

FAMILY PLANNING AND PREGNANCY

Decisions about family planning can be difficult and very emotional when one of the prospective parents has a genetic disorder, such as Marfan syndrome. Before making any decisions, parents should understand the many options now available, as well as the potential risks to the child and the mother. A genetic counselor or the nurse in The Marfan Foundation's help center can discuss the options with you and provide insights.

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I have Marfan syndrome and I want to have a baby. What should I consider before pregnancy?

Pregnancy poses additional risks to women with Marfan syndrome because of the increased stress on the heart and blood vessels. While there is no clear distinction between women who can and cannot tolerate pregnancy, several points seem well-established:

- Women who have significant heart valve problems or aortic disease should discuss pregnancy risks with their doctors before considering pregnancy. The risk of serious aortic complications such as a tear or rupture is considered significant once the aortic diameter reaches 4.0 centimeters. For women with Marfan syndrome with aortic dimensions less than 4.0 centimeters at the onset of pregnancy, some risk is still present.
- Women who have had composite graft surgery (including an artificial aortic valve) of the aortic root need special guidance because of the potential for harmful effects of warfarin (such as Coumadin®) on the developing fetus. While it is thought that prior aortic root surgery decreases the risks

associated with pregnancy for women with Marfan syndrome, this does not eliminate all risk since other aortic segments can enlarge and tear.

- Any pregnancy in a woman affected by Marfan syndrome should be considered “high-risk” (a term obstetricians use) and her aorta should be evaluated by echocardiography at least every three months.
- Delivery should be by the least stressful method possible. There is current controversy regarding whether a controlled vaginal delivery or a Cesarean section imposes less stress for the majority of women with Marfan syndrome. The decision regarding the best delivery method for a particular woman should be made after careful consultation with an obstetrician familiar with all relevant issues. Cesarean section is not absolutely necessary because of Marfan syndrome, but may be indicated for any of the usual reasons that would apply to any pregnancy.
- Women are often advised to complete childbearing early in life.
- Certain medications used in the treatment of Marfan syndrome cannot be used during pregnancy due to a risk of birth defects and fetal loss. These include angiotensin converting enzyme inhibitors (such as enalapril or captopril) and angiotensin receptor blockers (such as losartan).

Note: If a woman is diagnosed with Loeys-Dietz syndrome or vascular Ehlers-Danlos syndrome, there are additional risks when considering becoming pregnant. Women with Loeys-Dietz syndrome have a risk of aortic dissection and uterine rupture during pregnancy and directly after childbirth. Pregnancy may also be very dangerous for women with vascular Ehlers Danlos syndrome. Obstetric complications include risk of uterine rupture during labor, damage to the vagina and perineum, bleeding, and rupture of blood vessels and the colon. If you are diagnosed with Loeys-Dietz syndrome or vascular Ehlers Danlos syndrome, or think you may have one of these conditions, consult with a genetic counselor and knowledgeable doctors before considering pregnancy.

What should I do before I become pregnant?

- Have an examination with your family doctor or internist to evaluate your overall health.
- Visit your cardiologist and have an echocardiogram to make sure your aorta is not at a size that would make pregnancy too risky.
- See a perinatologist (maternal-fetal medicine specialist or high risk obstetrician) to talk about specific issues related to pregnancy and Marfan syndrome.
- Consult with a clinical geneticist or genetic counselor to help you and your partner understand how Marfan syndrome is inherited and to learn about the choices you have.

What is the chance that my baby will have Marfan syndrome?

When one parent has Marfan syndrome, each child has a 50 percent chance of inheriting the disorder, regardless of the gender of the child or the affected parent. If both parents are affected, there is a 75 percent chance that the child will be affected. A child who inherits the Marfan gene from both affected parents would be severely affected and is often associated with fetal loss or catastrophic complications shortly after birth.

It is important to remember that the severity of Marfan syndrome in the parent is not an absolute indication of how mild or severe the syndrome will be in the child. While affected members in the same family (with the same mutation) generally show similar disease severity, there can be variation even within a family.

Is there any way to make sure that I have a baby that does not have Marfan syndrome?

