Maitri Health Care for Women
Obstetrics, Gynecology and Midwifery

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Genetic Testing

Maitri believes that pursuing genetic testing is a personal decision, and we strive to help women/couples determine the best approach to these testing options.

We recognize that what is an obvious choice for one woman on whether to screen, or how to screen, may be just the opposite answer for another woman. We respect whatever decisions are made with regards to genetic testing.

We are happy to assist you in deciding what the best approach is for you. Below is a list of the services and tests available. You may want to check with your insurance company regarding coverage before you decide on which test to pursue.

Things to consider when deciding on genetic testing:

- Is this information I want? Some women do not wish to know in advance if their fetus/child has a genetic disorder.
- What will I do with this information? Some women feel strongly that they would terminate a pregnancy that was found to have a genetic problem, while other women may just want to prepare ahead of time for having a child with a certain condition. Keep in mind that there are no “in utero” cures for these conditions.
- Do I want to pursue invasive (definitive testing) or am I comfortable with a screening (risk assessment test)?
- Does my insurance cover these tests? Which ones does it cover?
- Based on my age, family, and personal history, how much risk do I have of having a baby with a genetic disorder?

What is Down syndrome?

Also called Trisomy 21, Down syndrome is a genetic disorder caused when an abnormal cell division results in extra genetic material from chromosome 21. This genetic disorder, which varies in severity, causes lifelong intellectual disability and developmental delays, and in some people can cause health problems. It is the most common genetic chromosomal disorder.

Frequency of Down syndrome per Maternal Age

Age (years)	Frequency of Fetuses with Down Syndrome to Normal Fetuses at 16 weeks of pregnancy	Frequency of Live Births of Babies with Down Syndrome to Normal Births
15-19	---	1/1250
20-24	---	1/1400
25-29	---	1/1100
30-31	---	1/900
32	---	1/750
33	1/420	1/625
34	1/325	1/500
35	1/250	1/350
36	1/200	1/275
37	1/150	1/225
38	1/120	1/175
39	1/100	1/140
40	1/75	1/100
41	1/60	1/85
42	1/45	1/65
43	1/35	1/50
44	1/30	1/40
45 and older	1/20	1/25

The numbers are approximated and rounded. Using this data, geneticists have set the number separating low-risk from high-risk at 1/250. Why is there a difference in frequencies between 16 weeks and time of birth? Because the spontaneous miscarriages of pregnancies with Down syndrome between these times.

What is Trisomy 18?

Also called Edwards syndrome, Trisomy 18 is a chromosomal condition which results from an extra copy of chromosome 18. It is associated with abnormalities in many parts of the body and intellectual disability. Due to the presence of several life-threatening medical problems, many individuals with trisomy 18 die before birth or within their first month. Trisomy 18 occurs in about 1 in 5,000 live-born infants.

What is Trisomy 13?

Also called Patau syndrome, Trisomy 13 is a chromosomal disorder which results from an extra copy of chromosome 13. It is associated with severe intellectual disability and physical abnormalities in many parts of the body. Due to the presence of several life-threatening medical problems, many infants with Trisomy 13 die within their first days or weeks of life. 5 to 10 percent of children with this condition live past their first year. Trisomy 13 occurs in about 1 in 16,000 newborns.

Genetic Testing Overview

Screening tests - Non diagnostic meaning not a "yes" or "no" answer, but a risk assessment (for example a 1 in 1000 chance):

- Integrated screen
- Cell Free DNA
- Ultrascreen
- Modified Sequential Screen
- Quad Screen
- Detailed Fetal Anatomy Screen- Ultrasound examination

Diagnostic tests - these tests give a definitive result- "yes" or "no" if the baby has a major chromosomal problem:

- CVS- chorionic villi sampling
- Amniocentesis

Prior to pregnancy or anytime during pregnancy

- Genetic counseling
- Cystic Fibrosis Carrier testing
- SMA Carrier testing
- Fragile X Carrier testing
- Ashkenazi Jewish Carrier Testing

Financial information on Genetic Testing

Health insurance coverage for genetic testing varies from plan to plan, company to company, and state to state. With this in mind, each patient is responsible for researching their own plan coverage with regards to genetic testing by calling the insurer, benefits representative, or both. Our medical team will not be able to answer questions regarding the expected cost that will be billed to you.

