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Title: Transgenerational Effects of Environmental Toxins on Avascular Necrosis Susceptibility

Environmental toxin exposure is increasingly recognized as a contributor to chronic disease through long-term molecular and epigenetic changes that may persist across generations. While much research has focused on outcomes such as cancer and reproductive disorders, less is known about whether ancestral exposure to toxins such as Agent Orange may influence susceptibility to musculoskeletal diseases, including avascular necrosis (AVN) of the hip. Here, I evaluated the current evidence to determine whether transgenerational exposure to environmental toxicants contributes to AVN risk through epigenetic, vascular, or bone-metabolic mechanisms. A literature review was conducted examining experimental animal studies, epidemiologic investigations, and clinical research on epigenetic inheritance, dioxin exposure, vascular dysfunction, and AVN pathogenesis. The evidence demonstrates that dioxin-containing compounds can induce heritable epigenetic modifications, including changes in DNA methylation, histone retention, and non-coding RNA expression, which are associated with increased susceptibility to adult-onset disease. Clinical studies also establish vascular compromise, thrombophilia, endothelial dysfunction, and impaired bone perfusion as central mechanisms underlying AVN. However, no studies directly link transgenerational toxin exposure to AVN, indicating that any potential association remains biologically plausible but unproven. Current evidence suggests that ancestral environmental toxin exposure may indirectly increase AVN susceptibility by altering vascular integrity, coagulation pathways, inflammation, or bone metabolism rather than directly causing the disease. These findings identify a significant gap in the literature and emphasize the need for future studies investigating the relationship between inherited epigenetic changes and skeletal vascular disease.