AUSTRALIAN Clinicalabs

Roche

Prenatal Testing Information

BASIC BIOLOGY

Our bodies are made up of trillions of cells.

Within each cell is our genetic material, or DNA.

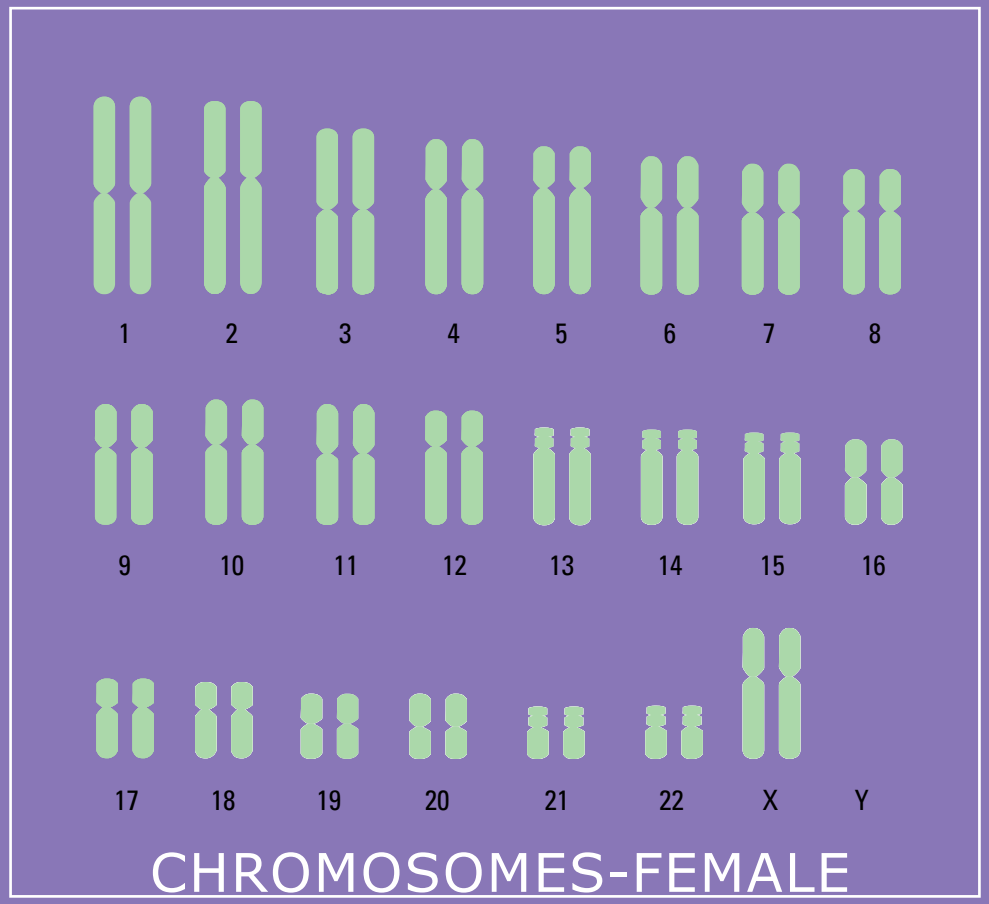
DNA is the instruction manual that tells our bodies how to grow and develop.

BASIC BIOLOGY

DNA is packaged into structures called chromosomes.

We inherit our chromosomes from our parents.

Humans typically have 46 chromosomes, occurring in 23 pairs. Females typically have two X chromosomes and males have one X and one Y chromosome.



