms disregards the complexity of interactions across biologic and structural factors, including the effects of structural racism. Structural racism is the totality of ways in which society fosters discrimination by creating and reinforcing inequitable systems through intentional policies and practices sanctioned by government and institutions. It is embedded across multiple levels, including the economic, educational, health care, and judicial systems, which are manifested in inequity in the physical and social environment. In this review, we present a conceptual framework and pull from the literature to demonstrate how structural racism is a root cause of atopic disease disparities by way of residential segregation, socioeconomic position, and mass incarceration, which may lead to aberrations in the innate and adaptive immune response and the augmentation of physiologic stress responses, contributing to a disproportionate disease burden for racial and ethnic populations. (*J Allergy Clin Immunol* 2021;148:1112-20.)

**Key words:** Racism, health disparities, asthma, allergic dermatitis, atopy

## Abbreviations used

DEP: Diesel exhaust particulate  
FLG: Filaggrin  
HOLC: Home Owners' Loan Corporation  
LOF: Loss-of-function  
SEP: Socioeconomic position  
STAT3: Signal transducer and activator of transcription 3  
Treg: Regulatory T

Racial and ethnic health disparities have persisted, and in the case of atopic diseases, they have worsened<sup>1</sup> despite scientific research dedicated to untangling the contributing biomechanisms and dedicated efforts to address poorly controlled disease,<sup>2-4</sup> including the rampant introduction of precision medicine therapy.<sup>5,6</sup> Asthma and atopic dermatitis are 2 of the most common chronic conditions of childhood in the United States, often persisting into adulthood.<sup>7,8</sup> Asthma affects more than 5.1 million children and more than 20 million adults, corresponding to 7.8% of the US population.<sup>7</sup> Approximately 7.3% of adults and 13% to 15% of children have atopic dermatitis.<sup>8-10</sup> As is the case with many chronic health conditions, the burden of atopic diseases disproportionately affects Black and Brown communities.<sup>11-17</sup> The persistence of disparities requires a shift of the biomedical framework to incorporate root causes, particularly the direct and indirect roles of structural racism.<sup>18</sup> Structural racism is both historically rooted and culturally reinforced.<sup>19</sup> It is the totality of ways in which society fosters discrimination by creating and reinforcing inequitable systems through intentional policies and practices sanctioned by various levels of government and institutions.<sup>19-21</sup> Structural racism is embedded across society, including in our economic, educational, health care, and justice systems, manifesting as inequitable distribution of resources.<sup>19</sup> This is distinct from interpersonal racism, which is the differential treatment with regard to race, skin color, ethnic origin, or immigration status.<sup>22</sup>

Although we have focused this review on the role of structural racism contributing to the disparities within the Black, Latinx, and Indigenous communities,<sup>11-14,16,23-25</sup> we recognize that the pervasive effects of structural racism have likely influenced disease outcomes in many—if not all—minoritized communities in the United States. For this review, we use the term *Latinx*. Although this term has not been fully adopted by all of the population, given the topic of this review, we believed it important to select a term that represents a global movement toward more gender-inclusive terms.<sup>26</sup> We also recognize that *Latinx*

From <sup>a</sup>the School of Medicine, the University of California San Francisco, and <sup>b</sup>the School of Public Health, University of California Berkeley.

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Corresponding author: Neeta Thakur, MD, MPH, Department of Medicine, University of California, San Francisco, 500 Parnassus Ave, PO Box 0841, San Francisco, CA 94143-0841. E-mail: [Neeta.Thakur@ucsf.edu](mailto:Neeta.Thakur@ucsf.edu).

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encompass diverse subgroups with unique migration to the United States; however, these groups also share cultural and environmental risk factors for atopic diseases that are influenced by structural and societal factors.<sup>27</sup> Indigenous populations refer to descendants of the peoples who inhabited the Americas before European colonization.

A deeper understanding of the history and the ongoing oppression of Black, Latinx, and Indigenous populations in the United States is needed to understand the deep-rooted and broad effect of structural racism on health outcomes, and specifically, on asthma and atopic dermatitis. This review examines the direct and indirect pathways by which structural racism may increase disease and worsen morbidity for asthma and atopic dermatitis. In the sections that follow, we provide a conceptual framework of structural racism and mechanisms of how it has been manifested in the United States, review the racial and ethnic disparities for asthma and atopic dermatitis, summarize the literature examining pathways of structural racism, and conclude with recommendations for future research and efforts that move toward reducing disease disparities.

