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SOCIAL IMPACT OF POVERTY AND TROPICAL DISEASES (C BLACKBURN, SECTION EDITOR)

Rural Embodiment and Community Health: an Anthropological Case Study on Biocultural Determinants of Tropical Disease Infection and Immune System Development in the USA

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Abstract

Purpose of Review Biocultural methods are critically important for identifying environmental and socioeconomic factors linked with tropical disease risk and outcomes. For example, embodiment theory refers to the process by which lived experiences impact individual biology. Increased exposure to pathogens, chronic psychosocial stress, and unequal resource access are all outcomes linked with discrimination and poverty. Through lived experiences, race and socioeconomic inequality can literally become embodied—get under the skin and affect physiology—impacting immune responses and contributing to lifelong health disparities. Yet, few studies have investigated tropical disease patterns and associated immune function using embodiment theory to understand lasting physiological impacts associated with living in a high-pathogen environment.

Recent Findings Here, we use preliminary data drawn from the Rural Embodiment and Community Health (REACH) study to assess whether pathogen exposure and immune stimulation within a sample of children from the Mississippi Delta are associated with household income. We also test whether immune marker levels—assessed with enzyme-linked immunosorbent assays using dried blood spot samples—vary between the REACH sample and a similarly aged nationally representative NHANES sample. Immune marker levels did not differ significantly between REACH participants living below vs. above the federal poverty line, yet immunoglobulin E levels—a marker of macroparasite infection—were higher among REACH study participants compared to the NHANES sample.

Summary These results may suggest community-level pathogenic exposures (i.e., parasitic infections) are embodied by REACH participants with implications for long-term immune function, potentially resulting in immune aspects that differ from nationally representative samples.

Keywords Parasitic disease · Immune function · Environmental racism · C-reactive protein · Immunoglobulin E · Immunoglobulin G

Introduction

Anthropology integrates complementary perspectives to comprehensively examine the historical and contemporary forces that shape human society, behavior, and biology. This holistic approach is helpful in identifying important biocultural determinants of well-being. Incorporating anthropological perspectives into tropical medicine research can consequently provide important frameworks for understanding disease progression and long-term health patterns. For example, embodiment theory considers how human bodies are shaped by lived experiences, physically transforming in response to social and environmental interactions [1, 2].

This article is part of the Topical Collection on Social Impact of Poverty and Tropical Diseases

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Incorporating embodiment theory into infectious disease research provides a framework to assess the ways that lived experiences translate into biological realities. Here, we argue that an understudied area of embodiment theory is how environmental interactions associated with sociopolitical and economic circumstances (i.e., inequality, marginalization, segregation, resource access, infrastructure quality) alter exposure to important microbes and pathogens—including those responsible for tropical diseases—with lasting implications for immune system development, function, and long-term health outcomes.

The importance of embodiment in shaping human health has been increasingly recognized and discussed in the field of biological anthropology [3–5], but additional work is needed to clarify how these pathways contribute to variation in immune system development and the emergence of enduring health and social inequities. In this article, we present an overview of the embodiment concept, briefly exploring the pathways by which embodiment may occur, focusing specifically on environmental correlates to pathogen exposure and resulting changes in immune function. We then present an anthropological case study on the immune-related embodiment of environmental conditions (e.g., exposure to neglected tropical diseases) using preliminary data from the Rural Embodiment and Community Health (REACH; REACHresearch.org) study, a project investigating how health inequities and systemic racism may shape long-term well-being in the USA.

Embodiment Overview

Embodiment is central to the study of human well-being and the emergence of health inequities. As first outlined by social epidemiologist Nancy Krieger, embodiment reflects an "ecosocial" theory of disease causation, recognizing that humans are both cultural and biological beings and considering how external interactions and exposures become internalized through physiological and developmental pathways to ultimately alter individual health [1, 2]. Central to the concept of embodiment is a focus on local ecology, necessitating examination of dynamic interactions between organisms sharing a particular ecosystem [6, 7], with implications for key health determinants (e.g., resource acquisition, disease exposure, experienced psychosocial stress) and associated downstream health inequities. Overall, an embodiment framework encourages researchers not to assume physical differences between individuals or populations are innate, but to instead consider how these differences may be shaped by dynamic variation in social and environmental contexts across the life course [1].

While embodiment research can be used to help explain positive health patterns [2], it has been more commonly used to document how poor health outcomes are shaped by patterns of power (e.g., constrained agency due to structural inequalities), production, consumption, and reproduction [5, 6, 8, 9]. For instance, increased exposure to pathogens, chronic psychosocial stress, and unequal access to resources are all outcomes known to influence long-term health patterns that have been linked with low socioeconomic status, institutional and interpersonal discrimination (e.g., racism, sexism, ageism, homophobia), and infrastructural neglect [4, 10–12]. Because sociocultural factors and lifestyle patterns impact individual interactions with the environment and subsequent exposure to microbes and pathogens, researchers using biocultural approaches are well suited to explore the process and consequences of embodiment. Relevant biocultural methodologies include interview data, biomarker and anthropometric measures, and epigenetic/metagenomic sequencing. Anthropological research across a variety of settings has demonstrated how biomarker analyses may capture hard to quantify aspects of lived experiences, such as chronic stress (i.e., through repeat measures of cortisol levels) and associated health patterns [5, 13], as well as links between structural lifestyle changes, exposure to important microorganisms (e.g., intestinal parasites and microbes that influence gut microbiota composition), and immune function [14–17]. As evidenced by these select studies, a biocultural toolkit is well suited to synthesize and connect lived experiences with downstream physiological effects, thus documenting how both large-scale structural forces and local-level realities shape the process of embodiment [8].

