Prenatal testing certification system

Executive committee

HPでさらに詳しく

Executive Committee for the prenatal testing certification system website

『Let's consider together about the different tests for your baby』

A site for pregnant women and their families. We provide information on various types of prenatal testing, where to consult, opinions of those who have undergone testing and those who chose not to, as well as information on living with a child with a congenital disease and information about welfare services.

For NIPT affiliated facilities: We are affiliated with the following facilities (core facilities).

Facility:

Doctor:

Address:

Consulation contact:

You can talk directly to a pediatrician (prenatal consultation pediatrician) before or after the test.

The prenatal consultation pediatricians who collaborate with our facility are as follows.

Doctor:

Facility:

Contact:

This booklet was produced in cooperation with the Japan Society of Obstetrics and Gynecology and the Japanese Society of Human Genetics.

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NIPT

Non-invasive prenatal genetic testing

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2021 Ministry of Health, Labor and Welfare Research Grant

(Next-Generation Development Fundamental Research Project for Overcoming Childhood Diseases)

「Research on creating a system for providing prenatal diagnosis」

Introduction

Amniocentesis and chorionic villus sampling are methods to reliably determine whether the baby in the uterus has a chromosomal disorder or not before birth, however they carry with them risks such as miscarriage (due to puncture of the uterus with a needle). Therefore non-invasive methods to test for chromosomal disorders in babies have been developed, one of which is NIPT (non-invasive prenatal genetic testing).

This document describes the information that you should know and be aware of in order to decide whether or not to undergo NIPT.

Outline of NIPT

- NIPT is a test to determine whether the baby in the uterus has a chromosomal disorder
- The chromosomal disorders tested are trisomy 21, trisomy 18 and trisomy 13.
- After about 9 to 10 weeks of pregnancy, 10 to 20 ml of blood is collected from the pregnant woman and cfDNA (fragmented chromosomes) floating in the blood are analyzed in order to obtain results.
- Results are reported as “Positive”, “Negative” or “Pending”. "Positive" means that there is a high possibility of that disease.
- About 10% of the cfDNA floating in the blood of pregnant women comes from the baby, or more precisely from the placenta. Therefore, although NIPT is a highly accurate test, it only determines the likelihood of a chromosomal disorder.
- If the test result is "positive", a confirmatory test using amniotic fluid cells or chorionic villus cells is required. In addition, in the case of "pending", it is necessary to consult with the doctor again about what to do next.

What are chromosomes?

- Most people have 46 chromosomes, consisting of a pair of autosomes (chromosomes 1 to 22) and a pair of chromosomes (XY chromosomes) that differ according to sex.
- Chromosomes are packed with many genes (blueprints for the human body and functions).
- Changes in the number or form of chromosomes can affect growth and development and can result in congenital diseases and distinct physical features.
- "Trisomy" is a condition in which there are 3 chromosomes instead of 2 (a pair). For example, trisomy 21 is a condition in which there are 3 chromosome 21s.

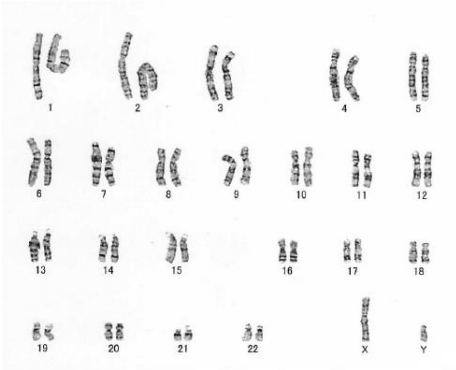


Fig. chromosomes (46, XY)

What we can learn and what we cannot learn from NIPT

- NIPT is a test that checks for possible chromosomal disorders such as trisomy 21, trisomy 18, and trisomy 13, but it does not detect other disorders.
  - ➢ About 3 to 5 out of 100 babies are born with congenital diseases.
  - ➢ In that number, chromosomal causes account for about 25%, and the three chromosomal disorders covered by NIPT account for another 70%. Doing the math, the number of babies born with the three chromosomal disorders covered by NIPT is about 0.7 in 100.

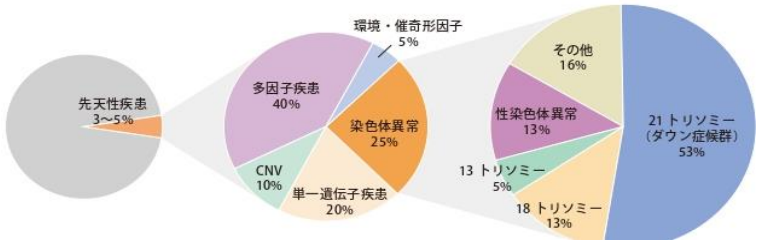


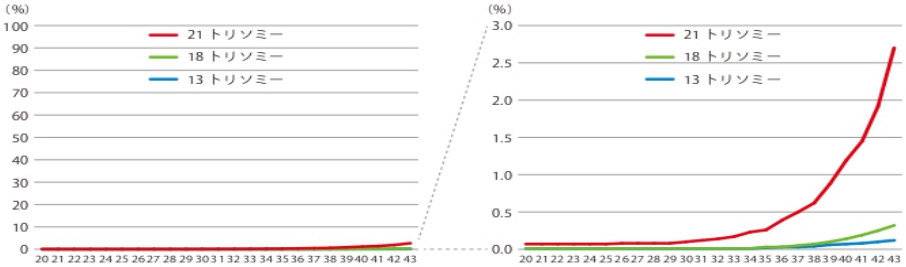
Fig. Frequency of congenital disorders and chromosomal disorders

