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FTS and NIPT

First Trimester Screening and Non-Invasive Prenatal Testing

Patient Information

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Conventional First Trimester Screening (FTS)

In addition to a few ultrasound scans performed by your gynaecologist, blood will also often be collected during your pregnancy for specific laboratory tests. For instance, your blood group will be determined, hormones and immune status will be checked and much more besides. Another test known as First Trimester Screening (FTS) is also available to every pregnant woman.
This screening test is used to detect whether your baby is at increased risk of having certain chromosomal conditions (trisomy) in which case you will be offered additional tests.

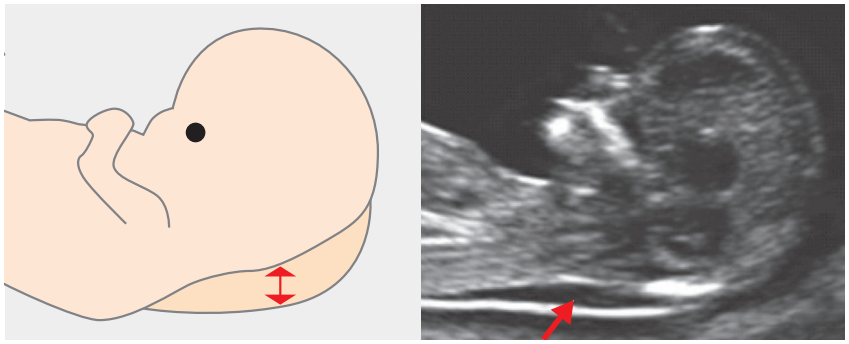
What is trisomy?

Each cell in the human body has 46 chromosomes, 23 from the father and another 23 from the mother. The chromosomes carry the genetic information. Trisomy is a chromosomal condition that occurs when a certain chromosome is present three times instead of twice. The extra genetic material in the cells has serious consequences.
Trisomy 21 (Down's syndrome) is the most common chromosomal condition. It is associated with intellectual disability and often affects other organs including heart. The risk of trisomy 21 pregnancy increases with maternal age. The age risk in a 40 year-old woman is 1:100 (1%) compared to a smaller risk of 1:1500 (0.07%) in a 20 year-old female. Trisomies 13 (Patau syndrome) and 18 (Edwards syndrome) are much rarer than trisomy 21. These chromosomal abnormalities are associated with severe malformations that make it impossible for the affected children to survive in most cases.

Principles of FTS

Ultrasound scans and laboratory tests

First trimester screening comprises an ultrasound scan and a blood test, both of which are carried out during the first trimester of pregnancy. The ultrasound scan also determines the precise gestational age in addition to numerous other aspects. This is carried out by measuring the unborn child from the crown of the head to the coccyx (crown-rump length, CRL). This measurement can be used to determine the precise week+day of pregnancy. It is far more accurate than a calculation based on the last menstrual period. Nuchal translucency (NT) is then measured. Nuchal translucency is the accumulation of fluid under the skin of the neck of the foetus. NT is increased in foetuses with trisomy 21.



An illustration and ultrasound image of nuchal translucency

Risk calculation

Two markers produced by the placenta, namely PAPP-A (Pregnancy Associated Plasma Protein A) and free β-HCG (Free Beta Human Chorionic Gonadotropin), are tested in the maternal blood in the laboratory. A special computer programme is then used to calculate the individual risk of trisomy for the current pregnancy based on a combination of the mother's age, history (weight of the pregnant female, smoking, ethnicity, diabetes, possible trisomy in the previous pregnancy), nuchal translucency, marker concentration and week of pregnancy. This risk is described as the final or combined risk. The background risk based on maternal age is called the baseline risk or age risk.