## CONCEPTUAL FRAMEWORK

Racial categories in the United States were originally established by European settlers to assert power over enslaved African and Indigenous people, who were falsely thought to be innately, intellectually, and morally inferior.<sup>19</sup> Over centuries, the concept of race and racial differences has been propagated by the field of medicine with the use of racial taxonomies in research and clinical practice.<sup>28</sup> To understand how structural racism contributes to disparities in asthma and atopic dermatitis, we propose the following conceptual framework (Fig 1) pulling from the work of Williams and Mohammed,<sup>29</sup> Williams et al,<sup>30</sup> Bailey et al,<sup>19</sup> Bailey et al,<sup>21</sup> and the World Health Organization's Commission on Social Determinants of Health framework.<sup>31</sup> The determinants of health include biology, geographic origin and ancestry, health behavior, and the socioenvironmental context as influenced by societal institutions and structural racism (Fig 1).<sup>29,31</sup> These determinants of health interact, and as is the case with health behaviors, they may be influenced heavily by socioenvironmental conditions.<sup>32</sup> In Fig 1, the concept of race and the resulting perceived hierarchy stem from the perpetuation of structural racism in legal, political, cultural, and economic institutions, which has led to residential segregation, disparate socioeconomic opportunities, and mass incarceration. Structural racism and the resulting intermediate pathways create racial inequity that contributes to interpersonal racism. The toll of interpersonal racism and discrimination additionally contributes to inequitable access to health-promoting resources (disease prevention) and health care access, as well as to chronic psychosocial stress, while also enhancing the effects of structural racism (Fig 1).

In our framework, structural racism leads to proximal pathways of inequity affecting the physical and social environments. In the physical environment, Black, Latinx, and Indigenous communities are exposed disproportionately to pollutants and/or environmental hazards, occupational hazards, and poorer housing quality,<sup>21,33,34</sup> all of which are factors with strong evidence of association with asthma and atopic dermatitis.<sup>25,34-36</sup> In the social environment, Black Latinx, and Indigenous people are more likely to experience financial strain, have less wealth, have decreased access to education, live in neighborhoods with

higher rates of violence, and have a greater number of adverse childhood experiences.<sup>33,37-41</sup> Several epidemiologic studies have demonstrated that these proximal pathways are associated with higher physiologic stress burden.<sup>42,43</sup> Independent of socioeconomic position (SEP), discrimination and segregation have also been associated with higher physiologic stress burden leading to increased inflammation.<sup>22,44,45</sup> Social adversity has also produced inflammation in animal models.<sup>46</sup> On the basis of this evidence, we hypothesize that these proximal pathways, along with experiences of interpersonal racism, become embedded in the biology through aberrations in the innate and adaptive immune response (Fig 1).<sup>47,48</sup> In the sections that follow, we critically appraise the gaps in our current knowledge and summarize the evidence supporting our framework, which extends from animal to human studies and spans the research fields of psychosocial stress to epidemiology.

## DISPARITIES IN ASTHMA AND ATOPIC DERMATITIS

In the United States, asthma prevalence is substantially higher in Black and Indigenous populations, at rates of 10.6% and 10.7%, respectively, compared with a 7.7% prevalence within the non-Hispanic White population.<sup>7</sup> In addition, Black and Indigenous populations experience higher asthma morbidity, with frequent asthma attacks and higher rates of asthma-related health care utilization.<sup>11-14</sup> When the Latinx population is considered as whole, the prevalence of asthma among Latinx people is lower (6.6%) than in most other racial and ethnic groups.<sup>7</sup> When examined by national subgroup, the prevalence of asthma in Mexican Americans (5.3%) is lower than in other subpopulations of Latinx people (8.5%),<sup>7</sup> with Puerto Ricans having the highest lifetime prevalence of asthma.<sup>49</sup> Mexican American children also have a 2-fold increased risk of hospitalization compared with the rate for White children, which is similar to the hospitalization rate of Black children with asthma.<sup>11</sup> The lower overall prevalence of asthma in Mexican Americans likely underestimates the impact of acculturation, which reflects an adoption of cultures of the dominant society and captures the duration of time spent in the host country.<sup>49,50</sup> Notably, the prevalence of asthma in Mexican Americans is increasing at a greater rate than in all other racial and ethnic groups.<sup>11</sup> Higher acculturation has been shown to be associated with higher prevalence of asthma in Mexican Americans<sup>49,51</sup> and other Latinx subgroups<sup>49</sup>; similar patterns are seen in several disease outcomes.<sup>27,52</sup> Proposed mechanisms include adoption of cultural and behavioral practices that lead to increased disease risk and increased exposure to environmental hazards.<sup>27,49</sup> It is important to consider the harmful health effects of being a racialized immigrant in the United States.<sup>53</sup> Structural racism may uniquely impart its influence on first-generation Mexican Americans and other racialized immigrants in the form of economic exploitation, including labor exploitation and curbing of access to economic resources and opportunities, and neighborhood disinvestment, thus contributing to concentration of poverty and increased exposure to environmental hazards.<sup>53</sup>

