

Historical perspective of pediatric health disparities in infectious diseases: centuries in the making

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Summary: COVID-19 is not the first infectious disease to affect certain communities to a greater extent than others. This article highlights lessons learned and proposed mechanisms of health disparities in common infections to provide context to the COVID-19 and future pandemics.

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Abstract:

COVID-19 laid bare the disproportionate effects of infectious agents on vulnerable communities. However, historically, infectious diseases have long been known to affect certain communities to a greater extent than others. The mechanisms behind these differences are multifactorial, and lie less in biological susceptibility and instead more on socioeconomic factors and other social determinants of health. This article highlights health disparities in common infections such as respiratory syncytial virus, tuberculosis, HIV, syphilis, and influenza and will use lessons learned from previous pathogens and infectious disease disparities in vulnerable populations to provide context to the COVID-19 pandemic.

Keywords: Infectious Disease; Disparity; Vaccination; Access; Children

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The COVID-19 (coronavirus) pandemic's arrival felt, in many ways, very new. This generation-defining global infectious diseases event unfolded before our very eyes as we all raced to understand it, to follow the epidemiologic curves, to learn its modes of transmission, and to serve as resources and experts to our patients, families, friends, and communities. As the pandemic evolved, it was quickly evident that its impact was not felt equally in all of those communities; studies repeatedly demonstrated that racial and ethnic minority communities and those with less wealth or access to housing in the United States experienced COVID-19 infections, hospitalizations, and deaths at higher rates than their counterparts. [1] The murders of Ahmaud Arbery, Breonna Taylor, and George Floyd in 2020 all added further national context to the health disparities occurring during the COVID pandemic and underscored the systemic racism in the United States (US) that helps drive these inequalities. While this review focuses on disparities in the US, these concerns are of course not limited to the US setting; similar disparities can be observed in many settings globally.

Yet while the COVID-19 pandemic felt new, the occurrence of health disparities in infectious diseases certainly was not. Race is a social construct, and not a biological fact. Thus, the differential impacts of infections on various communities arise not from biology, but instead from the sociologic context in which medicine is practiced. This context can be understood in terms of access: access to health care itself, access to diagnostic testing, access to therapies, and access to preventative measures. Differential access leads to differential impact of infectious disease on vulnerable communities. Understanding these disparities is critical to target screening, prevention, and treatment programs and achieve equitable outcomes for all.

Access to health care facilities

A comprehensive review of all pediatric health disparities related to infectious diseases is beyond the scope of this commentary, but examples are informative. Structural barriers such as racism, misogyny, transphobia, classism, and the US carceral system can conspire to limit access to health care in the first place. These forces can intersect in multiplicative ways. For example,

transgender women are a marginalized community that comprises just 0.28% of the US population, but the HIV prevalence in this community overall is 14% (compared to less than 1% for cisgender women in the US), and that prevalence differs substantially by race (44% among Black women, 26% among Hispanic women, and 7% among non-Hispanic White women).[2] Yet in a study in 6 US cities, less than half of transgender Black women who were seropositive for HIV had previously been diagnosed.[3]

Further highlighting the additive nature of social disadvantages and the concept that they may lead to decreased access to care, an increasing number of social disadvantages was associated with lower physical functioning quality of life in a dose-response manner among children hospitalized with respiratory infections.[4] The increased incidence of severe COVID-19 infection in non-Hispanic Black, Hispanic, and Indigenous children is considered to be due, in part, to delayed care due to limited access to physical clinics and decreased technical infrastructure for telehealth visits.[5] Incarceration and involvement with the justice system can likewise affect access to care and impact infection-related health outcomes as has been shown for HIV and sexually transmitted infections.[6,7] Difficulty with accessing care can also re-occur at transitions of care such as moving from adolescent to adult providers based on age.[8,9]