CHROMOSOMES-FEMALE

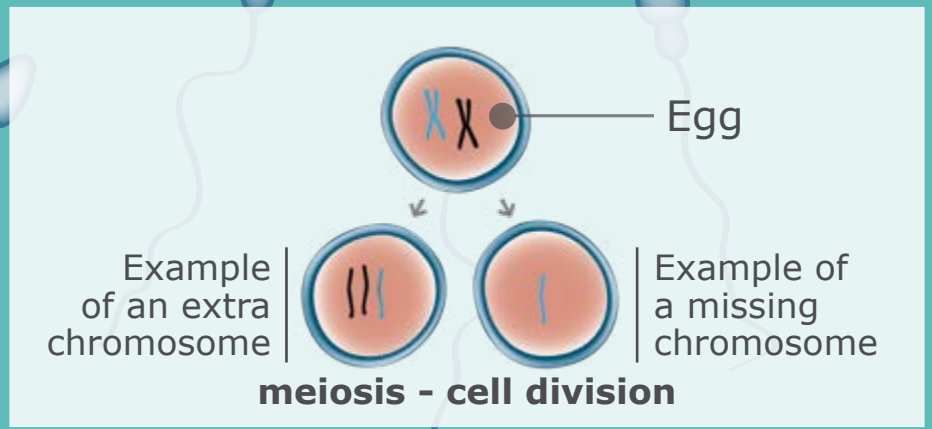
BASIC BIOLOGY

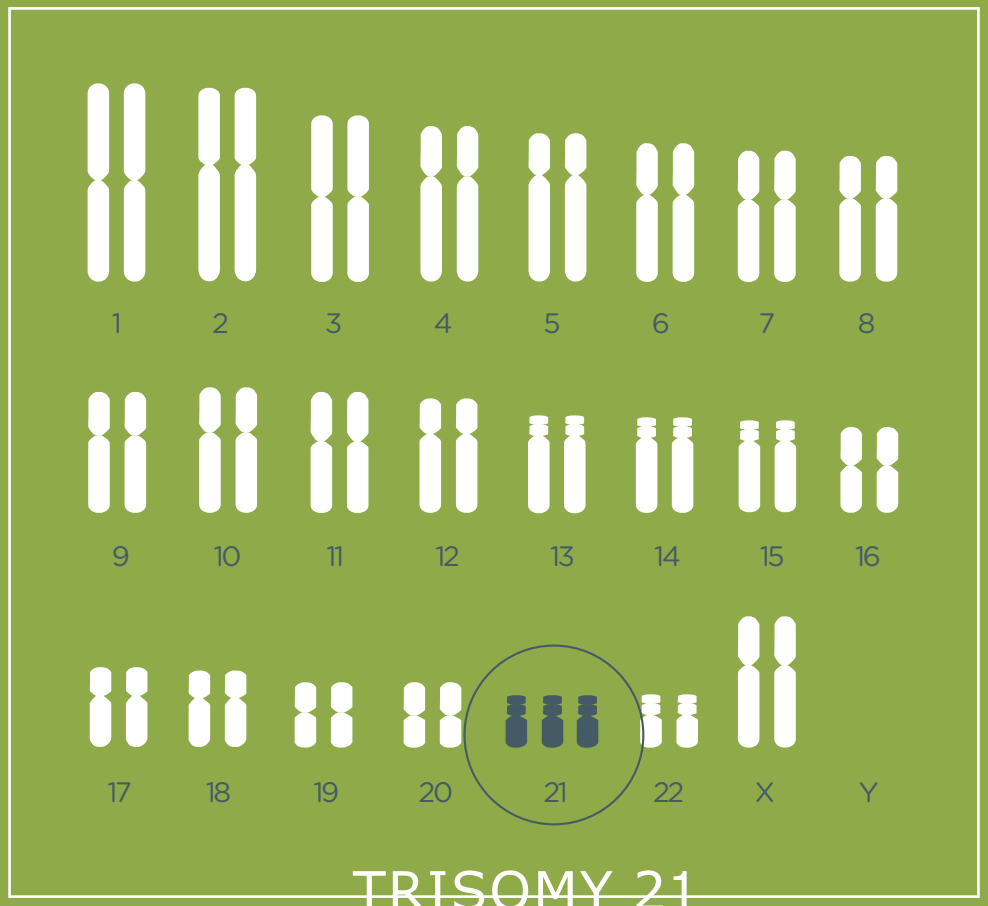
Sometimes, an error can occur that leaves a sperm or egg cell with a missing or extra chromosome.

If that happens, the resulting pregnancy may also have a missing or extra chromosome.

Sperm

Egg





TRISOMY 21

CHROMOSOME CONDITIONS

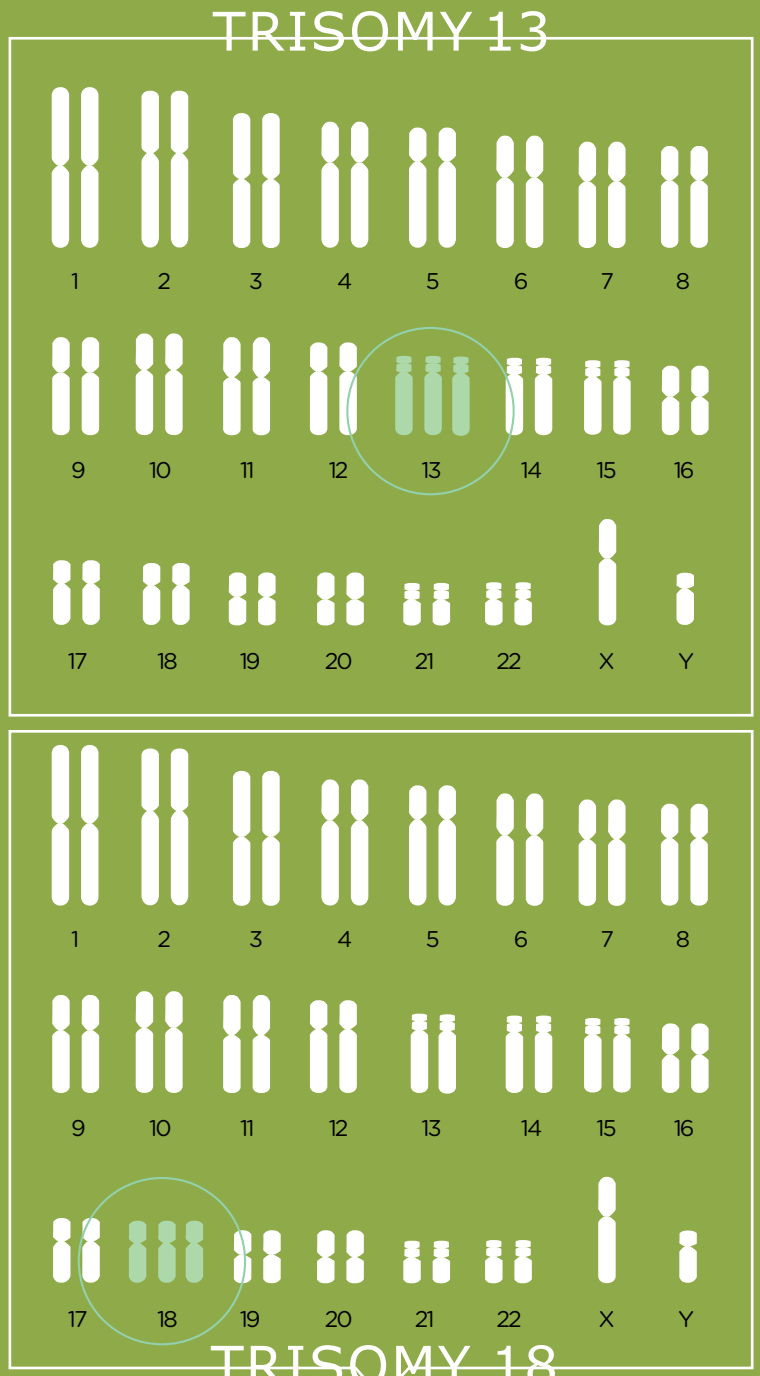
Trisomy 21:

Trisomy 21 refers to an extra copy of chromosome 21. Trisomy 21 causes Down syndrome.

