Malformations of this type are called congenital bilateral aplasia of the vas deferens (CBAVD).

If the malformation only affects one side (unilateral), the term used is CUAVD. In over 80% of men affected, a mutation in the CFTR gene is the cause of the CBAVD. Certain mutations in the CFTR gene can lead to a serious clinical picture, cystic fibrosis, in the offspring, e.g. if a mutant copy of the gene is also inherited from the mother. For this reason, tests for this genetic disease should also be carried out if CBAVD or CUAVD is present.

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Summary

Various genetic changes can result in infertility. Genetic causes of this type can also adversely affect the health of any child resulting from a spontaneous pregnancy or a pregnancy following reproductive medical intervention.

It is recommended that the possibility of genetic investigations such as chromosomal analysis or targeted examination of specific genes should be mentioned, particularly for the clarification of the causes of fertility problems or before reproductive medical intervention such as ICSI.

Based on the findings, a physician specializing in human genetics can estimate the risks of another miscarriage or of health problems during further pregnancies and for any future children.

If there is an increased genetic risk for future pregnancies, prenatal diagnosis can be carried out if desired, e.g. by a chromosomal analysis of the cells from the amniotic fluid.

Genetic counselling

It is recommended that genetic counselling be given prior to any genetic diagnosis.

During this, the various methods of diagnosis and their significance will be examined, and limits and risks discussed then so that each person receiving counselling can use the information to make a personal decision.

Requests and sample material

Request form
Prenatal diagnosis
Postnatal diagnosis
Molecular genetic diagnosis
(with informed consent form on the back)
These forms can be obtained from us or our local offices

Sample material and dispatch

For information on the coordination of sample dispatch, please contact us or our local offices

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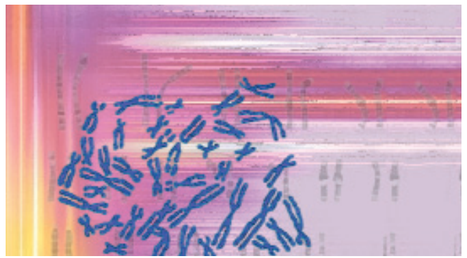

Infertility

Introduction

10-20% of all couples have an unfulfilled desire for children. About 20% of all identified pregnancies end spontaneously in a miscarriage and at least 1% of all couples experience several successive miscarriages. Reproductive problems are thus a common medical issue.

Numerous factors can lead to unwanted childlessness, so a variety of different medical specialists are involved in the clarification of the causes of infertility and its treatment within the framework of "reproductive medicine".

Because genetic factors can contribute to a not insubstantial proportion of cases of infertility and repeated miscarriages, in many cases it may be sensible to carry out a number of different human genetic investigations.

The human genetic investigations which can play a role in association with infertility or miscarriages are discussed below.

Genetic causes of miscarriage and impaired fertility

Chromosomal changes

One reason for the failure to have children can be the repeated occurrence of miscarriages (habitual miscarriages). These are relatively common. About 70% of pregnancies end spontaneously before the expected period, so they are not usually noticed.

The term "habitual miscarriage" is used when recurrent miscarriages occur. The risk of miscarriage recurring depends on the underlying problems responsible for the miscarriage.

Quite specific genetic changes are responsible for up to 50% of miscarriages. These genetic changes affect the so-called chromosomes.

Chromosomes are the carriers of genetic information. Almost all human cells contain 46 chromosomes, each of them in the form of a pair (Fig. 1A and 1B).

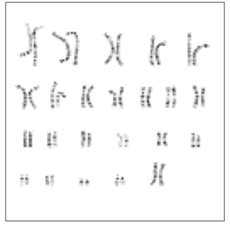

Fig. 1A:
Female chromosome set containing 48 chromosomes (46,XX)

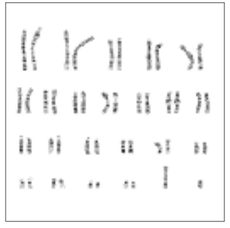

Fig. 1B:
Male chromosome set containing 48 chromosomes (46,XY)

Abnormalities involving the number of chromosomes can lead to miscarriages or, if a live birth occurs, to various consequences for the health of the child concerned. The most common abnormalities found in material from miscarriages are chromosome sets which lack the second sex chromosome – i.e. the absence of the X or Y chromosome (45,X) – or the presence of a third chromosome 16 – trisomy 16 (47,XY,+16 or 47,XX,+16).

