



GENETIC COUNSELING AND PRENATAL TESTING

GENETICS & IVF
Institute

Every parent hopes to have a healthy child. The good news is most babies are born healthy. However, sometimes a genetic disease or birth defect may occur. If your pregnancy is at increased risk for certain conditions, your Obstetrician may suggest that you meet with a genetic professional to learn more about available testing options. A Genetic Counselor can provide valuable information to women or couples who are planning a family. The following information reviews the genetic counseling process and presents some basic information on the most common screening and testing options available during pregnancy.

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GENETIC COUNSELING

Decisions about family planning, genetic testing and prenatal diagnosis are personal and complex. Genetic counseling is a process that will help you gather information and use that knowledge to make informed decisions that are in the best interest of you and your family. You will not be told what to do.

A typical appointment starts with a review of your family history, ethnicity, personal health and pregnancy history by one of GIVF's professional Genetic Counselors. Analysis of this information allows the Genetic Counselor to determine which, if any, tests would provide useful information for your reproductive and family planning. The appropriateness of prenatal diagnosis, genetic screening and other tests will vary, depending on your individual health and family history. The benefits, limitations, safety and accuracy of all the current testing options will be discussed with you. Deciding to pursue or decline a test are both equally valid choices. If desired, testing can usually be done on the same day as your consultation, or a separate appointment can be made.

If an appropriate genetic test is not currently available, the Genetic Counselor may be able to provide risk estimates based on the specific observed patterns in your family. Genetic testing is a growing field, with new tests being offered each year. You may also be able to enroll in research based studies.

Depending on the complexity of your situation and the number of questions you have, genetic counseling sessions vary from 30 to 60 minutes in length.

Common reasons for genetic counseling include:

- You, your partner or someone in your immediate family has a genetic disorder, birth defect, or mental retardation.
- You will be 35 years of age or more at the time of pregnancy delivery.
- You or your partner had a previous pregnancy with a birth defect or genetic condition.
- You have an abnormal pregnancy screening result.
- You have an abnormal CVS or amniocentesis result.
- Your ultrasound revealed a birth defect or marker associated with a genetic condition.
- You have a medical condition such as epilepsy or insulin-dependent diabetes that requires you to take medications during your pregnancy.
- You want to know more about screening for genetic diseases common in your ethnic background.
- You have experienced three or more miscarriages with no known explanation.
- You are seeking information about available screening and diagnostic testing or are undecided about the best option for you.



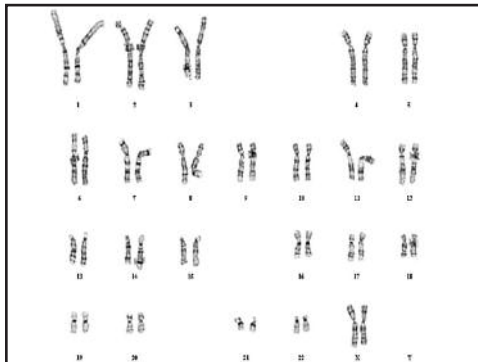


WHAT ARE CHROMOSOMES?

Humans grow and develop based on the instructions contained in our genetic material. A normal human cell should contain exactly 46 chromosomes. This material is bundled into **Chromosomes**. They are matched into 23 pairs. Pairs one through 22 are numbered by size and are the same in males and females. The 23rd pair is referred to as the sex chromosome pair. Typically, females have 2 X chromosomes, while males have an X and a Y. The short-hand way to refer to a normal set of chromosomes is 46,XX for females and 46,XY for males.



46,XY



46,XX

At conception, an egg containing 23 chromosomes from the woman combines with a sperm containing 23 chromosomes from the man. The two sets of genetic information combine so that the growing embryo has 23 pairs, or 46 total chromosomes, and is a mixture of genes from both biological parents.



WHAT ARE GENES?

Chromosomes contain smaller units of genetic material called **DNA**. DNA is a sequence of letters that spell out the genetic code. The DNA is organized into words and sentences called **genes**. Humans have approximately 20,000 genes and each one influences a part of development. Most genes come in pairs. One copy is inherited from our mother and one from our father. A change in the spelling of a DNA sequence or the gene is called a mutation.

Every person's DNA contains mutations which are usually harmless. However, some mutations are responsible for causing disease. A detailed assessment of your family history can determine if a pregnancy is at increased risk for a specific condition.