Access to diagnosis

Physical access to care is not enough to eliminate disparities in health outcomes. For example, once they are through the door to a clinic, some groups such as gender or sexual orientation minorities may find that screening forms do not include them, or that providers may be uncomfortable around them, as has been shown among young men who have sex with men seeking HIV care.[10] Interactions with less comfortable providers and a system that does not make one feel seen may therefore limit access to further care or to other services offered (such as infectious diseases screening). Primarily speaking a language other than English can similarly limit access to optimal care in that use of adequate interpretation might be limited, leading either to decreased

provider understanding of the patient's history or to the family's decreased understanding of treatment plans and follow up. As an example, a study of pediatric appendicitis found that patients who spoke a language other than English had both two-fold increased odds of having had additional healthcare visits to the Emergency Department or their pediatrician prior to their appendicitis diagnosis and hospitalization, and an increased hospital length of stay once eventually hospitalized.[11]

Syphilis, and therefore congenital syphilis, is an example of a condition wherein disparities persist despite improvements in public health overall. Syphilis rates in the United States have increased since 2000, disproportionately impacting men who have sex with men, people in lower socioeconomic status areas, and non-Hispanic Black and Hispanic people.[12] Congenital syphilis is significantly more common in infants born to non-Hispanic Black and Hispanic mothers than in non-Hispanic White mothers (19.9 and 10.3 times higher, respectively).[13] Early diagnosis and treatment of syphilis is critical to preventing congenital syphilis; non-Hispanic Black and Hispanic women are significantly less likely to have this testing.[13] Similar disparity exists for perinatal HIV, in which early diagnosis and maternal treatment significantly impact infant outcomes but infants of non-Hispanic Black and Hispanic mothers remain at higher risk of perinatal infection.[14]

Access to treatment

Even once an infectious diagnosis is made, access to appropriate therapy can be inequitable. The U.S. Public Health Service Syphilis Study at Tuskegee in which 400 Black men with syphilis were enrolled without informed consent and followed for 4 decades without being offered the penicillin antibiotic therapy that had become widely available during the study is simply the best-known and most appalling example of inequitable access to therapy for infections.[15] The many historical traumas perpetrated against marginalized communities in the US and Canada have entrenched the inequitable access to therapies for infections, including through generating appropriate reticence in these communities to seek care for fear that the care itself will be yet another trauma in the form of

medical experimentation without consent or inappropriate therapies. At the same time, these and other historical traumas due to systemic racism also perpetuate other aspects of socioeconomic disadvantage such as poverty, housing discrimination, access to clean water and suitable food, and inferior insurance. These systemic factors are proposed as possible explanations for the increased incidence of and worse outcomes during tuberculosis and lower respiratory infections among US American Indian / Alaska Native and Canadian First Nations populations or sepsis among Black children, for example.[16–18] Even when type of insurance is accounted for, disparities can persist, as was demonstrated in a cohort of children enrolled in military insurance that demonstrated increased surgical treatment of osteomyelitis for Black children in adjusted analyses.[19] Involvement in infectious diseases surveillance and research can also be inequitably distributed as has been shown in influenza, bronchiolitis, and HIV, perpetuating the cycle that those with increased social advantage to begin with will receive the advantages of care and therapy.[20–22]

Access to infectious disease prevention: Environmental factors

In many cases, infectious disease disparities arise from inadequate preventative measures, such as public health interventions and vaccination. In 1899 W.E.B. Du Bois reported increased tuberculosis mortality in Black Philadelphians, attributable to neighborhood factors such as crowding and unsafe housing.[23] Similarly, the US Department of Commerce reported a doubling in the relative annual risk of tuberculosis infection between non-Hispanic Black and non-Hispanic White Americans in US cities from 1910 to 1933, again attributable to crowding and poor housing conditions.[24] This disparity persists to modern times. From 1994 to 2002, North Carolina reported tuberculosis rates of only 0.2 per 100,000 non-Hispanic White children, as opposed to 3 and 4.2 per 100,000 in non-Hispanic Black and Hispanic children respectively.[25] In Stout's study, over 88% of pediatric tuberculosis cases were in non-Hispanic Black, Hispanic, and Asian / Pacific Islander children, demonstrating the sustained impact of health disparities across centuries.[25]

