NIPT

Non-Invasive Prenatal Genetic Testing

出生前検査認証制度等
運営委員会

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You have probably heard of prenatal tests called “amniocentesis” and “chorionic villus sampling” (CVS), which are both conventional methods used to detect chromosomal diseases in babies before birth. These tests are definitive, but invasive (including needle insertion into the uterus); therefore, the risk of miscarriage cannot be ruled out.

NIPT has been developed as a non-invasive screening test — i.e., without any invasion of the pregnancy — and offers a means to test for the risks of a baby having a chromosomal disorder.

This instruction contains important information for expectant mothers and their families considering whether to undergo NIPT.

Overview of NIPT

- NIPT is a test used to estimate the possibility of fetus having chromosomal anomalies called trisomies — such as trisomy 21, trisomy 18, and trisomy 13.
- The test is available from 9-10 weeks of pregnancy. It only requires 10-20 ml of blood from the mother.
- NIPT is a screening test that examines small fragments of DNA (cell-free DNA, cfDNA) circulating in the blood of pregnant women.
- Approximately 10% of the cfDNA floating in the mother’s blood is of placental origin. As it does not always match the DNA of the fetus itself, the results may be slightly less accurate. Therefore, the NIPT is considered a highly accurate test; however, it can only tell you how likely it is that your baby has a chromosomal difference.
- The results are reported as “positive,” “negative,” or “inconclusive.” “Positive” indicates a high probability of chromosomal disorders.
- If you test “positive” for NIPT, it is necessary to have a definitive test (amniocentesis or CVS) performed, while in the case of “inconclusive,” you need to consult again on the possible subsequent actions that can be taken.

What are Chromosomes?

- Most individuals have 46 chromosomes, consisting of 22 pairs of autosomes (numbered 1-22) and a pair of sex chromosomes (XX or XY).
- Each chromosome contains a large number of genes that provide a blueprint for the body’s structure and function.
- Changes in the number or structure of chromosomes can affect fetal growth and development, which can result in birth defects and physical characteristics.
- Chromosomes normally occur in pairs. Trisomy means that a person has three chromosomes instead of two. For example, trisomy 21 indicates that a baby has 3 copies of chromosome 21. (“Tri”- is Greek for “three”)

What NIPT can and cannot tell us

- NIPT is a test performed to estimate the possibility of trisomy 21, 18, and 13. No other abnormalities are detected.
  - ▸About 3-5 out of every 100 babies are born with congenital diseases.
  - ▸Of these, chromosomal abnormalities account for approximately 25% of all the diseases. Moreover, 70% of these abnormalities are trisomy 21, 18, or 13. According to the calculation, 0.7 out of 100 babies have one of those trisomies.

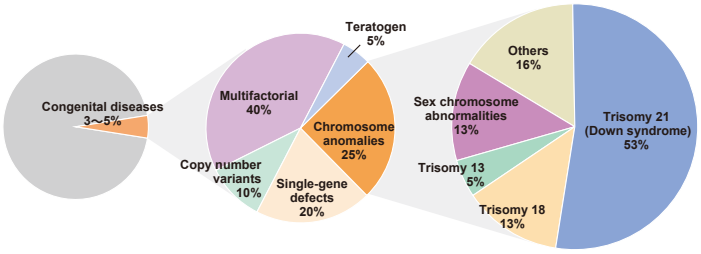

Figure. Frequency of congenital diseases and chromosome anomalies.

(Thompson & Thompson Genetics in Medicine 8th Edition Saunders 2016; Wellesley D, et al. Eur J Hum Genet 2012: 20:521)

Maternal age and trisomy

- It has been reported that the risk for trisomy increases with maternal age.
- Not every kind of chromosomal anomaly shows a clear correlation with maternal age.

Maternal age at delivery	Trisomy 21	Trisomy 18	Trisomy 13
20	1/1441	1/10000	1/14300
25	1/1383	1/8300	1/12500
30	1/959	1/7200	1/11100
35	1/338	1/3600	1/5300
40	1/84	1/740	1/1400
45	1/30		

Table. The frequency of trisomy in relation to maternal age

Congenital disorders as diversity

- Any baby can be born with a congenital disorder that is sometimes caused by chromosomal anomalies. Congenital disorders may give the baby unique characteristics which can be regarded as a part of their individuality, and what is more, human diversity as a whole.
- It would be a challenge to live with some congenital abnormalities, but this is not a critical factor in deciding whether or not you are happy.
- Whatever situation you are in, don’t forget that you are never alone. The government has attempted to build a mutually supportive and acceptable society that provides public services.
- Individual choice should be respected, including the decision to terminate or continue pregnancy. Some groups provide peer support to mothers and their families to help them make more informed decisions.

NPO for Family and Baby Wellness
https://fetalhotline.fab-support.org/

For prenatal testing, we are in collaboration with the facility (core hospital) below.

Facility Name:
Physician in charge:
Facility Address:
Contact:

Pediatricians could also be consulted before and after the test.
We collaborate with a “prenatal consult pediatrician” below.

Physician Name:
Facility Name:
Contact:

Health Labour Science Research Grant Project in FY2021 (Basic Research on Raising Next-Generation Children, including Overcoming Children’s Diseases)
“Research on the Establishment of a System for Providing Prenatal Diagnoses”

Characteristics of three targeted trisomies

Trisomy 21 (Down syndrome)

- Trisomy 21 occurs in approximately one in every 600–800 live births.
- Physical growth and language development are relatively slow in children with down syndrome. However, an appropriate environment (including therapeutic rehabilitation) can promote development.
- Some children with Down syndrome might have health problems, such as heart defects and gastrointestinal disorders.
- Many of them attend local schools and special support schools.
- Adults with Down syndrome sometimes need nursing care for daily activities, but many live in their own local communities with support from the government. Throughout their lives, they can receive various types of public support services.
- Down syndrome is listed by the Minister of Health, Labor and Welfare as one among many “specific pediatric chronic diseases.” Patients with specific pediatric chronic diseases can receive government support and welfare in several ways.
- You can find circles and group activities for parents and children with trisomy 21 across the country, from which you can obtain welfare services and opportunities to exchange information.