Some diseases are caused by a mutation in one copy of a gene. We refer to these conditions as **dominant genetic diseases**. Dominant diseases can be passed directly from one parent to a child. Examples of dominant genetic diseases include Achondroplasia and Huntington disease. For some dominant genetic diseases, there may be specific DNA tests available.

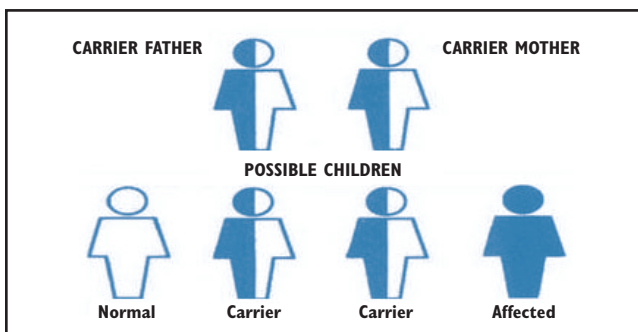
Other diseases are caused when a mutation occurs in both copies of a gene. These diseases are referred to as **recessive genetic diseases**. Examples of recessive genetic diseases include Sickle Cell Anemia and Cystic Fibrosis. In a recessive disorder, a carrier has one normal copy and one abnormal copy (mutation) of the disease-causing gene. Carriers are usually healthy since the presence of one normal copy of the gene is enough to prevent the disease. It is estimated that each individual is a carrier of four to eight recessive genetic diseases. Fortunately, most recessive diseases are rare and occur at a rate of 1 in 50,000 to 1 in 100,000 births. In most cases, it is not possible to anticipate if a rare recessive disease may occur, as there is usually no family history suggestive of the condition and carrier screening is frequently not available. Carrier screening is available for some common recessive diseases known to occur with an increased frequency in certain ethnic groups. (see page 4)

A smaller number of diseases are related to gene mutations on the X or Y chromosome and therefore affect males and females differently. These diseases are referred to as **sex-linked genetic diseases**. Some common examples include Hemophilia and color-blindness. Depending on your family history, testing for a sex-linked genetic disease may be available.



RISKS BASED ON ETHNICITY

Some recessive genetic conditions are known to occur with an increased frequency in certain ethnic groups. When both parents are carriers of the same recessive disease, there is a 1 in 4 (25%) chance that the pregnancy will have the disease, a 1 in 2 (50%) chance that the pregnancy will be a carrier, like the parents, and a 1 in 4 (25%) chance that the pregnancy will not be a carrier or have disease.



When there is no family history of a disease, there is still a risk for recessive diseases based on your ethnicity. Carrier status for a recessive disease is commonly passed silently from generation to generation. Frequently, carriers are identified only by a specific genetic test. Following is a table listing some of the more common diseases and carrier frequencies in different ethnic groups

ETHNIC GROUP	DISEASE	CARRIER FREQUENCY
Ashkenazi Jewish	Canavan Disease	1 in 40 (2.5%)
	Tay Sachs Disease	1 in 30 (3%)
	Cystic Fibrosis	1 in 25-29 (4%)
	Familial Dysautonomia	1 in 30 (3%)
African American/ West Africa	Sickle Cell Anemia	1 in 6-12 (8-16%)
	Other Hemoglobinopathy	1 in 30-75 (up to 3%)
European Caucasians	Cystic Fibrosis	1 in 25-29 (4%)
Mediterranean/ South Asian	Beta Thalassemia	1 in 20-30 (3-5%)
SE Asian (Loas, Vietnam, Thailand)	Alpha Thalassemia	1 in 20 (5%)
	Beta Thalassemia	1 in 30 (3%)



RISKS BASED ON FAMILY HISTORY

A family history of known genetic diseases, birth defects and/or genetic conditions can influence the health of a pregnancy, affect childhood development or determine who will be susceptible to certain adult onset conditions. If you are concerned about your genetic family history, a Genetic Counselor can help you determine what your specific risks may be. As previously discussed, testing may be available for dominant, recessive or sex-linked genetic diseases. Some of the most common concerns are due to multifactorial traits or structural chromosome rearrangements.

