PRENATAL GENETIC DIAGNOSIS

Prenatal genetic diagnosis consists on the detection of genetic or chromosomal abnormalities before birth.

This kind of diagnosis is recommended for couples wherein one member is a carrier of a genetic or chromosomal abnormality which may transferred to the progeny. Furthermore, it is also used in these cases where would exist a high likelihood of acute malformations even incompatible with life. Such relevant cases may be: advanced maternal age, previous problematic pregnancies. Estimations say that approximately 4% of the total of childbirth has some type of congenital defect.

Finally, prenatal diagnosis is recommended after obtaining high risk of chromosopathy at EBA-Screening (Echography and Biochemical screening for Aneuploidies), test carried out between weeks 11-13 of pregnancy. Below is the list where prenatal genetic diagnosis is recommended:

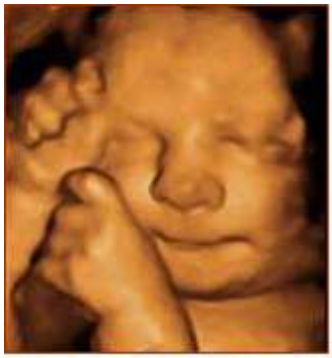
- ⇨ Advanced maternal age (from 30-35 years).
- ⇨ Advanced paternal age (from 50 years).
- ⇨ Positive chromosopathy biochemical study (risk over 1/270).
- ⇨ Previous sons with Down syndrome or others chromosomal aberrations.
- ⇨ Chromosomal abnormalities at any other member of the couple's family.
- ⇨ Familiar history of mental retardation, chromosomal aberrations or malformations.
- ⇨ Hereditary diseases antecedents.
- ⇨ Sterility problems or recurrent abortions.
- ⇨ Ultrasounds scan result suspecting of chromosomal aberrations or malformation.
- ⇨ Exposure to various harmful agents: contraception, drugs, radiation, etc.
- ⇨ Several obstetric situations: lack or excess of amniotic fluid in the fetus, delay on fetal growth, abnormalities on fetal cardiac rhythm,

To develop prenatal genetic diagnostics geneticists & gynecologists must obtain fetal cells using an invasive method ultrasound-guided: either amniocentesis or chorionic biopsy.

After sample collection it is necessary to extract fetal DNA in a sufficient quantity and quality to develop subsequent assays. At this point, it is worthy noting that the development in the recent years of the so-called next generation sequencing –and other developments on molecular biology– allow the production of millions of DNA sequences at an unprecedented speed with an increasing reduced cost per nucleotide. Although these technologies also became more demanding with regard to the quality and quantity of DNA usually needing culturing collected samples.

Amniocentesis is carried out between weeks 15-18 of pregnancy, and consists on the extraction of a small volume of amniotic fluid which surrounds the fetus by a puncture through the maternal abdomen. Chorionic biopsy is carried out between weeks 11-12 of pregnancy and is the extraction of placental tissue by transcervical route. In spite of both methods can lead to patient annoyances, both methods have very low rates of complications.

Once performed the sample collection, it is necessary to extract the fetal DNA either extracting by quickly but expensive automated systems or by culturing the samples until getting sufficient amount to carry out the molecular techniques (sequencing, PCR, etc.). Using these molecular biology techniques may be analysed a crowd of genetic and hereditary diseases by analysing corresponding genes.



In these kinds of assays, time became into a critical issue. For instance, when women have to make the decision to abort or not and wants to have all information, rapid results on prenatal genetic analyses gives information of help to make the decision. Time is crucial because legislations usually allow abortion only at early pregnancy stages (depending on the country).

There are advances which use peripheral blood of the mother to carry out these kinds of assays, but they still need improvements to get enough DNA concentration to develop sequencing, cutting-edge PCR, etc.

SUBSEQUENT ANALYSES

Examples of subsequent analysis on prenatal diagnosis are:

- Quantitative Fluorescent PCR.
- Amplification and direct sequencing of involved genes.
- Multiple mutation detection through SNaPshot technology.
- Specific mutations detection through ARMS technology.
- Analysis of microsatellite instability by TP-PCR technology.

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