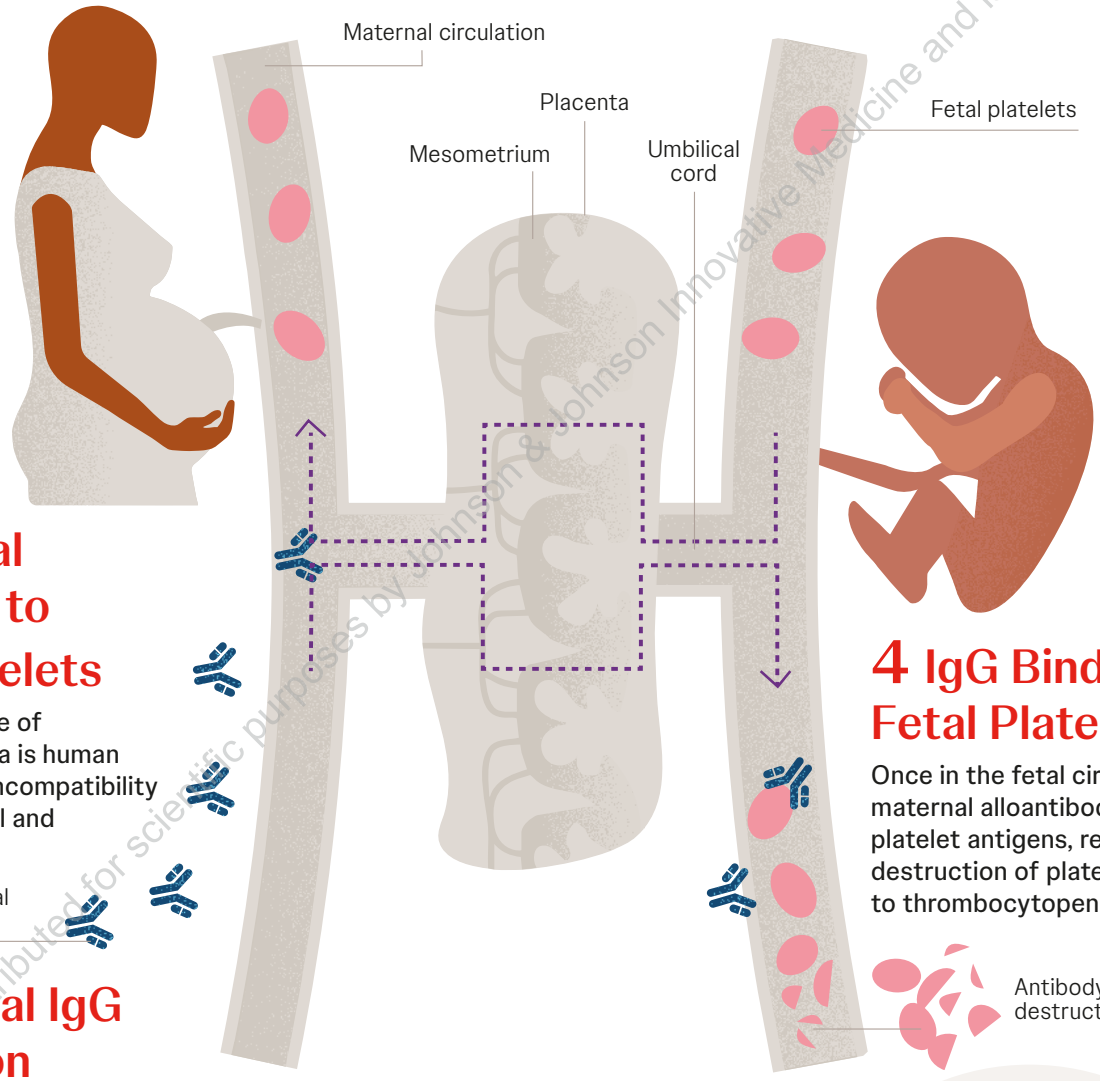
Fetal and Neonatal Alloimmune Thrombocytopenia

What is FNAIT?