Overarching Pathways of Embodiment

Continued methodological refinements have allowed researchers to more definitively demonstrate the specific mechanisms by which lived experiences become embodied, including recent work drawing on epigenetic, microbiome, and immune function measures. Here we discuss these embodiment pathways in more detail, with special focus on pathogen exposure and immune system development and function (Fig. 1).

Epigenetics

The field of epigenetics provides quantifiable insights into the mechanisms by which environmental conditions can produce embodied phenotypes. Epigenetic research measures environmentally sensitive DNA modifications that impact gene expression—including chemical modifications to DNA and DNA-associated proteins (i.e., histones) —but do not change an individual's underlying DNA sequence [18, 19]. These epigenetic modifications are functionally important because they affect which genes are expressed. Epigenetic measures are useful in embodiment research because, unlike DNA bases which are typically fixed across the lifespan,

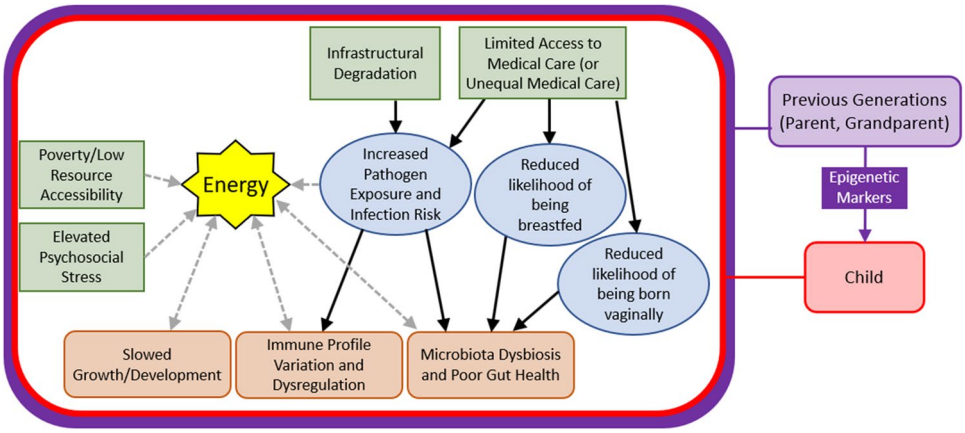

Fig. 1 Pathways and effects of embodied immunity. Solid black lines represent direct effects of disease exposure (linked with resource access and living conditions) and immune activity. Gray checked lines represent factors that alter energy availability, thereby shaping immune system development and function. Green rectangles are the social, political, and environmental factors that become embodied. Blue ovals are the immediate downstream effects of those environmental factors. Orange rounded rectangles represent measurable embodied outcomes. These embodied effects can occur in previous generations (purple box) and affect children (red box) through intrauterine environments, inherited living conditions, and epigenetic changes. While the measurable embodied outcomes are separated here, it is important to recognize that all three discussed here affect one another. Figure created with Microsoft PowerPoint

epigenetic modifications are sensitive to environmental exposures (e.g., nutrition, psychosocial stress, and toxins). A large body of research has focused on documenting links between environmental conditions and epigenetic modifications during early development [19, 20]. Furthermore, there is increasing evidence that the environmental experiences of prior generations may influence epigenetic patterns in descendants [21], which provides a biological basis for the embodiment of historical trauma [19, 22, 23].

Gut Microbiome Measures

The composition and activity of the gut microbiome—defined as the collective genome of the 100 trillion bacteria and other microbes residing in the intestinal tract—is also influenced by individual living conditions and local environment, including diet, household infrastructure, and healthcare access/medication history [17, 24]. The gut microbiome is established early in life and is influenced by a range of factors [19], including delivery method at birth [25–28], post-birth feeding method (i.e., breast vs. formula feeding) [29], and antibiotic use [30–33]. Importantly, each of these factors is shaped by resource access (e.g., to quality medical care and parental leave to support breastfeeding) and living conditions (e.g., exposure to microbes linked with unhealthy gut microbiota development), thereby providing a biological pathway by which embodiment may occur and shape long-term health outcomes.

The development of the microbiome during early development influences health outcomes throughout the life course and across generations [26, 27, 34]. Like epigenetic modification, pathological gut microbiome profiles can negatively affect the gestational environment and may therefore contribute to the intergenerational transmission of poor health [24]. Microbiome composition also appears to shape immune system and digestive tract development. A healthy and diverse microbiome protects against certain pathogens and supports digestive processes (e.g., vitamin synthesis and fiber break down), while a microbiome experiencing dysbiosis (i.e., an imbalance of beneficial/pathogenic species) can potentially lead to pathological states such as hyperinflammation [26, 27, 34]. Early microbiome-linked immune effects may in turn alter the risk of developing health inequity-related chronic conditions. For example, racial disparities in gastrointestinal health are evident in the USA, with Black adults exhibiting elevated rates of certain gastrointestinal cancers (e.g., stomach, small intestinal, and colorectal cancer) and higher resulting mortality rates than white adults [35, 36]. This pattern has been attributed in part to higher hyperinflammatory immune responses elicited by exposure to pathogenic bacteria or parasites, but also due to gut microbiota dysbiosis [15, 36–38]. Child environmental exposure and related microbiome development may consequently play a key role in the emergence of health disparities later in life.

Immune System Development and Function

Recent work has started to consider links between embodiment pathways and infectious disease patterns [15, 24, 39, 40], highlighting clear connections between embodiment pathways and infectious disease risk that should be explored further [15, 39]. For instance, the Eukaryotic Microbiome

(i.e., the collective genome of non-bacterial members of the intestinal microbiome that includes fungal, protozoal, and helminthic species) is an area of microbiome research that has received surprisingly little attention but may have important implications for embodiment processes and immune function [41]. Interactions with these microorganisms during development have been implicated in shaping long-lasting immune activity and subsequent long-term health outcomes.

