

Chromosomal Microarray Analysis (CMA) for Pregnancy Loss

- I. Chromosomal microarray analysis on products of conception (POC) may be considered **medically necessary** as an alternative to conventional karyotype analysis when:
 - A. The member meets one of the following:
 1. The member has a history of [recurrent pregnancy loss](#), **OR**
 2. The member has a pregnancy loss at or greater than 20 weeks of gestation (i.e., IUFD or stillbirth), **AND**
 - B. The member has received counseling regarding the benefits and limitations of chromosome microarray analysis on products of conception.
- II. Chromosome microarray analysis on products of conception (POC) is considered **investigational** for all other indications.

RATIONALE AND REFERENCES

Chromosomal Microarray Analysis (CMA) for Pregnancy Loss

American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM)

The ACOG and SMFM practice bulletin no. 682 supports the following evaluation for pregnancy loss in their 2016 statement (reaffirmed 2020 and 2023):

"Chromosomal microarray analysis of fetal tissue (i.e., amniotic fluid, placenta, or products of conception) is recommended in the evaluation of intrauterine fetal death or stillbirth when further cytogenetic analysis is desired because of the test's increased likelihood of obtaining results and improved detection of causative abnormalities" (p. e263).

Committee on Genetics and the Society for Maternal-Fetal Medicine. Committee Opinion No.682: Microarrays and Next-Generation Sequencing Technology: The Use of Advanced Genetic Diagnostic

Tools in Obstetrics and Gynecology. Obstet Gynecol. 2016;128(6):e262-e268.
doi:10.1097/AOG.0000000000001817

American Society for Reproductive Medicine (ASRM)

The American Society for Reproductive Medicine (2012) issued an opinion on the evaluation and treatment of recurrent pregnancy loss. The statement drew multiple conclusions, one of which states: "Evaluation of recurrent pregnancy loss can proceed after 2 consecutive clinical pregnancy losses" (p. 1108).

Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril. 2012;98(5):1103-1111.
doi:10.1016/j.fertnstert.2012.06.048

Papas, et al.

A review published in the Application of Clinical Genetics in 2021 by Papas and Kutteh recommends that genetic testing on products of conception should be performed after the second and subsequent pregnancy loss. Chromosome microarray is the preferred testing method (p. 321).

Papas RS, Kutteh WH. Genetic testing for aneuploidy in patients who have had multiple miscarriages: a review of current literature. Appl Clin Genet. 2021;14:321-329.

DEFINITIONS

1. **Amniocentesis** is a procedure in which a sample of amniotic fluid is removed from the uterus for prenatal diagnostic testing.
2. **Chorionic Villi Sampling (CVS)** is a procedure where a sample of chorionic villi is removed from the placenta for prenatal diagnostic testing.
3. **Major malformations** are structural defects that have a significant effect on function or appearance. They may be lethal or associated with possible survival with severe or moderate immediate or long-term morbidity. Examples by organ system include:

- Genitourinary: renal agenesis (unilateral or bilateral), hypoplastic/cystic kidney
 - Cardiovascular: complex heart malformations (such as pulmonary valve stenosis, tetralogy of fallot, transposition of the great arteries, coarctation of the aorta, hypoplastic left heart syndrome)
 - Musculoskeletal: osteochondrodysplasia/osteogenesis imperfecta, clubfoot, craniosynostosis, fetal growth restriction/intrauterine growth restriction (IUGR)
 - Central nervous system: anencephaly, hydrocephalus, myelomeningocele
 - Body wall: omphalocele/gastroschisis
 - Respiratory: cystic adenomatoid lung malformation
4. **Percutaneous Umbilical Cord Blood Sampling (PUBS)** is a procedure where a sample of fetal blood is extracted from the vein in the umbilical cord.
5. **Recurrent pregnancy loss (RPL)** is defined as having two or more failed clinical pregnancies, including a current loss if applicable.