

General information about positive NIPT results: Trisomy 9

My patient's NIPT is positive for trisomy 9. What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result suggests the presence of an extra copy of chromosome 9. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 9 depends on many factors, including the patient's clinical and family history.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. Globally, professional medical societies recommend that all women with a positive screening result should have genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm the results.^{1,2} Confirmation prior to birth can also help with pregnancy and neonatal management.

See below for more information about trisomy 9.

What is trisomy 9?

Trisomy 9 is a condition that is caused by an extra chromosome number 9 (three copies instead of two).

What are the features of trisomy 9?

Most pregnancies with trisomy 9 will miscarry spontaneously. If a developing fetus has mosaic trisomy 9 (where some cells are normal and some cells have trisomy 9), there is an increased chance for the pregnancy to progress and possibly survive to term. However, liveborn infants with full trisomy 9 are expected to die shortly after birth. Liveborn infants with mosaic trisomy 9 are expected to have serious medical problems. Key features include prenatal onset of growth deficiency, severe intellectual disability, dysmorphic features, cardiac defects, and skeletal problems. In reported cases of prenatally diagnosed trisomy 9, the outcomes have ranged from normal to live births with clinical sequelae. The variability in clinical presentation is believed to be due to confined placental mosaicism (CPM; when trisomic cells are present in the placenta, but not in the fetus) or the degree of fetal mosaicism.

What is the prevalence of this condition?

The exact prevalence of this condition is unknown. For this reason, positive predictive value (PPV) cannot be calculated. Trisomy 9 is a common cause for miscarriage early in pregnancy, accounting for 2.7% of all trisomic first-trimester miscarriages. This condition is very rare in liveborn infants.

What testing could be considered?

Specialized genetic tests such as karyotyping, fluorescence *in situ* hybridization (FISH), quantitative polymerase chain reaction (qPCR), and microarray are available to confirm the presence of trisomy 9.

These confirmatory tests are generally performed on cells from chorionic villus sampling (CVS) or amniocentesis during pregnancy, on cord blood or peripheral blood sample after the baby is born, or on products of conception (POC) in the case of a miscarriage. The type of invasive procedure and diagnostic testing should take into account the underlying chromosome anomaly.^{3,4}

Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 9, but a normal ultrasound cannot exclude trisomy 9.

Resources for trisomy 9

MedlinePlus Genetics
medlineplus.gov/genetics/chromosome/9

Unique, The Rare Chromosome Disorder Support Group
rarechromo.org

References

- Rose NC, Kaimal AJ, Dugoff L, et al. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. *Obstet Gynecol.* 2020;136(4):e48-e69.
- Benn P, Borrell A, Chiu RW, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. *Prenat Diagn.* 2015;35(8):725-734.
- Cherry AM, Akkari YM, Barr KM, et al. Diagnostic cytogenetic testing following positive noninvasive prenatal screening results: a clinical laboratory practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2017;19(8):845-850.
- Van Opstal D, Srebniak M. Cytogenetic confirmation of a positive NIPT result: evidence-based choice between chorionic villus sampling and amniocentesis depending on chromosome aberration. *Expert Rev Mol Diagn.* 2016;16(5):513-520.

Additional resources

Bruns DA, Campbell E. Twenty-five additional cases of trisomy 9 mosaic: Birth information, medical conditions, and developmental status. *Am J Med Genet A.* 2015;167A(5):997-1007.

Gardner RJM, Sutherland GR, Shaffer LG. *Gardner and Sutherlands's Chromosome Abnormalities and Genetic Counseling.* 5th ed. Oxford University Press; 2018.

Malvestiti F, Agrati C, Grimi B, et al. Interpreting mosaicism in chorionic villi: results of a monocentric series of 1001 mosaics in chorionic villi with follow-up amniocentesis. *Prenat Diagn.* 2015;35(11):1117-1127.

Schwendemann WD, Contag SA, Wax JR, et al. Sonographic findings in trisomy 9. *J Ultrasound Med.* 2009;28(1):39-42.

Tonni G, Lituania M, Chitayat D, et al. Complete trisomy 9 with unusual phenotypic associations: Dandy-Walker malformation, cleft lip and cleft palate, cardiovascular abnormalities. *Taiwan J Obstet Gynecol.* 2014;53(4):592-597.