CHAPTER 12

IMMUNITY AT MATERNAL FETAL EDGE

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How does normal placentation occur?

Human placentation is unique, as it allows an intimate contact between maternal and fetal cells at the maternal-fetal interface throughout pregnancy, which results in tightly controlled immune reactions between mother and her child. Implantation occurs around days 6 to 7 after conception. By day 10 after conception, the blastocyst is completely embedded in subepithelial stromal tissue and the uterine epithelium grows to cover the implantation site. Shortly thereafter, mononuclear extravillous cytotrophoblasts stream out of the trophoblastic shell to invade the entire endometrium and inner third myometrium as well as the maternal uterine vasculature. The latter process, which begins the process placentation, establishes the definitive uteroplacental circulation and places fetal trophoblast in direct contact with maternal blood. At a functional level, the placenta must integrate maternal and fetal physiology, immunology and endocrinology. Complications that present relatively late in pregnancy may reflect errors that occurred much earlier in placental development(1).

What is the immune paradox of pregnancy?

During pregnancy, the foreign antigens of the developing fetus and the placenta come into direct contact with cells of the maternal immune system but fail to evoke the typical tissue rejection response seen with organ transplants. Moreover, while the maternal immune system does not reject the fetus, it continues to protect the body against infections(2).

Which mechanisms are important in immune modulation of pregnancy?

There are at least two mechanisms for overcoming most immune reactions. One is active suppression, and the other is enhanced tolerance. Enhanced tolerance has been clearly demonstrated in normal pregnancy. Regulatory T cells, which are critical mediators of tolerance, become more numerous in pregnancy(3).

mune cells associated with recurrent miscarriage are natural killer (NK) cells and their cytokines. More evidence for NK cell dysfunction was partially impaired in women with recurrent miscarriage, and with that were less successful in inhibiting Th17 cells(18-19).

Does fetal or maternal immunity play a role in contractions in preterm labor?

Although preterm labor has multiple etiologies, infection and inflammation are the most common causes of spontaneous preterm labor. Preterm labor often associated with maternal infections, could potentially arise from a breakdown in maternal-fetal tolerance. For example, infections can activate the adaptive immune system and trigger T cell- mediated allograft rejection. In healthy pregnancies reactive T cells are prevented from crossing placenta, and their activation is kept under control by the expansion of regulatory T cells. In addition, uterine dendritic cells are unable to migrate into uterine draining lymph nodes and prime maternal T cells, and decidual B cells further counteract inflammatory responses during preterm labor. Another important mechanism for maintaining maternal-fetal tolerance arises on formation of fetal regulatory T cells. Activated fetal T cells can promote preterm labor through the induction of maternal uterine contraction(20).

What are the effects of maternal inflammation during pregnancy on neural development of the fetus?

Maternal immune perturbations alter fetal developmental trajectories, prenatally programming changes to the offspring brain that may present immediately and/or later in development. Changes at the level of offspring brain morphology may occur after maternal inflammation, either directly, through changing neuronal and glial progenitors, or indirectly, for example through microglial effects on neurodevelopmental processes such as neuronal survival and synaptic pruning(21).

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