

Purpose of inspection

Since the fetus floats in the amniotic fluid, the amniotic fluid contains fetal cells. By collecting this amniotic fluid, it is possible to investigate whether the fetus has a chromosomal change "chromosomal abnormality".

What is a chromosome?

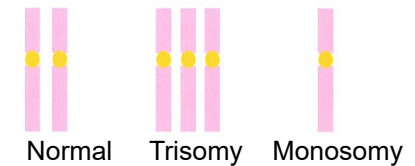
The human body is made up of small cells, each of which has a chromosome inherited from its parents. Chromosomes contain genetic information, which is a blueprint for humans. When sperms and eggs are fertilized, the fetus inherits 23 chromosomes from each. Therefore, humans have 23 pairs of chromosomes as shown in the figure below, for a total of 46 chromosomes. One of the 23 pairs is a sex-determining sex chromosome, with women having two X chromosomes and men having one X and one Y chromosome. The other chromosomes are called autosomal chromosomes.



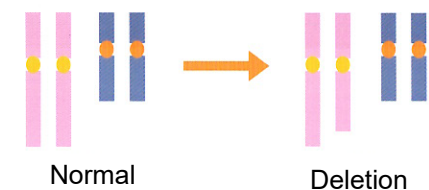
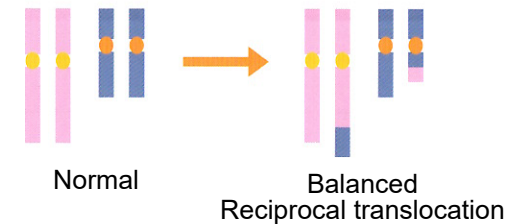
Example of a male without chromosomal abnormalities (46, XY)

What is a chromosomal abnormality?

"Chromosome abnormality" means that the human blueprint, which is a transmission information, changes. Chromosomal abnormalities can be broadly divided into two. One is "change in number" where the number of chromosomes, which is 46, increases or decreases, and the other is "change in structure" where the shape of chromosomes changes. Chromosome "changes in number" include trisomy (three chromosomes) and monosomy (only one chromosome). For example, Down's syndrome has three chromosomes 21 and trisomy 18 has three chromosomes 18.



"Structural changes" in chromosomes are those in which the chromosome is cut and the structure is partially changed, and there is no excess or deficiency in the entire chromosome (balanced type) and excess or deficiency (unbalanced type). An example of a balanced type is reciprocal translocation (parts of different chromosomes swapped with each other). An example of an imbalanced type is a deletion (a part of the chromosome is missing).



About the interpretation of the result

If a chromosomal abnormality is detected, consult with your doctor or chromosome specialist to find out about the fetal condition and prognosis estimated from the results.



Collection of data

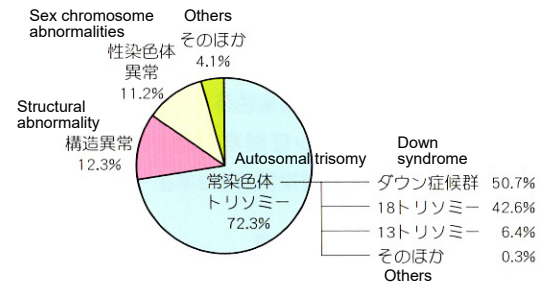
Relationship between chromosomal abnormalities and age

It is known, the older the pregnant woman, the more high probability that a baby with a chromosomal abnormality such as down's syndrome, etc. will be born. In the table below, at birth, by maternal age, babies born in Down Syndrome or all the probability of having a chromosomal abnormality.

Age at delivery	Down syndrome	All chromosomal abnormalities	Age at delivery	Down syndrome	All chromosomal abnormalities
25	1/1352	1/476	35	1/385	1/179
26	1/1287	1/476	36	1/308	1/149
27	1/1209	1/455	37	1/243	1/123
28	1/1120	1/435	38	1/190	1/105
29	1/1019	1/417	39	1/147	1/81
30	1/910	1/385	40	1/113	1/63
31	1/797	1/385	41	1/86	1/49
32	1/684	1/323	42	1/66	1/39
33	1/575	1/286	43	1/50	1/31
34	1/475	1/244	44	1/38	1/24

Breakdown of chromosomal abnormalities

Amniotic fluid analysis performed by Lab Corp Japan from 2006 to 2008. It shows the breakdown of chromosomal abnormalities in chromosomal analysis. Autosomal trisomy occupied about 70%. In addition, of autosomal trisomy, about half was Down Syndrome (Trisomy 21).