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

Relationship between maternal age and birth frequency of trisomic infants

- It is known that as maternal age increases, the frequency of births of babies with trisomy also increases.
- For other chromosomal disorders, the effect is not clear.

出産時年齢	21 トリソミー	18 トリソミー	13 トリソミー
20	1/1441	1/10000	1/14300
25	1/1383	1/8300	1/12500
30	1/959	1/7200	1/11100
31	1/837	1/7200	1/11100
32	1/695	1/7200	1/11100
33	1/589	1/7200	1/11100
34	1/430	1/7200	1/11100
35	1/338	1/3600	1/5300
36	1/259	1/2700	1/4000
37	1/201	1/2000	1/3100
38	1/162	1/1500	1/2400
39	1/113	1/1000	1/1800
40	1/84	1/740	1/1400
41	1/69	1/530	1/1200
42	1/52	1/400	1/970
43	1/37	1/310	1/840
44	1/38	1/250	1/750
45	1/30		



The frequency of the disease increases with the age of the pregnant woman, but if the maximum value on the vertical axis is set to 100%, the upward trend is not clear. If you expand it like the graph on the right, you can see the upward trend.

Fig. Birth rates of infants with chromosomal disorders by maternal age at birth

(Morris JK et al., J Med Screen 9:2-6,2002; Morris JK et at., Prenat Diagn 25:275-278,2005; Appendix in Savva GM et al.,Prenat Diagn 30:57-64,2010)

Our Diversity and Congenital Diseases

- Anyone can have a baby with a congenital disorder, including birth defects caused by chromosomal changes. This can make your baby different from most people, but that's a characteristic of human diversity and individuality.
- It cannot be denied that having characteristics different from other people due to congenital disorders may lead to a more difficult life. On the other hand, it can also be said that a person's happiness or unhappiness is not only determined by such characteristics.
- Regardless of our circumstances, we are all members of society, and public welfare services are provided in order to create a society that recognizes and helps all individuals.
- On the other hand, for various reasons, some people may decide not to give birth and that choice is also respected. .There are also organizations that provide peer support by those who have experience in these situations.

■ Association for supporting the future of parents and children (https://fetalhotline.fab-support.org/)

Characteristics of diseases that are tested

Trisomy 21 (Down Syndrome)

- In general, it is said to occur in 1 in 600 to 800 births.
- Physical and language development after birth is generally slow, but growth and development can be encouraged in an appropriate environment (by therapy).
- They may have issues such as heart disease and digestive problems.
- During school age, they attend local schools and special needs schools.
- After becoming adults, they may need nursing care, but many of them live in the community while receiving support from the government, and various support services are available throughout their lives.
- It is certified as a specified chronic childhood disease (see the site at the bottom of page 7), and there are support systems such as medical care, welfare, and the community of the person concerned.
- In each region, there are places for information exchange such as parent meetings and circle activities, and welfare support systems are also in place.

■ Japan Down Syndrome Association (https://www.jdss.or.jp)

■ Yokohama Project (https://livingwds.info/)

Trisomy 18 (Edwards' Syndrome)

- Generally, it is said to occur in 1 in 4,000 - 10,000 births.
- Ultrasound examinations performed during prenatal checkups may reveal abnormal growth in the baby, heart disease, digestive system disease, morphological changes in the limbs, etc.
- Babies may be born with multiple ailments and may require medical attention early in life, including respiratory and feeding support.
- They may die soon after birth due to illnesses such as heart disease and respiratory failure. On the other hand, aggressive medical intervention is reported to improve life span and prospects, and some people live longer, reaching adulthood.
- Although there is a delay in motor skills and intellectual aspects, by attending special support schools and continued medical management, these skills will develop slowly as they grow.
- It is certified as a specified chronic childhood disease (see the site at the bottom of page 7), and there are support systems such as medical care, welfare, and the community of the person concerned.

■ Trisomy 18 Association (http://18trisomy.com/)

■ Team 18 (https://team-18.jimdofree.com/)

Trisomy 13 (Patau Syndrome)

- Generally, it is said to occur in 1 in 5,000 - 10,000 births.
- Ultrasound examinations performed during prenatal checkups may detect diseases such as heart disease, central nervous system disorders, and morphological changes.
- Babies may be born with multiple ailments and may require medical attention early in life, including respiratory and feeding support.
- They may die soon after birth due to illnesses such as heart disease and respiratory failure. On the other hand, aggressive medical intervention is reported to improve life span and prospects, and some people live longer, reaching adulthood.
- They rarely learn to walk or speak on their own, but tend to grow and develop slowly.
- It is certified as a specified chronic childhood disease (see the site at the bottom of page 7), and there are support systems such as medical care, welfare, and the community of the person concerned.