The Old Friends Hypothesis, for example, contends that a specific branch of the immune system (i.e., type 2 immunity), evolved in response to macroparasite infection [42–44]. Relatively recent changes in sanitation infrastructure, hygiene practices, and medical care limit exposure to these "old friends," potentially resulting in immune dysregulation that favors pro-inflammatory pathways and causes the body to overreact to harmless or self-produced stimuli. These immune changes ultimately increase the risk of chronic inflammatory diseases (e.g., allergies, autoimmune diseases, cardiovascular disease) and are hypothesized to contribute to the relatively high prevalence of these conditions in high-resource, low pathogen areas [42, 45]. Still, while pathogen exposure during key developmental periods may produce enhanced immune regulation in later life, the immune responses elicited by contracting parasitic infections and other tropical diseases are also energetically expensive and may result in delayed growth and cognitive development, as well as other negative health outcomes [46–48]. Thus, by shaping long-term immune function and developmental outcomes, environmental exposures to pathogens and associated immune responses demonstrate how the embodiment of early life experiences (e.g., parasite load) may alter adult well-being (e.g., immune profiles, adult height, educational attainment).

Problematically, previous studies investigating links between infection-related changes in lasting immune function have largely been conducted in higher-resource areas (i.e., testing factors linked with allergies and asthma risk in these populations) [49–52]. Additional research is therefore needed to assess the embodiment of infectious disease exposure in low-resource, marginalized groups, particularly low-resource areas facing high tropical disease risk. Given that these communities are often characterized by harmful environmental exposures (e.g., pathogens and pollutants), widespread poverty, and high levels of psychosocial stress that may negatively impact immune function [4, 10–12], embodiment likely contributes substantially to health outcomes. Yet, few studies have conceptualized these health outcomes using embodiment theory to understand lasting immune impacts associated with living in a high-pathogen environment, especially during key developmental periods. Biocultural anthropological frameworks and methods are well suited to address this need. Here, we provide a preliminary case study that demonstrates the application of an anthropological embodiment framework to investigate how living conditions, resource access, and pathogenic exposures during development may interact to influence immune system development.

Embodiment Case Study: the Rural Embodiment and Community Health (REACH) Study

The Rural Embodiment and Community Health (REACH; https://www.reachresearch.org/) study was established in 2019 with the goal of investigating the prevalence of neglected tropical diseases and relationships between lifestyle variation, ecological factors, and health patterns in low-income rural regions of the USA through the lens of embodiment. The project focuses on the impact of exposure to intestinal parasites (e.g., protozoal and helminth infections) and pathogenic bacteria (e.g., *Helicobacter pylori*) on growth, development, and immune function. The long-term consequences of these infections can include malnutrition, iron deficiency, stunted growth, and delayed cognitive development for intestinal parasites [53], and possible intestinal inflammation and increased gastrointestinal cancer risk later in life for *H. pylori* [36]. However, infection symptoms vary substantially across populations and individuals, likely due to variation in both physiology and embodied experiences. Embodiment processes linked with exposure to parasites and other gastrointestinal pathogens remain poorly studied in the USA; it is therefore unclear how these types of environmental exposures may be embodied and contribute to prevalent health disparities evident among minoritized and low-resource communities within this high-income country [15, 54–57].

Moreover, the burden posed by gastrointestinal parasites in the USA is currently unknown due to limited research interest, medical testing, and national attention; however, historical data from the 1930s through 1980s suggest endemic levels of infection [55, 57–62]. The elimination of parasites has never been conclusively demonstrated, and there is good reason to believe that infections continue to be prevalent, especially in the Southern USA where high poverty rates and environmental factors (e.g., soil conditions and climate) favor infection spread [55, 63]. The hypothesis that parasite infection may still be prevalent in the USA has been gaining traction in recent years [15, 54–57]. Recent evidence from studies conducted in the Southern USA indicates that several types of parasitic infections are present, including protozoa (i.e., single-celled eukaryotes) and helminths (i.e., parasitic worms) [15, 54–57].

Thus, parasite infection may represent an underexplored set of lived experiences in the USA that alter individual biology and contribute to the development of long-term health inequities and associated socioeconomic disparities. As has been demonstrated in lower-income countries, the long-term

effects of infection-related embodiment may be especially impactful during childhood when the immune system is developing, leading to context-dependent lasting immune effects [46, 64]. Immune challenges during early life have been shown to affect long-term immune cell production patterns, with implications for lifelong immune function and later health outcomes. Measuring specific immune marker concentrations can consequently provide important information on immune system development, status, and exposure histories. For instance, the antibody immunoglobulin E (IgE) is critical in adaptive immune responses to macroparasites. Likewise, exposure to other pathogens, like viruses and bacteria, may elicit acute, inflammatory immune responses to clear the infections (e.g., the production of C-reactive protein [CRP]) and longer lasting humoral immune activity (e.g., immunoglobulin G [IgG]) [65–69]. These three immune markers reflect different forms of immune system activity and also represent distinct timescales of immune function (Table 1). Measuring all three immune markers therefore provides an opportunity to assess how embodiment processes may influence various types of immune function across different timescales.

In addition, exposure to different pathogens (or lack thereof) at different stages throughout the life course shapes health in several important ways, reflecting the embodied effects of exposure. Earlier exposure to certain parasites primes the immune response to favor adaptive immunity over innate inflammatory immune responses, which has been linked to reduced growth and shorter adult stature [70]. Conversely, limited exposure to parasites during immune system development may prime the immune system to favor innate, inflammatory responses and increase the risk of developing disorders associated with immune dysregulation (e.g., allergies, autoimmunity, and heart disease) [71–74]. However, these associations remain poorly tested among low-income communities within wealthy nations, despite the fact that children in these settings likely face environmental exposures that vary substantially from both nationally representative samples and nations/regions with known high-pathogen exposure. Specifically, children living in a rural, low-income setting likely experience poor nutrition, altered exposure to environmental toxins (e.g., pesticides and herbicides) used in agricultural settings, and high-pathogen loads associated with suboptimal sanitation infrastructure, all of which contribute to differential immune stimulation throughout immune system development.

