Inherited Genetic Diseases: Stem Cell Treatments

What genetic diseases are potentially treatable with stem cells?

There are a large number of inherited genetic diseases (like sickle cell anemia) that can now be accurately diagnosed early in fetal life by examining fetal DNA obtained by chorionic villus sampling or amniocentesis. In most cases the testing is done because the disease has been identified to run in the family.

Some of these diseases are treated after birth by bone marrow transplantation. However, successful bone marrow transplantation after birth is limited by lack of donor stem cells, damage already done to the baby by the disease, rejection of the donor cells by the baby’s immune system, and, in some cases, rejection of the baby’s tissue by the donor cells (graft-versus-host disease or GVHD).

Many of the problems associated with transplantation of stem cells after birth are related to immune rejection. Transplantation before birth into a fetus whose immune system is not fully developed may overcome these problems.

The strategy of transplanting normal stem cells into a fetus with a stem cell defect at a time when the graft will not be rejected could be applied to wide variety of inherited defects (listed below). This approach is potentially applicable to any congenital disease that can be diagnosed prenatally and can be cured or improved by bone marrow or stem cell transplantation after birth. Although we have demonstrated that injection of hematopoietic stem cells (the stem cells for blood) into fetal lambs and monkeys leads to long-term and successful growth of donor bone marrow stem cells in the recipient (hematopoietic chimerism). However, this strategy has so far been applied successfully in only a few human diseases.

Alpha Thalassemia Major

The UCSF Fetal Treatment Center and UCSF Benioff Children's Hospital Oakland Thalassemia Center have established the first multidisciplinary center for Alpha Thalassemia Major. The program is designed to address the complex diagnostic, prenatal, intrauterine, and perinatal management issues affecting a family with an Alpha Thalassemia Major pregnancy.

For more information please visit our page on Intrauterine Therapy for Alpha Thalassemia Major
Inherited Genetic Diseases Treatable with Stem Cells

### Hemoglobinopathies
- b-Thalassemia major
- a- Thalassemia major
- Sickle cell anemia

### Immunodeficiency Diseases
- Severe combined immunodeficiency syndrome
- Bare lymphocyte syndrome
- Chronic granulomatous disease
- Wiskott-Aldrich syndrome
- Infantile agranulocytosis (Kostman’s syndrome)
- Lazy leukocyte syndrome (neutrophil actin deficiency)
- Neutrophil membrane GP-180 deficiency
- Agammaglobulinemia
- X-linked lymphoproliferative syndrome
- X-linked hyper-IgM syndrome

### Inborn Errors of Metabolism
- Hurler’s disease (MPS-1) (a-iduronidase deficiency)
- Hurler-Scheie syndrome
- Hunter disease (MPS-II) (iduronate sulfatase deficiency)
- Sanfillippo B (MPS-IIIB) (a-glycosaminidase deficiency)
- Morquio (MPS-IV) (hexosamine-6-sulfatase deficiency)
- Maroteaux-Lamy syndrome (MPS-VI) (arylsulfatase B deficiency)
- Sly syndrome (MPS-VII) (b-glucuronidase deficiency)

### Mucopolysaccharidoses
- Hurler’s disease (MPS-1) (a-iduronidase deficiency)
- Hurler-Scheie syndrome
- Hunter disease (MPS-II) (iduronate sulfatase deficiency)
- Sanfillippo B (MPS-IIIB) (a-glycosaminidase deficiency)
- Morquio (MPS-IV) (hexosamine-6-sulfatase deficiency)
- Maroteaux-Lamy syndrome (MPS-VI) (arylsulfatase B deficiency)
- Sly syndrome (MPS-VII) (b-glucuronidase deficiency)
Mucolipidoses
- Fabry disease (a-galactosidase A deficiency)
- Gaucher disease (glucocerebrosidase deficiency)
- Krabbe disease (galactosylceramidase deficiency)
- Metachromatic leukodystrophy (arylsulfatase A deficiency)
- Niemann-Pick disease (sphingomyelinase deficiency)
- Adrenal leukodystrophy
- I-cell mucolipidosis II

Other Hematopoietic Diseases
- Osteopetrosis
- Diamond-Blackfan syndrome
- Fanconi anemia

What is the outcome for a fetus with an inherited genetic disease?

Because stem cell defects result in such a wide of variety of diseases (hemoglobinopathies, immunodeficiencies, inborn errors of metabolism, etc.), the outcome for the fetus depends on that particular disease. The wide range of outcomes are anywhere from death or severe lifelong impairment to survival and treatment after birth with minimal impairment. There are degrees of severity and variations in outcome even with a single disease. A good example is sickle cell disease: some children have very mild disease and do not need any treatment and others have very severe disease that requires frequent treatment and leads to severe impairment.

