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Letter to Editor

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Cellular Stressor in Female Reproductive Longevity in the Era of Climate Change

Dear Editor,

Climate change is not just an ecological issue, it is a biological emergency for women's health. Recent committee statements by the American College of Obstetricians and Gynecologists (ACOG) and the International Federation of Gynecology and Obstetrics (FIGO) (1) demonstrated the devastating effects of climate extremes on obstetric sphere (2), yet the potential sequelae for women's reproductive longevity, particularly the key intra-ovarian mechanisms and endocrine pathways that orchestrate ovarian aging, remain largely underreperched.

Extreme climatic changes including high temperatures, fine particulate matter (PM2.5), and endocrine-disrupting chemicals (EDCs) are cellular toxicants that compromise the biological basis of female longevity even before they become pregnant (3). The clinical focus ought to be shifted from an isolated perspective of a single pregnancy toward a lifelong gynecologic longevity.

The gynecologic vulnerability is triggered by a multi-system dysfunction. Damage starts upstream: thermal stress and EDCs directly affect hypothalamic signaling, downregulate kisspeptin expression, and hyperactivate the hypothalamic-pituitary-adrenal (HPA) axis (4).

At the same time, continuous exposure to ambient heat affects the hepatic metabolism, leading to the disruption of the detoxification pathways of the liver by the cytochrome P450 enzyme system (5). The compromised liver clearance results in unmetabolized EDCs and microplastics building up in the bloodstream and overwhelming ovarian tissue (6). While physiological follicular regression relies on non- inflammatory apoptosis, climate-derived toxic burden and oxidative stress cause ovarian granulosa cells to be destroyed in an inflammatory manner through non-apoptotic aggressive cell death, such as pyroptosis, necroptosis, and dysregulated autophagy (7). Finally, the destruction cascade occurs and quickly exhausts the non-renewable pool of oocytes, which accelerates premature menopause. This early withdrawal of estrogen increases women's long-life risk of cardiovascular disease and osteoporosis (8) (Figure 1).

Most importantly, these biological susceptibilities are magnified by structural and psychosocial disparities. In hot and low-resource settings, women are at risk of facing an extra crisis. When temperatures exceed 50°*C* for a prolonged period, power-grid failures disable the cooling system (9). However, when this extreme thermal stress coincides with other psychosocial trauma, post-conflict environments, or humanitarian emergencies, it produces a devastating double activation of the HPA axis, leading to an extended episode of high

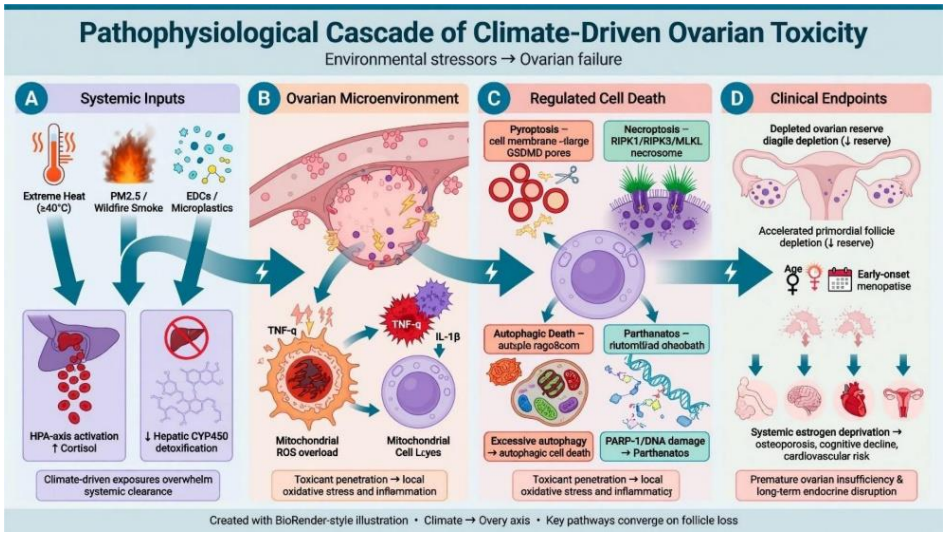


Figure 1. The pathophysiological cascade of climate-induced ovarian toxicity

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cortisol, which further diminishes female reproductive functions and fertility (10). Collectively, climate induced-cellular toxicity, neuroendocrine dysregulation, and fragilities of the health system converge to amplify women reproductive longevity across vulnerable population around the world (1, 9). The medical community needs to translate these cellular stressors into proactive clinical preventive strategies.

In line with ACOG's recommendations regarding climate-driven health disparities (1), a proactive approach is needed, one that incorporates short screening questionnaires about exposure to occupational heat and local chemical exposure, as well as thermal vulnerability assessments, into routine non-pregnancy gynecologic assessments. Still, environmental toxicity cannot be cured by screening alone; protecting women's reproductive longevity requires bold collaboration among government, environmental organizations, and medical committees, not a simple aspirin pill (2, 9). Preserving the ovarian reserve is not just about fertility; rather, it's about defending the underlying structure of a woman's lifelong health. Global climate resilience is not possible if environmental toxicity is escalating the biological ageing of half the world's population silently.

Conflict of Interest

The authors declare no competing financial or non-financial interests.

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