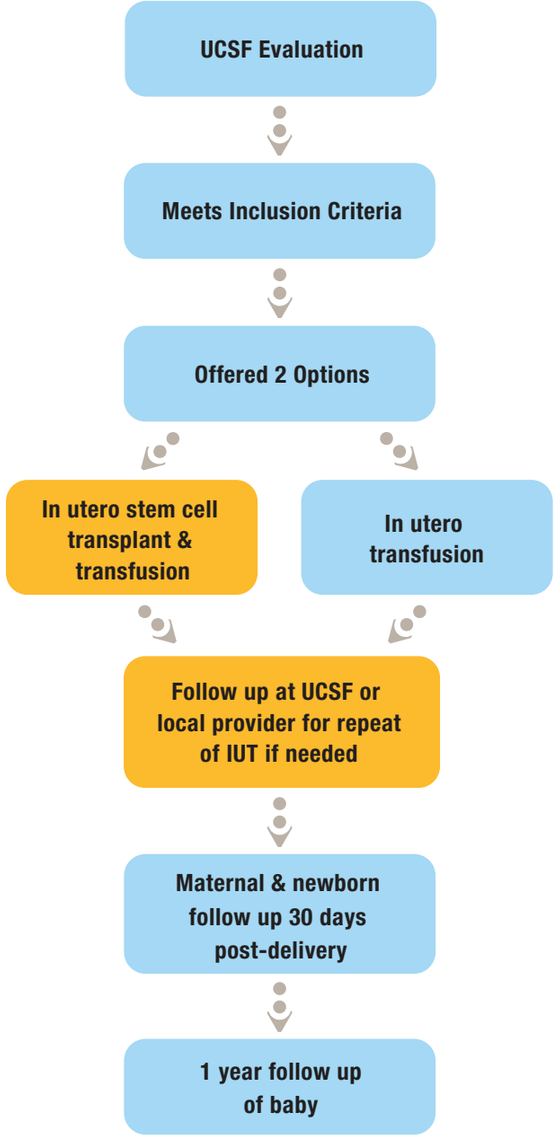
Referral Algorithm



UCSF Benioff Children's Hospitals
Oakland | San Francisco

For more information or to refer a patient please contact us at:

The Fetal Treatment Center
THE BIRTHPLACE OF FETAL SURGERY

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The Fetal Treatment Center
THE BIRTHPLACE OF FETAL SURGERY

Fetal intervention for Alpha Thalassemia Major

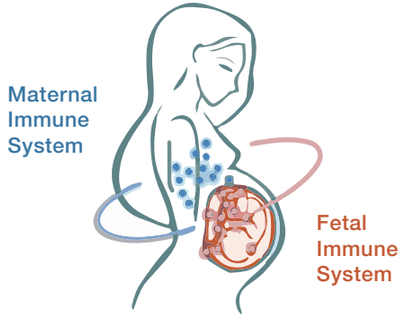
Alpha thalassemia major (ATM) is usually fatal in utero. Fetal blood transfusions are the only current treatment for supporting the fetus through pregnancy. Newborns need chronic transfusions to replace their red blood cells. Postnatal stem cell transplantation can be a definitive therapy but has numerous complications. In utero stem cell transplantation was developed as a strategy to address the challenges associated with transplantation after birth.

We have developed a new strategy of *in utero stem cell transplantation* with the goal to reduce postnatal morbidity and cure the fetus before birth.

UCSF Benioff Children's Hospitals

In Utero Stem Cell Transplantation

The fetal immune system has unique features that make stem cell transplant before birth safer than treatment after birth. Since the mother and fetus tolerate each other during pregnancy (maternal-fetal tolerance), transplanting stem cells from the mother gives the best results.



Our group has tested this idea for over a decade and we have recently obtained approval from the FDA to perform a phase 1 clinical trial of maternal stem cell transplantation in fetuses with ATM.

The trial plan is to harvest stem cells from the mother's bone marrow, prepare them for safe injection, and transplant them into the fetus along with an in utero tranfusion (IUT). Transplanting stem cells concurrently with IUT minimizes additional procedural risk to the fetus, and takes advantage of a unique time period in development when the mother can be an ideal stem cell donor for her fetus.

Even if in utero transplantion does not cure the disease, it may make a postnatal bone marrow transplant from the mother safer. After birth, the newborns may need additional transfusions or no further treatment depending on how well the transplanted cells survive.

The goal of this study is to determine how well the mother and fetus tolerate stem cell harvesting and transplantation.

Evaluation & Counseling

Step 0 – Identify at risk pregnancies

Thalassemia screening should be performed in patients of Southeast Asian, Middle Eastern, African, Mediterranean or Asian Indian ancestry with MCV <82 and normal iron studies.

Step I – Pre-UCSF Evaluation

Mothers who are carriers for the alpha thalassemia mutation and whose fetuses develop signs of anemia should undergo additional testing for confirmation of the fetal diagnosis or carrier status in both parents. Medical records can be sent to the UCSF Fetal Treatment Center for review.

Step II – UCSF Evaluation

Evaluation consists of an ultrasound, echocardiogram, and counseling by team members at the UCSF Fetal Treatment Center: fetal surgeon, hematologist, perinatologist, social worker, neonatologist, genetic counselor, and nurse practitioner. If the mother and fetus are found to be candidates, in utero stem cell transplantation will be offered.

Step III – In utero stem cell transplantation

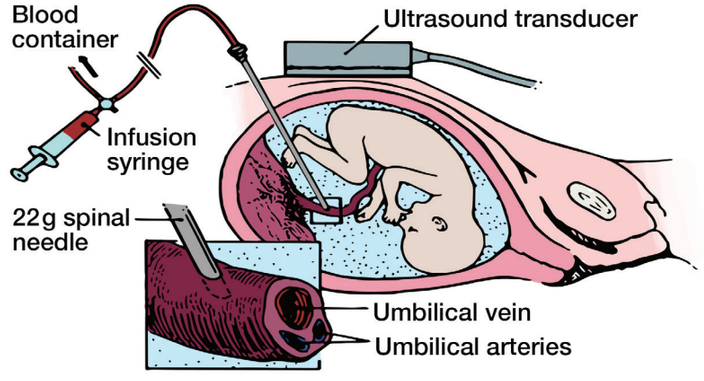
Prior to 25 of weeks gestation, the stem cell transplantation is performed concurrently with the IUT. Following this initial procedure, the fetus will likely require additional blood transfusions as part of standard ATM care. These transfusions can be coordinated through UCSF Fetal Treatment Center or patients may leave San Francisco to seek care with their local medical providers.

Step IV – Neonatal Follow Up

We will evaluate the blood of the newborn to determine how well the mother's stem cells survive and engraft. We will then follow each patient for one year after in utero transplantation.

Study Design

This phase I study will evaluate the safety and feasibility of in utero transplantation in fetuses with ATM.



Inclusion Criteria

- Fetal anemia secondary to ATM
- 18–25 weeks' gestation
- Adequate bone marrow harvest from maternal subject

Exclusion Criteria

- Presence of another birth defect that contributes to a significant morbidity or mortality risk
- Echocardiogram or ultrasound findings that indicate a high risk for fetal demise after intervention
- Maternal cardiac disease
- Evidence of mirror syndrome in mother
- Symptomatic maternal anemia
- Preterm premature rupture of membranes or active preterm labor