What is a trisomy?

Each human cell contains 23 pairs of chromosomes, a total of 46. Chromosomes carry genetic information. One half originates from the mother and the other from the father. A trisomy occurs when a chromosome exhibits three copies rather than the normal two. Advanced maternal age is a risk factor for trisomies. A trisomy is often associated with mental retardation and reduced life expectancy.

Trisomy 21, also known as **Down Syndrome**, is one of the most common genetic birth defects, affecting approximately 1 in 700 newborns. Down Syndrome is caused by an additional copy of the chromosome 21. It often involves a mild to moderate mental and physical development as well as heart defects and a reduced life expectancy.

Trisomy 18 also known as **Edwards Syndrome**, is ascribed to an additional copy of chromosome 18. Affected individuals often suffer from heart defects and other intellectual and physical impairments. The prevalence of trisomy 13 is approximately 1 in 5.000 births.

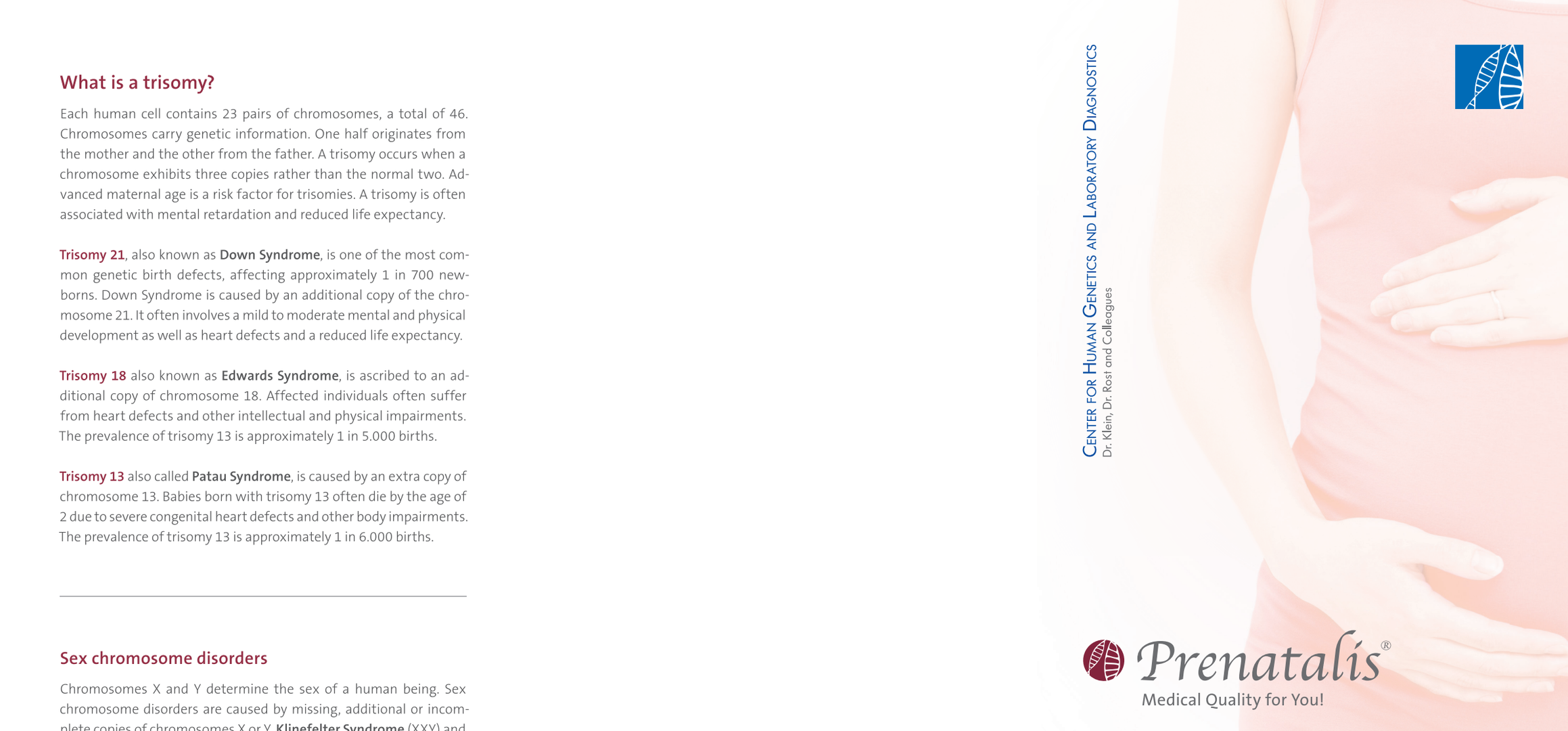
Trisomy 13 also called **Patau Syndrome**, is caused by an extra copy of chromosome 13. Babies born with trisomy 13 often die by the age of 2 due to severe congenital heart defects and other body impairments. The prevalence of trisomy 13 is approximately 1 in 6.000 births.