The prevalence of atopic dermatitis is estimated to be 1.7 times higher in Black children than in White children, particularly in early childhood.<sup>15-17</sup> Black children also have higher risk of persistent and severe disease.<sup>16</sup> Although the incidence of atopic dermatitis in Latinx children is similar to that in White children

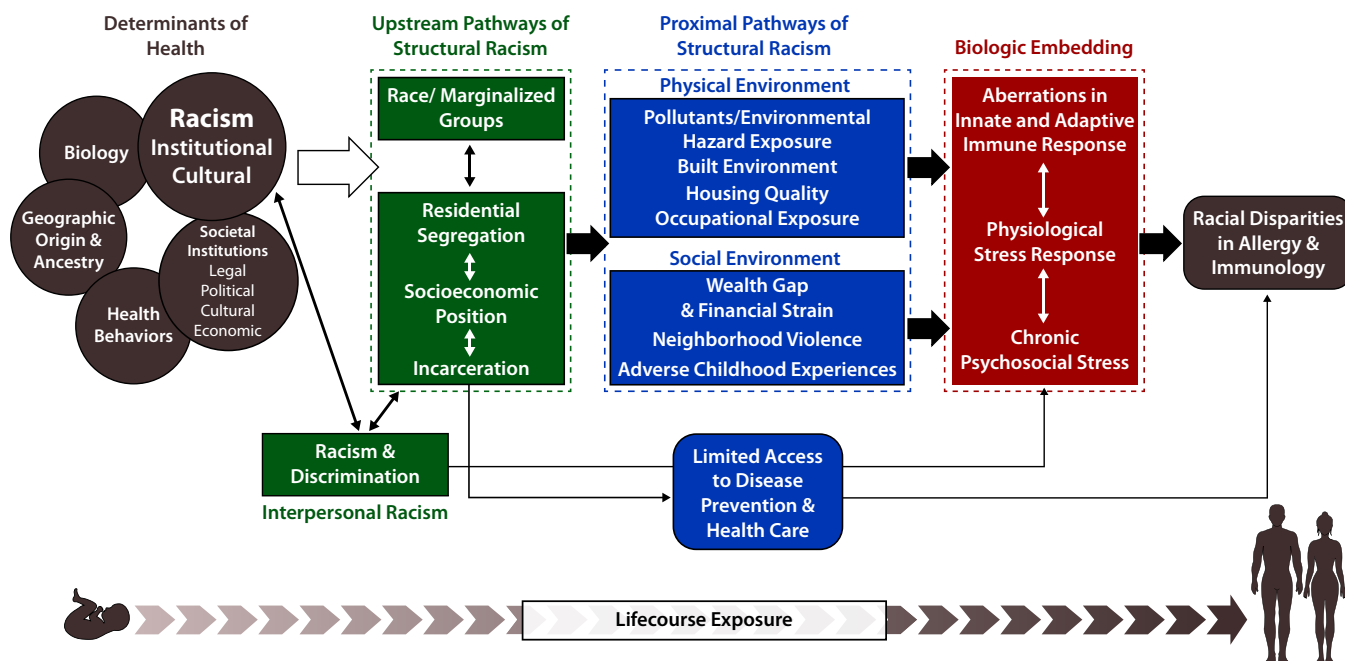


**FIG 1.** Structural racism as a root cause of allergy and immunology disparities. Conceptual framework of the upstream and proximal pathways of structural racism and its effect on health. Framework adapted from the work of Williams and Mohammed,<sup>29</sup> Williams et al,<sup>30</sup> Bailey et al,<sup>19</sup> Bailey et al,<sup>21</sup> and the World Health Organization's Commission on Social Determinants of Health framework.<sup>31</sup>