Importantly, unlike regions where parasitic infection is well-acknowledged, low-resource children living in high-income countries may also face additional health consequences from undiagnosed infections and lack of education about infection avoidance. The health impacts of these tropical diseases in higher income nations may be especially apparent among communities of color, where legacies of

Table 1 Three important immune markers linked with various environmental exposures during development. A brief description of each immune marker is provided, including information on typical immune activity, activation duration, and possible contribution to embodiment processes

Immune marker	Immune role	Relative activity duration	Embodiment contribution	Citations
C-reactive protein (CRP)	Concentrations increase quickly with infection onset, part of nonspecific defense critical for pathogen clearance	Produced within days of infection, generally a short-lived response lasting for a handful of days	If chronically elevated, may lead to low-grade inflammation and immune dysregulation	[68, 69]
Immunoglobulin G (IgG)	Associated with acquired humoral immunity in response to viral and bacterial infections	Acts over a period of several months	Robust IgG immune activity could reflect adaptive immune priming to bacterial and viral pathogens	[65]
Immunoglobulin E (IgE)	Often associated with responses to parasitic infection	Lasting many months (from stimulation to return to baseline concentration) or even years in the case of chronic reinfection	Greater reliance on IgE-related immune responses may dampen inflammation, although high IgE levels may also be tied with atopic and allergic conditions in some contexts	[66, 67]

environmental marginalization and associated lack of access to key health determinants (e.g., medical care, functional sanitation systems, adequate nutrition) may both increase parasite exposure and compound the negative impacts of infection [10, 11]. Clarifying immune patterns associated with these lived experiences may consequently help resolve the developmental and environmental causes of health inequalities starting early in life. To investigate these complex associations within an embodiment framework, the present pilot study was conducted in a rural community located in the Mississippi Delta. Previous 18 s rRNA amplification and sequencing from stool samples collected in this sample indicated that roughly one-third of child participants exhibited signs of parasitic infection [15], but is unclear how environmental pathogen exposure may be embodied with implications for lasting immune function and later health outcomes. To clarify these patterns, the following hypotheses were tested:

1) Pathogen exposure and immune stimulation within the REACH sample will correspond with household income status. These exposures will be embodied in ways that influence immune activity, such that (a) IgE levels will be higher, (b) IgG levels will be higher, and (c) the likelihood of elevated CRP concentrations (associated with increased reliance on inflammatory immune pathways) will be lower among REACH child participants living below the national poverty line.
2) In comparison to a nationally representative sample (National Health and Nutrition Examination Survey (NHANES)), the REACH sample (living in a rural, low-resource setting) will exhibit the following: (a) higher IgE levels (due to increased parasite exposure), and (b) a lower likelihood of elevated CRP concentrations (due to greater adaptive immune activity dampening inflammatory immune responses). Total IgG levels were not available for NHANES participants.

Methods

Study Sample

Preliminary data were collected between July and August 2019 in a community of approximately 2000 individuals from the rural Mississippi Delta region. Roughly 95% of individuals in the community identify as Black or African American, and the median household income is $20,265 based on US census estimates. The community experiences limited access to key resources. For instance, the nearest full grocery store is roughly 20–30 min away by car, limiting access to families without a car and leading many community members to rely on the limited food selection available at the local Dollar General and neighboring gas station. Furthermore, while care from nurse practitioners was available within the community, the nearest county hospital required a 30-min car ride for those able to afford medical services. Additional health concerns raised by study participants included environmental toxin exposure (e.g., from agricultural pesticides), which may compound existing poor nutrition and negatively affect child growth, development, and long-term health trajectories. The combination of poor nutrition, exposure to environmental toxins and pathogens, and limited access to medical care and relevant health information may contribute to the development of lifelong health disparities in this community through embodiment processes.

The pilot sample included 32 children (ages 3–15 years, across 18 households). All child participants either self-identified or were identified by their parents as Black or African American, consistent with the makeup of the community. Parental consent and child assent were obtained for all participants. All methods and procedures were approved by the Institutional Review Boards at University of Colorado Colorado Springs, Dartmouth College, and Washington University in St. Louis. It should be noted that these data were collected as part of an exploratory field season for the REACH project. During this community visit, the research team was primarily focused on developing partnerships for future collaborative research and community outreach, rather than data collection. Thus, only a small pilot sample was recruited for preliminary data collection. Although follow-up research was disrupted by the COVID-19 pandemic, additional data collection is underway to further test embodiment pathways, particularly in relation to the issues identified by community members.

Data Collection

(i) Interviews: Parents of child participants completed household interviews that provided the following information: child age, sex, number of people living in the child's home, and household income category (< $10,000; $10,000–$19,999; $20,000-$34,999; $35,000-$49,999; $50,000-$74,999; $75,000-$99.999; $100,000 +). Whether a family was considered to live above or below the national poverty threshold was then determined based on household income level and family size [75].
(ii) Anthropometric measurements: To account for the impact of body size on immune markers, anthropometric measures were collected following standard techniques [76]. Height was measured using a stadiometer (Seca Corporation 214, Hanover, MD) and a Tanita children's scale (model BF-689) was used to obtain participant weight. These height and

weight measures were then used to calculate BMI (kg/m^2). Child BMI *z*-scores were calculated using WHO standards, considering participant age and sex [77].

