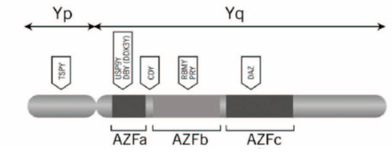
1. Measurement of the sperm ploidy index
2. Measuring of the percentage of apoptosis
3. Measurement and assessment of the DNA fragmentation index (DFI)
4. Measurement of leukocyte count in the sample
5. Analysis of acrosome integrity

The application flow cytometry as it has evolved today is regarded as a state-of-the-art reference method for the study of sperm.



4. Molecular genetic testing for Y chromosome microdeletions

Microdeletions of chromosome Y (del Y), namely the absence of specific chromosomal regions which contain genes important for the normal production of sperm, are often the cause of reproductive problems in men.

These microdeletions, depending on the region missing, may lead to azoospermia, oligozoospermia or oligo-teratozoospermia. In general, Y chromosome microdeletions are detected in approximately 10% of infertile men with the above indications.

The analysis is useful because, besides uncovering the etiology of infertility, the couple is informed about the risk of inheritance of the defect to male offspring and most importantly, will aid effectively in planning the appropriate IVF strategy.

5. Molecular genetic testing for cystic fibrosis

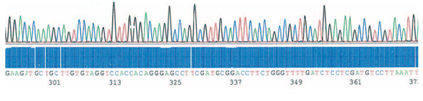
Cystic fibrosis (CF) is the most common genetic disease in the white Caucasian population, with serious consequences for the health and life span of the affected person.

There are two major problems with cystic fibrosis: a) carriers of the disease are perfectly healthy without any symptoms and therefore without some way to recognize them, and b) the gene (CFTR) is relatively large in size with many possible mutations (>1,500).

Furthermore, mutations in the CFTR gene are not identical in frequency in all populations, with important differences, for example, between ethnic groups of Northern Europe and the Mediterranean.

Especially in the investigation of male infertility, it is very important to note that a certain category of specific mutations in the CFTR gene in men may lead to congenital bilateral absence of the seminal duct (CBAVD), presenting with obstructive azoo-oligospermia. CBAVD is responsible for 1,5% of male infertility in general and ~80% of patients with CBAVD have at least one mutation in the CFTR gene.

Therefore, in men with obstructive azoospermia, it is highly recommended to test for the possible presence of cystic fibrosis mutations in order to confirm the diagnosis. Furthermore, the test is also important because if a mutation is found, due to the high carrier frequency in the population (1/25), testing of the mother must be performed to determine the couple's risk for having an affected child.



6. Molecular genetic testing for thrombophilia risk

Idiopathic thrombosis is a multi-factorial disease which occurs when a person predisposed to thrombosis is exposed to clinical risk factors.

Thrombophilia is not a disease in itself, but may be associated with a disease (e.g. cancer), exposure to drugs (e.g. contraceptives), other factors (e.g. pregnancy or postpartum) or may be inherited.

Thrombophilia may also be associated, with relatively low frequency, with spontaneous abortions and possibly stillbirth or other pregnancy complications. Currently, there is no single laboratory test or a specific battery of tests which may determine all types of thrombophilia.

Comprehensive laboratory testing for thrombophilia is recommended internationally to include the determination of the levels of several known hemostatic coagulation factors in plasma (e.g. fibrinogen, prothrombin time, etc.) and the genotypes of 4-5 specific mutations/polymorphisms (e.g. Factor V Leiden and R2, Factor XIII, Prothrombin G20210A, etc.) which are known to be associated, to varying degrees, with the genetically determined risk for thrombophilia.

Analysis of many other polymorphisms and mutations, which have no proven association with thrombophilia (e.g. ACE I/D, β-Fibrinogen -455G> A, APOE e2/e3/e4, ApoB R3500Q, etc.) is not recommended and will lead to erroneous interpretations.

Finally, it is important that the final test report of full laboratory testing for thrombophilia, and especially of genetic testing, clearly states the estimated risk in order to facilitate prompt management of the case.

InterGenetics
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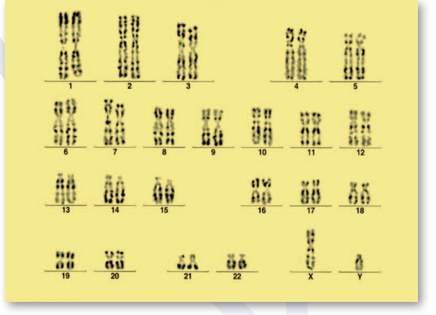
GENETIC TESTING IN REPRODUCTION



In-depth investigation through:

- ✓ *comprehensive clinical genetic evaluation, leading to the appropriate testing strategy*
- ✓ *analysis of chromosomal abnormalities utilizing high resolution techniques*
- ✓ *specially designed genetic testing for cystic fibrosis mutations*
- ✓ *multi-parametric sperm analysis by flow cytometry*

Infertility is today one of the most serious, frequent medical and social problems. The statistics speak for themselves:

- 1/6 couples experience reproductive problems
- 1/3 women over 35 are infertile, and
- 1/25 men have sperm-related problems

In ~ 80% of cases the problem is due to only one of the two partners (shared equally), in ~10% of cases both partners are infertile while in the remaining ~10% of cases the problem is of unknown etiology. What matters is that in 2/3 of the cases where the problem has been diagnosed, there is a solution and the couples succeed in having a child.

