Preterm birth and the mechanism of action of low-dose aspirin: a response

We are grateful for the opportunity to reply to the letter from Drs Norooznezhad and Nabavian regarding our study "Low-dose aspirin use in pregnancy and the risk of preterm birth: a Swedish register-based cohort study." Preventing preterm birth (PTB) is exceptionally important, and we thank Drs Norooznezhad and Nabavian for their interest in our findings.

We agree with Drs Norooznezhad and Nabavian that low-dose aspirin may have additional effects in pregnancy beyond inhibiting cyclooxygenase. The authors described how infectious conditions are associated with PTB and increased production of proinflammatory cytokines, such as interleukin (IL) 1β, IL-6, and tumor necrosis factor-alpha (TNF-α). Furthermore, they provided evidence that aspirin can inhibit nuclear factor kappa B and TNF-α transcription. TNF-α elicits several cellular responses and is involved in both term labor and preterm labor independent of the presence of infection.[1] Importantly, aspirin has been shown to prevent TNF-α–mediated endothelial cell dysfunction and insufficient trophoblast invasion. The latter is a cause of uteroplacental ischemia,[2] a common finding in spontaneous PTB.[3] Although the pathophysiology of PTB is not fully understood, it is thought that the onset of labor is accompanied by a transition from an anti-inflammatory state to a proinflammatory state,[1] and as such, TNF-α and other proinflammatory cytokines may play a key role. Thus, targeting these molecules with anti-inflammatory drugs, such as aspirin, is a promising approach to preventing PTB. Further insights into aspirin's mode of action may shed light on the pathophysiology of PTB. ■

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