

The Child Is Father of the Man, and Mother of the Woman

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KEY WORDS

aging, childhood, intrauterine environment, telomere, perinatal period

ABBREVIATION

DOHaD—Developmental Origins of Health and Disease

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Well before Wordsworth, it was recognized that early life experiences shaped adult personality and behavior. However, until much more recently, the dominant medical model posited virtually a complete disconnect between childhood and adult health. It was as though emerging from childhood without major disease or disability miraculously reset the “health-o-meter” to 0, only to rebegin registering its scores in midlife. A quarter century ago, David Barker and colleagues showed the biological implausibility of such a simplistic model.¹ Since then, accumulating evidence has strengthened the “Barker hypothesis” and now “developmental origins of health and disease,” or DOHaD, is an increasingly accepted concept.

Although acknowledgment that childhood, fetal, and even preconceptional events can influence later health is growing, skeptics remain, partly because the link is still largely based on association, not proven mechanisms of causation. Mechanistic research is urgently needed to convince naysayers and, more importantly, to devise treatments and preventions, for the many “adult-onset” conditions that actually are rooted in much earlier exposures and events.

An example of such mechanistic research is the report by Shalev et al,² which used a prospective longitudinal birth cohort from New Zealand to investigate the relationship between perinatal complications and indicators of aging at midlife. In 829 adults age 38, they assessed the leukocyte telomere length (a fairly objective measure of aging) and estimated perceived facial ages (a more subjective measure of aging). By midlife, individuals with history of higher frequency of perinatal complications tended to have shorter leukocyte telomere lengths, and 8 undergraduate students tended to rate their facial ages as older than their chronological ages. Surprisingly, measures of adverse family history and social risks in childhood did not significantly attenuate the association between perinatal complications and aging measures.

Because telomere length has been linked to cellular aging, the findings of this study provide a hint at a possible molecular mechanism underlying accelerated aging associated with early-life adverse events. And, if perceived facial aging does prove to be a reliable external marker (a signature of sorts for cellular aging), this study's findings, as the authors note, reveal an “inside and outside” look at the aging process, linking early life stressors to adult diseases (a central dogma of DOHaD) and suggesting at least 1 biologically plausible mechanism underlying the link.

But, this study has limitations. The authors used a perinatal risk index, a composite measure of a large heterogeneous group of perinatal variables, all of them weighted equally. However, many maternal variables are not etiologically linked (eg, epilepsy, diabetes, placenta previa, or “having had a small baby”). Similarly, many neonatal variables in the

composite index were vague and poorly defined (eg, jitteriness, tenseness, limpness) or were common, relatively mild neonatal conditions (eg, nonhemolytic jaundice, a history of Rh or ABO incompatibility). And, it is not clear how many infants received what forms of intensive care. From such a long list of diverse perinatal factors, how can one define an etiological link among “perinatal stress,” allostatic load, and premature aging? Similarly, it is unclear whether specific telomere lengths among the 88 (11%) subjects which had just 2 or more perinatal complications matched the facial aging ratings by a small group of students which, in their commendable acknowledgment of study limitations, the authors note as being “somewhat noisy.”

So questions remain: Are shorter telomere lengths measured at age 38 the consequence of early-life programming? Are there no premature aging effects from later-life adverse events? If so, what are the molecular pathways linking these phenomena? Clearly, more light needs to be focused on the DOHaD etiological black box. But, this is a useful step in that direction. And we look forward to many more such efforts, which will gradually illuminate this black box and fundamentally change how we understand health and disease. And, how we practice pediatrics.

Arguably the most important advance in the health care of children, and in establishing pediatrics as a medical specialty, was the cultural awakening that children were not simply small

adults. Ironically, DOHaD greatly expands the impact of pediatrics by reversing that shift and focusing on how children actually are smaller versions of the adults they will become. Once the biological and behavioral pathways that underlie DOHaD are identified and understood, the role of pediatrics should expand in fundamental and powerful ways. Anticipatory guidance in the future will not be just about the next 6 weeks or 6 months or even 6 years of the child's life, but the entire life span. The pediatrician and other children's health care providers will inform parenting and behaviors, including diet and exercise, and even prescribe presymptomatic medication targeted to the individual child. The pediatrician will become the gatekeeper to lifelong health.

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