MULTIFACTORIAL TRAITS

The most common birth defects and diseases are those that occur due to the complex interactions and combinations of maternal, environmental and genetic influences. These conditions are usually called multifactorial traits, referring to the many different factors that come together to cause the problem. Common multifactorial birth defects include congenital heart defects and cleft lip. Spina bifida, or open neural tube defect, is a multifactorial trait that occurs in approximately 1 or 2 in 1000 births. Taking the vitamin folic acid (folate) helps reduce the chance of having a baby with spina bifida. Common examples of multifactorial diseases include depression, diabetes, and high blood pressure.

In most cases predictive genetic testing is not available for multifactorial traits. However, a Genetic Counselor can perform a detailed review of your family history to assess your personal risk factors. You will be asked questions about your medical history and the history of your siblings, parents and cousins. Depending on your specific concerns, information may be needed on more distant family members as well. Your partner's personal, medical and family history will also be reviewed. Any genetic patterns will be discussed with you. You may receive information about recurrence risks and early warning signs, or you may be offered ways to gather more information.

STRUCTURAL CHROMOSOME ABNORMALITIES

Random changes in the number of chromosomes can occur in any pregnancy (see *age related risks* on page 6). A second type of chromosome abnormality is a change in the structure or organization of the chromosomes. These changes include deletions (a small missing piece), inversions (a piece flipped upside down), insertions (an added piece) or translocations (exchange of pieces involving two or more chromosomes). Structural changes are not associated with maternal age. They can be the cause of multiple unexplained miscarriages, birth defects or apparent infertility.



RISKS BASED ON AGE

As a woman gets older, the chance that she may have an abnormal pregnancy involving an extra or missing chromosome increases. There appears to be no association with most family histories, ethnicity, diet or lifestyle.

When a fertilized egg does not contain exactly 46 chromosomes, the resulting pregnancy will have a chromosome abnormality. It is not known why a particular egg or sperm may have missing or extra chromosomes.

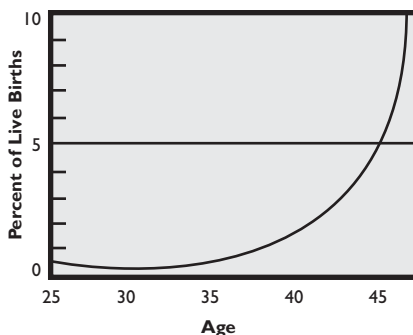
A COMMON EXAMPLE IS DOWN SYNDROME

In Down syndrome there is an extra copy of chromosome #21, creating a total of 47 chromosomes. For this reason, it is also known as Trisomy 21. The chromosomes of a person who has Down syndrome are shown here.



Approximate chances of having a liveborn child with a chromosome abnormality at different maternal ages

MATERNAL AGE	CHANCE FOR ABNORMALITY
Age 20	1 in 525
Age 25	1 in 475
Age 30	1 in 380
Age 35	1 in 180
Age 38	1 in 105
Age 40	1 in 65
Age 42	1 in 40
Age 45	1 in 20





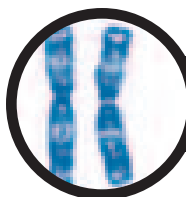
CHOOSING A TEST: DIAGNOSTIC VS. SCREENING

It is important to understand your testing options during pregnancy. Although there is no test that covers all genetic diseases or birth defects, diagnostic and screening procedures are available to evaluate your pregnancy. The next few pages provide some background information on common diagnostic and screening procedures.

A **diagnostic** test provides definite information for specific conditions. There is no medical procedure that tests for all diseases. While no test can give a complete guarantee, diagnostic testing is the most accurate technology available for detecting chromosome or genetic problems during a pregnancy. Commonly available diagnostic procedures include CVS (chorionic villus sampling), amniocentesis, and certain types of high-resolution fetal ultrasonography. Most diagnostic tests are invasive and carry a small risk of complications.

A **screening** test provides a personalized risk assessment for certain medical conditions. Blood tests and ultrasounds are commonly available genetic screening tests in pregnancy. Screening tests are not invasive and carry no risk to the pregnancy. A 'normal' result on a screening test does not mean you have a healthy pregnancy, but your chances of having a baby with certain problems are lower than most. If you have an 'abnormal' result from a screening test, you most likely have a healthy pregnancy, but you may want to have a diagnostic test performed for definite information.