Down syndrome is a condition that can affect physical and mental development.[1]

For further information about Down syndrome or to be connected with other families visit downsyndrome.org.au

1. O'Connor, C. Nature Education. 2008 1(1):42.



CHROMOSOME CONDITIONS

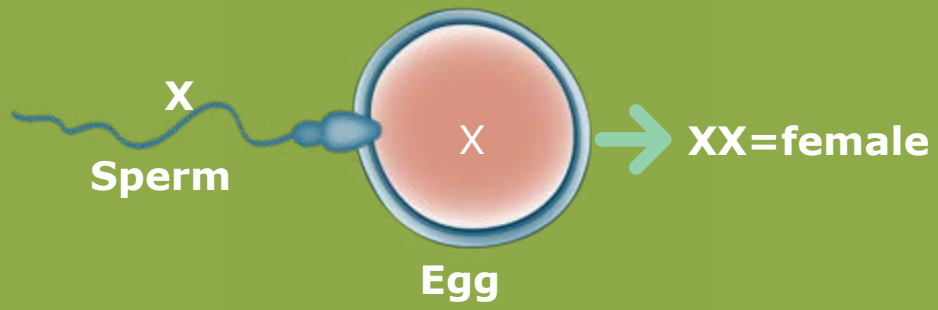
Trisomies 13 and 18:

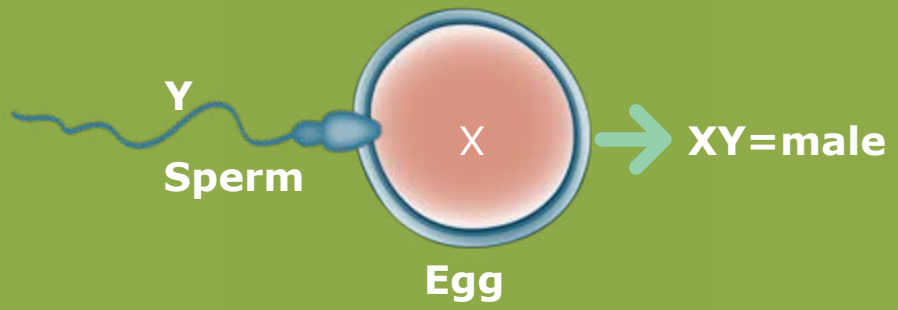
Trisomies 13 (Patau syndrome) and 18 (Edwards syndrome) are rare conditions caused by an extra copy of chromosome 13 or chromosome 18. These are often tested for during pregnancy.

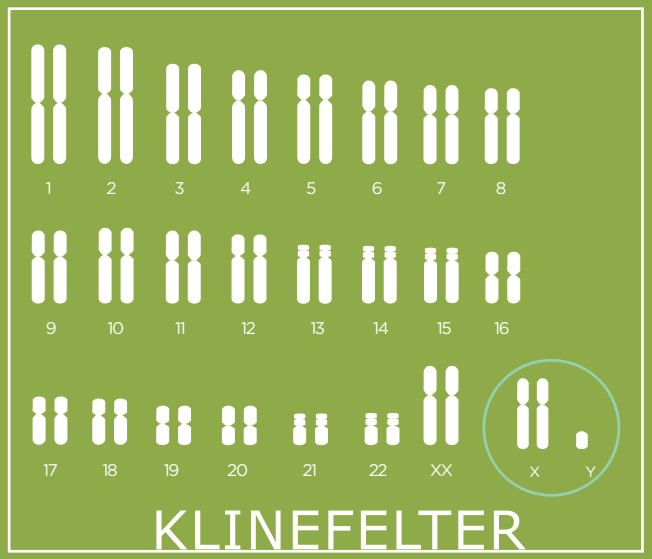
These conditions are more severe than Down syndrome. Some babies with these conditions may survive and live[2] for a short time after birth.[1, 2]

1. A.D.A.M. Medical Encyclopedia. Atlanta (GA): A.D.A.M., Inc.; ©2005. Trisomy 13;2015 Jan 8.
2. A.D.A.M. Medical Encyclopedia. Atlanta (GA): A.D.A.M., Inc.; ©2005. Trisomy 18;2015 Jan 8.

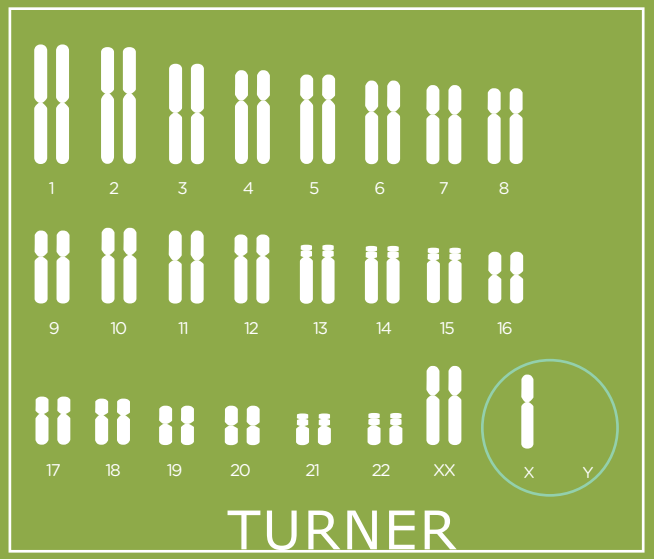
CHROMOSOME CONDITIONS







KLINEFELTER SYNDROME



TURNER SYNDROME

Chromosomes that determine whether we are male or female are labelled "X" and "Y" and are also called 'sex chromosomes'.