Many chromosomal abnormalities found in material from miscarriages may be associated with an increased risk of recurrence of future miscarriages or an increased risk of health problems for future children.

This applies in particular to changes in the structure of the chromosomes, such as in so-called translocations.

In 4-6% of couples with previous miscarriages, one of the partners has such a translocation. This is also the case for up to 10% of couples with fertility problems. In a translocation, break events have occurred in the chromosomes. Parts of the chromosome material involved in the break events may be lost or they attach themselves to other chromosomes (Fig. 2).

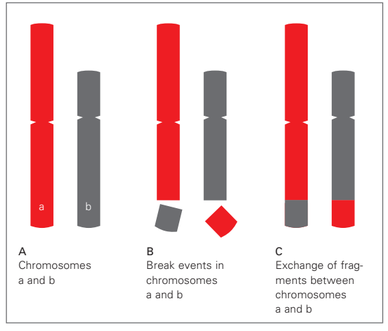

Fig. 2:
Translocation

If the quantity of chromosome material remains the same, and none is lost, the changes are called "balanced" translocations. Chromosomal changes of this type are generally of no clinical significance to the carrier, but balanced translocations can lead to unbalanced chromosome sets in the carrier's offspring.

The term "unbalanced chromosome set" is used when not enough or too much chromosome material is present. Unbalanced chromosomal changes can lead to impairment of physical or mental development.

Changes to DNA, the genetic material

Some cases of impaired fertility are signs of a specific genetic disease (syndrome). Syndromes can be caused by changes to the genetic material DNA. DNA has a long thread-like structure. It is the part of the chromosome that includes all the genetic information (Fig. 3).

All the genetic information relating to any product (protein) produced by a cell in the body is called a gene. Genes contain coded information in the form of a defined sequence of the different building blocks of DNA. These building blocks are called adenine, cytosine, guanine and thymine and are abbreviated to the letters A, C, G and T. Changes in the sequence of the building blocks are called mutations.

Serious genetic diseases are a rare cause of impaired fertility. They should, however, be ruled out if there are clinicaly corresponding signs.

Changes to the DNA however, are a relatively common cause of impaired fertility in the male partner. These mutations affect the AZF region of the CFTR gene.

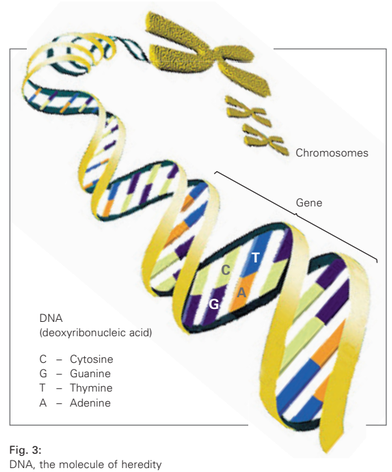

Fig. 3:
DNA, the molecule of heredity

Azoospermia factors (AZF)

In 10-20% of men who are not found to produce any mature, motile sperm (azoospermia) and in whom this cannot be explained by malformation of the seminal ducts, mutations of various gene regions are the cause. For example, sections of the genetic substance DNA which contain information for azoospermia factors (AZF) may be missing (deletions). Deletions in the AZF regions are also found in men with reduced sperm counts (oligospermia). If the partner of the man becomes pregnant following medical intervention such as ICSI (intra cytoplasmatic sperm injection), all male offspring will also be affected by the mutation.

Mutations in CFTR

A reduced sperm count or the absence of mature sperm cells can also be caused by a congenital malformation of the seminal ducts. This is the cause of 1-2% of cases of impaired fertility.