Prenatal chromosomal analysis: investigation techniques and collection of cells

Prenatal chromosomal analysis and also other genetic tests or tests for deformities are carried out using cells from the unborn child. These can include analyses of the genetic material DNA or, for example, tests for neural tube defects (spina bifida). To obtain fetal cells, amniocentesis or chorionic villus sampling (invasive techniques) are needed which carry a risk of miscarriage. The risk of miscarriage due to amniocentesis for example is given as 0.5 to 1 % (1 : 200 to 1 : 100). For this reason too, the decision on whether to perform this or not should be taken with care.

Non-invasive investigation techniques of prenatal diagnosis are sonography (ultrasound examinations) and biochemical measurements carried out as part of the first trimester screening or the triple test. With these techniques it is impossible to draw any direct conclusions regarding the chromosomes of an unborn child, however.

Invasive methods for collecting fetal cells are **amniocentesis** (collection of a sample of amniotic fluid), **chorionic villus sampling** (CVS, collection of certain parts of the placenta), and **cordocentesis** (umbilical blood sampling).

Amniocentesis (Fig. 3) can be performed from the 13th week of pregnancy. Sufficient amniotic fluid is collected – about 10-15 ml – to provide enough cells for chromosomal analysis.

To obtain a result for the most common numerical chromosomal changes as fast as possible, a **prenatal rapid aneuploidy test** (interphase FISH) can be performed as well. With this technique it is possible to detect trisomies of chromosomes 13, 18, and 21 and determine the number of sex chromosomes. The result is obtained in 24 hours. When the prenatal rapid aneuploidy test is performed, it is always performed in conjunction with conventional chromosomal analysis, as the structure of the chromosomes can only be established by the latter method.

bioscientia

Center for Human Genetics Ingelheim

Konrad-Adenauer-Strasse 17
55218 Ingelheim
Germany

Phone +49(0)6132-781-203
+49(0)6132-781-224
+49(0)6132-781-165
Fax +49(0)6132-781-236

int.support@bioscientia.com
www.bioscientia.com

Authors:

Bioscientia
Center for Human Genetics
Konrad-Adenauer-Strasse 17
55218 Ingelheim
Germany
Prof. Dr. med. Daniela Steinberger
Dipl. Biol. Anja Kron

1/2007

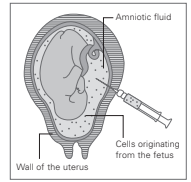

Fig. 3:
Amniocentesis (www.singer.ch/praenat.htm)

The amniotic fluid can also be used for biochemical determination of the substances AFP and ACHE. These tests can provide evidence of certain deformities such as neural tube defects (spina bifida).

Chorionic villus sampling (CVS) is performed from the 10th week of pregnancy. 15-20 mg of chorionic tissue is removed and used for short-term and long-term culturing. The final result is available in 8-10 days. An advantage of CVS is that the results can be obtained at an earlier point in the pregnancy than is possible with amniocentesis. The risk of miscarriage after CVS is reported to be 1-2 %.

In **cordocentesis** a 0.7-2 ml sample of fetal blood is collected by puncturing the umbilical cord. This investigation, which can be used from the 20th week of pregnancy, is suitable for obtaining a chromosomal analysis result as quickly as possible following the detection of an abnormality.

Requests and sample material

Request form
Chromosome analyses prenatal and postnatal
This form can be obtained from us or our local offices.

Sample material
Prenatal chromosome tests are carried out on amniotic fluid cells, chorionic villi (CVS), miscarriage material, and cord blood. Since the sample material is to be used for cell cultures, it must not be frozen.
For information on the coordination of sample dispatch, please contact us or our local offices.

Time taken to get the test result
Please refer to out current test list.

Accredited by Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
ZLG-P-366.07.02

Bioscientia has been CAP accredited since 1987

bioscientia

Center for Human Genetics Ingelheim

Prenatal chromosomal diagnosis

Introduction

The last few years have seen continuous further development of prenatal test methods, resulting in various diagnostic possibilities. The information presented below gives an overview of a special area of prenatal diagnosis: prenatal chromosomal diagnosis.

Foundations of chromosomal diagnosis

Chromosomes are structures found in the nucleus of somatic cells and containing information important to their functioning. This information is organized in the form of genes on the genetic material DNA (Fig. 1). Chromosomes consist not only of DNA but also of proteins and are passed on to an individual's descendants in accordance with specific laws. By using special techniques, chromosomes can be isolated from the relevant somatic cells, stained, and viewed under a light microscope.