during early childhood, Latinx children have higher risk of persistent and severe disease.<sup>9,16</sup> As is the case with asthma, the cultural and environmental changes associated with acculturation may play a significant role for Latinx children, as children who were not born in the United States but have resided in the United States for more than 10 years have higher odds of developing atopic dermatitis than do those who recently migrated.<sup>54,55</sup> Extrapolating from small population-based studies, the prevalence of atopic dermatitis Indigenous population of the United States is estimated at 8% to 11%.<sup>56,57</sup> There are even fewer studies that have examined the severity of atopic dermatitis in Indigenous populations in the United States. This is a needed area for research; specifically, research focused on identifying and addressing risk factors that may be unique to this community.

Even after traditionally measured socioeconomic factors have been accounted for, racial and ethnic disparities in asthma and atopic dermatitis persist, contributing to controversy over the reason for this residual difference and is used to support theories of biologic determinism.<sup>15,58</sup> However, there is sparse evidence supporting the idea that biologic differences between racial groups drive disparity in disease prevalence and severity. For example, Abuabara et al demonstrated that neither genetic ancestry nor a polygenic risk score nor a genetic skin pigment score explained the prevalence or morbidity disparities in atopic dermatitis between Black and White participants.<sup>59</sup> Several studies have identified that loss-of-function (LOF) mutations of the filaggrin (*FLG*) gene result in epidermal barrier dysfunction. For people of European ancestry,<sup>15,60</sup> *FLG1* LOF mutations are associated with more severe atopic dermatitis. Past studies have noted that the 4 most common *FLG* LOF mutations are rare or even absent in individuals of African ancestry.<sup>15,60,61</sup> However, with advancement of measurement and availability of whole genome sequencing, more recent reviews have identified the

presence of variants across the *FLG* LOF gene in individuals of African ancestry, with mutations of this gene also causing more severe disease regardless of mutation type.<sup>59-61</sup> These studies highlight why biomedical research in allergy and immunology stands to benefit from the inclusion of more diverse study populations; however, narrowly focusing on genetic variations disregards the complexity of interactions across biologic and structural factors, which together contribute to disease risk. Instead, we argue that the persistent racial and ethnic disparities in asthma and atopic dermatitis likely reflect residual confounding from both unmeasured social and structural determinants, including the downstream effects of structural racism.<sup>62</sup> In this work, there is also a need to consider the degree to which structural racism is transmitted transgenerationally through epigenetic modification, as well as the consequences of such modifications on health across populations.<sup>63-67</sup>

## UPSTREAM PATHWAYS OF STRUCTURAL RACISM

### Residential segregation

Soon after the abolishment of slavery, in the Reconstruction Era segregation policies were established in the form of Black Codes to ensure continuation of a cheap labor force and, later, as “Jim Crow laws” under the premise of “separate but equal.”<sup>68</sup> Although zoning laws segregating neighborhoods were viewed as unconstitutional by the Supreme Court in 1917, during recovery from the Great Depression, the federal government sanctioned this practice with preferential investment in current and future homeowners through the Home Owners’ Loan Corporation (HOLC).<sup>69</sup> HOLC created maps of at least 239 US cities, ranking communities in terms of mortgage worthiness.<sup>21</sup> Inner-city communities with large Black or immigrant populations were systematically graded and outlined in red (“redlining”), flagging them as

hazardous investment areas.<sup>21,33,69</sup> This practice barred residents from these communities from receiving HOLC loans and thus systematically prevented the procurement of assets and accumulation of transferable wealth.<sup>33</sup> Although overt redlining is illegal today (it is prohibited under the Fair Housing Act of 1968), its effects have endured.<sup>70</sup> Communities that were previously redlined have a persistent pattern of economic inequity and segregation.<sup>70</sup>

Nardone et al demonstrated that historical redlined census tracts have 2.4 times higher rates of asthma-related emergency department visits than do census tracts deemed to be good investments.<sup>33</sup> There are several indirect mechanisms by which redlining may lead to worse asthma and atopic dermatitis outcomes for Black and Latinx communities. Redlining led to an inequitable distribution of wealth, and over generations it has resulted in concentration of poverty, low rates of home ownership, and poor housing quality in Black and immigrant communities.<sup>33</sup> In asthma and atopic dermatitis, there is a large body of literature documenting the negative effects of poor housing quality on outcomes.<sup>25,34-36</sup> Presently, structural racism continues to operate by denying improved housing opportunities for communities of color via housing and mortgage discrimination.<sup>71</sup> Because of these discriminatory practices, people living in disinvested neighborhoods continue to have limited opportunities to move out of those neighborhoods despite earning higher incomes.<sup>71</sup>

