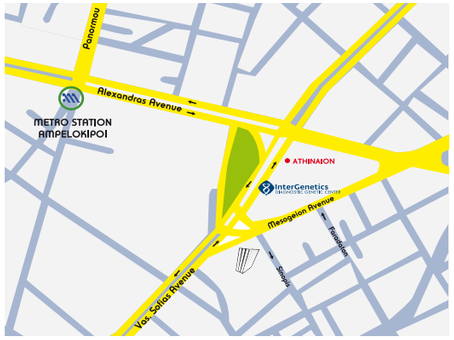

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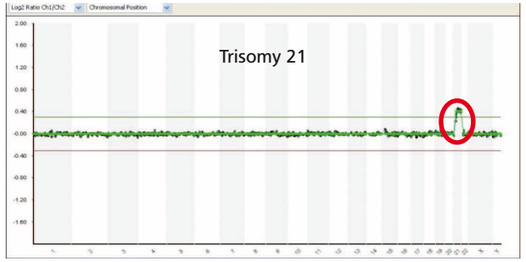
This test will detect genetic syndromes and other abnormalities that appear suddenly in an otherwise normal pregnancy and usually without a previous history or ultrasound findings. Therefore, it may be applied to all samples requiring prenatal diagnosis. For all the aforementioned reasons, the test is nowadays gradually replacing traditional karyotype analysis.



4. Prenatal testing for neurogenetic disorders

In all prenatal chromosomal diagnosis tests, both standard karyotype analysis and prenatal molecular karyotype (from amniotic fluid or CVS samples), we perform, without additional charge, a specially designed panel of neurogenetic disorders, which includes the diagnosis of Fragile X syndrome (FRAXA) in the majority of affected male embryos only, and of Spinal Muscular Atrophy (SMA) detecting approximately 95% of affected embryos.

Which diseases may be detected and how is prenatal genetic testing performed concerning gene disorders

Today, more than 8,000 diseases are known to be associated with mutations in one or more genes. Examples of common gene disorders are β-thalassemia and cystic fibrosis. At present, there is no single prenatal test (the way karyotype analysis is applied for chromosomal abnormalities) which may massively diagnose all gene disorders. Therefore, prenatal testing can be applied only in families where we already know the mutation(s) in one or both parents and this prior knowledge is an absolute requirement for prenatal diagnosis in these cases. Genetic testing is performed from a fetal DNA sample, primarily from chorionic villi cells or amniotic fluid cells, directly or after culture of the cells.

In all cases requiring prenatal genetic testing, parallel analysis of polymorphic DNA markers is performed from a maternal blood sample, in order to exclude the presence of maternal cell contamination.

Therefore, the fetal sample should be accompanied by 1-2ml of a peripheral blood sample from the mother.

Genetic counseling

Proper clinical genetic assessment of each case and genetic counseling, both before and following the test, is essential in order to determine the appropriate strategy for laboratory testing and to interpret correctly the concepts of pathological and normal.

InterGenetics
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PRENATAL TESTING FOR GENETIC DISORDERS

- ✓ *More than 85,000 tests and 32 years experience*
- ✓ *Multi-faceted testing, with multiple options and in-depth analysis, using the latest molecular genetics and cytogenetic techniques*
- ✓ *Comprehensive genetic counseling*
- ✓ *Pioneering application of an extended prenatal panel (EPP) followed by*
- ✓ *Pioneering application of molecular karyotype (array CGH) as a routine test in prenatal chromosomal diagnosis*

What is prenatal testing and why is it performed

Prenatal testing refers to all the investigations carried out during pregnancy, in order to uncover severe genetic diseases in the fetus, which occur with an overall frequency of approximately 1/20 pregnancies. Prenatal testing may involve:

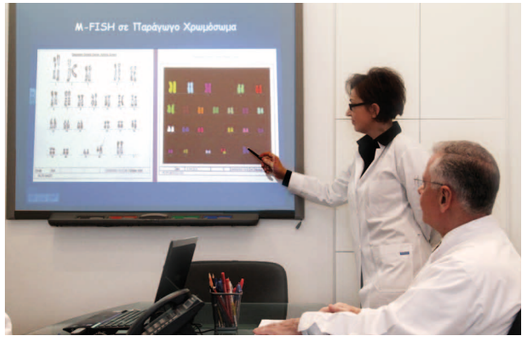
1. risk assessment for potential genetic defects, especially chromosomal abnormalities, such as Down syndrome, mainly in the 1st trimester of pregnancy, with the integration of sonographic markers such as nuchal translucency and biochemical markers in maternal blood, which in the 1st trimester are PAPP-a and β-hCG