Amniotic fluid chromosome analysis and About Rapid FISH

This is a test to check the chromosomes of the fetus using fetal cells contained in amniotic fluid.

参考文献 References

- 1) Test and Technology Transfer Committee. Genet Med. 2000;2:356-361.
- 2) Jacobs PA, et al. J Med Genet. 1992;29:103-108.
- 3) 社内データ In-house data
- 4) Cuckle HS, et al. Br J Obstet Gynaecol. 1987;94:387-402.
- 5) Hook EB. Obstet Gynecol. 1981;58:282-285.

医療機関名 Medical institution name

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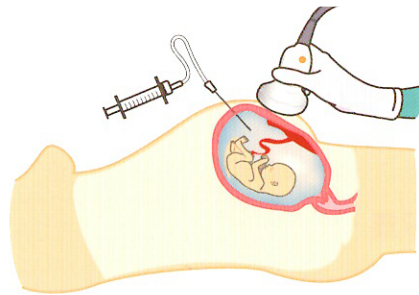
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Before undergoing amniotic fluid chromosome analysis. Be sure to consult your doctor to get genetic counseling.

"Rapid FISH" used be called called "Insight rapid test".

How to collect amniotic fluid

A thin needle is inserted into the abdomen of a pregnant woman to collect amniotic fluid. This procedure is called "amniocentesis". Ultrasonography is performed before collecting amniotic fluid to check the position of the placenta, amniotic fluid volume, etc., as well as the position and posture of the fetus. Check if the tip of the needle is in the amniotic fluid using ultrasound during amniocentesis. Ultrasonography is performed even after amniocentesis confirm there is no abnormality in the condition of the fetus. Amniocentesis is done, in facilities after the 15th week of pregnancy when amniotic fluid increases. For more information, please confirm with your doctor.



Safety of amniocentesis

Amniotic fluid chromosome analysis has been performed since the late 1960's and many pregnant women have undergone the test so far. However, when collecting amniotic fluid, a thin needle is stabbed in the abdomen, so it's not completely free of danger. Complications of amniocentesis are, miscarriage, water rupture, bleeding, abdominal pain, intrauterine infection, fetal injury, and premature births. These problems can be dealt with by appropriate measures in most cases, but in some cases it will eventually lead to miscarriage or fetal death. the probability is said to be 0.2% to 0.3% (1/300 to 1/500).

Amniotic fluid chromosome analysis and Rapid FISH method

Chromosome analysis of amniotic fluid is divided into two categories. One is "Amniotic fluid chromosome analysis", the other is "Rapid FISH".

Rapid FISH is a cleaning inspection. This test can only be added when performing definitive diagnosis water chromosome analysis.

Categories	Positioning	Days Required	Target chromosomal abnormality		
			Change in number		Structural changes and mosaics
			13th, 18th, 21st Chromosome X, Y chromosome	Other Chromosomes	
Amniotic fluid chromosome analysis	Definitive diagnosis	Approx. 2-3 weeks	○	○	○
Rapid FISH	Screening Test	Approx. 1 week	○		

○ Can be detected × Cannot be detected

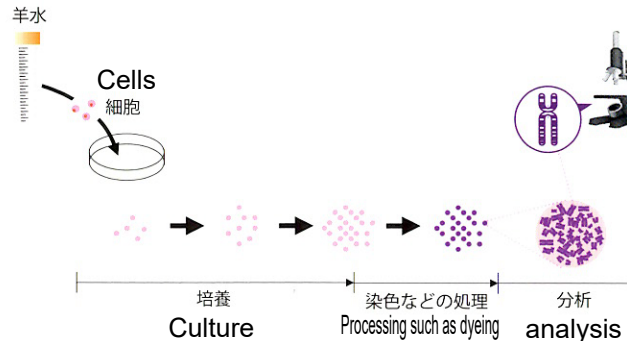
* 13 • 18 • 21st chromosome, X and Y chromosome structural changes and mosaics may be detected.

Amniotic fluid chromosome analysis

In amniotic fluid chromosome analysis, fetal cells in amniotic fluid are tested. However, since the number of cells is small, the number of cells should be increased by culturing. When cells increased enough, select cells at a time when the characteristics can be identified and stain the chromosomes with a stain solution. Then, observe the chromosomes under a microscope.

