Menopause status and COVID-19

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Dear Editor,

We greatly appreciate the publication of this important research article, for its exploration of the connection of estradiol levels and menopausal status with outcomes from infections with SARS-CoV-2 in women. (1) This study has been greatly needed from the inception of the COVID-19 pandemic. Sadly, unlike this research, most published data lacks stratification of women into pre and postmenopausal categories, making the determinations made in this article an impossibility. (2)

A pervasive lack of understanding of the myriad effects that estradiol plays throughout the female body has resulted in the exclusion of this critical information being considered in much research and in the clinical care of women.

We advocate for the use of physiologically dosed human-identical transdermal estradiol as hormone replacement, combined with human-identical cyclic progesterone, in appropriate recently menopausal women. Our recommendations are based on a significant body of preclinical and clinical data. (3) This study's findings of a distinctly protective effect of estradiol in women with functioning ovaries is in complete alignment with our position and with science. (4)

Estradiol has receptors on all innate and adaptive immune cells and is a key player in the immune response, which includes both pro-inflammatory and anti-inflammatory functions. (5) Estradiol (E2) is a modulator of the renin-angiotensin-aldosterone system, a major force in the instigation of the inflammatory response and in the resolution of inflammation. (6) E2 plays a major role in regulating lipid mediators and peptides involved in the processes needed for an optimal immune response, improving the likelihood of a successful outcome in the fight against an infectious agent such as SARS-CoV-2. (7)

The use of hormone replacement therapy gains further support from this excellent study. The harmful impact of ovarian senescence affects all organ systems, inclusive of the cardiovascular system, the neurological system, the gut, the musculoskeletal system, the genitourinary system, and now in the age of the COVID-19 pandemic, its vital role with the immune system is clear. (8)

Given the potential for serious negative effects ensuing from a state of estradiol deficiency, heightened by the COVID-19 pandemic, not only should appropriate postmenopausal women be considered for hormone replacement therapy, but women being treated with aromatase inhibitors and estrogen receptor antagonists should be counseled on the risks and benefits of those drugs, personalized in each case, in light of the findings of this study.

None of the authors has any potential conflicts of interest.

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