Inflammatory Pathways and Parturition

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Preterm labor, defined as childbirth occurring earlier than 37 completed weeks of gestation, is a major determinant of neonatal mortality and morbidity, many times with long-term adverse consequences for the health of both mother and child.[1] According to the World Health Organization, the rate of preterm birth across 184 countries is reported to be between 5% and 18% of all babies born. Therefore, it is urgent to find ways of preventing preterm labor, and in order to do so, it is essential to better understand the mechanisms behind it and those involved in parturition in general.

An increasing body of evidence suggests that parturition is an inflammatory process, in which progesterone also plays a major role.[2-6] In the current issue of *Reproductive Sciences*, this idea is explored further by 3 unrelated groups that report different findings leading to this same interpretation of the onset of labor being linked to inflammation.

Pavlicev and Norwitz elegantly describe their provocative view of parturition as just a delayed menstruation. In their review, the authors discuss the fundamental characteristics of human pregnancy, in which intrauterine inflammation takes part, to propose that many of the physiological problems that lead to pregnancy and parturition complications, such as preterm labor, are fetus independent and can already be detected during spontaneous decidualization in menstruation. Importantly, their idea suggests that these complications may indeed be determined before the onset of pregnancy.[7]

In another report, Patel et al hypothesize that human parturition involves hormonal interactions that, through the regulation of pro-inflammatory cytokines, are able to induce type-A progesterone isoform (PR-A) to inhibit type-B progesterone receptor (PR-B), leading to labor triggering. The authors tested their hypothesis using an immortalized human myometrial cells line, in which levels of PR-A and PR-B can be experimentally controlled. Their findings showed that the ability of PR-A to repress PR-B was increased by serum supplementation and interleukin-1β, strongly suggesting that in myometrial cells this repressing activity of PR-A on PR-B increases with gestation time and is induced by pro-inflammatory cytokines.[8]

Last but not least, Vaswani and colleagues aimed to characterize the changes occurring in cytokine and chemokine gene expression through mid to late gestation, using the rat placenta as a model. The authors analyzed messenger RNA expression of various cytokines, chemokines, and genes of the transforming growth factor beta (TGF-β) and tumor necrosis factor (TNF) family in rat placentae at E14.25, E15.25, E17.25, and E20. Their results show that 46 genes were differentially expressed, of which 21 presented increased expression in late gestation (E20). These findings highlight the importance of cytokines and chemokines in the later stages of pregnancy, further supporting a link between inflammation and parturition.[9]

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