The decision about whether to opt for a screening or diagnostic test is personal. There is no right or wrong choice. As you discuss your options with a Genetic Counselor you should consider how much information you wish to gain during your pregnancy and how you feel about the chance for complications that accompany some of the testing options. During your appointment, your Genetic Counselor will outline the benefits and limitations of each test and review your personal situation so that you are comfortable with your final decision.



DIAGNOSTIC OPTIONS

Prior to having a chorionic villus sampling (CVS) or amniocentesis at GIVF, you will meet with a Genetic Counselor to discuss the test. After reading the following information, write down any questions that you may have and take them to your appointment.

If you are taking a blood thinning medication such as Lovenox or Fragmin, please contact a GIVF Genetic Counselor at least 2 days prior to your appointment for directions.

CHORIONIC VILLUS SAMPLING (CVS) (10TH THROUGH 12TH WEEK)

CVS is a specialized alternative to amniocentesis. This test can be helpful to couples who desire to have highly accurate test results as early as possible in the pregnancy. It involves removing a small amount of tissue called the chorionic villi, which is located on the outside of the fetal gestational sac and will later become the placenta. The chorion is a fetal tissue, and shares its genetic makeup with the fetus, not the mother. The chorion has many small, finger-like projections on its outer surface, and a few of these may easily be removed without disturbing the pregnancy. The chorionic villi cells may be used for chromosome analysis or other genetic testing. The chorionic villi cannot be used to test for open neural tube defects.

CVS is available at GIVF from 10 to 13 weeks of pregnancy. The CVS may be performed transabdominally by guiding a thin needle through the abdominal wall to the chorionic villi, then withdrawing a small amount of this tissue (See diagram on page 10, part A). Occasionally, particularly if the thickest location of the villi is in the lower portion of the uterus, the CVS is performed transcervically by using a thin flexible plastic catheter (hollow tube) which is guided through the cervical opening, somewhat like having a Pap smear done. This catheter is then used to remove a small amount of the villi (See diagram on page 10, part B).

Most women do not report the CVS procedure to be painful. It usually takes a minute or two to perform, and is commonly described as feeling like pressure rather than pain. Some women experience mild cramping for up to a few hours afterwards or rarely experience light spotting that usually goes away within a day or two.



DIAGNOSTIC OPTIONS

Because the procedure involves going inside the uterus, there is a small chance of bleeding or infection. Any of these complications may cause a miscarriage. At GIVF, we have observed this risk to be approximately 1 in 200 (0.5%). GIVF is one of the most experienced centers in the world at performing this first trimester diagnostic test, having provided over 30,000 women with this early option.

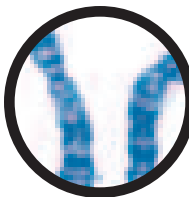
AMNIOCENTESIS (15TH THROUGH 22ND WEEK)

During an amniocentesis a small amount (usually 2 tablespoons) of amniotic fluid that surrounds the fetus is removed. The amniotic fluid contains cells that have been shed by the fetus during normal development. These cells may then be used for chromosome tests and/or specific genetic tests. The fluid itself is tested for the level of alpha fetoprotein (AFP) or for biochemical genetic disorders, if appropriate.

Amniocentesis is available at GIVF from 15 to 22 weeks of pregnancy. The amniocentesis procedure involves guiding a thin needle through the mother's abdomen and into the amniotic sac (See *diagram on page 10*). Ultrasound is used to determine the location of the fetus and the best place to withdraw the fluid. The entire procedure is done under ultrasound guidance.

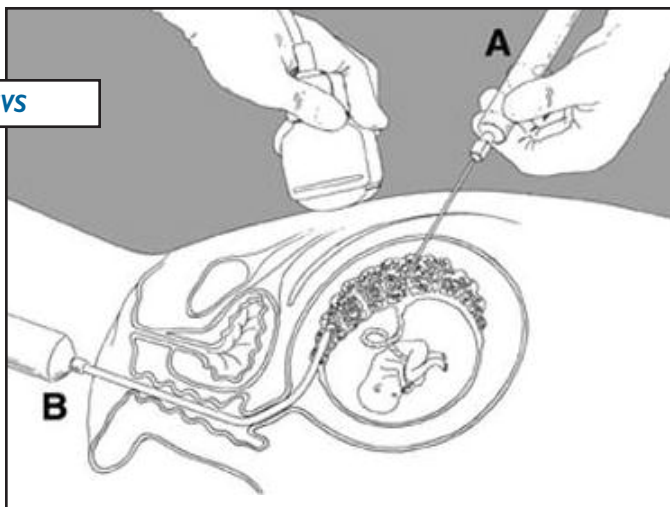
Most women do not report the amniocentesis procedure to be painful. It usually takes a minute or less to perform, and is commonly described as feeling like pressure rather than pain. Some women experience mild cramping for up to a few hours afterwards.