(iii) Dried blood spot collection: To measure IgE, IgG, and CRP levels, dried blood spots (DBS) were collected from the older children. Three to five drops of whole blood were collected on filter paper from a single finger prick following standard minimally invasive collection methods [78]. Samples were dried 4 h and stored in a − 20 °C portable freezer until transport on dry ice to the Global Health Biomarker Lab at the University of Oregon for analysis (see Online Resource 1 for additional details) following established methods [70, 79, 80].

NHANES Immune Marker Data

To test whether REACH child participant IgE and CRP levels varied significantly from nationally representative samples, NHANES data were used. Specifically, the publicly available 2005–2006 dataset containing IgE and CRP concentrations was downloaded and the data for similarly aged children (ages 3–15; $n = 2364$) were extracted and merged with the REACH study dataset. To facilitate comparisons with NHANES data, serum-equivalent values were calculated from REACH participant IgE and CRP DBS concentrations following established methods [64, 68].

Statistical Methods

Preliminary analyses indicated that the REACH project participant IgG concentrations were normally distributed (with a skew between ± 1). However, IgE concentrations were not normally distributed and were subsequently transformed. Consistent with previous work [48], serum-equivalent CRP concentrations were dichotomized for use during analysis. Specifically, a binary variable was created to indicate the presence (CRP ≥ 1 mg/L) or absence (CRP < 1 mg/L) of an acute inflammatory immune response [81]. Previous work suggests this cutoff value (CRP ≥ 1 mg/L) accurately identifies elevated inflammatory responses [48].

(i) Hypothesis 1: To test whether IgE or IgG levels were elevated among participants considered to live below the national poverty line compared to living above this cutoff point, BCa bootstrap linear regression was used, controlling for participant BMI *z*-scores. Due to the small sample size, Fisher's exact test was used to test whether acute CRP level classification was significantly less likely among individuals living below the federal poverty level (compared to those living above this level).

(ii) Hypothesis 2: To assess whether IgE levels were significantly higher among REACH study participants compared to those of similarly aged children in the NHANES dataset, a Wilcoxon rank-sum test was used. This non-parametric test is appropriate given the small REACH sample size and non-normal data distribution (due to the presence of meaningful outliers). Likewise, a non-parametric Fisher's exact test was run to determine whether elevated CRP level classification was significantly more likely among REACH participants compared to similarly aged children in the NHANES dataset.

Results

Descriptive Statistics

Sample descriptive statistics for age, sex, body mass, interview data, and biomarker data are presented in Table 2. According to WHO cutoffs for BMI *z*-scores [82], 12

Table 2 Descriptive statistics of key variables. Sample means (with standard deviation and range) or frequency (percent) of key variables, for 32 participants (across 18 households) providing DBS samples. Untransformed values are presented for ease of interpretation

Variable	Mean (SD; range)
Age (years)	8.28 (3.42; 3–15)
BMI (kg/m^2)	20.7 (4.44; 14.9–32.1)
Immunoglobulin E concentration (ng/mL)*	1282.3 (2132.0; 354.2–9188)
Immunoglobulin G concentration (g/L)	1.77 (0.460; 0.991–2.86)
CRP concentration (mg/L)	0.398 (0.145–4.21)
	Frequency (%)
Sex	
Female	16 (50.0%)
Male	16 (50.0%)
Household income level	
< $10,000	16 (50.0%; 10 households)
$10,000-$19,999	4 (12.5%; 2 households)
$20,000-$34,499	8 (25.0%; 3 households)
$35,500-$49,999	3 (9.38%; 2 households)
$50,000-$74,599	1 (3.13%; 1 household)
Federal poverty-level classification	
Below	23 (71.9%; 13 households)
Above	9 (28.1%; 5 households)
CRP level classification	
Acutely elevated	2 (6.25%)
Not elevated	30 (93.8%)

*IgE concentration average calculated omitting participant with high CV% value ($n = 31$).

Table 3 Bootstrap regressions for the prediction of IgE and IgG concentrations from participant BMI *z*-score and federal poverty line classification (accounting for household annual income and number of people living in the household). Observed coefficients with bootstrap S.E. Comparisons are statistically significant at *$=p<0.05$, **$=p<0.01$, and ***$=p<0.001$

	Immunoglobulin E	Immunoglobulin G
Constant	0.001 (0.0004)*	2.16 (0.230)***
BMI *z*-score	0.0001 (0.0001)	−0.135 (0.077)
Federal poverty line classification (0 = above cutoff, 1 = below cutoff)	0.0005 (0.0004)	−0.329 (0.206)

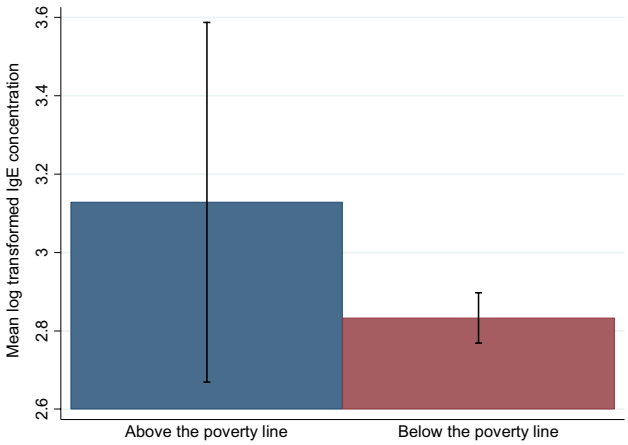

Fig. 2 REACH participant average log transformed immunoglobulin E (IgE) concentrations. Among children classified as living above or below the federal poverty level, as defined by household income and number of people within the household. Figure created with Stata 14