■ Children with Trisomy 13☆PROJECT13☆(http://trisomy13.blog.jp/)

■ Association of Parents Supporting Children with Trisomy 13 (http://www.13trisomy.com/next.html)

■ Specified Chronic Diseases in Pediatrics "Overview of Countermeasures for Specified Chronic Diseases in Pediatrics Ministry of Health, Labor and Welfare" (mhlw.go.jp)

Things to reconfirm before undergoing the test

- NIPT can be performed only by drawing blood from pregnant women, but it is a test to check for chromosomal disorders in babies before birth. Any result other than "negative" can lead to various difficulties.
- NIPT can be said to be a test that pregnant women who are worried about whether to undergo invasive tests with a risk of miscarriage, such as amniocentesis, can undergo as a basis for deciding whether to do so or not.
- A NIPT “positive” result means that there is a high probability of one of the 3 trisomy disorders.
  - ➢ This test cannot confirm the diagnosis. In order to confirm the diagnosis, it is necessary to undergo amniocentesis or chorionic villus sampling, but since these examinations involve inserting a needle into the uterus from the abdomen, there is a 1 in 300 probability of miscarriage.
  - ➢ The test result may be positive, but the chromosomal disorder may not be present (called a false positive). For example, even if a 35-year-old pregnant woman is "trisomy 21 positive", there is about a 20% chance that the baby will not have Down's syndrome.
  - ➢ If the test is "positive", genetic counseling should be sought for further explanation of the results and follow-up.
- A NIPT "negative" result means that the probability of one of the three trisomy disorders is low.
  - ➢ The probability that it is not one of the three trisomies is over 99.9%, but they cannot be 100% ruled out. Although very rare, it is possible to have a chromosomal disorder even with a negative result (false negative).
  - ➢ There are many congenital disorders other than trisomal disorders, so a "negative" test does not mean the baby is free of any disease.

- A NIPT “pending” result is when the result cannot be determined as “positive” or “negative”.
  - ➢ According to national data, there is a 0.3 to 0.4% chance that the result will be "pending".
  - ➢ In this case you will need to consult with the doctor again about what to do next (repeat NIPT, give up on the NIPT test, undergo amniocentesis, etc.).
- Even if the test reveals the possibility of a chromosomal disorder in the baby in the uterus, the actual symptoms of the baby and the state of subsequent development cannot be clearly determined because there are individual differences. In addition, this test is not directly related to the treatment of any disorder.
- Although the original purpose of the test is to investigate chromosomal disorders in the baby, chromosomal disorders and malignant tumors in the pregnant woman may also be discovered during this test.
- Before you decide whether to undergo the test, make sure you understand the process well through pre-test genetic counseling and consider whether it is necessary for you and your partner.
- Regardless of whether you decide to undergo NIPT or not, your well-thought out decision will be respected.
- We are always available to discuss any concerns or worries about the future of your baby or family. If you would like a more detailed explanation, we can refer you to an on-site pediatrician or an appropriate outside facility.
- Don't forget that even if your baby has some form of congenital disease, there are always support services who will work together with you to find the best way forward for your baby, such as medical and welfare services.

References

Types of tests for examining chromosome disorders in babies during pregnancy

	Inconclusive test (non-invasive test)			Conclusive test (invasive test)	
	Ultrasound marker test (combined test)	Maternal serum marker test	NIPT Non-invasive prenatal genetic testing	Chorionic villus sampling	Amniocentesis
Timing	11 - 13 wks	15 - 18 wks	9 - 10 wks and beyond	11 - 14 wks	15 - 16 wks and beyond
Chromosomal disease	Trisomy 21 Trisomy 18 (Trisomy 13)	Trisomy 21 Trisomy 18	Trisomy 21 Trisomy 18 (Trisomy 13)	General chromosomal disorders	General chromosomal disorders
Method	Ultrasound (NT etc.) ⋆Combined test requires blood sampling	Blood sampling only	Blood sampling only	Chorionic puncture	Amniocentesis
					
Detection rate (sensitivity) for trisomy 21	NT: about 60% Combined test: 80%	80%	99%	99.9%	99.9%
How results are shown	Probability (1/○○○) or positive/negative	Probability (1/○○○) or positive/negative	Positive/negative/pending	Chromosome photo/Karyotype	Chromosome photo/Karyotype
Test characteristics	Many false positives No risk of miscarriage Limited facilities Inexpensive Early implementation	Many false positives No risk of miscarriage Many facilities Inexpensive	High positive predictive value No risk of miscarriage Limited facilities Expensive Early implementation	Risk of miscarriage (1%) Limited facilities Early implementation Affected by placental mosaicism⋆	Risk of miscarriage (0.3%) Relatively many facilities

⋆Placental mosaicism: A difference in the number of chromosomes between the placenta and fetus.