Genetic testing in couples with reproductive problems (miscarriages, sperm-related problems, repeated IVF failures, etc.) is designed according to the indications.

Genetic testing includes:

1. Peripheral blood karyotype

The test is applied in cases with problems related to male or female infertility of known or unknown etiology and in couples with multiple miscarriages, especially in the 1st trimester.

It is possible that the karyotype of an individual may reveal the presence of a numerical abnormality involving the sex chromosomes X and Y, in all the cells or in a proportion of the cells, and this may cause reproductive problems.

It is also possible that the karyotype may detect the presence of a balanced structural chromosomal abnormality, e.g. chromosomal translocations or inversions, which means that although there is no danger to himself, the person is a carrier (to some extent) of chromosomally unbalanced gametes, which when fertilized they lead to embryos with unbalanced genetic material, which are then usually quickly aborted or (rarely) they are born and are affected.

Due to its special importance, the test is internationally recommended and applied to all couples with reproductive problems, especially those undergoing assisted reproduction (IVF).

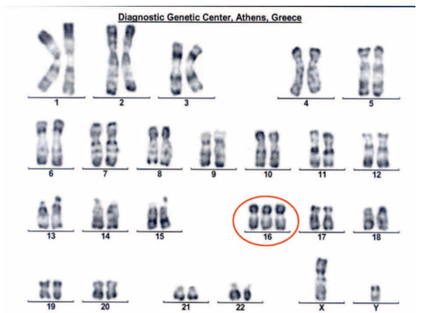
2. Karyotype of products of abortion

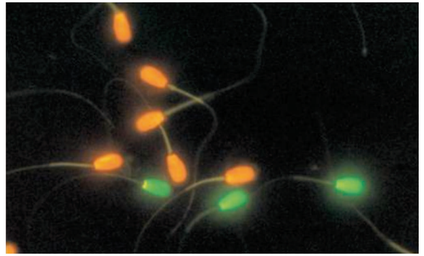
The test is particularly useful for uncovering chromosomal abnormalities, which are the cause of 60% of spontaneous abortions in the 1st trimester and 20% in the 2nd trimester.

About 95% of chromosomal abnormalities detected in products of abortion are numerical abnormalities (extra or missing copies of a chromosome), occurring for the first time in the couple and therefore sporadic and in this case the parental blood karyotypes are normal. In the remaining 5% of cases a structural chromosomal abnormality is detected in the abortus, which is usually inherited from a normal parent-carrier.

If a chromosomal abnormality is detected, then the cause of pregnancy loss in the couple has been established and any other non-genetic investigations are of secondary importance and referral for further time-consuming and costly testing is avoided. It is therefore easily to realize why the application of this test is of special value in all products of abortion.

Please note that the tissue sample of choice for genetic analysis of products of abortion is chorionic villi (CVS) and sampling should be performed with care in a manner that minimizes the presence of maternal cell contamination.





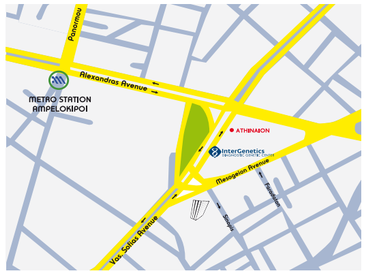
3. Sperm analysis by flow cytometry

It is known that, among other things, genetic and epigenetic lesions affect the 'quality' of sperm and lead to male infertility.

For example, increased rate of aneuploidy in sperm occurs with relatively high frequency in infertile men, particularly those with non-obstructive azoospermia while increased rate of apoptosis in sperm (programmed cell death) leads to a population of spermatozoa with low fertilization potential and preservation support of the developing fetus in the early stages.

The hitherto commonly applied laboratory techniques (FISH) for the study of aneuploidy and apoptosis in sperm, have significant limitations, such as very expensive reagents, long processing time, failure to analyze a large number of sperm cells, etc. Therefore, the laboratory investigation of these parameters still remains largely subjective and incomplete.

In contrast, analysis of sperm by flow cytometry allows, for example, the simultaneous, objective and accurate:



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