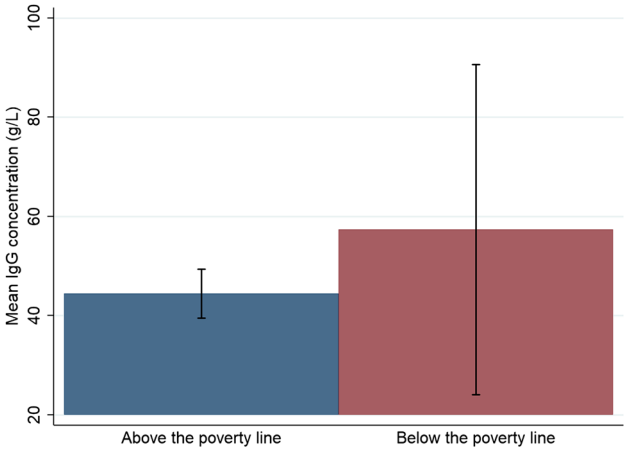

Fig. 3 REACH participant average immunoglobulin G (IgG) concentrations. Among children classified as living above or below the federal poverty level, as defined by household income and number of people within the household. Figure created with Stata 14

(37.5%) of sampled children were at risk for being overweight and 7 (21.9%) were overweight; none were underweight (although one child was approximately one standard deviation below the mean). High rates of poverty were evident in the sample, with half of the participants living in households making less than $10,000 annually (10 out of 18 households sampled) and 23 children (nearly three-quarters of the sample) classified as living below the federal poverty level based on household size (13 out of 18 households sampled). A substantial range of IgE values were evident (354.2–9188 ng/mL), while only two participants (from different households) exhibited CRP levels indicative of acute elevation.

> Hypothesis 1: IgE, and IgG will be higher, and rates of acute CRP elevation will be lower among participants living below the poverty threshold.

BCa bootstrap linear regression results testing the association between IgE and IgG concentration and federal poverty-level classification are presented in Table 3. No significant associations were observed between IgE level and federal poverty-level classification (Fig. 2) or BMI *z*-score (all $p>0.200$, model $R^2=0.0901$). Likewise, no significant associations were evident between IgG level and federal poverty classification (Fig. 3) or BMI *z*-score (all $p>0.05$, model $R^2=0.102$). Additionally, Fisher's exact test indicated that participants classified as living below the federal poverty level were not significantly less likely to exhibit acutely elevated CRP levels ($p=1.000$) (Fig. 4). The hypothesis was consequently not supported by these analyses.

> Hypothesis 2: Study participants will have higher IgE levels and lower rates of elevated CRP compared to a nationally representative sample.

A significant difference between the underlying distribution of IgE values was observed ($z=-6.54$, $p<0.001$). Specifically, as hypothesized, REACH study participants displayed greater mean IgE levels (512.2 IU/mL) compared to similarly aged NHANES child participants (184.9 IU/mL) (Fig. 5), even when the sample was filtered to only include non-Hispanic Black NHANES participants ($n=703$; $z=-5.29$, $p<0.001$; 252.9 IU/mL). Additionally, a higher proportion of NHANES children exhibited elevated CRP levels (19.7% of the sample) compared to REACH

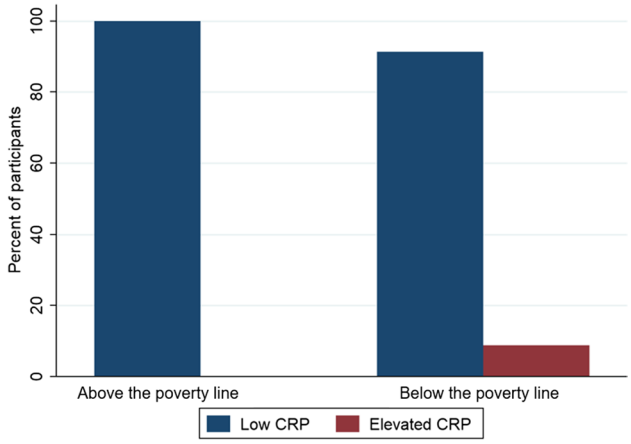

Fig. 4 Percentage of REACH participants exhibiting low vs. elevated C-reactive protein (CRP) levels. Among children classified as living above or below the federal poverty level, as defined by household income and number of people within the household. Figure created with Stata 14

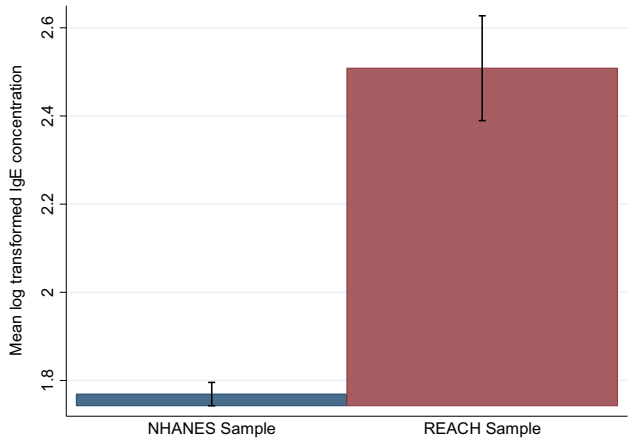

Fig. 5 Child average Immunoglobulin E (IgE) concentrations. Among children drawn from the NHANES and REACH study datasets. Figure created with Stata 14

participants (6.25% of the sample) (Fig. 6); however, these analyses did not indicate a statistically significant difference (two-tailed $p = 0.070$). These results were also consistent when only non-Hispanic Black NHANES participants ($n = 701$, 19.1% of this sample displayed elevated CRP levels) were compared to REACH study participants (two-tailed $p = 0.099$).

