



Discussion

The path ahead: From global pandemic to health promotion

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ABSTRACT

The current COVID-19 pandemic represents an acute threat to the health of adults and children across the globe. In addition, it has the potential to worsen the health of future generations through intergenerational health effects. Examples from history, including the Dutch famine (*Hongerwinter*), suggest that *in utero* and early life environments may have significant implications for health outcomes throughout the lifespan and are important in determining risk of chronic disease in adulthood. Parental health status, stress, and nutrition appear to affect offspring health and are all affected by the COVID-19 pandemic. Thus, it is critical that we consider the potential impacts of the current pandemic on pregnant women, infants and children and take public health and medical actions to mitigate risk and promote health in future generations.

1. Introduction

Over the winter of 1944–1945, the Netherlands experienced months of widespread famine and infectious diseases primarily caused by ration issues under the Nazi occupation. This humanitarian crisis, later referred to as the *Hongerwinter*, was a period of acute biological stress that also provided long-term scientific insight into the health effects of famine and, more broadly, the origins of chronic disease. Over many decades, researchers have followed babies born to mothers affected by the *Hongerwinter*, finding that the effects of the *Hongerwinter* have persisted throughout their lives. Women who were impacted by the famine during pregnancy gave birth to babies who were more likely to develop chronic diseases such as obesity, diabetes, and cardiovascular disease, even when the offspring experienced adequate access to food after birth (Roseboom et al., 2011). In fact, effects of the *Hongerwinter* have been observed among the grandchildren of women affected by the famine, demonstrating the multi-generational legacy of short-term humanitarian and health crises (Veenendaal et al., 2013). This perspective demonstrates the potential for long-term consequences of COVID-19 and suggests a need to investigate and act accordingly.

Across much of the world, significant energy, resources, and attention have been devoted to the immediate impact and management of COVID-19 including preventing transmission, detecting cases, buffering healthcare services, and investigating novel therapeutic interventions. This crisis has demanded extreme, relentless focus on the delivery of emergency and critical care, resulting in heroic actions from individual

clinicians, healthcare systems, and certain government officials. Less attention has been paid to understanding and mitigating the risks of this pandemic to the health of future generations through long-lasting effects of socio-economic challenges and biological exposures.

Research focused on the *Hongerwinter* and other exposures have emphasized the importance of early life conditions in the development of adult health outcomes, known as the Developmental Origins of Health and Disease (DOHaD) (Swanson and Ph, 2010; Heindel and Vandenberg, 2015). Complex interactions between parental health, social stress, local environment, nutrition and infectious disease exposure during pregnancy and early life have been shown to have significant implications for adult health – either by conferring risk or promoting biological resilience. While pregnancy represents a critical window in which we can influence offspring health, increasing evidence suggests the importance of preconception health for young men and women as well as the opportunity to modify prenatal risks through interventions during childhood (Stephenson et al., 2018). The implications of these insights are two-fold: first, to understand the high rates of chronic diseases among adults in many countries around the world, we must better examine their early lives and investigate the recent historical factors that contributed to their current health status (Ng et al., 2014). Second, to promote healthy adults in the future, we must focus on young people – from infants to adolescents – today.

As more individuals and communities are impacted by the pandemic, it is estimated that an increasing number of people will experience food insecurity and economic instability (Nicola et al., 2020; Pérez-Escamilla

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et al., 2020). It is critical that we consider the multiple mechanisms through which the socio-economic consequences of the pandemic can possibly produce intergenerational effects on the health of children who are not yet born. A modified social ecological model provides a useful framework for conceptualizing the broad array of interwoven mechanisms by which early child development will potentially be impacted by the pandemic (Golden et al., 2015). Within the home, increased exposure to domestic violence, marital strife, child abuse and substance use disorder can have significant and lasting impacts on child and adolescent development that last into adulthood (Felitti et al., 1998). At the broader level of political and economic concerns, the framework acknowledges the potential effects of poverty, food insecurity, social inequity, discrimination, social isolation, and educational disruption on health outcomes for future generations (Shonkoff et al., 2012; Osmani and Sen, 2003). Historical insights from the *Hungerwinter* suggest that these population-level exposures represent not only an immediate risk for depressed immune function associated with malnutrition among adults and children, but also a chronic risk to future generations who will be impacted intergenerationally through preconception, in-utero, and early life effects. This process may occur through establishment of the endocrine axis in fetal and early childhood development, anatomic remodeling in the malnourished fetus, and metabolic programming throughout childhood and adolescence (Karrow, 2006; Villanueva-Ortega et al., 2016). Furthermore, the intergenerational transmission of social disadvantage conferred by low economic capital, reduced educational attainment, and maladaptive parenting could have consequences for children now and in the future (De Nardi, 2004).