If a couple—one of whom has Marfan syndrome—decides that they want to ensure that they have a biological child without Marfan syndrome, there are two basic approaches:

- Conduct prenatal testing, such as chorionic villus sampling or amniocentesis
- Use in-vitro fertilization with pre-implantation genetic diagnosis

Both methods require specific knowledge regarding the mutation that is present in the affected parent. Currently, this generally involves sequencing of the FBN1 gene. This test takes time to obtain the test results. Therefore, it is important to undergo the testing prior to becoming pregnant. This is a complex and rapidly changing area of medicine; therefore, prospective parents should discuss the latest status of available options with their doctors and genetic counselor.

Prenatal testing for conditions such as Marfan syndrome can be carried out approximately 10–12 weeks into the pregnancy using chorionic villus sampling, which involves taking a small sample of cells from the placenta (the organ that links the mother's blood supply with her unborn baby's) through the entrance of the womb. The sample can then be tested for the presence of the mutation.

Marfan syndrome can also be tested for using amniocentesis. This test is carried out at about 16–18 weeks into the pregnancy. It involves taking a small sample of amniotic fluid for examination. Amniotic fluid surrounds the unborn baby in the womb. It is important to remember that although prenatal tests may show whether your child has the defective gene, they will not give you an absolute indication as to how serious their Marfan syndrome will be.

In some cases, the results of chorionic villus sampling or amniocentesis could be negative, suggesting that your child does not have the gene defect present in the affected parent. The fetus could still have inherited gene alterations from the parents for other genetic conditions (that were not tested for) and would have the same risk as anyone else in the general population to have a new mutation (not present in either parent) causing genetic disease (including Marfan syndrome).

In-vitro fertilization with pre-implantation genetic diagnosis is possible if the affected parent's gene mutation is known. The in-vitro fertilization (IVF) process is the same as used for infertility patients. However, when the embryo reaches the 6–8 cell stage (2–3 days after fertilization), 1 or 2 cells are removed from the embryo. These cells are then analyzed for the Marfan syndrome mutation using molecular genetic technology. Embryos apparently lacking the Marfan gene are selected for implantation in the uterus. While there is no consequence to the developing embryo of removing 1–2 cells at this very early stage of development, the implantation process is somewhat inefficient, often requiring multiple rounds of IVF before a pregnancy is established.

Am I at greater risk of medical problems while I am pregnant?

All women with Marfan syndrome are at increased risk for complications during pregnancy. Therefore, it is important that you are cared for by an obstetrician with the experience and expertise needed to

manage potentially life-threatening heart problems. You should also be carefully followed by your cardiologist throughout the pregnancy, with echocardiograms done at least every three months. There are not a lot of studies in this area, but available research shows that:

- Women with an aortic root less than 4.0 cm are at very low risk for a rapid change in aortic size or aortic tear during or immediately after pregnancy.
- Women with an aortic root above 4.0 cm are at greater risk, and this risk appears to increase proportionally to aortic size.
- Women with Marfan syndrome with an aortic root of more than 5.0 cm are at extreme risk during pregnancy. In this case, pregnancy is not recommended.

Am I more likely to have a miscarriage?

The miscarriage rate in women with Marfan syndrome is no different than in the general population.

Is there anything special I need to do during pregnancy?

A woman with Marfan syndrome should have an echocardiogram before she becomes pregnant. While she is pregnant she should have an echocardiogram at least every three months. If a woman's aorta measures close to 4.0 cm, more frequent echocardiograms may be indicated to check for any sudden increase in the size of the aorta. Women who experience a significant increase in their aortic root diameter during the course of the pregnancy should also have more frequent echocardiograms.

I am currently on Coumadin® (or another anticoagulant). Can I continue to take this medication while I am pregnant?

Coumadin® (warfarin) has been associated with birth defects if taken during the 7th–11th week of a pregnancy. For this reason, women with Marfan syndrome who require anticoagulation during pregnancy are generally placed on another kind of medication, heparin, which does not cross the placenta and is not associated with birth defects. Frequent monitoring of the time it takes the blood to clot (prothrombin time, PTT) is necessary to make sure that the blood is thin enough and won't clot. Heparin is stopped briefly for 24–48 hours around the time of birth.