In Black and immigrant communities, the lasting effects of redlining are also seen in the concentration of hazardous air pollutants,<sup>33,69</sup> which have been demonstrated to be associated with asthma morbidity.<sup>72</sup> Historically, redlined census tracts were subjected to downstream policies, such as eminent domain, industrial zoning, and racial zoning, which affected where highways and toxic hazard sites were built.<sup>33,69,73</sup> Historically, redlined census tracts have high diesel exhaust particulate emissions that are nearly twice high as those in nonredlined areas.<sup>33</sup> This is particularly important when it comes to disparities in asthma and atopic dermatitis, which have been shown to be triggered by hazardous environmental exposures.<sup>25,74-77</sup> Residential segregation—the contemporary manifestation of redlining, Jim Crow laws, and the legal separation of races—has also been linked to higher prevalence of asthma and worse disease outcomes for both asthma and atopic dermatitis.<sup>25,36,78,79</sup> In a study examining asthma prevalence in low-birth-weight children, Black children had higher rates of asthma than non-Black children did.<sup>79</sup> However, when non-Black children lived in Black zip codes (defined as zip codes in which more than 50% of the children identified as Black) and were exposed to the same environments, their rates of asthma were comparable.<sup>79</sup> This suggests that structural environment affects disease disparities, not biologic differences between races.<sup>79</sup> The systemic disinvestment in public and private sectors and concentrated industrialization within segregated communities of color has led to disproportionate exposure to environmental hazards,<sup>78</sup> highlighting one of the mechanisms through which segregation practice and policy lead to greater burden of asthma and atopic dermatitis in Black, Latinx, and Indigenous communities.

As a result of systemic disinvestment of communities of color, residential segregation is also associated with underresourced public services, including health care facilities<sup>21,80,81</sup> and health care providers,<sup>21,80</sup> thus directly affecting the care that is accessible by Black, Latinx, and Indigenous communities. Residential segregation has led to highly segregated schools with poorer quality of education because of the lack of community resources and

funding caused by concentrated poverty and low property tax revenue.<sup>82</sup> This has led to lower average test scores, fewer students in advanced placement courses, limited curriculum, less-qualified teachers, less access to academic counseling, and higher dropout rates in segregated schools, all limiting future employment potential<sup>82</sup> and influencing SEP, which is a well-described risk factor for asthma prevalence and morbidity due to asthma and atopic dermatitis.<sup>9,83-87</sup>

## SEP

Similar to socioeconomic status (SES), SEP measures differential access to resources but also encapsulates social class and social stratification.<sup>83</sup> Given the overlap in definitions, in this review SEP and SES are used interchangeably. SEP is strongly associated with the development of asthma, worse symptom burden, and higher health care utilization.<sup>78-86</sup> There is a 2-fold increase in the prevalence of asthma in individuals of low SEP as compared with in those of high SEP.<sup>7</sup> The link between SEP and risk of atopic dermatitis is less clear.<sup>87</sup> Although studies have observed higher prevalence of atopic dermatitis in children and adults with higher SEP, severe atopic dermatitis is associated with lower SEP, lower income, dilapidated housing, and living in a community with garbage in the streets.<sup>9,87</sup>

Although SEP is a strong predictor of atopic disease severity, it cannot be viewed independently of structural racism. In addition to lower educational opportunities, Black, Latinx and Indigenous people have poverty rates (ie, the proportion of those living below the federal poverty line) as high as 20.8%, 17.6% and 25.4%, respectively, as compared with 8.1% in White populations.<sup>88</sup> As already highlighted, residential segregation has contributed to this difference, shaping the distribution of resources and reinforcing racial differences in education and employment opportunities.<sup>37,78</sup> Structural racism and discrimination on both institutional and interpersonal levels have also contributed to racial disparities in SEP.<sup>37,39,78</sup> Even at the same education level, Black and Latinx people receive less income than their White counterparts and have markedly less wealth at equivalent incomes,<sup>37</sup> barring generations of Black and Latinx people from escaping the cycle of poverty and the exposures associated with higher severity of atopic diseases.