Because the needle must pass through the amniotic sac, there is a chance of the fluid leaking or the sac rupturing. As with all invasive procedures, there is also a chance that an infection may occur. Any of these complications may cause a miscarriage. The risk for complications from an amniocentesis when performed by the highly experienced physicians at GIVF is approximately 1 in 400 (or 0.25%). The board-certified clinicians at GIVF have provided amniocentesis testing for over 40,000 women.



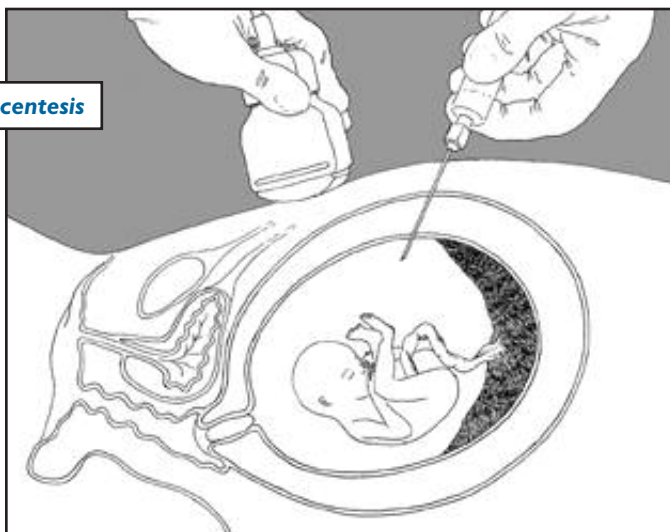
DIAGNOSTIC OPTIONS

CVS

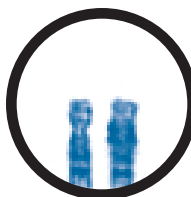


The diagram above shows the transabdominal (part A) and transcervical (part B) methods used for Chorionic Villi Sampling (CVS)

Amniocentesis



The diagram above shows the method used for Amniocentesis.



DIAGNOSTIC OPTIONS

COMMON REASONS FOR CVS OR AMNIOCENTESIS

- Maternal age of 35 years or more at expected time of delivery
- Abnormal screening results in the first or second trimester
- Ultrasound finding suggesting a higher risk for a chromosome abnormality
- Previous pregnancy or family history of certain chromosomal or genetic disorders
- Pregnancies at risk for certain genetic diseases

MEDICAL CARE AFTER YOUR CVS OR AMNIOCENTESIS

Most women do not experience significant medical complications after chorionic villus sampling (CVS) or amniocentesis. Strict bed rest is usually not required; however, we will recommend that you minimize physical activities for at least two days, or 48 hours. We recommend no exercise or heavy lifting (items over 10 pounds) or sustained standing for the first 48 hours following either procedure. You may walk short distances, travel by car or plane and continue your normal pregnancy diet after amniocentesis or CVS. Minimizing stair use is recommended. Showering is permitted but we ask you to refrain from taking a bath or placing medication in the vagina for 48 hours.

You may return to work as long as your job does not involve standing, heavy lifting or physical exertion. We can provide documentation for your employer, if this is necessary.

If you have any questions regarding appropriate activities, please contact your Genetic Counselor.





SCREENING OPTIONS

FIRST TRIMESTER SCREENING (11TH THROUGH 13TH WEEKS)

A newer screening option, the First Trimester Screen (FTS), is available at GIVF to women of all ages who are interested in early information about the health of their pregnancies. The FTS is the earliest screening option available in pregnancy and poses no health risks to the pregnancy. Offered during the 11th through 13th weeks in pregnancy, this screening combines a specialized ultrasound examination with maternal blood testing.