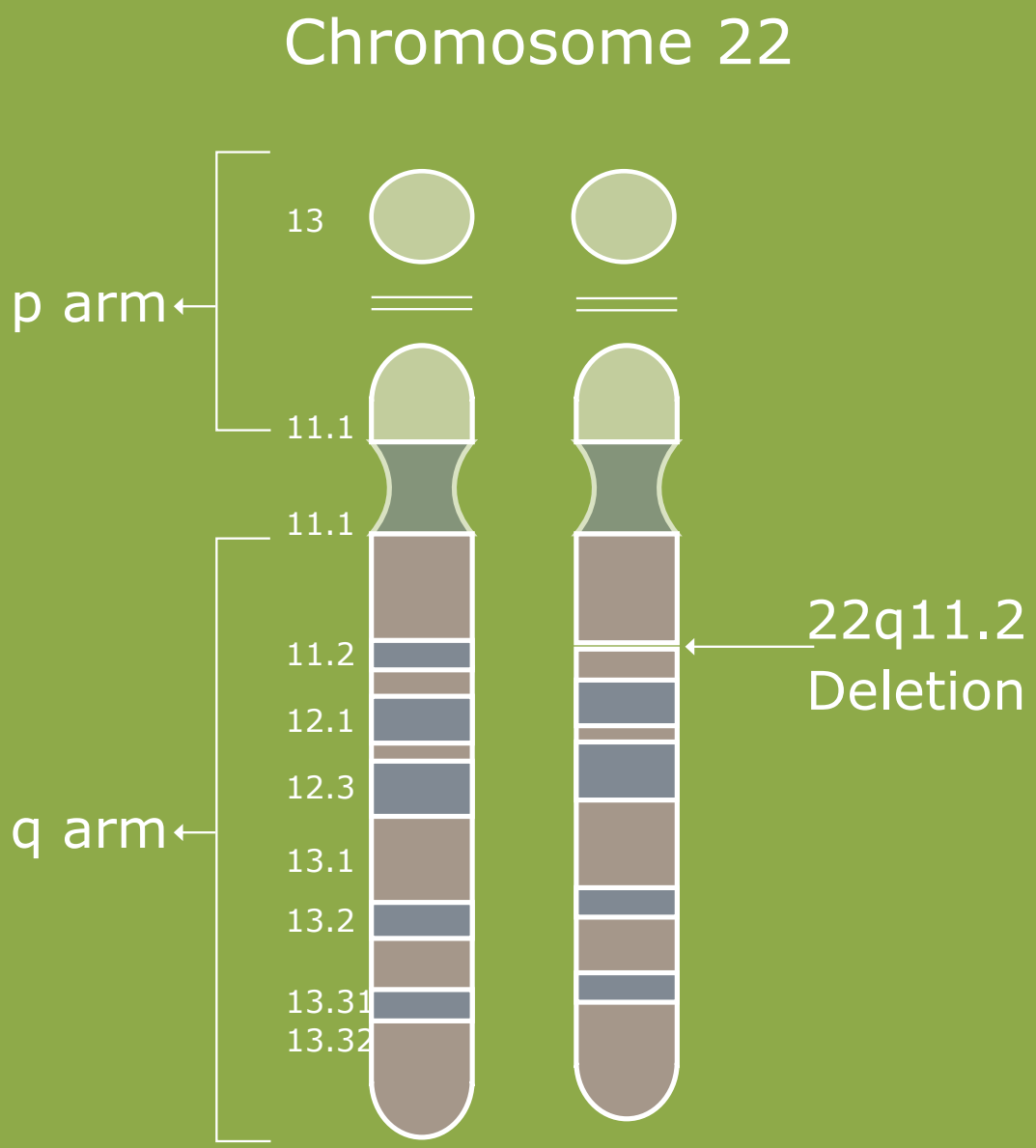
Some people have a missing or an extra sex chromosome.

The effects of these conditions are typically less severe than the trisomies already discussed but may include learning disabilities and sometimes infertility, or the inability to have children.[1]

Many people who have these conditions will not be identified because they do not cause any effect.

1. Visootsak J, Graham JM. Orphanet J Rare Dis. 2006;1:42.

CHROMOSOME CONDITIONS



22q11.2 deletion:

22q11.2 deletion refers to a small deletion found on chromosome 22.

Some people with a 22q11.2 deletion may not know they have the condition due to the variability in effect and severity. 22q11.2 deletion can affect many different systems.[1]

The effect and severity of a deletion at 22q11.2 cannot be determined during pregnancy however some cardiac anomalies associated with the condition may be seen on ultrasound.[1]

For further information about 22q11.2 deletion syndrome visit 22q.org.au

1. McDonald-McGinn DM et al. Nature reviews Disease primers. 2015;1:15071.

CHANCE OF THESE CONDITIONS

Most pregnancies will not have a chromosomal condition.

The chance of some chromosome conditions can be influenced by the age of the mother and, in some cases, family history.

Regardless of a woman's age, there is always some chance for every pregnancy to be affected by a chromosome condition.

COMBINED FIRST TRIMESTER SCREENING*

Combined first trimester screening* measures protein and hormone levels in a blood sample from the pregnant woman and estimate the chance that the developing baby has a chromosome condition.

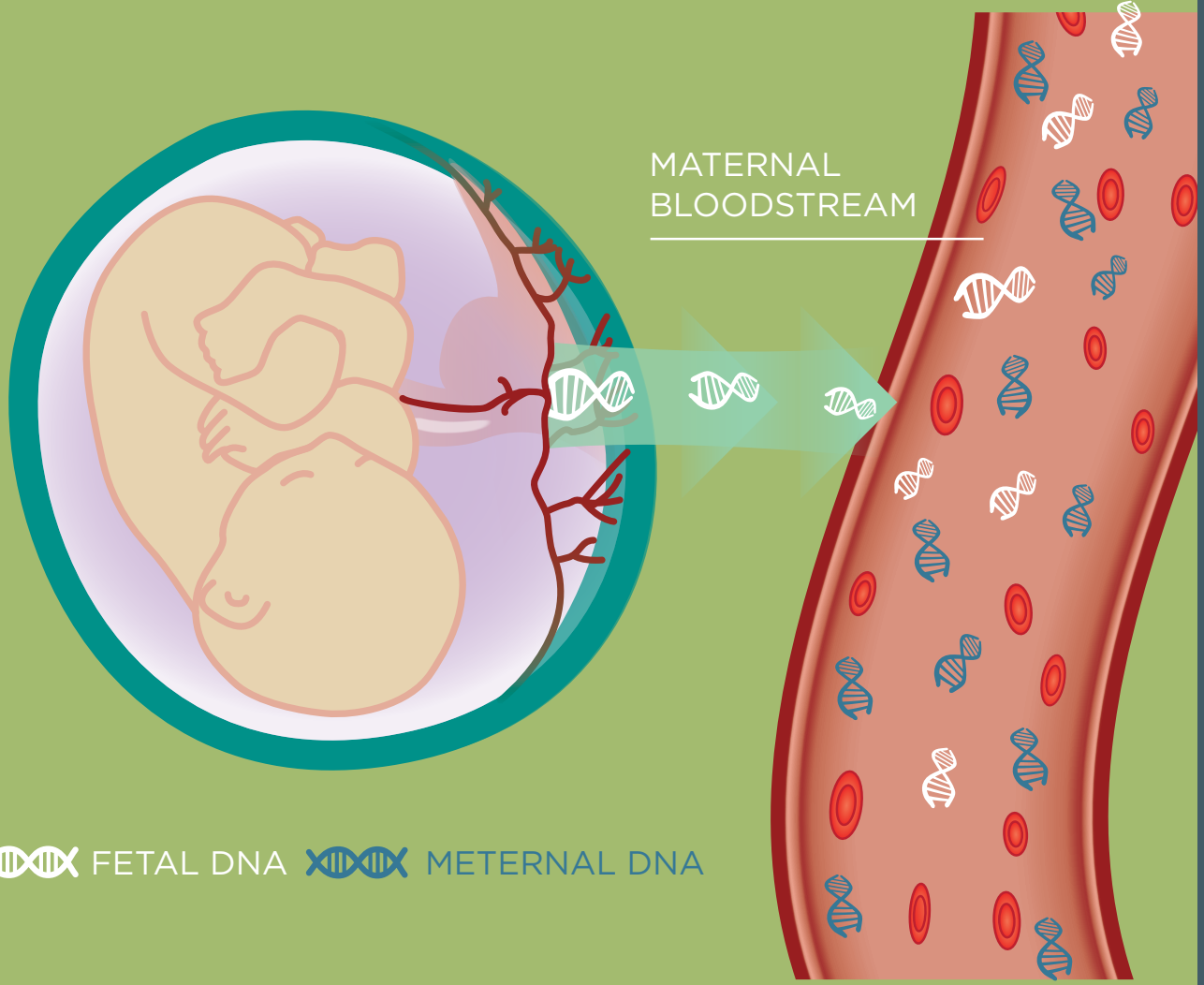
The blood test is often combined with an ultrasound measurement, called the nuchal translucency (NT), to improve result accuracy.

