

# Alpha Thalassemia Major

## Diagnosis and Treatment



The Fetal Treatment Center  
THE BIRTHPLACE OF FETAL SURGERY

### What is Alpha Thalassemia Major?

Alpha Thalassemia Major (ATM) is a genetic blood disorder that causes hemoglobin deficiency. Hemoglobin is a protein in red blood cells that carries oxygen throughout the body. In individuals with ATM, the red blood cells are missing normal hemoglobin and cannot deliver oxygen throughout the body.

### How do I know if my pregnancy is affected with ATM?

Prenatal diagnosis is available by chorionic villus sampling (CVS) or amniocentesis.

### What are the risks of ATM to my pregnancy?

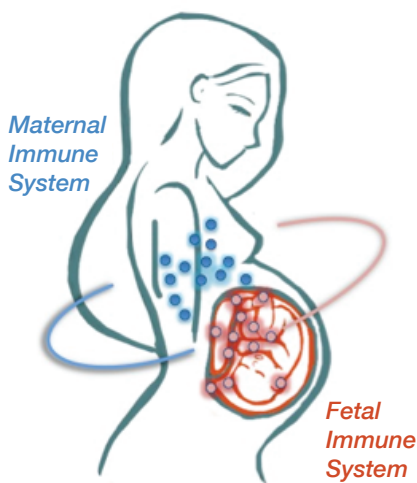
*Mothers carrying a pregnancy with alpha thalassemia major should be followed closely for signs of any of these complications.*

#### Risks for the fetus with ATM

- » **Fetal Hydrops** – a severe swelling (edema) which can cause in utero demise or preterm delivery

#### Risks for the mother with ATM

- » **Anemia** – low blood count
- » **Maternal “Mirror” Syndrome** – with fetal hydrops, the mother may show preeclampsia-like symptoms, mimicking the sick fetus. These may include vomiting, high blood pressure, body swelling, excessive protein in urine, and build-up of fluid in the lungs.



### What are the options for my pregnancy with ATM?

#### Expectant management or pregnancy termination

You could continue the pregnancy without interventions. Since ATM is a severe disease, it would be unusual for a fetus to survive until birth without fetal therapy for the anemia. With this approach, there is also a high risk of maternal complications (such as mirror syndrome). Babies born without any therapy can have neurological problems because of low oxygen delivery to the brain.

Some families may choose not to continue the pregnancy, and termination is an option until 24 weeks of pregnancy in the state of California.

#### Serial in utero blood transfusions

In utero blood transfusions (IUTs) can supply working red blood cells to the developing fetus and are commonly performed for many fetal diseases. This treatment is repeated in the pregnancy every few weeks until delivery. The goal of IUT is to increase oxygen delivery to the fetus, thereby reducing the risk of other pregnancy complications and improve long-term neurological outcomes. There is still a risk of pregnancy loss or preterm delivery after this procedure.

A child born with ATM after in utero transfusions will require chronic blood transfusions (usually every three weeks) to supply working red blood cells to the body. This therapy results in lifelong challenges managing iron overload.

Stem cell transplantation may also be an option and provide a definitive cure. Challenges with stem cell transplantation after birth may include:

- » Difficulty in finding a suitable donor
- » Side effects associated with the medications needed to prepare the bone marrow for this treatment (conditioning)
- » Transplanted cells attacking the patient (graft vs. host disease)

#### In utero stem cell transplantation: A Novel Approach

In utero stem cell transplantation was developed as a strategy to address the challenges associated with transplantation after birth. In this approach, the mother's stem cells are transplanted into the fetus, taking advantage of the fact that the mother and fetus tolerate each other's cells during pregnancy.

If the transplant is successful and the mother's stem cells are “engrafted” (incorporated into the baby's own bone marrow), the baby will be able to make normal blood cells. If the transplantation is not fully successful and engraftment is weaker, a “booster” transplant of the mother's stem cells may be performed after delivery. Since even low engraftment could result in long lasting tolerance to the mother's cells, this booster transplant can improve the baby's ability to make normal blood cells. A booster transplant is expected to be safer than current methods of stem cell transplantation after birth.

Mothers who choose to participate in this clinical trial will have stem cells harvested from their bone marrow. These cells will then be prepared for safe injection and transplanted into the fetus at the same time as an in utero transfusion (IUT). The fetus will have additional blood transfusions until birth. The success of the transplant will be evaluated after birth.

While we believe in utero transplantation can be performed safely, it is possible that it may not be effective. Potential risks of the procedure are that the fetus may become sick after the in utero transplantation or may not survive the therapy. Additionally, the mother may need a blood transfusion after donating bone marrow. In the event that in utero transplantation is not successful, repeated blood transfusions will be performed after birth and stem cell transplantation may be considered.



UCSF Benioff Children's Hospital

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## Treatment Options Flowchart

### Prenatal Treatment Options

#### Expectant Management

#### Serial In Utero Transfusions

#### In Utero Stem Cell Transplantation (New Option)

**Goals:** treat fetal hypoxia and survive birth

**Goals:** create lasting tolerance to mother's stem cells; possibly a single definitive therapy

**Serial In Utero Transfusions**  
IUT may reduce the risks of maternal mirror syndrome, preterm labor, and neurological damage



Stem Cell Transplant occurs during an IUT between 18-25 weeks

### Delivery

The majority of fetuses who do not receive any fetal therapy will not survive the pregnancy

#### Engraftment Success

None

Low

Good

#### After Birth Treatment Options

##### Continue Transfusions

Many patients have a good quality of life. Challenges may include: iron overload, chronic medications & cost

##### Stem Cell Transplantation

Transplant can be a definitive cure but also has an associated risk of mortality. Challenges may include: difficulty in finding donor, toxic medications to prepare the bone marrow for transplant, and graft vs host disease

Booster stem cell transplant with maternal cells

Possibly a definitive therapy

**Goals: To improved developmental outcomes and reduced medical management**

For more information please contact us at:



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