It takes more days than Rapid FISH because cells are cultured and tested.

Amniotic fluid



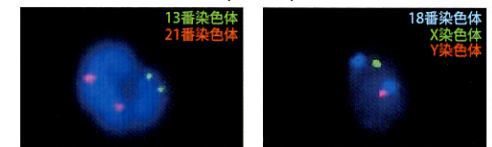
Rapid FISH

Rapid FISH does not culture fetal cells contained in amniotic fluid. It is a screening test that detects quickly the changes in the number of fetal 13th, 18th, 21st, X and Y chromosomes. Changes in the number of these chromosomes account for about 65-70% of the chromosomal abnormalities found in prenatal testing. Although the test results are not final, the correct diagnosis rate of the test results is high for changes in the number of chromosomes subject to this test. So it can predict the result of the definitive diagnosis which is an amniotic fluid chromosome analysis.

This test counts the glowing signals by adding a reagent that binds to a specific location the cells of the fetus which are 13, 18, 21, X and Y and develops a fluorescent color. In addition, count the glowing signals. Of the photo below, if there are two chromosomes, two signals and if there is one, one signal and if there are three, three signals are emitted.

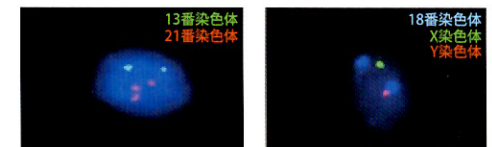
The signals of 50 cells are counted for each reagent. The result is judged according to the proportion of cells with abnormal signal and the number of normal signal

Normal results (male)



Two signals each are glowing on the chromosome 13, 18, and 21. The signal each is glowing on the X and Y chromosomes.

In the case of abnormal results (male with Down syndrome)



Two signals each on chromosome 13 and 18 and three signals on chromosome 21 are glowing. One signal each is glowing on the X and Y chromosomes.

Inspection limits

Amniotic fluid chromosome analysis

Subtle changes cannot be investigated

Many of the changes in the number of chromosomes and the changes in the structure can be analyzed accurately, but the changes in the minute structure and the changes in the gene level cannot be detected.

Mosaic may or may not be diagnosed

If one fetus has both abnormal chromosomal cells and normal cell, it is called a "mosaic". If abnormal and normal cells are found, the mosaic can be diagnosed. However, if only normal cells increase, or even if both cells increased. In such cases, if only normal cells were detected, it may result in a mosaic baby after birth.

Not all illnesses can be diagnosed

Chromosomal abnormalities are part of the baby's illness and this test cannot diagnose all illnesses. Any baby can have illness and about 3-5% have symptoms that require some treatment. In addition, the frequency of a baby with a chromosomal abnormality is 0.92%. Also, even if the baby has a chromosomal abnormality, there are individual differences in the degree of complications and development. However, this test cannot predict various growth and development possibilities.

Results may not be reported

Even if amniotic fluid can be collected, about 0.2% of cases, the number of fetal cells in it does not increase sufficiently and in such case the chromosomes cannot be observed and analyzed to produce results be reported.

Rapid FISH

Not applicable chromosomal abnormalities cannot be investigated

Detects changes in the number of chromosomes 13, 18, 21, X and Y. Therefore, such as structural abnormalities, mosaics, and the number of non-target chromosomes, approximately 30 ~ 35% of chromosomal abnormalities observed in prenatal diagnosis cannot be detected.

Not a definitive diagnosis

In case of abnormal result (positive) in Rapid FISH, 99.83% of those will have the same abnormal result with amniotic fluid chromosome analysis. Also, in case of normal (negative) with this test, 99.96% of those will also have the same normal result with the amniotic fluid chromosome analysis. (Chromosomal changes, not detected by this test, may be observed). For a definitive diagnosis, Please wait for the result of amniotic fluid chromosome analysis.

There are some cases where the test result cannot be judged.

It may not be possible to determine the test result for the following reasons. Please wait for the result of amniotic fluid chromosome analysis.

- When amniotic fluid and fetal cells contained in amniotic fluid are deficient: Since Rapid FISH does not culture cells, so this test needs lot of cells.
- If maternal blood is mixed and the fetus is a girl: Because it is not possible to distinguish between pregnant women's cells and fetal
- Report results only if the percentage of cells with abnormal signal counts and the normal signal counts meet the criteria.