Test Codes

Ultrascreen: 76813- US, 36416- finger prick, 84704, 84163

Integrated Screen: 76813- US, 82105, 82677, 84163, 84704, 86336

Modified Sequential Screen: 76813- US, 36416- finger prick, 84704, 84163, 82105, 82677, 86336

Quad Screen: 82105, 82677, 84702, 86336

Genetic Counseling: 99243

Amniocentesis: 59000, 76946

CVS: 59015, 76945

AFP: (alpha fetoprotein) 82105 (approximately $150)

Cell Free DNA (Invitae NIPS): 81420

Genetic Counseling

Not sure which test is best for you? Concerned about your test results? A genetic counselor is available to discuss testing options and/or the results from any prenatal testing with you and your partner or family. As part of the counseling, a detailed family history is obtained in order to determine if there are any other tests that might specifically apply to you, your partner, or fetus. Genetic counselors have specialized training in genetics and counseling. Genetic counseling is recommended to discuss any abnormal prenatal screening or diagnostic test results. Genetic counselors are there to help you decide on the best testing options for you, your baby's diagnosis, and to discuss with you the variety of options available if abnormal testing occurs. They can help you understand choices regarding:

- continuation of the pregnancy and making arrangements for appropriate medical services at and after delivery
- termination of pregnancy

Genetic counselors are also available for the following examples:

- Couples with questions or concerns about carrier screening for genetic conditions more commonly seen in ethnic groups. For example: Tay-Sachs disease, Thalassemia, Sickle Cell Anemia, and Cystic Fibrosis
- Concerns about exposure to radiation, medications, chemicals, infections, or drugs during pregnancy.
- Couples in which one or both partners have a personal and/or family history of:
    - Physical differences present at birth
    - Learning problems, developmental delay, or mental retardation
    - Extreme tall or short stature
    - Hearing loss
    - Recurrent miscarriages, still births, or early infant loss

- Chromosomal abnormality

Screening Tests

These tests are a risk assessment. The results return as a probability, or chance, of your baby having a chromosomal abnormality. For example: a 1 in a 1000 chance of having a child with an open neural tube defect.

Cell Free DNA (NIPS)

Invitae Non-Invasive Pranatal Screening (NIPS) analyzes whether a pregnancy is at increased risk for the chromosomal disorders listed below:

Testing for: Down syndrome (Trisomy 21) and Edwards syndrome (Trisomy 18) and Patau syndrome (Trisomy 13), sex chromosome abnormalities (listed below), and microdeletions

Y Analysis (which detects Gender and 47XYY Jacobs Syndrome) and/or XY Analysis (which will detect Turner Syndrome 45X, Klinefelter Syndrome 47XXY, Jacobs Syndrome 47XYY, Triple X 47XXX).

Turner Syndrome – (Monosomy X) when a female is born with instead of two X chromosomes, only one or one is altered in some way. It presents itself in short stature and infertility.

Klinefelter Syndrome – (XXY) when a male is born with an extra X chromosome. This typically causes underdeveloped testicles which may lead to a decreased production of testosterone. This may in turn cause such problems as infertility.

Triple X and XYY Syndrome – when a child is born with an extra X or Y chromosome. This increases the risk of learning disabilities and developmental delays.

Invitae NIPS tests for the following microdeletions: Prader-Willi/Angelman syndrome, 1p36 deletion, DiGeorge syndrome, Wolf-Hirschhorn syndrome, Cri-du-chat syndrome

Microdeletion: A microdeletion is a small, missing piece of a chromosome. While many microdeletions have little impact on a child's health or life, there are some that cause intellectual disabilities and birth defects.

Twin pregnancy: Invitae NIPS is unable to do microdeletions for twin pregnancies. The sex chromosome analysis for twins can tell you if you are carrying at least one male baby. However, it is unable to determine if there is more than one male or identify which twin is male.

How it is performed: Blood test (from a vein in your arm) after 10 weeks gestational age, analyzing cell-free DNA (cfDNA) in maternal blood.

Detection rate:

- Downs Syndrome – >99% (false positive rate <0.1%)

Pros:

- High detection rate and low false positive rate.

- This is a noninvasive test, and poses no threat to the fetus- there is no increased risk of pregnancy loss following this test

Cons:

- Increasing maternal weight is associated with lower fetal fraction of cell free DNA, therefore a second blood draw may be required for women weighing over 200 pounds. Maternal weights over 220 pounds may need to wait until 12 weeks to have this blood work drawn.
- Cell Free DNA does not test for open neural tube defects. A separate blood test (AFP) is recommended (15-20 weeks) to screen for those defects.