Crowding is also thought to play a role in the increased incidence of both influenza and COVID-19 in children. Crowding, defined as >1 person per room in the household, is more common in non-Hispanic Black, Hispanic, and American Indian/Alaskan Native (AI/AN) families.[26,27] O'Halloran et al., reported a 3- to 4- fold increase in influenza-related in-hospital mortality for Black, Hispanic, and Asian children under the age of 4.[28] Similarly, COVID-19 disproportionately impacts non-Hispanic Black, Hispanic, and Indigenous communities. In addition to an increase in multi-generational family homes, essential workers in service industries are more likely to be non-Hispanic Black or Hispanic and therefore less able to isolate during the pandemic.[29] Household factors like crowding and food insecurity associated with poverty are also thought to contribute to the severity of COVID-19 and other illnesses in children by impacting on-going care and recovery.[5] Outside the US, it is important to note that the World Health Organization estimates that the vast majority of parasitic and helminth infections occurs in developing nations.[30] In this way, the simple accident of where one is born drives one's lifetime likelihood of acquiring these infectious diseases.

Access to infectious disease prevention: Vaccination

Vaccination is a cornerstone of infectious disease prevention and highlights the importance of targeted interventions to close gaps in child health outcomes. Prior to the introduction of 7-valent pneumococcal conjugate vaccines, invasive pneumococcal disease was 3.3 times more common in Black children than non-Hispanic White children, particularly in the first 2 years of life; in 2002, this disparity in infection rates had decreased to 1.6 times higher but nonetheless persisted.[31] The increased incidence of Hepatitis B in non-Hispanic Black, American Indian/Alaskan Native (AI/AN), and Asian/Pacific Islander children similarly improved after introduction of Hepatitis B vaccination, but these children remain at higher risk of Hepatitis B infection than their non-Hispanic White peers (0.43-0.55 per 100,000 compared with 0.16 per 100,000).[32] Lower vaccination rates in non-White groups have been reported for many infectious diseases, including influenza, COVID-19, meningococcus serogroup B, and human papillomavirus (HPV), all of which are associated with

increased rates of illness for unvaccinated children.[26,28,33] Targeted delivery of vaccines, including reducing barriers to access and developing culturally appropriate educational materials for families, can be a powerful tool to improve the lives of children.

The introduction of HPV vaccines is already impacting rates of cervical cancer. Early gaps in vaccine uptake in non-Hispanic Black and Hispanic adolescents have significantly improved, but continued vigilance is required.[34] Young Black women are more likely to be diagnosed with cervical cancer than their peers, and for both non-Hispanic Black and Hispanic women, cervical cancer is more likely to be caused by oncogenic HPV types other than 16 and 18.[34] This makes uptake of the 9-valent HPV vaccines, which do cover the oncogenic types more common in non-Hispanic Black and Hispanic women, critical. Knowledge and initiation of HPV vaccination in adolescents is decreased in immigrant families and in many parts of the country, particularly Southern and rural states, thus targeted and culturally-tailored outreach will be needed to adequately protect adolescents and young women in these groups.[34–37]

AI/AN children have historically experienced similar increases in infectious disease morbidity and mortality compared with their peers. In the 1960s, post-neonatal mortality was 3.5 times higher in AI/AN children than all other races and the increase was largely attributable to infectious diseases preventable with vaccination, sanitation, and other public health measures.[38] AI/AN children continue to have higher post-neonatal mortality and overall childhood mortality compared with all children combined. While mortality attributable to infectious disease has dropped from 22% in the 1960s to <1% in 2000, it remains 1.7 – 2.2 times higher in AI/AN children than all races.[38] Lower respiratory tract infections remain more common in AI/AN children than non-Hispanic White children, particularly in households without indoor water for handwashing.[26] Respiratory syncytial virus (RSV) bronchiolitis is also more common in AI/AN children, particularly those who live in environments with household crowding (>1 person per room) and/or lack of indoor water.[26] Hepatitis A outbreaks were similarly much more common in AI/AN children than other children