Sex chromosome disorders

Chromosomes X and Y determine the sex of a human being. Sex chromosome disorders are caused by missing, additional or incomplete copies of chromosomes X or Y. **Klinefelter Syndrome** (XXY) and **Ulrich-Turner Syndrome** (X0), also known as Monosomy X, are associated with sex chromosome abnormalities.

First Trimester Screening (FTS)

The **FTS** is a non-invasive test that combines a blood test, a specialized ultrasound, and the age of the pregnant woman. This information provides a risk factor for a chromosomal abnormality.



CENTER FOR HUMAN GENETICS AND LABORATORY DIAGNOSTICS
Dr. Klein, Dr. Rost and Colleagues

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Non-invasive prenatal test (NIPT)

Information for Expectant Mothers

Accredited according to DIN EN ISO 15189:2014

Dear expectant mother,

Right now you are probably experiencing an emotional journey of joy, hope and at times, even concerns. Your gynecologist is able to provide expertise and advice concerning all aspects of pregnancy, especially about diagnostic options to protect your health and that of your unborn child.

Procedures, such as the diagnosis of infectious agents and coagulation defects or rhesus incompatibilities are part of your routine prenatal care. There are methods **available for the identification of chromosomal abnormalities**; amniocentesis or chorionic villus sampling (CVS), and although the rate of complications from these invasive procedures has steadily reduced, a risk of miscarriage of 0.3-1% remains. As an alternative to invasive procedures, an optional non-invasive method (non-invasive prenatal test, **Prenatalis® NIPT**) screens your blood for fetal chromosomal disorders, for example, **Down Syndrome** (trisomy 21). The sex of your unborn child can also be determined. However, in compliance with the German Genetic Diagnostics Act (GenDG), gender information may only be disclosed from the 14th week of pregnancy.

Since mid-2014 **Prenatalis®** NIPT is part of the diagnostics portfolio of the **Center for Human Genetics and Laboratory Diagnostics in Martinsried, Germany**. The accredited genetic blood test serves to reliably detect the most common fetal chromosomal abnormalities (**trisomy 21, 18, 13, X** and **Y**) and is applicable for single and twin pregnancies from 10 weeks gestation.

The test is conducted entirely by medical and scientific staff in Martinsried. It complies with strict data privacy standards and high quality demands set down by Germany's National Accreditation body (DAkkS). **Prenatalis®** is a safe and riskless method to find out if your unborn child has a specific genetic condition.

Am I eligible?

An NIPT may become relevant for you if any of the following apply:

- advanced maternal age (≥ 35)
- noticeable findings in laboratory values in first-trimester screen
- abnormal ultrasound findings
- personal or family history of chromosomal defects
- previous pregnancy with a fetal chromosomal abnormality (chromosome 21, 18, 13)

How does the test work?

During pregnancy your blood contains cell-free DNA fragments, both your own and fetal. NIPT is based on 1) extracting cell-free DNA from your blood-sample and 2) analyzing the cell-free fetal DNA by modern technology to detect numerical deviations, from the normal number of 46 chromosomes, specifically for the chromosomes 21, 18, 13 X and Y.

Three steps to your test result:

1. Patient education and genetic counseling

The patient education and genetic counseling must be conducted by a certified geneticist, who remains your principal contact person throughout the entire **Prenatalis®** procedure.

To find a genetic counseling service in your area, please contact us.

2. Blood collection

Following your written consent to the test, your physician will collect a blood sample (10 ml).

3. Analysis

Your sample will be sent by courier to the Medical Laboratory Martinsried where it will be analyzed by modern analytical methods.

Result

After 8-10 working days* (**Prenatalis®** Prior: within 5 working days) your physician will review the test result with you.

*working day ≙ mo – fr

What does the test result tell me?

If the test indicated a **negative** (inconspicuous) or low risk result, it means that your pregnancy is unlikely to be affected by any of the screened chromosomal conditions.

A **positive** (conspicuous) or a high risk NIPT result is a reliable indicator for a chromosomal defect. In reference to the Germany Society of Human Genetics, we recommend invasive diagnostic examinations such as amniocentesis or chorionic villus sampling to confirm the result. Your genetic counselor can direct you to resources with accurate up-to-date information about the genetic conditions mentioned.

The costs for **Prenatalis®** NIPT are reimbursed on a case-by-case basis by individual health insurance providers.

Why Prenatalis®?

- reliable risk evaluation for trisomy 21, 18, 13, X and Y in early pregnancy (from 10 weeks gestation)
- avoidance of risks associated with invasive prenatal diagnostics in corresponding indication
- applicable for twin pregnancies and in-vitro fertilization (IVF)
- quality testing, accredited to DIN EN ISO 15189:2014 by DAkkS
- part of a professional and comprehensive prenatal medicine concept
- test evaluation by a medical laboratory in Germany
- meets strict data protection laws

Limitations

The **Prenatalis®** blood test is a riskless and highly accurate method to detect the most common trisomies (21, 18, 13) and sex chromosome disorders. Other chromosomal structural changes, translocations or mutations in single genes cannot be identified by NIPT. If the cell-free DNA concentration in your blood is too low, a result might not be obtained. In these rare instances, the test has to be performed again.

Please find more information about Prenatalis® at

www.prenatalis.com