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Lung Development as Initiating Birth

The lungs are among the last of the mammalian organs to fully differentiate. The lungs must be able to draw in oxygen at the newborn's first breath. To accomplish this, the alveolar cells secrete a surfactant into the fluid within the lungs. This surfactant, consisting of specific proteins and phospholipids such as sphingomyelin and lecithin, is secreted very late in gestation; in humans, surfactant usually reaches physiologically useful levels at about week 34 of gestation. Surfactant enables the alveolar cells to touch one another without sticking together. Thus, infants born prematurely—that is, before their surfactant has reached functional levels—often have difficulty breathing and have to be placed on respirators until their surfactant-producing cells mature.

Mammalian birth occurs very soon after lung maturation. Some evidence suggests that the embryonic lung may actually signal the mother to start parturition (the expulsion of the fetus from the uterus) and labor (the birth of the baby). Mendelson and colleagues (Condon et al 2004; Mendelson et al 2017) showed that Surfactant Protein A as well as the surfactant glycerophospholipids Platelet Activating Factor and dipalmitoylphosphatidylcholine -- the final products produced by the embryonic mouse lung—activates macrophages in the amniotic fluid. These macrophages migrate from the amnion to the uterine muscle, where they produce immune system proteins such as interleukin-1β (IL1β). IL1β initiates the contractions of labor, both by activating cyclooxygenase-2 (which stimulates production of the prostaglandins that contract the uterine muscle cells) and by antagonizing the progesterone receptor (Figure 1). Mice deficient in surfactant proteins have a significant delay in the onset of labor, while surfactant-stimulated macrophages injected into the uteri of female mice induce early labor (Montalbano et al. 2013). Thus, one of the critical signals initiating birth is given only when the lungs have matured to the point where a newborn can take its first breath, and this signal may be transmitted to the mother via her immune system.

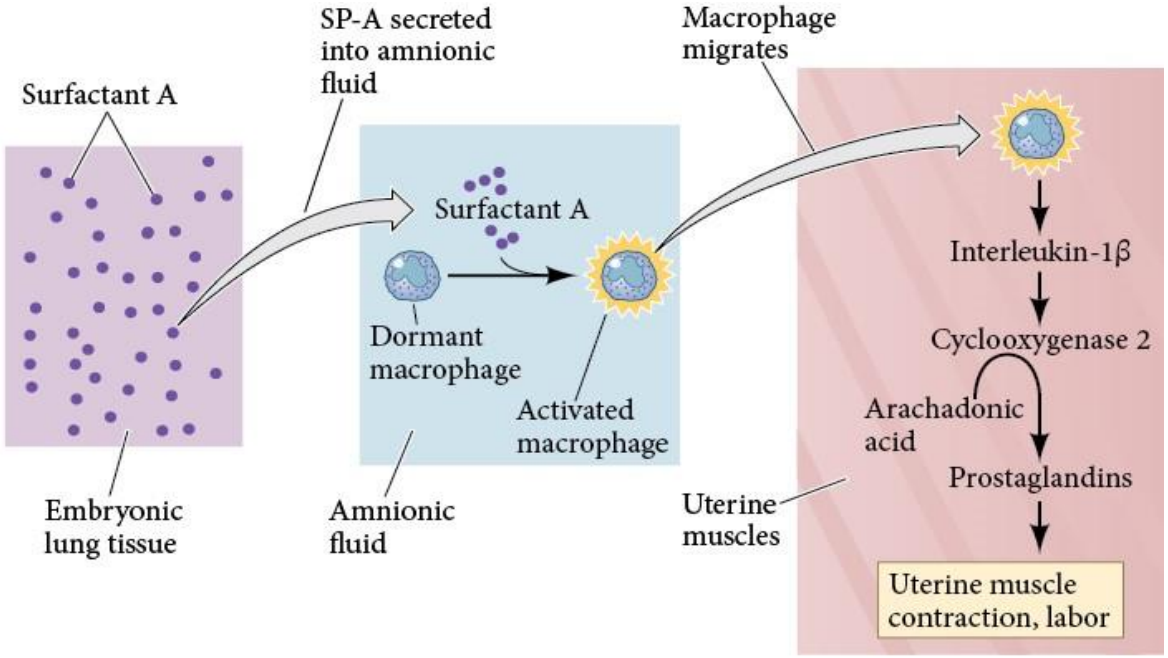

Figure 1 A model for immune regulation of labor through lung maturation. The immune system relays a signal from the

embryonic lung. Surfactant protein A (SP-A) activates macrophages in the amniotic fluid to migrate into the uterine muscles, where the macrophages secrete IL1β. IL1β stimulates production of cyclooxygenase-2, an enzyme that in turn triggers the production of the prostaglandin hormones responsible for initiating uterine muscle contractions and birth.

Indeed, as we discussed in Chapter 16, normal implantation of embryos can occur when the inflammatory response to the embryo is initiated but not completed. Parturition, the expulsion of the fetus from the uterus, may involve the completion of the inflammatory response. Indeed, immune responses leading to inflammation may have been the ancestral mechanism of parturition (Hansen et al 2017; Chavan et al 2021). In marsupials, the full inflammatory response comes rapidly after the attachment of the embryo to the uterus, so pregnancy is very short.

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