OBJECTIVE: We sought to determine the ability of single-nucleotide polymorphism—based noninvasive prenatal testing (NIPT) to identify triploid, unrecognized twin, and vanishing twin pregnancies.

STUDY DESIGN: The study included 30,795 consecutive reported clinical cases received for NIPT for fetal whole-chromosome aneuploidies; known multiple gestations were excluded. Cell-free DNA was isolated from maternal blood samples, amplified via 19,488-plex polymerase chain reaction, and sequenced. Sequencing results were analyzed to determine fetal chromosome copy number and to identify the presence of additional fetal haplotypes.

RESULTS: Additional fetal haplotypes, indicative of fetal triploidy, vanishing twin, or undetected twin pregnancy, were identified in 130 (0.42%) cases. Clinical confirmation (karyotype for singleton pregnancies, ultrasound for multifetal pregnancies) was available for 58.5% (76/130) of cases. Of the 76 cases with confirmation, 42.1% were vanishing twin, 48.7% were viable twin, 5.3% were diandric triploids, and 3.9% were nontriploid pregnancies that lacked evidence of co-twin demise. One pregnancy had other indications suggesting triploidy but lacked karyotype confirmation. Of the 5 vanishing twin cases with a known date of demise, 100% of losses occurred in the first trimester; up to 8 weeks elapsed between loss and detection by NIPT.

CONCLUSION: This single-nucleotide polymorphism—based NIPT successfully identified vanished twin, previously unrecognized twin, and triploid pregnancies. As vanishing twins are more likely to be aneuploid, and undetected residual cell-free DNA could bias NIPT results, the ability of this method to identify additional fetal haplotypes is expected to result in fewer false-positive calls and prevent incorrect fetal sex calls.

Key words: noninvasive prenatal testing, single-nucleotide polymorphism, triploidy, vanishing twin

The recent introduction of cell-free DNA (cfDNA)-based noninvasive prenatal testing (NIPT) has offered pregnant women a more accurate method for detecting fetal aneuploidies than traditional serum screening methods.1-12 NIPT noninvasively determines fetal chromosome copy number by interrogating cfDNA isolated from maternal plasma, with the fetus contributing anywhere from <2% to >30% of the total cfDNA.3,7,13 Other NIPT approaches use quantitative “counting” methods where fetal chromosome copy number is determined by comparing the absolute number of sequence reads from the chromosome(s) of interest (eg, chromosome 21) to reference chromosome(s), and inferring fetal trisomy when this ratio is above a predetermined threshold. This approach cannot determine the source of DNA (fetal or maternal) and is therefore unable to detect additional fetal haplotypes associated with triploidy or vanishing twins. Vanishing twins were reported to account for 15% of false positives in a...
recent counting-based NIPT study. This likely results in unnecessary invasive prenatal testing. A more recent approach using a single-nucleotide polymorphism (SNP)-based method along with sophisticated informatics can resolve this potential source of false-positive results. This approach identifies the presence of additional fetal haplotypes, indicative of a triploid or dizygotic multifetal pregnancy, and determines parental origin.\(^\text{10,12}^\)

Using the SNP-based approach, the prevalence of cases found to have additional fetal haplotypes within 30,795 consecutive cases undergoing routine clinical NIPT was determined, and is reported here. Clinical follow-up of these cases is also described.

**Materials and Methods**

**Patients**

The current study included all samples from participating centers received for commercial testing from March 1, through Nov. 30, 2013, that received a NIPT result. This study received a notification of exempt determination from an institutional review board (Ethical and Independent Review Services, no. 14064-01). All samples were analyzed at Natera’s Clinical Laboratory Improvement Act–certified and College of American Pathologists–accredited laboratory in San Carlos, CA. Analysis was performed for all samples on chromosomes 13, 18, 21, X, and Y, and included detection of trisomy 21, trisomy 18, trisomy 13, monosomy X, sex chromosome abnormalities (47,XXX/XXY/XYY), fetal sex, and additional fetal haplotypes.

**Sample collection and NIPT**

Maternal blood samples (>13 mL) were collected in Streck (Omaha, NE) blood collection tubes and processed at Natera (San Carlos, CA) within 6 days of collection. All samples were accompanied by a requisition form from the ordering clinician, and included the following patient information: gestational age, maternal date of birth, maternal weight, whether it was a multigestation pregnancy, and whether a paternal buccal swab was included. Ordering clinicians determined indication(s) for testing. Cases accepted for analysis were indicated as singleton pregnancies by ordering clinicians. Results were reported directly to the ordering clinician or distribution partners.

Samples were considered outside of the specifications for testing and were not analyzed if there was insufficient blood volume or the wrong tube was used, the sample was damaged, the sample was received at the laboratory >6 days after collection, the gestational age was <9 weeks, the patient used an egg donor, or the patient had a confirmed multiple gestation.\(^\text{13}^\) Testing was performed on all samples with sufficient blood volume (>13 mL) as described previously using validated laboratory methodologies (cfDNA isolation, polymerase chain reaction amplification targeting 19,488 SNPs, high-throughput sequencing, and analysis using the Next-generation Aneuploidy Test Using SNPs [NATUS] algorithm).\(^\text{9-12,15}^\) Samples were subject to a stringent set of quality-control metrics\(^\text{9-13,15}^\) before reports were sent to ordering clinicians.

