Clinical Pearl: Age is just a number: Evidence of Accelerated Biological Aging in Adults Born Extremely Low Birthweight (ELBW)

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With the increasing rates of preterm birth and survival worldwide, a number of studies have started to focus not only on the immediate consequences of prematurity seen in the neonatal intensive care units but also on its long-term effects on adult health. There is now evidence that individuals with a history of preterm birth are at a greater risk of developing hypertension, strokes as well as type 1 and type 2 diabetes (1, 2). These chronic medical conditions have been classically associated with increasing age, raising whether ex-preemies are at risk for accelerated aging.

The extent of DNA methylation increases with chronological age. Various "epigenetic clocks" are available to quantify the relationship between methylation and chronological age to determine an individual's "epigenetic" or "biological" age. Increased biological age has been linked to a greater risk of age-related morbidities (3). In their study, Van Lieshout and colleagues collected buccal cells from 45 extremely low birth weight (ELBW) survivors and 49 normal birthweight controls at 30-35 years of age. Epigenetic age was calculated from the weighted average of DNA methylation at 353 cytosine-phosphate-guanine sequences within the DNA methylation sites. The technique used is called the Illumina Infinium Human Methylation EPIC 850k BeadChip array devised by Horvath. They found that men born at ELBW demonstrated accelerated biological aging when compared to age-matched adults born at normal birth weight. The authors suggest that these findings could potentially be related to the increased psychological and physiologic stress premature infants endure (4, 5).

At this time, further studies are still needed to establish the link between accelerated cellular aging in individuals with a history of prematurity and specific outcomes, as well as to identify which subgroups are at the highest risk. Van Lieshout and colleagues point out that male preterm infants are susceptible to worse outcomes, and thus, are at risk for increased stress, which could potentially explain why the differences were only found in males (4, 5). Their findings appear to be supported by Parkinson et al., who used a different molecular marker, telomere length, to study cellular aging in patients with a history of prematurity. They have demonstrated a greater proportion of shorter telomeres in preterm men when compared to term men but were unable to find similar differences in women (6). Interestingly, in a recent study by Raffington et al., the authors analyzed DNA methylation to determine a methylation-based "pace of aging" in children. They have found that a greater socioeconomic disadvantage among white and Hispanic children was associated with a significantly faster pace of aging. This topic should be explored further. It would be imperative to determine if racial and socioeconomic disparities enhance the risk of accelerated aging in individuals with a history of prematurity (7).

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All the emerging evidence has important implications for clinicians, researchers, and policymakers. At the policy level, more data is still needed to establish appropriate screening and preventative guidelines. However, when caring for children, adolescents, and adults with a history of prematurity, physicians should closely monitor blood pressure and weight and encourage appropriate nutrition and physical activity. They should also be reminded of the importance of inquiring about preterm birth when obtaining routine medical history, even when encountering patients later in life. Lastly, family members of children born preterm should be counseled on the risk for accelerated aging and increased risk of cardiovascular and metabolic disorders.

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