Discussion

These findings provide mixed support for the study hypotheses. IgE, IgG, and CRP levels were not significantly associated with federal poverty-level classification. Yet,

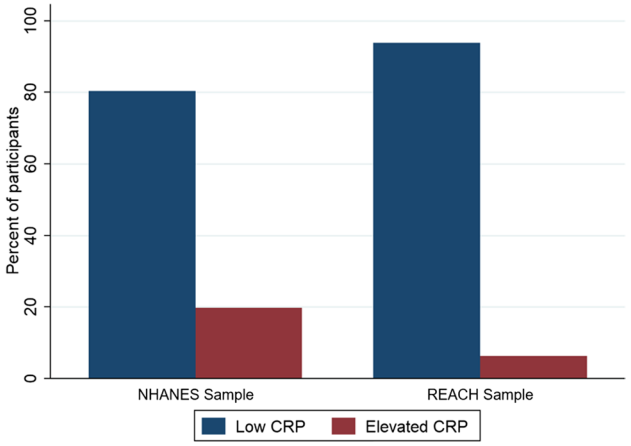

Fig. 6 Children exhibiting low vs. elevated C-reactive protein (CRP) levels. Among children drawn from the NHANES and REACH study datasets. Figure created with Stata 14

as expected, IgE levels were significantly higher among REACH study participants compared to the NHANES sample. Rates of elevated CRP levels were also lower among REACH participants; however, this relationship was not significant. These results may suggest community-level embodied environmental exposures (e.g., to macroparasites) among REACH participants with implications for long-term immune function, potentially resulting in immune aspects that differ from nationally representative samples.

Associations Between Immune Markers and Poverty Level

Meaningful differences in IgE, IgG, or CRP levels were not observed between REACH study participants classified as living above or below the federal poverty level. This lack of variation may reflect community-level factors that influence all households, regardless of socioeconomic status. For instance, high rates of poverty were evident across this sample, with most participants classified as living below the federal poverty level. Only one household reported an annual income of over $50,000, while 10 of the 18 households sampled made less than $10,000 annually. It is consequently likely that there was not enough income variation present in the small sample to document any associations between poverty-level classification and immune marker concentrations, and REACH participants were likely exposed to similar environmental conditions and shared embodiment processes within the small community. Suboptimal community infrastructure (e.g., sanitation systems) leading to frequent sewage backups, exposure to environmental pathogens in contaminated water and soil (e.g., parasitic infections), and limited access to medical care and a full grocery store may

all shape embodied immune system development and health in the community.

For example, many participants reported that the local bayou that runs through town regularly floods and leads to sewage backups during periods of heavy rain. Compromised sanitation systems as described here have been linked with elevated infection risk for a range of pathogens, including viral diarrheal illness, hepatitis A virus, measles, typhoid, cholera, and various parasites that spread through human waste [83, 84]. Furthermore, previous work in other regions of the Southern USA has documented links between infection and sewage backups, including documented cases of parasitic infection in parts of Alabama and Texas where community members are exposed to raw sewage due to failing sanitation systems [54, 56, 85, 86]. Signs of parasitic infection have also been documented in the REACH sample [15] likely shaping immune responses. The range of different pathogens transmitted through flooding and associated community-wide sanitation system failures may elicit a range of immune responses, including acute inflammation (e.g., elevated CRP levels) at the onset of infection and longer lasting antibody production in response to viruses and bacteria (e.g., elevated IgG production), as well as extracellular parasites (e.g., sustained IgE production).

Limited access to nutritious food and healthcare may exacerbate these issues. Previous research using NHANES data has demonstrated that children with larger body sizes—consistent with diets composed highly of calorically dense, processed foods—exhibited elevated signs of low-grade inflammation, as indicated by CRP levels [87, 88]. While BMI *z*-scores were not significantly associated with elevated CRP concentrations in the present study, future work should examine associations between diet composition and inflammation. Likewise, the inability to access a full hospital—as was the case for many low-income families included in this sample—may preclude the diagnosis and management of health conditions early in life. Embodiment processes linked with limited access to healthcare may also prolong parasitic infections, leading to increased chronic infection risk, compromised immune function in response to established infections, and an inability to treat infections medically [89]. These prolonged infections may, in turn, shape immune system development (e.g., through sustained IgE production) in ways that influence later health outcomes. Cumulatively, these early life exposures may lead to distinct immune activity patterns and health trajectories that differ from nationally representative data.

Immune Marker Differences Between REACH and NHANES Participants

Consistent with the hypothesis that children living in low-resource rural areas of the Southern USA are exposed to a set of environmental conditions that influence embodiment processes and long-term immune function, the results of the present preliminary study suggest that children from the rural Mississippi Delta experience elevated humoral immune activity—as indicated by IgE levels—compared to national samples. These long-lasting immune responses can result from parasitic infection during childhood [64]. Although current parasitic disease prevalence in the Mississippi Delta are unknown, high infection rates were documented in the past [55]. Additionally, preliminary 18 s rRNA sequencing of stool samples collected by the REACH study from 24 children (20 of whom are included in this sample) found signs of helminthic and protozoal infections in one-third of the participants, suggesting that parasite infection is an important health concern in this community [15, 40]. It is also possible that contact with environmental toxins due to the regular use of pesticides in the area may lead to immune dysregulation and elevated IgE levels [90, 91], although this remains to be tested in this population. Cumulatively, these environmental exposures during childhood may be embodied in ways that substantially influence developmental patterns and long-term immune activity.