Coumadin® can be safely used while breastfeeding because the level of the medication that is in breast milk is very low and does not have any anticoagulation effect in the infant. Therefore, after delivery, heparin should be restarted and Coumadin® also started. The heparin can be discontinued once the Coumadin® has reached the level where it has its desired effect.

Pregnancy and the postpartum period are times of markedly increased risk of clot formation; therefore, women who require anticoagulation should be fully anti-coagulated throughout this time.

I am currently on a beta-blocker. Can I take this medication while I am pregnant?

Many women with Marfan syndrome, especially those who have moderate or marked aortic dilatation, are treated with beta-blockers to lower the risk of aortic enlargement and dissection. Beta-blockers can be continued throughout the pregnancy, including the first trimester.

There have been some studies that showed a lower birth weight in infants exposed to beta-blockers during pregnancy. This happened most often with atenolol (Tenormin), a commonly used beta-blocker for people with Marfan syndrome. In addition, two beta-blockers—atenolol and propranolol—have been associated with minor heart problems immediately after birth, but these heart problems seem to correct themselves within two days after birth.

Babies who have been exposed to beta-blockers should be closely watched after they are born. This can be done in the traditional nursery setting. Make sure that your pediatrician is aware of the use of beta-blockers during pregnancy.

It is important to note that certain blood pressure medications, including angiotensin receptor blockers such as losartan and angiotensin converting enzyme inhibitors such as enalapril, should not be used during pregnancy due to a risk of birth defects or fetal loss.

Should I expect any additional bone and joint problems during pregnancy?

Pregnancy often causes an increase in joint and bone pain, especially in the lower back, pelvis, and legs. Walking around usually causes more pain; sitting and reclining reduce pain. Occasionally, bed rest is required during pregnancy if sitting or reclining does not help.

Is it safer for me to have a vaginal delivery or a C-section?

Research shows that women with Marfan syndrome who have an aortic diameter of less than 4.0 cm have similar outcomes with a vaginal delivery and a C-section. Some recommendations to reduce risk include:

- Use of an epidural to keep the blood pressure stable
- Avoid bearing down or "pushing." Instead, forceps should be used to assist with the delivery once the cervix is dilated.

There is some controversy about whether vaginal delivery or C-section is safer for women with a larger aortic diameter. It may be less risky to deliver these women by C-section before they go into labor, but this requires further study.

Can I have an epidural?

Epidural anesthesia is safe for the vast majority of women with Marfan syndrome. However, it is not advised for women with moderately severe dural ectasia. Dural ectasia causes the sac around the spinal cord (dura) to balloon out, leaving virtually no epidural space. The chances of a spinal fluid leak may be increased. Dural ectasia is best identified through MRI imaging, particularly of the lower spine with a person standing upright.

Are there any special considerations for the baby at birth?

At birth, the pediatrician should conduct a basic examination, as would be done for any newborn.

Usually, the only pressing issue for a newborn with Marfan syndrome is the presence of severe mitral regurgitation (the back flow of blood from the left ventricle to the left atrium of the heart through a defective mitral valve; also known as mitral incompetence). This is the most common

cause of significant problems in infants. A doctor can hear severe mitral regurgitation with a stethoscope. This problem in infancy can be seen in routine cases of Marfan syndrome, but is much more common in infants with the most severe form of Marfan syndrome, generally caused by a new gene mutation (neither parent is affected). Importantly, new gene mutations can cause the full spectrum of Marfan syndrome, from very mild to very severe. Just because a newborn has a new mutation, this does not mean that you should expect particularly severe Marfan syndrome.

Whether your baby inherited the disorder or is the first in the family affected—an early evaluation of his/her eyes is important to be sure that eyesight develops normally. Because lens dislocation may be present at birth or shortly after, a dilated eye exam is recommended. In general, a comprehensive evaluation of the baby by the pediatrician is important and should be done in conjunction with evaluation by a geneticist, cardiologist, ophthalmologist, and other specialists, as needed.

Do you have questions? Would you like more information?

- Call our help center, 800-862-7326, ext. 126 to speak with a nurse who can answer your questions and send you additional information.
- Visit our website at marfan.org. You can print information that interests you and ask questions online.