historically, and this disparity was completely eliminated with robust vaccination programs.[39] The substantial improvements since the 1960s are the result of multiple interventions including targeted community interventions based on robust epidemiologic data, culturally aware engagement with indigenous communities, and partnerships such as the one between the Indian Health Service and the American Academy of Pediatrics to bring pediatric care to clinics serving AI/AN communities, demonstrating the potential of strategic investment in reducing infectious disease health disparities for children.[38,40]

Summary and conclusions

Though the COVID-19 pandemic increased national attention on the existence of health disparities, the truth is that children and families in non-Hispanic Black, Hispanic, and Indigenous communities have been significantly and disproportionately impacted by infectious diseases for centuries. There are countless lessons from tuberculosis, sexually transmitted illnesses, respiratory illnesses, and other infectious diseases about the importance of community level interventions to improve access to care for all children. Our approach to conceiving of access to care as a significant factor in the pervasive health disparities impacting children and adolescents – access to health care facilities, diagnostic studies, treatments, environmental prevention, and prevention through vaccines – is likely an incomplete way to identify ways in which health disparities can result between groups but highlights key areas for potential intervention. Other contributing factors beyond the scope of this commentary but equally relevant include implicit and explicit bias; systemic factors in medicine such as decades of flawed teaching around race as a biologic construct and unethical research; and the profound impact of adverse childhood experiences on development and long-term outcomes.[41] Deepening our understanding of how these disparities develop is critical to level the playing field for all children, especially those who are at high, yet modifiable, risk based on the current state of society and the structural factors (including systemic racism) that perpetuate these health disparities.

There are practical steps that individual care providers, researchers, funders, and institutions can take to identify and eliminate health disparities. The American Academy of Pediatrics' recent policy statement on racism in medicine appropriately frames this as "eliminating race-based medicine and moving toward race-conscious medicine." [41] Dismantling race-based medicine requires active effort on the part of institutions, professional organizations, and individuals to revise policies, educational materials, and treatment guidelines through a lens of ensuring equity and removing flawed race-based recommendations; to monitor and improve both written and spoken language to diminish the barriers words can, perhaps inadvertently, create for patients; and to engage with communities and practices to create an inclusive environment for all families. [41]

Data are essential to mitigate health disparities impacting underserved children: public health interventions can only successfully target disparities we have identified, and thus it is imperative that we continue to examine the health outcomes of our patients stratified across social determinants of health to identify persistent or new disparities. It is particularly critical for epidemiologic studies and treatment trials to include social determinants of health to right-size solutions for the communities at highest risk in real-world settings. Additionally, clinical trials must be designed and implemented in partnership with traditionally underrepresented communities to ensure that the solutions identified in trials are solutions appropriate for all children. [42] While strides have been made through increasing awareness of and attention to eliminating health disparities, our work is far from done. On-going work is needed from funders, institutions, and investigators to design studies that identify and close the gaps in healthcare across the U.S. Institutional investments are also critical to provide culturally aware broadscale training in conscious and unconscious bias, race and medicine, and social determinants of health that contribute to gaps in health. The social determinants of health impacting child health will be further exacerbated by the many and far-reaching effects of climate change, through increasing food insecurity, poverty, and vector-borne illness in many areas, and potentially leading to increased migration as life becomes more challenging in some areas. [43] Funders and institutions must work proactively to prepare for

these impacts of climate change. We must commit to these on-going efforts and more to address and correct these disparities if we hope to fulfill the mission of the Pediatric Infectious Diseases Society: to promote the health and well-being of (all) children through the prevention and control of infectious diseases worldwide.

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