Approximate cost: We will always order this test to be run through your insurance. Invitae will reach out to you via text and email with an Estimation of Benefits of what it would cost through insurance. You then have 3 days to decide if you want to go through insurance or opt for the Self Pay option of $99. The Self Pay option does not go towards your deducible. See Invitae payment options handout for more details.

Ultrascreen

Testing for: Down syndrome (Trisomy 21) and Trisomy 18 and 13

How it is performed:

- Blood test (finger prick) between, 9 weeks plus 1 day and 13 weeks plus 6 days, measuring the hormone levels PAPP-A and Beta HCG
- Ultrasound measuring the nuchal translucency (thickness of the skin on the back of the baby's neck)- done between 11 weeks and 1 day and 13 weeks and 6 days

Both parts of the test can be performed at the same time, with results coming back in 1 week. Or the blood test can be obtained a week before the ultrasound, with results returning on the day of the ultrasound.

Detection rate:

-Down syndrome-> 85%
-Trisomy 18-> 80%

Pros:

- This is a noninvasive test, and poses no threat to the fetus- there is no increased risk of pregnancy loss following this test

Cons:

- It is not as accurate as the Integrated Screening test
- Ultrascreen also does not test for open neural tube defects. A separate blood test (AFP) is recommended (15-20 weeks) to screen for those defects.

Approximate cost: $1,000

Integrated Screen

Testing for: Down syndrome, Trisomy 18, open neural tube defects (such as Spina Bifida)

How it is performed: 3 Required Steps-

- Ultrasound (Nuchal Translucency Measurement) between 11 weeks +3 days, and 13 weeks +6 days

- Blood test (measuring hormone PAPP-A) between 10 weeks + 3 days and 13 weeks +6 days
- Blood test (measuring hormones AFP, HCG, uE3, inhibin A) between 15 weeks and 20 weeks +6 days

Detection rate:

-Down syndrome- 94-96%
-Trisomy 18- 90%
-Open neural tube defects: 80%

Pros:

- This is a non-invasive test, and poses no threat to the fetus. There is no increased risk of pregnancy loss following this test

Cons:

- Results are complete only after all steps of the Integrated Screen have been analyzed together (usually about a week after the second blood test).

Approximate cost: $1,500

Modified Sequential Screen

Testing for: Down syndrome, Trisomy 13, Trisomy 18, Open Neural Tube defect

How it is performed:

- Ultrasound (Nuchal Translucency Measurement) between 11 weeks +1 day and 13 weeks +6 days
- Blood Test (measuring hormone levels PAPP-A, Free Beta hCG) between 9 weeks +1 day and 13 weeks +6 days
- Blood test (measuring hormone levels AFP, Free Beta hCG, uE3, inhibin A) between 15 weeks and 20+6 weeks

Results are available approximately one week after each step. First trimester risk is provided first. If the risk is high enough, and you want to pursue diagnostic testing, you can choose to have CVS (Chorionic villi sampling) immediately, or an amniocentesis at 15 weeks. If the risk is low, indeterminate from the first part of the test, or for women who want more accurate results, the second trimester blood test is done and revised risk is provided.

Detection rate:
-Down Syndrome: 95% if both parts are done- 82-87% if only the first part is done
-Trisomy 18- 90%
-Neural Tube defects: 80%

Pros:

- First trimester risk estimate is provided, which allows for an earlier diagnostic test
- This is a noninvasive test and poses no threat to the fetus-there is no increased risk of pregnancy loss following this test.

Cons:

- Some women who are determined to be high risk after the first trimester screening may choose to pursue diagnostic testing, which runs a small risk of miscarriage.

Approximate cost: $1,500

Quad Marker Screening

Testing for: Down syndrome, Trisomy 18, and Open Neural tube defects

How it is performed:

- Blood draw is performed (measuring hormone levels AFP, HCG, uE3, inhibin) between 15 weeks and 20 weeks +6 days
- Results are available approximately one week after the blood draw

Detection rate:

-Down syndrome: 81%

Pros:

- Test has only one part. It can be done at the office, no hospital visit necessary.
- This is a noninvasive test and poses no threat to the fetus- there is no increased risk of pregnancy loss following this test.