In contrast to long-lasting IgE production, CRP elevation generally reflects an acute innate immune response. Only one child in the REACH sample reported being recently ill—although this child did not display acutely elevated CRP levels—which may partly explain why only two children exhibited signs of elevated CRP production. Contrary to study hypotheses, the results do not support the idea that embodiment processes associated with immune-priming parasitic pathogen exposure lead to lower levels of inflammation among REACH study participants relative to a nationally representative sample. The small sample size undoubtedly impacted our ability to detect meaningful differences between the two groups. It is also possible that while REACH participants exhibited signs of immune activity in response to certain pathogens (e.g., parasite infections) that vary from the NHANES sample, their exposure to pathogens eliciting an acute inflammatory immune response (e.g., viral infections) does not differ significantly from national trends. However, it is worth noting that REACH participants exhibited signs of significantly elevated intestinal inflammation, as indicated by fecal calprotectin levels (a common marker of gastrointestinal inflammation). Measured fecal calprotectin levels were significantly higher than those documented among similarly aged children living in Sweden, Norway, the UK, or Amazonian Ecuador [15].

It is therefore possible that environmental conditions experienced in the rural Mississippi Delta do lead to inflammation in certain parts of the body, but that more localized measures of inflammation are needed to detect these immune patterns. In other words, a generalized measure of inflammation like CRP may not detect these system-specific

inflammatory responses. Conversely, it is also possible that the exposure to intestinal macroparasites throughout immune system development in this sample may be reducing systemic inflammation as hypothesized. The Old Friends Hypothesis suggests that infection with parasitic worms during childhood may steer the immune system toward more anti-inflammatory pathways due to coevolutionary mechanisms that favor tolerating non-lethal chronic parasitic infection over complete resistance and clearance of infection [46, 92–96]. In this case, high levels of pathogen exposure during development may be embodied in a way that ultimately favors immune system regulation (vs. dysregulation) and may prevent the development of allergy/autoimmune diseases, while also potentially leading to poor developmental outcomes (e.g., stunted growth), although this requires further testing.

Limitations and Future Directions

This study had several important limitations. First, as previously noted, the sample size was small, and these results should be regarded as preliminary. Furthermore, due to the small sample size, simple non-parametric analyses were used for some of the analyses; multiple model covariates and interaction terms were consequently not included. Second, data on child diet were not collected. It was therefore not possible to directly test whether child nutrition may have influenced immune function. Future work will include the collection of dietary data to investigate these associations. Likewise, community levels of environmental toxin exposure were not measured, and it was not possible to test whether local pesticide use may have influenced child immune marker levels and general health (a concern reported by many parents in the community). Environmental samples will be collected in the future to ascertain local pesticide levels.

Another limitation is that only three immune markers were measured in the present study. While these measures reflect different aspects of immune function, the measurement of additional immune markers is needed to better test how childhood environmental exposures may be embodied in ways that affect immune function. For instance, other immune markers associated with inflammation (e.g., interleukin-6) and response to parasitic infection (e.g., interleukin-10) could be used to further test how living conditions and resource access are associated with immune regulation among REACH study participants. Still, the present preliminary study suggests that certain immune markers may prove more useful in future embodiment research. For example, long-lasting immune responses—like those associated with IgE production—may prove more useful in documenting the enduring physiological changes related to the embodiment of local environmental conditions. Immune markers that are typically produced during acute, transient inflammatory immune responses—such as CRP—may be too fleeting to capture biologically meaningful changes resulting from embodiment processes in children, but may prove useful for understanding the development and maintenance of chronic low-grade systemic inflammation in adulthood. Although parents were asked to report current signs of child illness, longitudinal DBS sample collection (i.e., multiple samples from the same participant over the course of the field season) and subsequent CRP analyses would have helped to address this limitation, distinguishing between high CRP levels related to fleeting, acute infections, and elevated levels caused by chronic low-grade inflammation (e.g., related to high adipose levels).

Finally, while these findings provide some preliminary evidence suggesting that early life conditions may significantly influence aspects of immune function, additional work is needed to establish the specific mechanisms by which these experiences might become embodied. Future REACH study data collection and analyses will include measures of participant gut microbiota, offering a more direct test of embodiment pathways and resulting immune activity in the study population. Incorporating measures of the microbiome will also provide an important assessment of how cohabitating intestinal parasites and gut microbiota interact to influence host immune regulation. These data will cumulatively offer additional insight into the emergence of persistent health inequities during childhood.

Conclusions

These preliminary findings suggest that children from low-income, rural US communities exhibit immune profiles that may differ in some respects from nationally representative samples, likely due in part to exposure to neglected tropical infections that go unacknowledged in the USA. More work is needed using larger samples to identify key ecological conditions and lifestyle factors impacting immune marker levels, as well as to establish the pathways by which these environmental exposures become embodied and contribute to immune activity variation. Still, the results of this pilot study demonstrate the importance of embodiment perspectives within tropical medicine to elucidate the emergence of health inequities in early life in relation to relevant lifestyle factors (environmental exposure to pathogens and toxins, living conditions, resource access). A biocultural anthropological framework can help construct a more holistic picture of embodiment mechanisms by accounting for evolved human physiological responses to environmental stimuli, while also recognizing that these processes are highly dynamic across individual life histories and circumstances. A biocultural lens allows researchers to account for the

influence of cultural norms, individual behavior, environmental conditions, and lifestyle in shaping physical health, while concomitantly considering the impacts of sociocultural phenomena (e.g., constructs of race) and structural inequalities [97–100]. Beyond clarifying how lived experiences may lead to lasting physiological changes, this type of work also has the potential to assist in ongoing efforts in tropical medicine and associated fields to address persistent racial and socioeconomic health disparities, both in the USA and abroad.

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Data Availability Due to the sensitive nature of this data and because this is a preliminary study collected from a very small sample, the authors and associated IRBs are concerned that even deidentified data may be identifiable within communities if made public. For this reason, these data are not posted publicly to a third-party server. However, the complete de-identified dataset will be made available to qualified researchers, clinicians, and others upon request. Researchers must agree to privacy and data use expectations. Requests can be made on the Rural Embodiment and Child Health website (REACHResearch.org) under the Data Sharing/Contact Us tab.

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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