Immunology-Inflammation

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Medawar recognized the paradox that the fetus is (in genetic terms) a semi-allograft which escapes rejection.

The presence of immune cells at the implantation site has been considered as a proof of a response by the maternal immune system to the fetus.
Immunology of Pregnancy

- The studies in the area of Immunology of Pregnancy have focused on Graft-Host response
Immunology of Pregnancy: Old Paradigms

- Mechanical Barrier
- Suppression of the Maternal Immune System
- Th-2 type Immune Response
Mechanical Barrier: Old

- The placenta prevents the movement of cells and antigens from the fetus to the mother and from the mother to the fetus.
Mechanical Barrier: New

- Evidence for traffic in both directions across the maternal-fetal interface includes studies reporting migration of maternal cells into the fetus and the presence of fetal cells in the maternal circulation.
Suppression of the maternal Immune System: Old

- Pregnancy is characterized by a state of immune suppression
Suppression of the Maternal Immune System: New

- Maternal antiviral immunity is not affected by pregnancy
- HIV+ pregnant women do not suffer from AIDS-like disease

Systemic Immune Suppression represents a danger to the species
Pregnancy is a TH2 inflammatory condition: Old

- Pregnancy is a TH2 condition and inflammation is detrimental for pregnancy
Inflammation and Pregnancy: New

- Inflammation is necessary for Implantation and parturition
First Trimester

Inflammation TH1

Second Trimester

Growth TH2

Third Trimester

Inflammation TH1

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8-12 WEEKS

<table>
<thead>
<tr>
<th>IMMUNE REACTION</th>
<th>3-6 MONTHS</th>
<th>7-9 MONTHS</th>
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</thead>
<tbody>
<tr>
<td>Open-wound stage: embryo elicits mother's immune response (inflammation)</td>
<td>No inflammation: mother and fetus reach symbiosis</td>
<td>Another inflammation leads to labor</td>
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<tr>
<td>Nausea, fever; contributes to &quot;morning sickness&quot;</td>
<td>None (mother feels good)</td>
<td>Fatigue, muscle contractions, possible fever</td>
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<tr>
<td>Infection leading to miscarriage; Lack of inflammation, leading to failure of pregnancy</td>
<td>Viral infection (may lead to preterm labor)</td>
<td>Preeclampsia, prolonged pregnancy, intrauterine fetal death</td>
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</tbody>
</table>

Mor G. Natural History April 2007
Inflammation and Wound Repair: The implantation wound
New Aspects for Placenta-Maternal Immune Interactions

- Role of the maternal immune system during pregnancy
- Role of the placenta as an immune regulator
- Role of the placenta during infection
The Role of Maternal Immune Cells During Pregnancy: Effect of Depletion of Maternal Immune cells
Maternal Immune System: Necessary for the Success of Pregnancy

- Natural Killer Cells - transformation of the blood vessels by the trophoblast
- Macrophages - Migration and survival of the trophoblast
- T Regs - Maintenance of tolerance
- Dendritic Cells - Implantation
Redefining the Immunology of Pregnancy
The Placenta is an Immune Regulatory Organ
Inner Cell Mass
Trophoblast
Blastocyst Cavity

Natural Killer Cells
Macrophage
Blood Vessels
Dendritic Cells
Neutrophils
Bacteria

T reg

TLR
Trophoblast Maternal Immune Interactions

- Graft/Host response vs Tumor/immune interactions
The Placenta as a Natural Tumor
Immune cells Promote Cancer cells migration, invasion and vascularization
Immune cells Promote Trophoblast cells migration, invasion and vascularization.
Infection and Pregnancy: Old Paradigms

- Response to infection during pregnancy has focused on the maternal immune system as the main and only player.
- Maternal immune system is suppressed to prevent responses to paternal antigens.
- Increased mortality during pregnancy due to infection has been attributed to maternal immune suppression.
Mother

Placenta

Fetus

Response

Virus

Bacteria

- The maternal immune system is not suppressed during pregnancy.
- The placenta plays a critical role in the response to infections, affecting not only the fetus but the maternal systemic immune response.
Infection and Pregnancy

Therefore:

– There are major limitations to our understanding of the role of infection during pregnancy.

– These limitations have a severe impact on how we:
  • Identify women at risk for preterm birth
  • Treat pregnancy complications due to infections
  • Prevent maternal mortality during pandemics
The inflammatory status of the placenta will influence the development of the fetal immune system as well as the maternal immune responses.