The **First Trimester Screen (FTS)** involves an ultrasound examination measuring the tiny fluid filled sack at the back of the fetal neck, called the **nuchal translucency**. An increased measurement may indicate a chromosomal disorder, a congenital heart defect or other birth defect, but can also be seen in normal fetuses. A maternal blood test that measures pregnancy hormones (β -hCG and PAPP-A) is combined with the ultrasound measurement and maternal age to calculate a specific risk for Down syndrome and for Trisomy 18 or 13.

Current studies indicate the FTS has a greater detection rate for Down syndrome and Trisomy 18 than second-trimester screening. In addition, the FTS screens for Trisomy 13, which is not included in second trimester screening. However, the FTS does not screen for open neural tube defects, so a detailed ultrasound or AFP only measurement is recommended in the second trimester.

One of GIVF's Genetic Counselors will call you to inform you of your results, which are usually available in three to four business days. If your results indicate an increased risk, additional diagnostic testing will be discussed with you by the Genetic Counselor. If appropriate, this testing can be performed at GIVF.

If your pregnancy is already at high risk for chromosomal disorders due to maternal age or other factors, results from your FTS may be helpful in deciding if a CVS is right for you. Since CVS is only available until early in the 13th week, it is best to schedule your FTS so that you have time to consider your results.

SECOND TRIMESTER SCREENING (15TH THROUGH 20TH WEEKS)

For many years the established standard of care for women under 35 has been second trimester screening in the obstetrician's office. It has multiple names including: maternal serum screening, triple screen, quadruple screen, or alpha feto-protein (AFP) test.

Second trimester screening measures three or four different pregnancy hormones (AFP, human chorionic gonadotropin (hCG),



SCREENING OPTIONS

unconjugated estriol (uE3), and dimeric inhibin A (DIA)) produced by the pregnancy. The levels of these hormones are collectively compared to estimate risks for three conditions: open neural tube defects (spina bifida), Down syndrome (Trisomy 21), and Trisomy 18. The results also incorporate maternal age, recognizing the chance for Down syndrome and Trisomy 18 increases with advancing maternal age.

A positive, or abnormal, screening result does not mean that your pregnancy has a genetic problem. Abnormal screening results only indicate that the pregnancy is at increased risk for an abnormality and that additional, more definitive, fetal testing such as amniocentesis should be considered. A negative, or normal, screening result indicates the pregnancy is at a low risk for these abnormalities. Second trimester screening alone cannot rule out any of these conditions. Therefore it is important not to make decisions about a pregnancy based only on the blood test.

GENETIC ULTRASOUND (18TH THROUGH 22ND WEEKS)

High-resolution fetal ultrasonography (also called Level II ultrasound) uses sound waves produced by an ultrasound machine to create an image of the fetus called a sonogram. The genetic ultrasound is usually performed by a specialty center such as GIVF, in order to evaluate the detailed growth and physical development of the fetus.

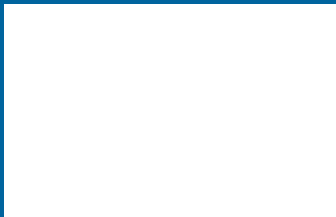
The ability of the ultrasound to detect physical variations is affected by gestational age, the fetal position and the ability to visualize clear images. In all pregnancies there is a 3-4% chance to have a child with a birth defect. If there has been a previous pregnancy with a birth defect or a family history of a birth defect or genetic syndrome, this risk may be increased. However, small physical abnormalities may be undetectable even under the best circumstances.

During the fetal ultrasound, pregnancies are evaluated for the presence or absence of specific ultrasound markers, or physical variations. Many markers are also seen in healthy pregnancies and carry no clinical significance. However, the presence of one or more markers may increase the chance for a chromosome disorder or other genetic syndrome. Ultrasonography alone does not diagnose Down syndrome or other chromosome disorders; only the CVS or amniocentesis can provide this information during pregnancy.

If an ultrasound marker or major physical abnormality is identified by your Level II ultrasound at GIVF, you will be immediately informed and counseled regarding the finding(s). Additional genetic counseling, testing, or follow-up evaluations may be recommended.



Our team of physicians, genetic counselors, ultrasonographers, and administrative staff is dedicated to providing comprehensive, compassionate care for each patient of Genetics & IVF Institute. If you would like more information about the services described in this brochure, or would like to schedule an appointment, please call (703) 698-7355.



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