Origins of the “great” obstetric and gynecologic syndromes

TO THE EDITORS: A.T. Hertig¹ (Harvard, MA) described narrowed arterioles in the placental bed in preeclampsia in 1945. In 1967, it was proposed that the narrowed uterine arterioles resulted from a “failure of physiological transformation” between 8 and 18 weeks’ gestation.² Dr Staff and colleagues³ updated this long-standing hypothesis in their recent review.

Narrowed arterioles with perivascular injured nerves are key features of many gynecologic syndromes but are also found in the isthmic region of pregnancy hysterectomy specimens (Figure, A and B). Injuries to vasomotor nerves release cytokines and have the following 2 distinctive effects: (1) proliferation of injured nerves from the proximal stump; and (2) hyperplasia of the now-denervated, distal arteriole. In pregnancy, these nerves do not extend to the placental bed, although their nerve sheaths may do so, creating varying patterns of “halos of hyalinized cells” around the narrowed arterioles. We propose that most of the great obstetrical and gynecologic syndromes result from prepregnancy injuries to uterine nerves caused by “difficult” first labors, physical efforts during defecation, or gynecologic surgery.⁴ In preeclampsia, “new” intrauterine, purinergic (P2X3), “stretch” receptors activate urogenital nerves; in preterm labor or preterm premature rupture of the membranes, there is an increased susceptibility to infection, and injured uterine arteries are more likely to rupture in placental abruption.⁵

“Failure of physiological transformation of uterine arterioles in pregnancy” has been the dominant research hypothesis for preeclampsia (although not other obstetrical syndromes) for more than 50 years.²,³ Prepregnancy injuries to uterine nerves with their diverse and varying consequences is a simple, uncomplicated explanation that may account for the pathophysiology of many of the “great” obstetrical and gynecologic syndromes. It has the persuasive benefits of being simple, inclusive, and comprehensible.

Ling Cui, MD
M. J. Quinn, MD, LLM
Hui Juan Zhang, MD, PhD
Department of Pathology
International Peace Maternity and Child Health Hospital
School of Medicine
Shanghai Jiao Tong University
910, Hengshan Rd.
Xujiahui, Shanghai 230000
China
mjquinn001@icloud.com
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FIGURE
Injured uterine nerves in pregnancy hysterectomy specimens

A, Depleted nerve bundles (anti-S100, ×100) with B, injured perivascular nerves (anti-S100, ×200) in the isthmic regions of pregnancy hysterectomy specimens. Prepregnancy injuries to uterine nerves may represent an improved explanation of the histologic findings in the “great” obstetrical and gynecologic syndromes rather than the long-standing “failure of physiological transformation of the uterine arterioles” hypothesis.