Cons:

- Not as accurate as other tests. Results are not available in the first trimester

Approximate cost: $500

*****The American College of Obstetrics and Gynecology recommends doing dual trimester screening (screening in the first and second trimester)

Alfa Fetoprotein (AFP)

Testing for: Risk of neural tube defect such as spina bifida or anencephaly

How it's performed:

- Blood draw is performed between 15 weeks and 20+6 weeks
- Results are available approximately one to two weeks after the blood draw

Detection rate:

- 75-90% of babies with neural tube defects are detected through the AFP screening
- Down syndrome: 85%

Pros:

- This is a noninvasive test and poses no threat to the fetus and there is no risk of pregnancy loss following this test.
- Test has only one part. It can be done at the office, no hospital visit necessary.

Cons:

- This test is a screening and is NOT diagnostic. If the test comes back positive, you would require more diagnostic testing.

Approximate cost: Approximately $150

Detailed Fetal Anatomy Screen Ultrasound Examination

Testing for: Birth defects and/or structural markers which can be related to some chromosomal abnormalities. This is performed between 18-22 weeks at UVM Medical Center.

This Ultrasound examination of the baby provides the most detailed fetal anatomic evaluation. This exam evaluates the fetal brain, spine, heart, urinary tract, lips, palate, arms and legs, and a number of other measurements that can help identify babies with our without birth defects, including major and minor markers for Down Syndrome.

The Ultrasound examination is designed to detect structural abnormalities. If the ultrasound exam results are considered normal, the risk of major structural defects is reduced to about 1%. However, this test cannot rule out chromosomal abnormalities. While it is able to assist with Down syndrome risk assessment, only about ½ of fetuses with Down syndrome will exhibit a marker on a detailed ultrasound.

Since the ultrasound cannot guarantee a baby does not have Down syndrome, we recommend that women who want the most accurate Down syndrome risk assessment also obtain other screening from maternal blood samples. For women who wish to know with complete certainty, only a diagnostic test (CVS or amniocentesis) can provide that assurance.

Pros:

- This is a noninvasive test and poses no threat to the fetus-there is no increased risk of pregnancy loss following this test.

Cons:

- Not a diagnostic test, some abnormalities develop later in pregnancy, and may be missed.
- Does not rule out chromosomal abnormalities or some birth defects.
- May identify a finding of unclear significance for the health of the baby.

Approximate Cost: $1,200
CPT code: 76811

Diagnostic Testing

These tests give a definitive answer if the baby has a major chromosomal problem.

CVS - Chorionic Villi Sampling

Testing for: Chromosomal abnormalities including Down syndrome, Trisomy 18 and Trisomy 13. It is the earliest diagnostic test available. It identifies chromosomal abnormalities with an accuracy of 99%.

How it's performed:

- During this procedure, a doctor obtains a small sample of the placenta. The procedure includes passing a small tube through the vagina and cervix, into the uterus, to obtain the sample. At times, the procedure cannot be performed vaginally. Therefore, a needle would be inserted through the abdomen after a local anesthetic is administered.
- CVS is done between 12 and 14 weeks of gestation, and the final results are available in 2 weeks

Pros:

- This is a diagnostic test which means its accuracy is in the 99% range (definitive, "Yes" or "No" answer)
- Performed early in the pregnancy

Cons:

- It is an invasive test which carries a miscarriage risk of 1:150 to 1:200
- There is the possibility of obtaining an inadequate sample for testing, identifying two different cell types, and failure of the cells to grow. If two different cells are identified, amniocentesis may be recommended as an additional diagnostic procedure.
- A maternal serum AFP is suggested at approximately 16 weeks to screen for open neural tube defects as CVS does not screen for this

Approximate cost: $1,500

Amniocentesis

Testing for: Chromosomal abnormalities- including Down syndrome, Trisomy 13, Trisomy 18, and Open Neural Tube Defects

How it is performed:

- Amniocentesis is a procedure in which the doctor obtains a small sample of amniotic fluid (which surrounds the developing fetus) by passing a fine needle through the abdominal wall and into the uterus. This is performed under ultrasound guidance.