This type of testing is restricted to certain periods of time during the pregnancy (11+0 to 13+6 weeks).[1]

* Maternal serum and ultrasound markers

1. RANZCOG Guideline: Prenatal screening and diagnosis of chromosomal and genetic abnormalities in the fetus in pregnancy (C-Obs 59). Amended July 2018.

harmony®
PRENATAL TEST



HARMONY

During pregnancy, the pregnant woman's blood contains fragments of the developing baby's DNA. The Harmony Prenatal Test is a screening test that analyses this DNA in a blood sample to predict the probability of trisomy 21 (Down syndrome), as well as trisomies 18 and 13, in the pregnancy.[1,2] These type of tests are also called cell-free DNA tests or non-invasive prenatal test (NIPT).

The Harmony Prenatal Test is more accurate than traditional screening tests and can be ordered any time after 10 weeks of pregnancy.[1]

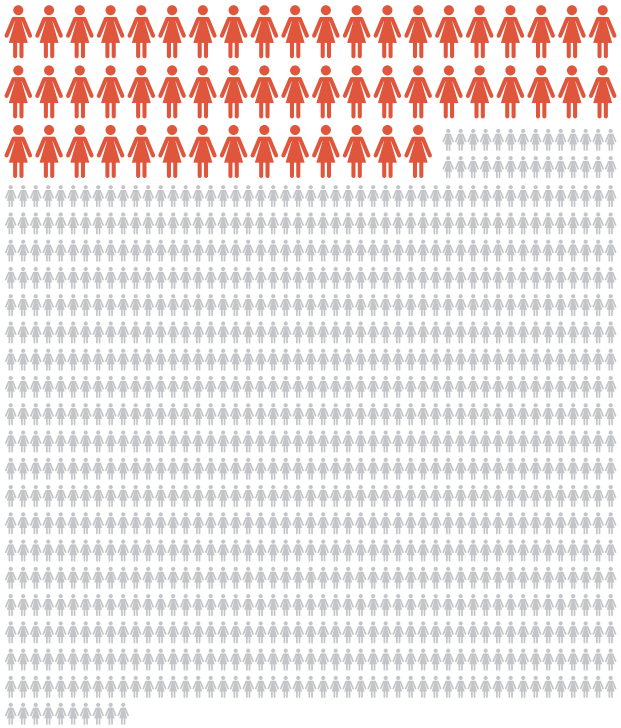
With the Harmony Prenatal Test, you may also opt to test for conditions caused by having an extra or missing copy of the X or Y or test for a deletion of the 22q11.2 region.

1. Norton et al. N Engl J Med. 2015 Apr 23;372(17):1589-97.
2. Nicolaides et al. Am J Obstet Gynecol. 2012 Nov;207(5):374.e1-6.

COMBINED FIRST TRIMESTER SCREENING*:

1 in 20 OR THE EQUIVALENT OF 50 in 1000

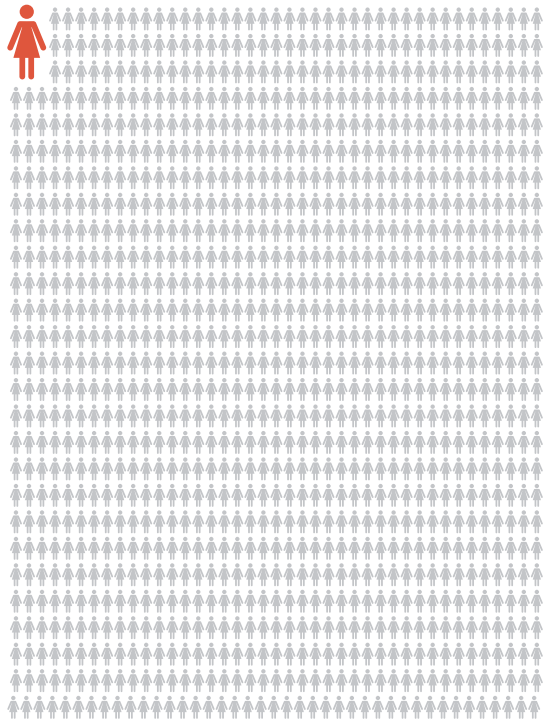
will have a false positive result



HARMONY PRENATAL TEST:

Less than 1 in 1600

will have a false positive result



The Harmony Prenatal Test is a screening test that is more accurate than traditional screening tests for trisomy 21 (Down syndrome).[1]

With Harmony, there is a lower chance that your doctor will recommend follow-up testing, such as amniocentesis.[2]