Informative value

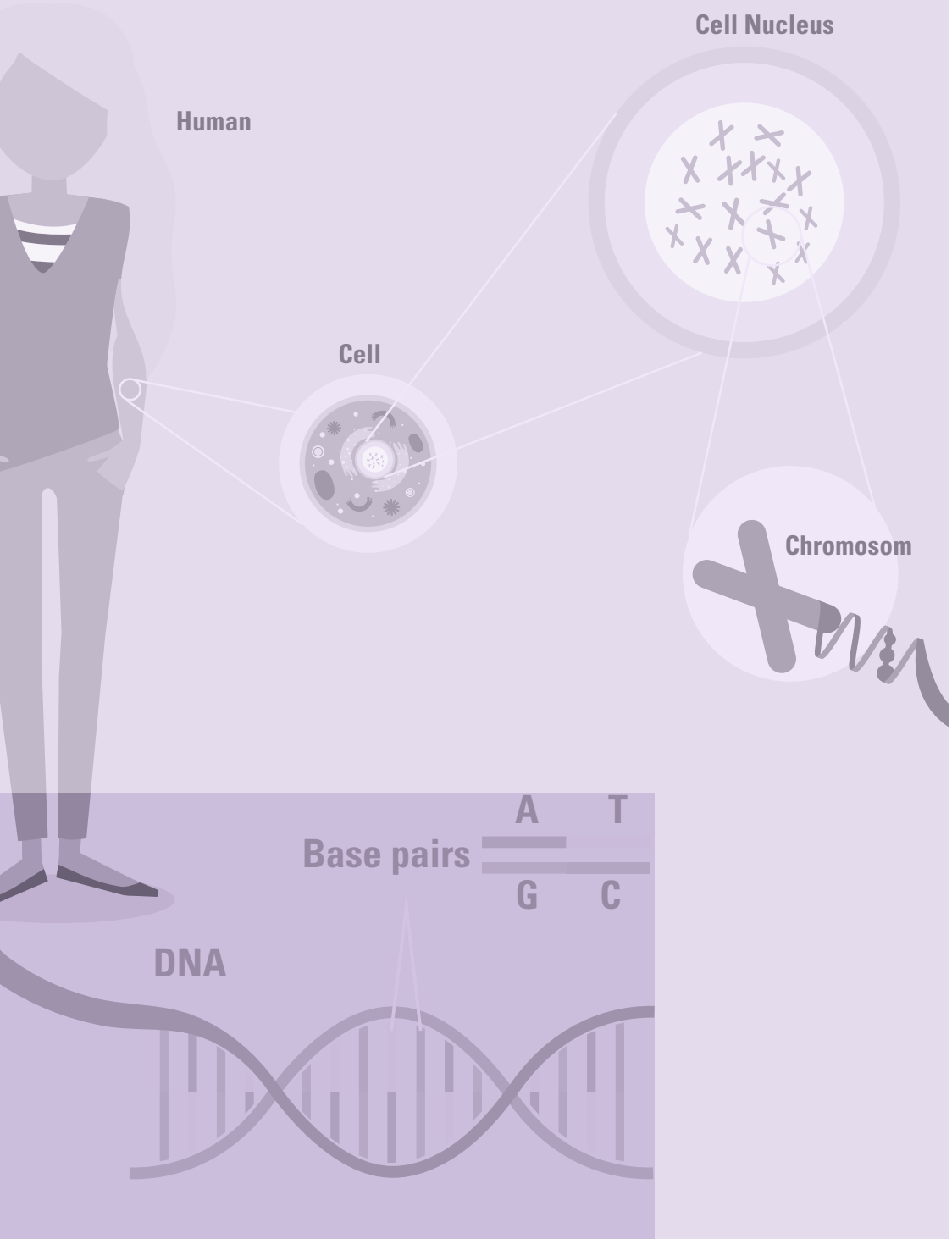
Most FTSs are uneventful, i.e. they show that there is no increased risk of trisomy 21, 18 or 13 in your pregnancy. However, the test can also highlight an increased risk. An abnormal result does not mean that your unborn child has a chromosomal condition as the FTS is only a screening procedure as opposed to a definitive diagnostic test. In the event of an abnormal FTS result, you must discuss with your doctor which further tests (NIPT = Non-Invasive Prenatal Test, chorionic villus sampling or amniocentesis) can be carried out.
The FTS can detect approximately 85–90% of all trisomy 21 pregnancies, i.e. 10% of all trisomy 21 pregnancies have an unremarkable FTS result.
Anomalies and malformations other than trisomies 13, 18 and 21 cannot be detected with FTS.

Specific conditions (twins, IVF, egg donation)

First trimester screening can also be performed for twin pregnancies and IVF fertilisations. In the case of egg donation, the age of the donor on the day on which the egg is collected is taken into account.