## Mass incarceration

The United States has the highest rate of incarceration in the world, with a prison population of more than 2 million.<sup>21,68</sup> Structural racism at various levels of the criminal justice system has accounted for a gross overrepresentation of imprisoned Black, Latinx, and Indigenous people.<sup>68</sup> Black Americans have the highest rates of incarceration, at a level 5 times higher than White Americans.<sup>89</sup> Latinx and Indigenous people are not far behind, at rates that are, respectively, 2 and 4 times higher than those of their White counterparts.<sup>89,90</sup> Despite studies showing that people of all races and ethnicities use and sell drugs at similar rates, Black men are imprisoned on drug charges at rates 20 to 50 times higher than those of their White counterparts.<sup>68</sup>

Overpolicing, imposition of police control in minoritized communities at a level unlikely to occur in the dominant society, and imprisonment of racial and ethnic communities in the United States can be traced back to the enslavement of Black and Indigenous people.<sup>21,68</sup> Policing began with the formation of

slave patrols in the 18th century in an effort to capture and retrieve runaway slaves.<sup>21</sup> After the abolition of slavery, slave patrols evolved into contemporary police, who not only enforced the unequal laws that targeted communities of color but also participated in the lynching of Black individuals.<sup>21</sup> Contemporaneous policies set in the past half-century have accelerated incarceration rates for Black, Latinx, and Indigenous populations. In 1971, President Nixon announced the war on drugs, directly leading to a 7-fold increase in the incarcerated population.<sup>68</sup> This was followed by passage of the Violent Crime and Law Enforcement Act during the Clinton administration, further enhancing the disparities in mass incarceration.<sup>21,68</sup> Recent evaluation of these policies demonstrates that the “war on drugs” and “tough on crime” policies, including stop-and-frisk laws, are deliberate and systematic examples of racism.<sup>91,92</sup>

Although literature exploring the relationship between incarceration and atopic diseases is in its infancy, a community-based study of approximately 2000 adults found that a personal history of incarceration was associated with an increased prevalence of asthma, higher health care utilization, and more severe asthma symptoms.<sup>93</sup> We propose that the impact of mass incarceration on asthma and atopic dermatitis operates via 3 potential pathways: enhancing racial socioeconomic inequities, amplifying the effects of chronic psychological stress, and exposing individuals to harmful physical environments (Fig 1). As a result of structural racism in the US legal system and policies being disproportionately enforced in minoritized communities, Black individuals in major cities are more likely than White individuals to have criminal records despite several reports documenting similar rates of commission of crimes in both groups.<sup>68,91,92</sup> After release from prison, individuals with criminal records are subject to legal barriers, limiting employment and economic opportunities.<sup>68,94</sup> This contributes to lower SEP and higher psychosocial stress, both of which are associated with an increased risk of asthma.<sup>93-96</sup> Incarceration also exposes individuals to stressful or traumatic environments, which may enhance the psychological stress response and thus predispose individuals to more severe asthma symptoms, as discussed later in this review.<sup>93,97</sup> Similarly, parental incarceration can also be a source of chronic stress in childhood and has been well studied as one of the 10 original items included in the Adverse Childhood Experiences questionnaire.<sup>98,99</sup> Higher exposure to adverse childhood experiences has also been associated with higher prevalence asthma in children and adults.<sup>100-103</sup> Mass incarceration may also expose individuals to harmful physical environments, including secondhand smoke, dilapidated prison conditions, indoor allergens such as pests, and hazardous external air pollutants,<sup>93</sup> all of which have been associated with asthma.<sup>74-76,104,105</sup> Following release, formerly incarcerated individuals are more likely to live in neighborhoods with substandard housing,<sup>93</sup> thus further increasing the potential exposure to conditions known to be associated with asthma and atopic dermatitis.<sup>25,34-36</sup>

## BIOLOGIC EMBEDDING OF STRUCTURAL RACISM

The effects of structural racism may become biologically embedded over the life course.<sup>47</sup> Fig 2 highlights empiric pathways by which racism may contribute to immune dysregulation and the development or worsening of atopic disease. We recognize that this includes pathways through increased exposure to environmental hazards, specifically, poor indoor and outdoor air

quality. For this review, we have focused on how structural racism may operate through the physiologic stress response to modulate immune function and promote atopic diseases through the following mechanisms: (1) T<sub>H</sub>1 cell–T<sub>H</sub>2 cell polarization, (2) T<sub>H</sub>17 cell–regulatory T (Treg) cell balance, (3) the microbiome, and (4) epigenetic modifications. Much of the evidence presented is drawn from the large empiric base of biomechanisms of chronic psychosocial stressors at the individual level (ie, socioeconomic status and perceived stress), as there is limited research directly examining the effects of structural racism on these biologic processes. Future research in these areas would advance our understanding of the biomechanisms of structural racism.