In addition, there are likely to be implications for children of women and men infected with SARS-CoV-2 in the peri-conception and gestational period regardless of exposure to socio-economic disadvantage. For example, mechanisms more closely tied to the clinical and sub-clinical manifestations of COVID-19 include the physiologic stress of transient hypoxia, inflammation, and infection experienced by offspring of parents affected by COVID-19 during pregnancy. While questions remain regarding transplacental transmission of coronavirus, the sequelae of gestational COVID-19 may be compared to other conditions affecting pregnancy and offspring health (Patanè et al., 2020). Data documenting the effects of smoking, high altitude residence, and previous respiratory pandemics (e.g., the 1918 influenza pandemic) during pregnancy have been associated with poor intergenerational health outcomes regardless of vertical viral transmission. Studies suggest that fetuses affected by such conditions during gestation face especially high risks of cardiovascular disease later in life (Mazumder et al., 2010; Giussani and Davidge, 2013). Furthermore, the demands of quarantine have contributed to the risk of obesity and overweight due to reduced opportunities for physical activity (Mattioli et al., 2020). This will have lasting consequences for children as well as offspring of adults who are an unhealthy weight in the preconception period (Bhutani and Cooper, 2020; Pellegrini et al., 2020). Additionally, epigenetic alterations in offspring of parents affected by COVID-19 due to parental stress and unaddressed chronic diseases during pregnancy such as hypertension and diabetes may be responsible for the intergenerational legacy of this pandemic (Lagraauw et al., 2015; Marciniak et al., 2017).

Overall, various pandemic-induced exposures, ranging from socio-economic concerns to viral infection itself, may contribute to a number of different biological, behavioral, and socio-economic pathways that impact vulnerable populations, including children, who already bear a disproportionate set of developmental risks associated with low access to resources.

Therefore, promoting health in the future involves action to bolster socio-economic support on the societal level while reducing risk of infection and investigating proximate pathways and their implications at the individual level.

Given the interaction between acute health crises and long-term intergenerational health outcomes, this pandemic serves as a call to increase attention on preventive medicine and public health rather than

shifting focus and funding completely towards emergency and critical care. By turning our attention towards mitigating risk and promoting health in future generations, we are likely to impact healthcare systems and global populations in mutually beneficial ways. First, preventing chronic diseases in the next generation will reduce ongoing demand on hospital systems related to complications of chronic disease, thereby freeing up capacity for response to future public health crises. Simultaneously, improved baseline health across global populations likely will decrease susceptibility to novel viruses should they affect our planet in the future. Thus, in one set of interventions, we can simultaneously bolster our capacity to cope with future pandemics while reducing the toll they would take on us. In doing so, we will also improve quality of life, productivity, and sense of wellbeing among children and adults.

Applying a DOHaD lens to COVID-19 provides a novel viewpoint and call to action, and we already have much of the knowledge and many of the tools required to make significant progress if our governments and healthcare systems choose to invest accordingly (Penkler et al., 2019). While long-term recovery from this pandemic will require a comprehensive and collaborative effort across nations and governments, there may be steps that can be taken on the local, state and national level within the United States or other individual countries even in the absence of a unified global effort. We can start by resuming and strengthening primary care services for children and pregnant women. Such programs may assist in the optimization of outcomes for those currently living with chronic diseases while providing health maintenance to prevent disease onset in healthy children and adolescents. In addition, we should ensure easy and equitable access to contraception so that individuals can plan for healthy pregnancies. Federal and community-level funding must work together to bolster public and non-governmental programs – such as food assistance, public education, and employment services – all of which promote baseline health and wellbeing and are associated with reduced risk of chronic disease in adulthood. We should focus on providing equitable access to nutritious foods, opportunities for physical activity, and healthy social systems across populations globally. We need to serve as stewards of the environment to reduce toxic exposures and promote sustainable neighborhoods, cities, and ecosystems in which current and future generations can thrive. We must work across sectors to increase economic opportunity and decrease socioeconomic disparities, which in and of themselves contribute to disease risk. Given the economic and social consequences of the COVID-19 pandemic worldwide, socioeconomically vulnerable populations will require dedicated attention as they are most vulnerable to coping with food insecurity and other risks of economic deprivation that may confer health risks over their lifetimes (Laborde, 2018; Uauy et al., 2011).

This pandemic will represent a central event in many of our lives; however, it need not define the legacy that we leave our children and grandchildren. While this crisis will likely come to an end within months to years, it will behoove us to consider the lasting effects of this period so that we can continue to mitigate adverse outcomes and promote health equity once this pandemic has passed. Thus, it is morally, economically, and politically incumbent upon us to take actions now to protect current and future generations by preventing chronic disease and promoting healthy, resilient children and adults. By curtailing chronic disease risk early in life, we are investing in healthy adults far into the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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