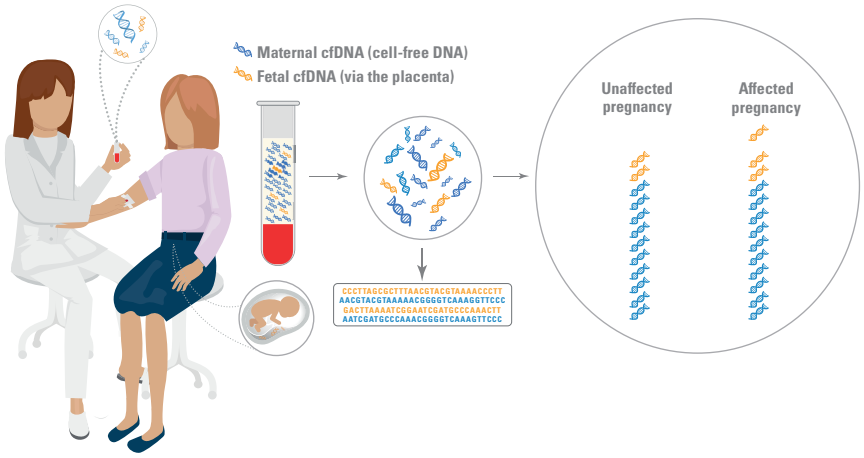
Cost coverage

First trimester screening is covered by health insurance. The cost of additional testing is also covered if an abnormal FTS result is obtained.



Non-Invasive Prenatal Testing (NIPT)

Principle



1 Collection of maternal blood and isolation cell-free DNA (cfDNA)

2 Sequencing of cfDNA

3 Analysis by numbers

The placenta releases tiny fragments of the unborn baby›s genetic material (DNA) into your blood. They represent approximately 10% of the cell-free DNA (cfDNA) in maternal blood. With NIPT (Non-Invasive Prenatal Testing), this cell-free foetal DNA can be analysed and quantified from maternal blood samples using the **CE-IVD certified Illumina-VeriSeq® NIPT-Solution System** to highlight extra or missing chromosomal material.

Advantages of the VeriSeq principle

- High sensitivity (>99%) and specificity (>99%) in the most common non-mosaic trisomies (trisomies 21, 18 and 13) and single pregnancies.
- Short processing time due to fully automated, lean laboratory processes and Next Generation Sequencing (NGS) technology
- The VeriSeq principle can also successfully analyse samples with low foetal cfDNA (<4%)
- Worldwide, over 99% of all published NIPT analyses are performed with Illumina systems.

Test options

Basic NIPT identifies the most common foetal chromosome abnormalities (Trisomies 21, 13 and 18). The sex of the child can also be determined. Rare maldistribution of the sex chromosomes [e.g. Turner syndrome (45,X) or Klinefelter syndrome (47,XXY)] can also be detected.

Extended NIPT detects rarer trisomies/monosomies or certain autosomal anomalies (deletions/duplications >7 Mb).

Costs

Basic trisomy NIPT costs are covered by basic insurance if an increased risk (≥1/1000, e.g. 1:800 for trisomies 21,18 or 13) is detected in first trimester screening.

If you wish, further genetic testing in the form of screening (extended NIPT) can be arranged at your own expense with your treating physician.

Timing

NIPT can be performed from a gestational age of 10+0 weeks through to the end of pregnancy.

Determination of sex

The sex of the baby can be determined. On legal grounds, the sex may only be disclosed from the 12th week of pregnancy. Of course, you can choose, whether or not you want to be informed about your baby's gender.

Specific cases (e.g. twins, IVF, egg donation)

NIPT can also be carried out during IVF pregnancies, twin pregnancies or egg donation. Gonosomal aneuploidies (maldistribution of sex chromosomes X and Y) cannot be detected in twin pregnancies.

Short diagnostic period

Diagnosis is generally confirmed in just 4 to 5 working days.

Potential problems

In certain cases, not enough fetal DNA can be obtained from the first blood sample – hence a second blood sample is necessary. There is no need to worry in this instance. This is not related to the test result.

Good to know

The screening procedure correctly identifies over 99% of all trisomy 13, 18 and 21 cases and 95.5% of rare autosomal trisomies or monosomies are detected. For deletions and duplications >7 Mb, the detection rate is around 70%. However, there are rare cases which are incorrectly assessed due to a specific feature in placental development. Any abnormal findings must be confirmed by chorionic villus sampling (CVS) or amniocentesis.

We recommend that all expectant parents attend a genetic counselling session before each NIPT to discover test options and limitations.

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Notes

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Your doctor will choose the best laboratory to suit you

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