## Physiologic stress response

Stressful events stimulate activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, leading to the secretion of glucocorticoids (cortisol) and catecholamines (epinephrine and norepinephrine), respectively, into the bloodstream. These molecules exert effects by binding glucocorticoid receptors and  $\beta$ -adrenergic receptors present throughout the body, including lymphocytes and other immune cells.<sup>106,107</sup> Chronic activation of these receptors leads to aberrant physiologic responses and desensitization, which increases morbidity due to allergic disease by reducing responsiveness to corticosteroid and  $\beta_2$ -agonist treatments.<sup>108</sup> For example, among children with asthma, chronic life stress was associated with decreased expression of the glucocorticoid and  $\beta$ -adrenergic receptors.<sup>48</sup>

**T<sub>H</sub>1 cell–T<sub>H</sub>2 cell polarization.** T<sub>H</sub> cells present allergens that are taken up by dendritic cells and have 2 predominant phenotypes, T<sub>H</sub>1 and T<sub>H</sub>2. T<sub>H</sub>1 cells release type 1 cytokines (IFN- $\gamma$  and IL-2), whereas T<sub>H</sub>2 cells produce type 2 cytokines (IL-4, IL-5, and IL-13) that induce production of IgE and eosinophilia characteristic of atopic diseases.<sup>109</sup> Dendritic cells also induce T<sub>H</sub>2 cell proliferation when exposed to allergens such as cockroach antigen, which is a health hazard common in poor housing quality and urban environments.<sup>110-112</sup> We show in Fig 2 that differential exposure to environmental hazards may mediate the association between SEP and T<sub>H</sub>2 cell polarization, but studies have yet to explicitly investigate these potential pathways with downstream exposures resulting from structural racism. Extrapolating from literature exploring the relationship between SEP, psychosocial stress, and type 2 inflammation,<sup>113</sup> 1 study found that levels of type 2 cytokines and circulating eosinophils were elevated in children of low SEP versus in children of high SEP.<sup>97</sup> This relationship between SEP and T<sub>H</sub>2 cell polarization was partially mediated by psychological stress in children with asthma and adolescents.<sup>97,114</sup> Subsequently, authors demonstrated that T<sub>H</sub>2 cytokine production by PBMCs stimulated with cockroach or dust mite antigen did not differ by SEP, suggesting that the SEP effect on T<sub>H</sub>2 cell polarization may operate through pathways independent of allergen exposures.<sup>115</sup> Glucocorticoids and catecholamines may mediate stress-associated T<sub>H</sub>2 cell polarization by inhibiting the production of type 1 cytokines in T<sub>H</sub>1 cells and promoting the T<sub>H</sub>2 phenotype.<sup>116,117</sup>

**T<sub>H</sub>17 cell–Treg cell balance.** Recent work has also investigated the role of T<sub>H</sub>17 cells in allergic pathogenesis.<sup>118</sup> Although effector T<sub>H</sub>17 cells promote inflammation, Treg cells express FoxP3 and limit excessive inflammatory responses. Psychosocial stressors may promote inflammation by decreasing the

