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On the long-term impact of COVID-19

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There is a very large body of research on the long-term effects of the 1918 flu pandemic. An important part of this literature focuses on the impact of *in-utero* exposure to the virus and invokes fetal programming and other mechanisms identified within the Developmental Origins of Health and Disease (DOHaD) paradigm. The outcomes vary broadly from elevated adult mortality risks and poorer health status of older adult survivors, under par educational attainment, poorer labor market performance and lower wages, unemployment, excess disability, and deficient physical markers of nutritional status. There are, of course, studies that focus not on the effects of exposure to the virus *per se* but on outcomes related to the chaos that ensued and the economic recession that followed the pandemic. Most of these studies rely on the reasonable assumption that the 1918 flu pandemic created conditions of a natural experiment: it was unexpected and could not be anticipated, with some identifiable exceptions exposure to it could not be avoided, and there were no competing events whose effects could be confounded with those of the flu. There is, however, an exception to this last requirement that some colleagues have described: the case of Puerto Rico where the same year that the flu made its appearance, a tsunami, and earthquake of large proportions hit the Western part of the island. This double whammy created the conditions for a double experiment as, in addition to the timing of pregnancy/birth, there is also discernible geographic variability for the earthquake caused significant damages only in the West coast of the island. The consequences in that region were dire and equally felt by those who had not been born at the time (*in utero* exposure) and infants and children. The adult survivors of these cohorts bear deep scars as markers of nutritional status attained by age 5 are significantly below normal.

The current COVID-19 pandemic will certainly offer future researchers another opportunity to probe its effects on many of the outcomes already examined by those engaged with research on the 1918 flu. Of particular importance are those associated with exposure in embryonic life, fetal growth, early infancy, and early childhood. But, there is something else: the economic crisis that will follow the (possibly) multiple waves of the COVID-19 epidemic will prolong and augment the agony as the consequences of exposure to the virus will be replaced and/or added to experiences of adverse economic conditions. The post COVID-19 economic recession may not be equivalent to the earthquake and tsunami in Puerto Rico. However, because it (as well as exposure to and experience with COVID-19) will vary greatly, there will be massive heterogeneity across social groups, regions and countries in the intensity of exposures and experiences to tease out more cleanly the role of both classes of exposure.

Why not take advantage of the possibilities that this calamity opens up? Why not offer future researchers the possibility of assessing effects of interest more robustly than their ancestors could with the scant data available from the 1918 pandemic? There are many initiatives one could identify and elaborate at length. We choose to highlight only one: a children longitudinal study.

Draw a national sample of females who were pregnant during the pandemic, those who gave birth and their children aged 0-4. Gather hospital records with information about pre-pregnancy, pregnancy and delivery, take full blood samples from mothers and children and establish a protocol to follow them up for a period of time until, say, physical growth comes to a halt. Do not forget to include in the sample sibs and twins! In addition to adult and child biomarkers (including, of course, having or not contracted and being exposed to the virus) one could retrieve conventional demographic and socioeconomic information reflecting various child outcomes, from markers of physical growth to cognitive scores, to school performance, to exposure to risk behaviors (poor diet, lack of exercise, smoking initiation). If, in addition, the child study leads to the creation of a large data bank with identifiers, it will make possible the formulation of additional studies to investigate outcomes at different stages of the life cycle of the population.

The consequences of the COVID-19 pandemic and the economic aftermath will leave deep scars on many but especially the poor and disadvantaged. The study will be a platform to assess those differentials and, perhaps, could also provide the foundation for interventions that prevent or minimize subsequent deleterious effects. Just a few examples:

a. Online instruction will probably remain in place for some time. The inequalities this mode of instruction can generate are huge and will have potentially sizeable effects on educational attainment, labor market performance and all those outcomes we know are related to education. Well designed and timely interventions can minimize the damage that the inequality of access to the internet (including laptops, tablets, wireless service). Implementation of different interventions can also generate the opportunity to evaluate differentials in the rate of success;

b. In utero and infant and early childhood exposure to viral infection and nutritional deprivation can cause lasting effects. Inevitably, this class of impact will be felt more strongly in low- and middle-income countries. But it may also impact some subpopulations in high income countries that are already facing adverse conditions (e.g. migrant populations and minorities). The children study will provide an opportunity to assess physical growth trajectories and identify those most in need of intervention to reestablish normal patterns of growth when these are derailed. Here again, the utilization of multiple types of interventions generates additional knowledge that may be useful in the future.

c. Parental unemployment and the hardship it creates could lead to hopelessness, desperation, and fatalism. This will inevitably affect parental mental health (depression, chronic anxiety) but also could alter their behaviors, from those associated with uptake of risky behaviors to those related to labor market participation. What will these conditions do to adult mortality rates (suicides for example), to union stability, to domestic violence, to norms and practices about elderly care and, more generally, kin relations?). Importantly, how will the new household environment for children change? What will it do to their own view of the world? How will their parents ' drastically altered future outlooks alter their own?

Will they too become fatalistic, hopeless, prone to adhere to risky behavior? Will the pandemic become a vehicle to transmit hopelessness and despair? Will inequalities beget even stronger inequalities?

d. Traditional children's social relations will inevitably change. Peer contact will be altered by lock downs and post-pandemic policies to prevent or reduce social contacts. Children activities such as summer camps, athletic and other sport competitions and even birthday celebrations may be suspended for a while and, when reinstated, they will adopt very different styles whose effects will not be known for quite some time. Could these changes mark children, say, between ages 2 and 5? In what ways? Could there be large social class differentials? It is not far-fetched to think that even child-adult relations will be stained by distance, separation and mistrust as children are taught to avoid adults.

e. Children of health care workers might be particularly affected, as many parents choose to self-isolate and stay for weeks and months without physically spending time with their children while being available virtually via social networks and video chats. How does this influence childhood development when your parent is celebrated as a hero on the one hand but absent from your daily life during this crisis where support and love are more important than usual? And, what about the very real possibility (as has already been verified in some settings) that children of healthcare workers and their parents are shunted because they are perceived as high-risk individuals?

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