FNAIT is an immune-mediated disorder in which maternal alloantibodies lead to the destruction of fetal or newborn platelets. The primary cause is human platelet antigen (HPA) incompatibility between the mother and fetus. Maternal alloimmunization is the most common cause of fetal thrombocytopenia in otherwise healthy newborns in the United States.[1-3]

The most common alloantibodies in FNAIT are anti-HPA-1a and anti-HPA-5b in Caucasians,[4-6] anti-HPA-5b and anti-HPA-4b in East Asians,[7] and anti-HPA-5b, anti-HPA-5a, and anti-HPA-2b in women of African descent.[8,9]



1 Maternal Exposure to Fetal Platelets

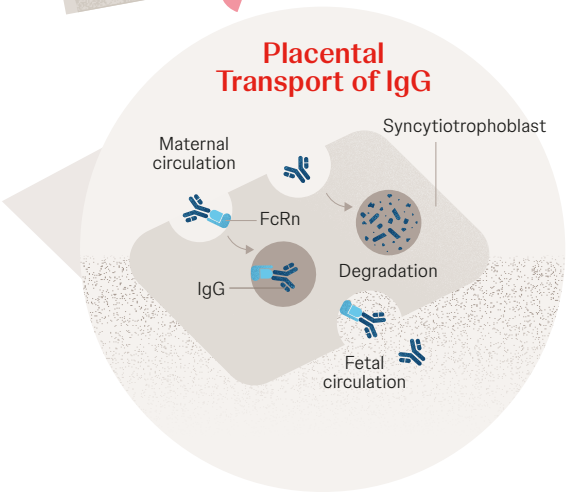
The primary cause of thrombocytopenia is human platelet antigen incompatibility between maternal and fetal platelets.[1,2]

2 Maternal IgG Production

Following exposure to fetal platelets, the maternal immune system produces IgG that targets paternally-inherited fetal platelet antigens. IgG is the only antibody class that is transported across the placenta.[1,2]

3 FcRn Mediates IgG Transport Across the Placenta

FNAIT occurs following the transport of platelet-specific IgG alloantibodies across the placenta. Antibodies cross from maternal to fetal circulation by binding to FcRn.[2]



4 IgG Binds to Fetal Platelets

Once in the fetal circulation, the maternal alloantibodies bind to platelet antigens, resulting in the destruction of platelets, leading to thrombocytopenia.[1,2]

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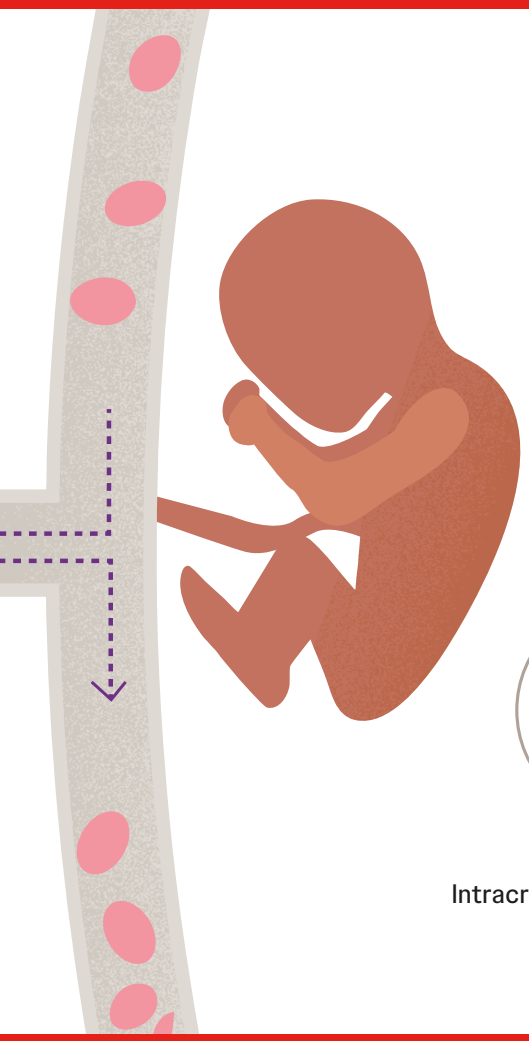

Impact on Fetus

Alloantibodies cause thrombocytopenia via destruction of fetal platelets, increased clearance of fetal and neonatal platelets, damage to vascular endothelial cells and suppression of new platelet production.[1,2,10]

FNAIT can manifest as bruising and potential bleeding into other organs, with the most severe outcome being an intracranial hemorrhage.[1]

Outcomes in Untreated FNAIT Affected Pregnancies

Intracranial hemorrhage (ICH): 4–25%[5,11-13]

Petechiae: <47%[14]

Severe thrombocytopenia (<50×10⁹/L): 43–74%[5,15]

Research Horizons

Advancing research in FNAIT involves a thorough understanding of the transplacental journey of maternal IgG alloantibodies, the differences between various maternal IgG alloantibodies, the extent to which maternal antibody titers rise, and the resulting effects on fetal development. These insights may help us to understand why some fetuses and newborns are more severely affected by FNAIT than others, and may help drive treatment innovations for pregnancies at risk for FNAIT.

FcRn, neonatal fragment crystallizable receptor; FNAIT, fetal and neonatal alloimmune thrombocytopenia; HPA, human platelet antigen; ICH, intracranial hemorrhage; IgG, immunoglobulin G.

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