HARMONY

Clinical studies show that the Harmony Prenatal Test will detect greater than 99% of cases of trisomy 21 (Down syndrome).[1]

Less than 1 in 1,000 women will have a false positive test result with Harmony Prenatal Test. This is at least 50 times lower than combined first trimester screening.[1]

In a small percentage of women, a result from NIPT may not be obtained. This is most often due to not enough fetal DNA within the maternal blood stream.[1]

* Maternal serum and ultrasound markers

1. Norton et al. N Engl J Med. 2015 Apr 23;372(17):1589-97
2. Wax et al. J Clin Ultrasound 2015 Jan; 43(1):1-6.

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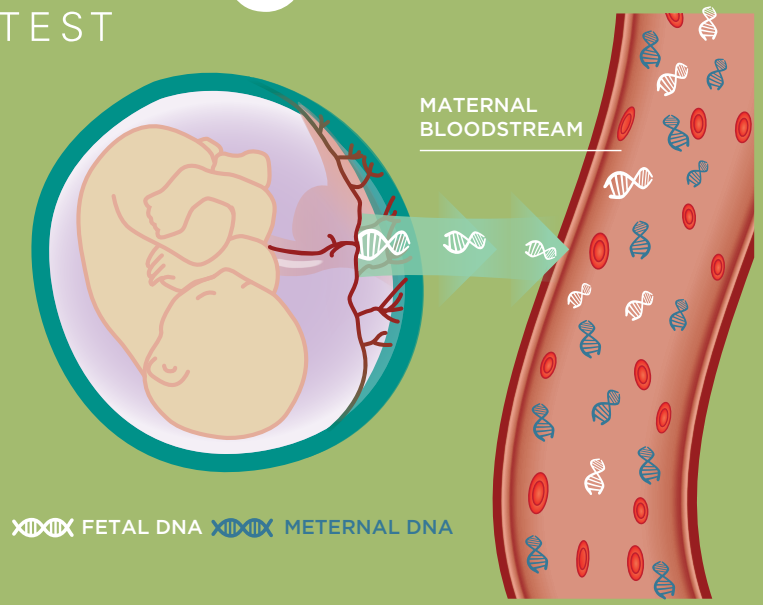
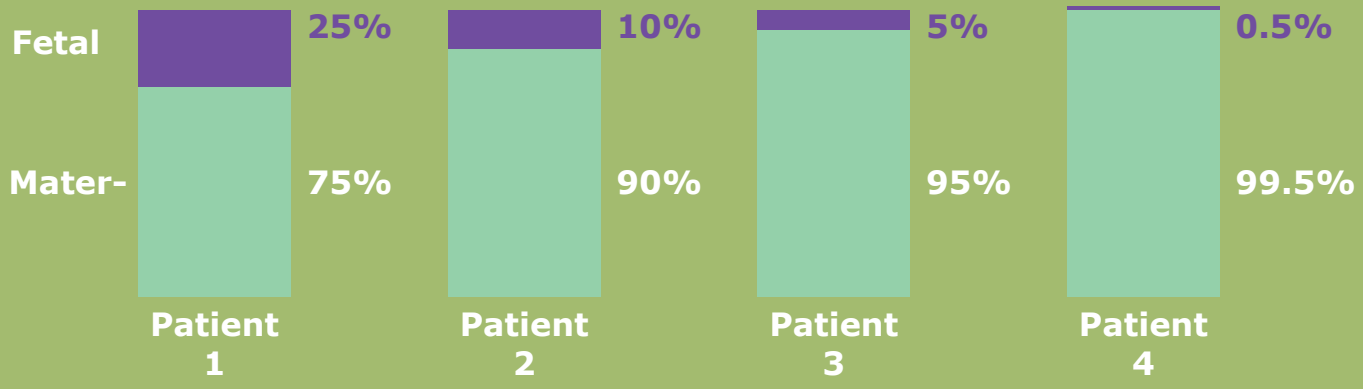
PRENATAL TEST



Fetal Fraction in Circulation



Percentage of maternal to fetal DNA in circulation can vary from woman to woman, and changes throughout gestation[4]

FETAL FRACTION

Fetal fraction is the term used for the amount of DNA that comes from the baby out of the total amount of DNA in the sample.

Each sample will have varying fetal fractions. Below 4% fetal fraction the result may become compromised and this could lead to a sample that is high risk for a trisomy being reported as a low risk.[1, 2, 3]

The ability to accurately measure fetal fraction is an essential requirement. Harmony provides a fetal fraction measurement for every eligible sample.

The presence of fetal cell-free DNA must not be assumed.

1. Palomaki et al. Genet Med 2012;14:296-305.
2. Canick et al. Prenat Diagn. 2013 Jul;33(7):667-74.
3. Sparks A et al, Am J Obstet Gynecol. 2012 Apr;206(4):319. e1-9.
4. Wang E et al, Prenat Diagn. 2013 Jul;33(7):662-6.

REDRAW REQUESTS

Over 97% of women will receive a result first time with Harmony Prenatal Test.[1]

Some women will receive a redraw request and a very small number of these women will not be able to get an answer with NIPT at all. These women should discuss with their health care provider other methods for screening their pregnancy.

A redraw request is not a cause for alarm. It is due to stringent quality control measures of the Harmony Prenatal Test or possible biological factors.

The most common biological reason is insufficient fetal DNA in the mother's blood. The ability to accurately measure fetal fraction is an essential requirement for accurate NIPT results.