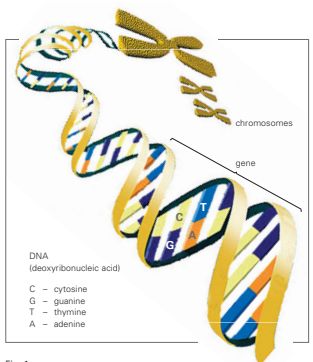

Fig. 1:
The heredity molecule DNA (after www.ornl.gov/hgmis)

Diagnosis of this kind is also referred to as cytogenetic diagnosis. With a cytogenetic investigation, the number of chromosomes can be determined and their structure analysed. The chromosomes are evaluated using light microscopy and arranged according to their structure, using an international classification system. The result is presented in a short form, the "chromosome formula" (ISCN – International System for Human Cytogenetic Nomenclature – formula). The classification and visual representation of an individual's set of chromosomes is called a karyogram (Fig. 2). The complete set of chromosomes of a human somatic cell as represented in a karyogram consists of a total of 46 chromosomes. Of these, 22 chromosome pairs are referred to by numbers, according to their assigned position (chromosomes 1-22). There is also a pair of sex chromosomes: in addition to chromosome pairs 1-22, a woman has two so-called X chromosomes (Fig. 2A) and a man has an X and a Y chromosome (Fig. 2B). Thus the corresponding short formula is 46,XX for a woman or 46,XY for a man.

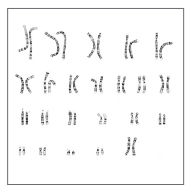

Fig. 2A:
Female set of
46 chromosomes (46,XX)

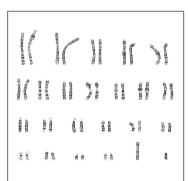

Fig. 2B:
Male set of
46 chromosomes (46,XY)

Changes in chromosomes and their significance

Deviations from the usual number of chromosomes or deviations in their structure (chromosomal aberrations) are detectable in approximately 0.5 % of all live-born babies. Chromosomal aberrations can even be diagnosed before birth.

The most common chromosomal variation – a deviation in the number of chromosomes (numerical aberration, aneuploidy) – is called Down syndrome, after the person who first described it. In the somatic cells of people with Down syndrome, there are three copies of chromosome 21 rather than two. Down syndrome is therefore also known as "trisomy 21". The ISCN short formula for a male affected by Down syndrome is 47,XY,+21; for a female affected by Down syndrome it is 47,XX,+21. Other relatively common trisomies are Edwards' syndrome (trisomy 18 or 47,XY,+18 or 47,XX,+18) and Patau's syndrome (trisomy 13 or 47,XY,+13 or 47,XX,+13).

From the chromosome banding patterns which can be seen after the use of appropriate staining techniques it is possible to detect not only numerical aberrations, but also aberrations in the structure of the chromosomes (structural aberrations). Such changes include translocations (when a segment of one chromosome switches to another chromosome), deletions (the absence of segments from chromosomes), duplications (doubling of segments of chromosomes), or inversions (incorporation of a chromosome segment in reversed order). Structural chromosomal aberrations too can have various health consequences for those affected.

Reasons for prenatal chromosomal diagnosis

Possible reasons (indications) for performing a prenatal cytogenetic test are:

The age of the mother
Chromosomal aberrations can occur in children born to mothers of any age group. However, the likelihood of a woman's giving birth to a child with trisomy increases with increasing age of conception.

Results of biochemical tests
The likelihood of giving birth to a baby with certain trisomies or deformities can be assessed with the help of serum tests of the kind carried out in "first trimester screening" or the "triple test". Certain results in these tests can indicate that a chromosomal aberration is present. Diagnosis is not possible with these methods, however. This can only be done by analysing the chromosomes of the unborn child.

Chromosomal aberrations in a previous child
If a couple already have a child with a free trisomy, the probability of having another child with a chromosomal abnormality of this kind is increased.

Chromosomal structure changes in the parents
Healthy people can have changes in their chromosomal structure that have no consequences for those people themselves. Such can include, for example, translocations in which there is neither too little nor too much chromosomal material present in the somatic cells (balanced translocations). If one or both of the parents has a balanced translocation, there is an increased risk that their offspring will have too little or too much chromosomal material (unbalanced translocations). This can lead to substantial impairment in those affected. If any of these indications is present, it is advisable to seek genetic counselling. In this way, previous findings, further prenatal diagnostic options, and the indication for these can be individually explained. On the basis of this information a personal decision can then be taken about whether or not to proceed with further diagnostic measures.

Birth of a child with physical deformities
Physical deformities are often the result of chromosomal abnormalities. Chromosomal aberrations are detectable in approximately 30 % of all live-born children with deformities and in 5 % of stillborn children without external abnormalities. Prenatal diagnosis is indicated whenever a previous child has had a deformity due to a chromosomal aberration or some other genetic cause (gene mutation).

Repeated miscarriage (habitual spontaneous abortion)
can be indicative of a chromosomal aberration. In at least 50 % of miscarriages (spontaneous abortions) that have no discernible cause, the fetus has chromosomal abnormalities. If a chromosomal change was present in previous miscarriages, the probability of subsequent pregnancies' also being affected by aneuploidy is increased. Repeated miscarriage can be a sign of chromosomal changes in the parents.

Abnormal ultrasound findings
such as, for example, certain values for hygroma colli (accumulation of fluid in the neck region) can indicate a chromosomal change in the fetus.

If any of these indications is present, it is advisable to seek genetic counselling. In this way, previous findings, further prenatal diagnostic options, and the indication for these can be individually explained. On the basis of this information a personal decision can then be taken about whether or not to proceed with further diagnostic measures.

Some of these diagnostic measures involve collecting cells from the unborn child, cells which can then be used for prenatal chromosomal analysis or for other genetic tests or tests for deformities.