The best information about the consequences of each of these many inherited stem cell defects can be found on websites, support groups, and publications devoted specifically to that disease. We have provided links to some of these very helpful and informative websites. Another way to find information on any specific inherited defect is to use a search engine such as Google or by logging onto Medline/PubMed.

How serious is the inherited genetic disease in my fetus?

For you to make the best decision, you will need accurate and complete information about your fetus’s condition, including the type and severity of the defect determined by DNA testing. In addition, you will want to know if there are associated defects, or if this problem is
part of a cluster of problems (syndrome). Genetic testing of fetal material either from the placenta, or from the amniotic fluid, or obtained directly from the fetus is the most important part of this evaluation. Examination of DNA from the mother, father, and other family members may be necessary. Imaging of the fetus by transvaginal or transabdominal ultrasound or magnetic resonance imaging (MRI) may also be helpful. In considering possible fetal therapy, it is very important to know the age of the fetus. This is most accurately determined by early ultrasound.

When all the information is available, you will want to discuss it with a knowledgeable genetic counselor or perinatal geneticist. If appropriate, you may be referred to specialists for that particular inherited genetic disease.

What are my choices during this pregnancy?

The most important consideration is the accuracy of the diagnosis through genetic counseling about the consequences of that particular inherited stem cell defect. If after full and complete counseling about the defect and its consequences, you choose to continue the pregnancy, you will start planning the proper time and place of delivery for optimal care after birth.

For inherited stem cell defects that cause trouble at birth and require immediate treatment, the place of delivery will be the most important consideration. You may choose to deliver in a center that has special expertise in treating that particular defect. Babies with some types of defects will need support in an intensive care nursery, and may require transfusion with blood, dialysis to cleanse the blood, or even postnatal hematopoietic stem cell transplantation. In some cases, the disease may make the baby vulnerable to infection and thus require special precautions. For some rare diseases, there are only a few centers specialized in the treatment of that disease.

In some types of inherited genetic defect, intervention before birth may be considered. The reasons to consider intervention before rather than after birth are:

1. the genetic defect causes ongoing damage to the fetus that can prevented by earlier treatment; and
2. the disease will require hematopoietic stem cell transplantation and this can be better accomplished before birth.

The potential advantage of stem cell transplantation in utero is to take advantage of fetal immunologic immaturity or tolerance, thus avoiding the need for immunosuppression or myeloablation (destroying some of the bone marrow in order to make room for the new donor bone marrow). Some disadvantages are the risk of the procedure itself, which requires injecting the donor cells into the very small fetal abdomen or bloodstream. There is also the risk of causing infection or of the transplant not working. All these factors must be carefully considered before deciding whether to attempt this novel and presently unproven form of treatment.

What will happen after birth?

Management after birth will depend on the nature of the inherited genetic defect. In many
cases, very specialized therapy by experts in that disease is only available at highly specialized tertiary care centers. For many diseases, hematopoietic stem cell transplantation, usually in the form of a bone marrow transplant, will be planned after birth. Often, repeated testing and careful follow-up are necessary to protect the baby until the transplant is performed.

Even when stem cell transplantation has been performed before birth, careful follow-up after birth will be necessary. In some cases, transplantation of stem cells from the same donor may be repeated after birth, taking advantage of the fact that the prenatal transplantation has been used to establish immunologic tolerance to those donor cells.

For many of the inherited genetic defects, it is very helpful for families to get involved with other families caring for babies or children with similar problems.

**Support Groups & Other Resources**

- March of Dimes [6] ? Researchers, volunteers, educators, outreach workers and advocates working together to give all babies a fighting chance
- Birth Defect Research for Children [7] ? a parent networking service that connects families who have children with the same birth defects
- Kids Health [8] ? doctor-approved health information about children from before birth through adolescence
- NIH - Office of Rare Diseases [10] ? National Inst. of Health - Office of Rare Diseases

Contact Us
Privacy Policy
UCSF Benioff Children's Hospital

© 2013 The Regents of the University of California

**Source URL:** https://fetus.ucsf.edu/stem-cells

**Links**
[1] https://www.youtube.com/watch?v=Rf4hKMV7IG4
[2] https://fetus.ucsf.edu/node/406
[4] https://www.youtube.com/watch?v=wbw0qirt8IQ