1. Norton et al. N Engl J Med. 2015 Apr 23;372(17):1589-97.

TEST OPTIONS

The Harmony Prenatal Test is validated for use in singleton, twin, and IVF pregnancies, including self and non-self egg donor pregnancies.[1]

		AVAILABLE FOR		
		SINGLETON	EGG DONOR & IVF	TWINS
Harmony Prenatal Test	Evaluates the probability of fetal trisomy 21, trisomy 18 and trisomy 13.	✓	✓	✓
The following test options are also available from the same blood draw:				
☐ **Fetal Sex**	Provides information regarding fetal sex. Assessment of fetal sex does not include assessment of sex chromosome aneuploidy. In twin pregnancies, a female result applies to both fetuses; a male result applies to one or both fetuses.	✓	✓	✓
☐ **Monosomy X**	Evaluates the probability of monosomy X, but no information regarding other sex chromosome aneuploidies.	✓	✓	
☐ **Sex Chromosome Aneuploidy Panel**	Evaluates the probability of X and Y chromosome aneuploidies, including monosomy X, XXX, XXY, XYY and XXYY.	✓	✓	
☐ **22q11.2**	Evaluates the probability of 22q11.2 deletion	✓	✓	

For both Monosomy X and the Sex Chromosome Aneuploidy Panel, fetal sex will only be reported if the Fetal Sex box is checked separately. However if the result indicates a high risk for sex chromosome aneuploidy, then this risk assessment will indirectly provide information regarding fetal sex. The Harmony Prenatal test is not available for more than 2 fetuses.

1. Stokowski et al. Prenatal Diagnosis 2015, 35, 1–4

The Harmony Prenatal Test offers assessment for trisomies 21, 18 and 13.

After discussion with a healthcare provider, patients carrying one fetus can choose to include an assessment for 22q11.2 deletion syndrome, fetal sex, monosomy X or the sex chromosome aneuploidy panel. This information will not be reported unless specifically requested.

Twin pregnancies requesting the Harmony Prenatal Test will have an assessment for trisomies 21, 18 and 13 and a single result will be reported for the pregnancy. On request, fetal sex can be reported for the pregnancy.

Sometimes NIPT is not an option for screening a pregnancy. Reasons include pregnancies with more than two fetuses, pregnancies where an empty sac can be identified or some maternal conditions.

SCREENING TESTS

Harmony Prenatal Test is a screening test. No screening test is designed to detect all possible conditions. Screening tests help identify pregnancies with an increased chance of certain chromosome conditions. With screening tests, false positive and false negative results will occur.

Other types of screening tests, such as an early structural scan, may be able to provide information about other conditions during pregnancy and can be discussed with a medical professional.

Women who have an increased chance on their screening test should consult a medical professional who can recommend additional invasive confirmatory testing.

INVASIVE CONFIRMATORY TESTING

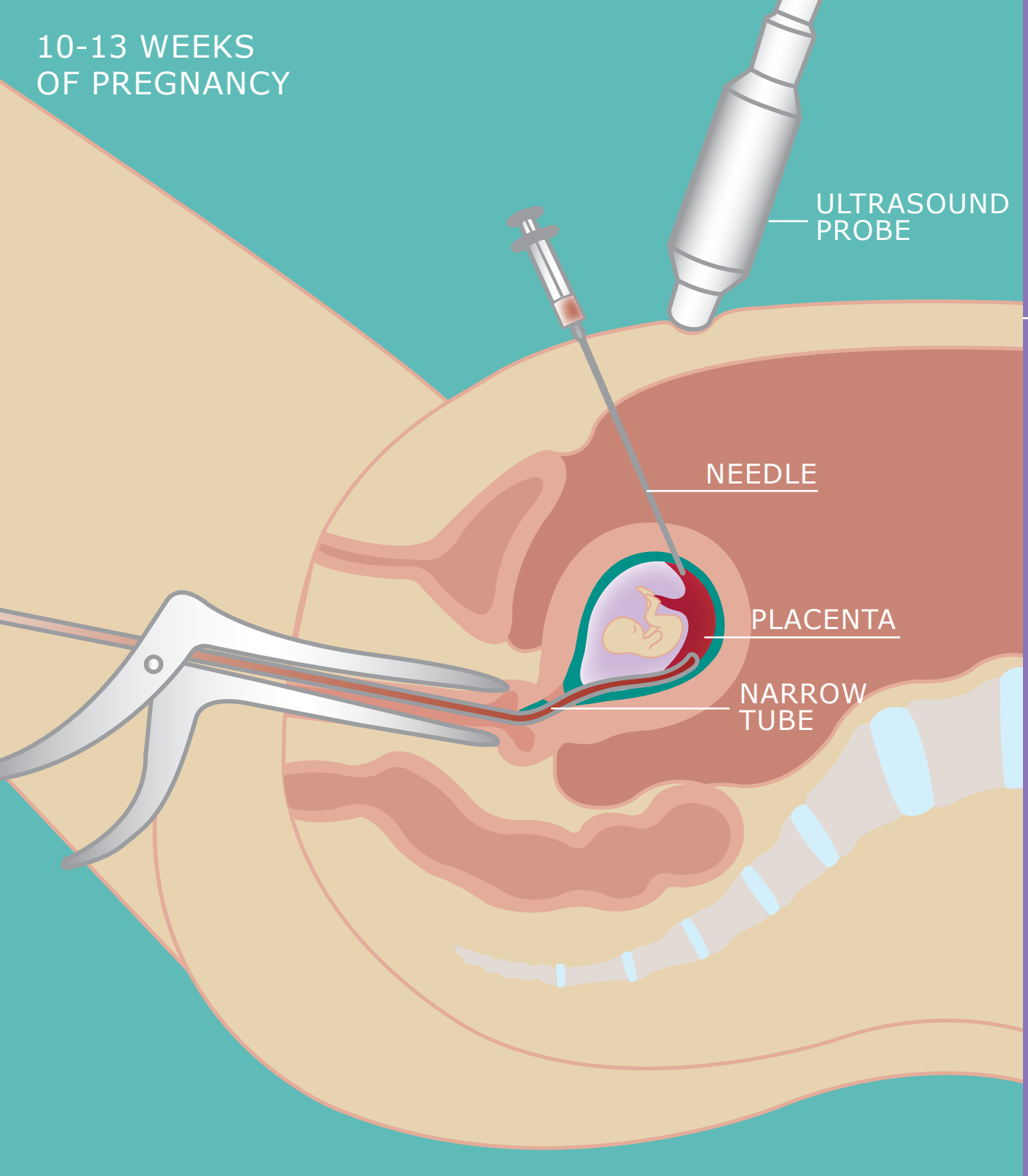
Invasive confirmatory testing involves a procedure to obtain cells from the pregnancy for testing.[1]

Invasive confirmatory testing can give a definitive answer about most chromosome conditions in a pregnancy.

It is most often performed for pregnancies with an increased chance for a chromosome condition.