2. diagnosis of genetic abnormalities in the fetus, by direct analysis of genetic material, chromosomes or DNA, from embryonic cells, and finally

3. diagnosis of severe congenital anomalies of the fetus, using ultrasound examination

When is prenatal genetic testing performed

- when the mother is >35 years old (advanced reproductive age)
- due to a high risk for chromosomal abnormalities of the embryo, following fetal ultrasound examination and / or prenatal biochemical marker testing
- parents carriers of a genetic abnormality, e.g. both parents carriers of β-thalassemia or parent carrier of a chromosomal abnormality
- family history or previous pregnancy with a recognizable genetic disorder



How is prenatal genetic testing performed

In order to be able to perform genetic testing, it is first necessary to obtain genetic material from the fetus. This may be done mainly:

a) by amniocentesis, which involves drawing an amniotic fluid sample in the 2nd trimester of pregnancy (17th – 22nd week). Today, it has been shown that the risk of a complication due to the procedure is extremely low, approximately 1/500 and therefore amniocentesis is regarded as relatively safe.

b) by chorionic villi sampling (CVS), which is performed in the 1st trimester of pregnancy (11th – 13th week) and the sample has the same genetic makeup as the fetus. The risk of a complication due to the procedure is approximately 1/100.

Prenatal chromosomal diagnosis

The study of the chromosomes in prenatal diagnosis serves to uncover potential pathological abnormalities related to numerical or structural changes of the chromosomes of the fetus. Depending on the type of changes detected, the geneticist will assess the risk to the fetus for being affected from a syndrome or other genetic disease.

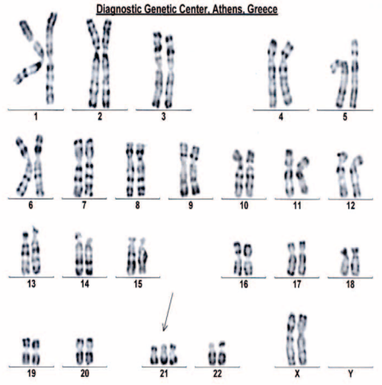
What are the tests for prenatal chromosomal diagnosis

1. Rapid aneuploidy detection by QF-PCR.

This test is completed within 24 hrs and will detect only numerical chromosomal abnormalities for chromosomes 13, 18, 21, X and Y (e.g. Down syndrome) and also the presence of the F508del mutation of cystic fibrosis. The method can be applied both in chorionic villi cells (1st trimester) and in amniotic fluid cells (2nd and 3rd trimester of pregnancy).

2. Karyotype analysis of amniotic fluid or chorionic villi cells.

Is the numerical and structural analysis of chromosomes, as visualized under a microscope, following culture of about 10 days and the test is completed in two weeks. The resolution of the method is relatively limited, compared with recent methods currently applied routinely. Today, the proportion of abnormal embryos revealed by this test is approximately 2/100 samples analyzed.



3. Prenatal molecular karyotype of amniotic fluid or chorionic villi cells.

This method, also known as array comparative genomic hybridization (array CGH), permits the 'micro-analysis' of the human genome at 100-1,000 fold higher resolution compared to classic karyotype, for the detection of abnormalities of whole chromosomes (e.g., trisomy 21, etc.), but also for the detection sub-microscopic abnormalities involving small areas of the chromosomes which are either missing (deletions) or are duplicated (duplications), and which are associated with a large number of genetic diseases and syndromes (about 120), presenting with different congenital anomalies and/or mental/psychomotor retardation and which would have otherwise remained undiagnosed through classic karyotype analysis.

Currently, the proportion of abnormal embryos detected by this test is approximately 3/100 samples analyzed. Furthermore, the application of the test does not require the lengthy culture of amniotic fluid or chorionic villi (CVS) and therefore it is completed within 4-5 days, while it requires a smaller amount of sample, for example 5-8 ml of amniotic fluid.