Pros:

- This test is the less risky of the invasive diagnostic ("Yes" or "No") tests
- It predicts open neural tube defects with 97% sensitivity
- It predicts the major chromosomal defects, with an accuracy of 99.8%

Cons:

- It is an invasive test that carries a risk of miscarriage of less than 1:500 when it is performed after 15 weeks
- There is also a small risk of fetal puncture. The procedure is performed under ultrasound guidance to lower that risk.

Approximate Cost: $1,000

** Even though both Amniocentesis and CVS are definitive tests, they cannot rule out micro deletions or small chromosomal problems

Carrier Testing

This is performed by a blood test which can be done at any time prior to or during pregnancy. A carrier is an individual who does not develop the disease, but can pass on the gene with a mutation to his or her children.

If both parents are carriers of the same disease, there is a 1-in-4 chance, with each pregnancy, that their child will be born affected with that disease, a 2-in-4 chance that their child will be a carrier of that disease and a 1-in-4 chance that their child will be neither affected nor a carrier of that disease.

In an autosomal recessive condition (such as CF and most Jewish genetic diseases), persons who inherit only one mutated gene show no signs of disease, but persons who inherit two mutated genes will be affected by the disease.

Cystic Fibrosis Carrier Testing

In the Caucasian population, about 1 in 2500-3000 infants are born with Cystic Fibrosis, making it one of the most common genetic diseases.

Cystic Fibrosis does not affect intelligence, but does cause many health problems. Cystic Fibrosis can affect several organs in the body including the lungs, pancreas, intestines, liver, and reproductive organs. Children with CF have a thick mucus in their lungs, which increases the risk of infections and causes damage to the lungs. Cystic Fibrosis can cause problems with digestion, and children with Cystic Fibrosis are often small for their age. Currently, the average life expectancy of someone with Cystic Fibrosis is about 30 years. Individuals born with CF today are living longer as treatments improve.

At Maitri, we offer carrier testing for cystic fibrosis which is performed by a blood test. To be at risk to have a child with cystic fibrosis, both parents must be carriers. If both parents are carriers, there is a 25% chance that they will have an affected baby. Prenatal testing for Cystic Fibrosis is available through amniocentesis or Chorionic Villus sampling. There is no “in utero” gene therapy or cure for Cystic Fibrosis.

Approximately 1 in 25 Caucasians of Northern European descent are carriers of Cystic Fibrosis, and most carriers have no symptoms. Other ethnic groups are less likely to be Cystic Fibrosis carriers. A negative family history does not rule out the possibility of Cystic Fibrosis in your baby. Direct testing of the Cystic Fibrosis gene can detect approximately 85-90% of those who carry this specific gene. Thus, while most carriers are identified, it is possible to have a negative test result and still be a carrier for cystic fibrosis.

Carrier testing may not be covered by your insurance plan. This test only needs to be performed once. You do not need to be tested with each subsequent pregnancy. This test ALWAYS needs to be prior authorized by insurance before performing. In order to expedite this process please let us know as soon as possible that you would like this test performed as the prior authorization process can be cumbersome.

Approximate Cost: $1540
CPT: 81220

Ashkenazi Jewish Carrier Testing

There are a number of genetic diseases for which persons of Jewish heritage (at least one grandparent) are more likely to be carriers of than the general population. These diseases are all serious and can be fatal and or life altering to children born with them.

There are different genetic concerns for people of Ashkenazi Jewish background (German, French or Eastern European), and people of Sephardic (Mediterranean) or Mizrahi (Persian/Iranian or Middle Eastern) background. The conditions for which carrier screening is offered are more common in individuals of Ashkenazi Jewish descent than other ethnic groups because of specific mutations that occurred in the "founders" of the population. Because Jewish individuals historically married within their own ethnic group, these mutations increased in frequency over generations. Regardless of specific Jewish background, all Jewish and interfaith couples may have preconception carrier screening for the Jewish genetic diseases**.** This typically begins with an appointment with one of the Genetic Counselors at UVM Medical Center.

Screening is available for eleven genetic disorders. Carrier frequency is different for each condition – the overall chance of being a carrier for at least one of these diseases is 1 in 4 to 1 in 5 for someone of AJ descent. All of these disorders are also found in non-Jewish individuals, but with lower incidence (with the exception of CF).

As with Cystic Fibrosis testing, if one parent undergoes screening initially and all tests are negative, then no further screening or testing is needed.

Approximate Cost: $800

CPT codes: 81220, 81200, 81251, 81242, 81209, 81255, 81260, 81330, 81290, 81250, 81205

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