There are two types of invasive procedures, chorionic villus sampling and amniocentesis.

1. RANZCOG Guideline: Prenatal screening and diagnosis of chromosomal and genetic abnormalities in the fetus in pregnancy (C-Obs 59). Amended July 2018.



CHORIONIC VILLUS SAMPLING (CVS)[1]

CVS can be done between 10-13 weeks of pregnancy.

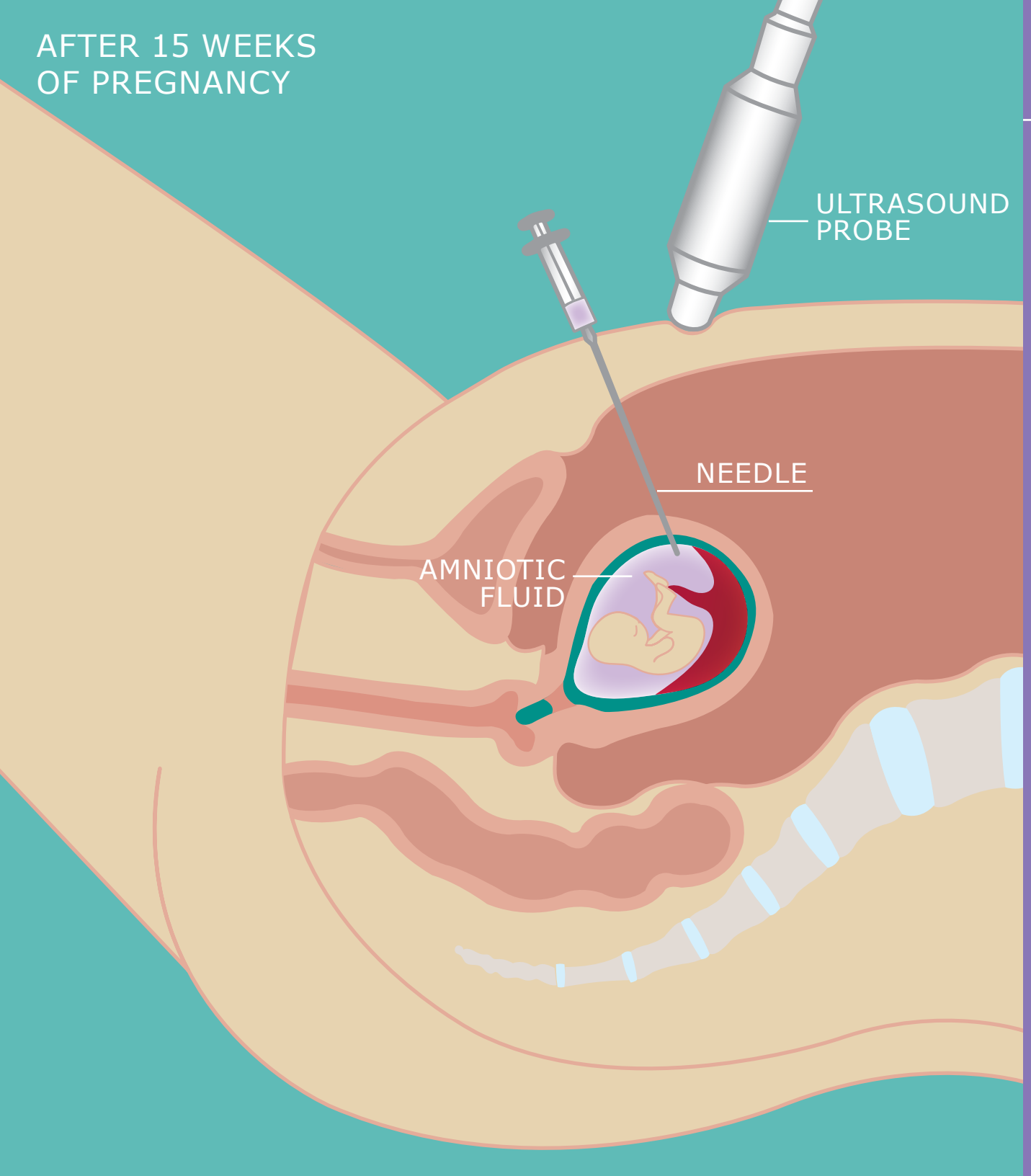
This procedure removes a small sample of cells from the placenta using a needle (through the abdomen) or narrow tube (through the vagina).

All chromosomes within these cells are studied to see if there are any extra or missing.

CVS can provide greater than 99% detection rate for all chromosome conditions.

There is a small chance of miscarriage following the procedure.

1. Chorionic villus sampling. Retrieved from http://www.mayoclinic.com/health/chorionic-villus-sampling/MY00154/DSECTION=chances - 29 June 2017.



AMNIOCENTESIS[1]

An amniocentesis is performed after 15 weeks of pregnancy.

Amniotic fluid contains cells from the developing baby, and a small sample of this fluid is removed using a needle that is inserted through the abdomen.

All chromosomes within these cells are studied to see if there are any extra or missing.

Amniocentesis can provide a 99.8% detection rate for chromosome conditions.

This procedure also carries a small chance of miscarriage.

1. Amniocentesis. Retrieved from http://www.mayoclinic.com/health/amniocentesis/MY00155/DSECTION=chances - 29 June 2017.

THE CHOICE IS YOURS!

Now that you have learned about the non-invasive screening and invasive confirmatory testing options to help identify the chance for chromosome conditions in your pregnancy, the choice is yours.

It is recommended that you discuss your preferences with your healthcare provider or genetic counsellor to help make the best choice for you.

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Visit us at **antenatal.clinicallabs.com.au**
For assistance email harmony@clinicallabs.com.au

The Harmony non-invasive prenatal test is based on cell-free DNA analysis and is considered a prenatal screening test, not a diagnostic test. Harmony does not screen for potential chromosomal or genetic conditions other than those expressly identified in this document. All women should discuss their results with their healthcare provider who can recommend confirmatory, diagnostic testing where appropriate. The Harmony Prenatal Test is validated for use in women ≥ 18 years. The Harmony Prenatal Test was developed by Ariosa Diagnostics. The Harmony Prenatal Test is performed in Australia.

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DECISION MAKING