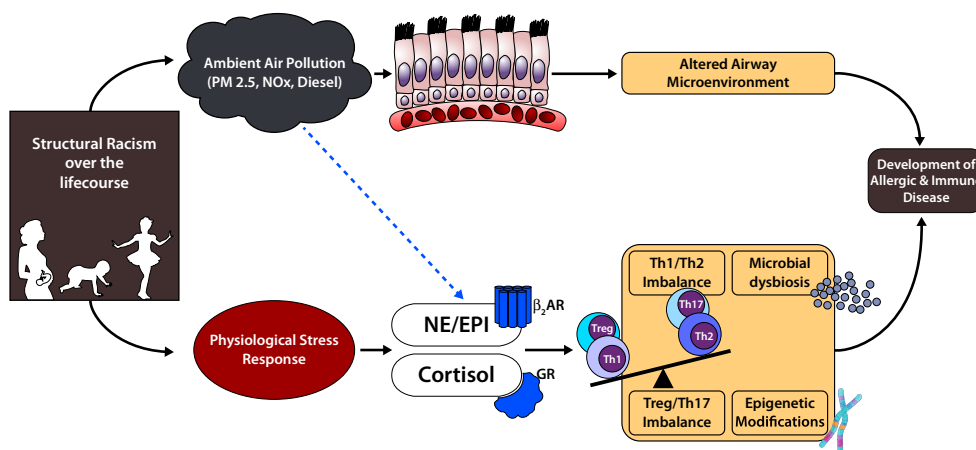


**FIG 2.** Empiric pathways for biologic embedding of structural racism. Structural racism may modulate immune function and promote atopic diseases through the following mechanisms: (1)  $T_H1$  cell– $T_H2$  cell polarization, (2)  $T_H17$  cell–Treg cell balance, (3) the microbiome, and (4) epigenetic modifications

number of Treg cells and enhancing  $T_H17$  cell differentiation.  $T_H$  cells from low-SEP children with asthma had elevated expression of ROR $\gamma$ t, a transcription factor critical for  $T_H17$  cell function.<sup>119</sup> The effect of psychosocial stressors on  $T_H17$  cell–Treg cell balance may be mediated by cortisol.<sup>120</sup> PBMCs treated with a synthetic glucocorticoid at concentrations equivalent to the cortisol levels observed during periods of high stress had decreased FoxP3 expression.<sup>121</sup>  $T_H17$  cell differentiation is also regulated by IL-6 (a proinflammatory cytokine present at elevated levels in individuals from racially segregated communities<sup>122</sup>) by activation of the signal transducer and activator of transcription 3 (STAT3) protein and release of Foxp3 from ROR $\gamma$ t.<sup>123</sup>

**Microbiome.** Psychosocial stressors may produce shifts in gut microbial diversity that contribute to allergic pathogenesis. For example, infants born to mothers with high prenatal stress and/or elevated cortisol levels had a greater abundance of pathogenic Proteobacteria in their gut microbiome and higher reports of allergic reactions.<sup>124</sup> Respiratory microbial communities may also contribute to the development of atopy. Children with uncontrolled asthma who were living in urban environments had nasopharyngeal microbiomes dominated by *Moraxella*, a type of Proteobacteria, which was also associated with increased eosinophilic inflammation.<sup>125</sup> In children with severe asthma, bronchial Proteobacteria positively correlated with  $T_H17$  cell–related gene expression in airway epithelia.<sup>126</sup>

**Epigenetic modifications.** Biochemical alterations to the DNA, such as methylation and histone modifications, influence gene expression and accessibility. Allergic asthma was previously associated with differentially methylated genes in the nasal epithelia.<sup>127</sup> Psychosocial stressors may also induce epigenetic changes that increase susceptibility to allergic disease.<sup>128</sup> Methylation of *ADCYAP1R1* was associated with both exposure to violence and increased odds of asthma in a study of Puerto Rican children.<sup>129</sup> Chronic stress may also affect epigenetic regulation of genes involved in  $T_H$  cell polarization.<sup>130</sup>

## CONCLUSION

By fostering discriminatory policies and practices, government and institutions have reinforced the inequitable distribution of resources and opportunities for Black, Latinx, and Indigenous

people via residential segregation, SEP, and mass incarceration. These upstream pathways of structural racism have led to inequity in the physical and social environment that are associated with alterations in biologic processes, including the physiologic stress response, which may contribute to the increased risk for atopic disease and severe symptoms. Exposure to inhaled environmental pollutants may also increase risk of allergic respiratory disease by altering the airway microenvironment and activating neuroendocrine mediators.<sup>131,132</sup>

To address racial and ethnic disparities, the field of allergy and clinical immunology must take part in dismantling the proximal effects of structural racism. This is not a simple feat, as these factors are rooted in centuries of discrimination and enslavement. Additional investigation is needed to understand the health impact of racism, including further elucidation of the biologic processes and physiologic responses associated with experiencing the effects of structural racism. Research is also needed to identify ways in which the effects of racism can be mitigated through community-based participatory research. This should be done simultaneously with efforts to address the root causes of health disparities. Avenues to achieving a more diverse research workforce reflecting Black, Latinx, and Indigenous communities are also needed. Lastly, to truly address health disparities caused by structural racism, the medical and research community must actively participate in policy reform, advocacy, community redevelopment, and place-based partnerships.

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