Japan Down Syndrome Society
https://www.jdss.or.jp

Yokohama Project
https://yokohamapj.org/

Trisomy 18 (Edwards syndrome)

- Trisomy 18 occurs in approximately 1 in every 4,000–10,000 live births.
- A fetal ultrasounds during pregnancy can show features suggestive of trisomy 18 — such as growth deficiencies, heart defects, gastrointestinal disorders, and changes in limb morphology.
- Babies with trisomy 18 are often born with numerous difficulties, including breathing and feeding, which require medical management during the early postnatal period.
- Due to the presence of several medical problems, such as heart disease and respiratory failure, babies with trisomy 18 sometimes die shortly after birth. However, aggressive medical interventions have been reported to improve patients’ lives and life expectancies. With this, some individuals can even reach adulthood.
- Patients may show motor and intellectual delays after birth. However, receiving suitable medical treatment and attending special support schools will promote their development slowly, but steadily.
- Trisomy 18 is listed by the Minister of Health, Labor and Welfare as one of a range of “specific pediatric chronic diseases.” Patients with specific pediatric chronic diseases can receive government support and welfare in several ways.

Trisomy 18 Support Group
http://18trisomy.com/

Team18
https://team-18.jimdofree.com/

Trisomy 13 (Patau syndrome)

- Trisomy 13 occurs in approximately 1 in 5,000–10,000 live births.
- Fetal ultrasounds performed during pregnancy can show features suggestive of trisomy 13 — such as heart defects, central nervous system abnormalities, gastrointestinal disorders, and changes in body morphology.
- Babies with trisomy 13 are often born with numerous difficulties, including breathing and feeding, which require medical management during the early postnatal period.
- Due to the presence of several medical problems, such as heart disease and respiratory failure, infants with trisomy 13 sometimes die shortly after birth. However, aggressive medical interventions have been reported to improve patients’ lives and life expectancies. With this, some individuals can reach adulthood.
- Children with trisomy 13 may not learn how to do things that typical children do, such as walking or talking. However, they are able to learn and develop at their own pace.
- Trisomy 13 is listed by the Minister of Health, Labor and Welfare as one among a number of “specific pediatric chronic diseases.” Patients with specific pediatric chronic diseases can receive government support and welfare in several ways.

☆ PROJECT13 ☆
http://trisomy13.blog.jp/

Parents' Association for Children with Trisomy 13
http://www.13trisomy.com/next.html

Before you make a final decision on having NIPT, please note the following

- NIPT is a non-invasive test used to screen for chromosomal abnormalities in the fetus by using maternal blood. Please keep in mind that you will have a significant hurdle to overcome if you test either as “positive” or “inconclusive.”
- This non-invasive test can provide an important indication of whether you will undergo further invasive procedures, such as amniocentesis, which carries a risk of fetal loss.
- A “positive” result means that there is a higher chance for the baby to have trisomy 21, trisomy 18, or trisomy 13.
  - NIPT does not give you a definitive answer. The only way to be sure is to have a diagnostic test, such as amniocentesis or CVS. During this invasive procedure, a needle is inserted through the belly into the uterus, increasing the risk of miscarriage by up to 1 in 300.
  - Sometimes NIPT gives a “positive” result when the fetus does not actually have the chromosomal disorder (a so-called “false positive”). For example, if a 35-year-old pregnant woman receives a positive result for Down syndrome, there is a 6.4% chance that the result is wrong and that the fetus does not have the condition.
  - Any individuals with “positive” results should be provided genetic counseling for a discussion of NIPT results, and what to do next.
- A “negative” result means the chance for the baby to have trisomy 21, trisomy 18, or trisomy 13 is generally very low.
  - Although the negative predictive value for those three trisomies is greater than 99.9%, NIPT is not 100% accurate. The test has a very small chance for a “false negative” (a baby who tests “negative” for NIPT but born with the condition).
  - Since trisomies are not the only kind of congenital disorders that occur in babies, a “negative” result does not indicate that the baby is free of diseases.
- An “inconclusive” result indicates that the test did not provide clear positive or negative results.
  - Japanese data shows that there is about a 0.3-0.4% chance of getting an “inconclusive” result.
  - When receiving an “inconclusive” result, it is necessary to consult again on possible subsequent actions (e.g., having a repeat NIPT, receiving diagnostic testing, or having no further tests conducted).
- NIPT reveals the possibility of chromosomal disorders in your baby. However, it cannot tell you precisely what kind of symptoms your baby will be born with or how it will grow after birth, since these can vary considerably between babies. The test also does not tell you how to treat the disorder.
- Although NIPT is designed to detect chromosomal disorders in fetuses, it may incidentally detect maternal chromosomal abnormalities, including malignant diseases.
- In order to make a fully informed decision, genetic counseling is essential before undergoing NIPT in order to make fully-informed decisions. With a full understanding of the test, please think again if it is necessary, for you and your partner.
- Whatever conclusion you and your partner come to after careful consideration, the decision will be respected as much as possible.
- If you have fears concerning the future of your baby and family, please feel free to contact us for consultation. We can also make referrals to pediatricians in our facility, or even to appropriate outside facilities, if needed.
- Even if you are told that your baby has a congenital disorder, there is no need to feel helpless. There are various support groups in the country, and you can receive continuous medical and social support from the government.

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