The NATUS algorithm incorporates parental genotypic information, uses numerous quality control metrics, and determines a sample-specific accuracy for each interrogated chromosome.\(^\text{9-12,15}^\) Briefly, the algorithm considers parental genotypic information, crossover frequency data, and possible fetal chromosome copy numbers (monosomy/disomy/trisomy) at 19,488 evaluated polymorphic loci. By comparing the observed fetal allele distributions from the sequencing data to the predicted distributions, the algorithm determines the fetal ploidy state with the maximum likelihood for each interrogated chromosome; this maximum likelihood probability is incorporated into a risk score for reporting purposes.\(^\text{15}^\) The NATUS algorithm is currently only validated to call aneuploidy in singleton gestations. However, the algorithm is able to determine when cfDNA sequencing results do not match the modeled fetal copy numbers with a high likelihood, and can identify the presence of additional fetal haplotypes that indicate either fetal triploidy or the presence of an undetected dizygotic multiple gestation. The presence of an additional fetal haplotype was identified when all tested chromosomes failed to match the disomy hypothesis, and when the additional haplotype was apparent from allele distributions. At this time, the algorithm cannot distinguish dizygotic twin gestations from triploidy pregnancies due to similar allele distributions (Figure 1); therefore, these are reported as a single call. Specifically, in a euploid singleton pregnancy, where the maternal alleles are AA (with dimorphic alleles arbitrarily labeled as A and B), the 2 expected fetal genotypes include AA and AB. By contrast, in dizygotic twin and triploid pregnancies where the maternal alleles are AA, there are 3 expected fetal genotypes for both triploid (AAA, AAB, ABB) (Figure 1, A) and dizygotic twin (AA/AA, AA/AB, AB/AB) (Figure 1, B) pregnancies. This results in equivalent B allele distributions (0, 1, or 2 B alleles), and very similar A allele distributions in triploid (1, 2, or 3) and dizygotic twin (2, 3, or 4) pregnancies.

For cases with an identified additional fetal haplotype, a report was sent to the ordering clinician or laboratory indicating that the results were consistent with a possible triploid or vanishing twin pregnancy, and recommending follow-up counseling and testing; after report delivery, a Natera genetic counselor contacted the ordering clinician/provider to answer questions related to the NIPT findings.

**Clinical outcomes**

Follow-up information on cases identified with an additional fetal haplotype was requested by telephone at regular intervals from ordering clinicians and partner laboratories. All information detailing ultrasound findings and pregnancy outcomes were recorded in the laboratory follow-up database. Follow-up information directly reported to Natera by providers was also recorded. Multifetal pregnancies were confirmed by ultrasound, which is consistent with how they are clinically diagnosed in practice. Cases were categorized as follows: (1) “confirmed vanishing twin pregnancy” if ultrasound detected a second empty sac or second sac containing a deceased fetus;
Graphical representation of sequencing data obtained from A, a paternal triploidy sample and B, a vanishing twin sample. It is important to note that this is not how the algorithm makes copy number calls, but is one method for visualizing data. All interrogated single-nucleotide polymorphisms (SNPs) are assumed to be dimorphic and are designated as A and B for simplicity. Briefly, for each graph, the number of A allele reads as a fraction of total reads is plotted (y-axis) against the position of each of several thousand interrogated SNPs on chromosomes of interest (x-axis). X-axis represents the linear position of each SNP along the chromosome, and each spot corresponds to a single SNP. As plasma cell-free DNA (cfDNA) is a mixture of fetal and maternal cfDNA, the vertical position of each spot represents the sum of contribution of both fetal and maternal allele reads, and is a function of the fetal proportion. To more readily visualize maternal and fetal contributions, spots are colored according to maternal genotype: SNPs for which the mother is homozygous for the A allele (AA) are red, SNPs for which the mother is homozygous for the B allele (BB) are blue, and SNPs for which the mother is heterozygous (AB) are green. Since the majority of plasma cfDNA is maternal in origin, spots mainly distribute according to the maternal genotype. The contribution of fetal allele reads results in segregation into distinct clusters. Because loci targeted on the Y chromosome are homologous to loci on the X chromosome, but differ by 1 nucleotide, probes hybridize to both chromosomes. However, targeted alleles have chromosomally distinct, nondimorphic identities, so are not color-coded; all alleles from the X chromosome are assigned as A alleles, and all alleles from the Y chromosome are assigned as B alleles. A, Confirmed paternal triploidy, 22.6% fetal cfDNA fraction. Position of peripheral red and blue clusters indicates additional haplotypes, as indicated to the right of the plot. Alleles for the X chromosome are indicated (X). Presence of B alleles from the Y chromosome shifts the cluster downward, indicating the presence of a single Y chromosome (based on distribution of reads). Together, this suggests a fetal chromosomal complement of 69,XXY. B, Confirmed vanishing twin, 19.6% fetal cfDNA fraction. Position of peripheral red and blue clusters indicates additional haplotypes, as indicated to the right of the plot. Presence of B alleles from the Y chromosome shifts the cluster downward, indicating the presence of a single Y chromosome (based on distribution of reads). Together, this suggests the presence of vanishing twins, as indicated to right of plot; “Fetus 1/2” indicates genotypes of fetus 1/fetus 2. Center green clusters only segregate and are readily visible at higher fetal fractions.

REFERENCES

(2) “confirmed ongoing twin pregnancy” if ultrasound showed an ongoing and viable twin pregnancy; (3) “confirmed fetal triploidy” if triploidy was confirmed by invasive testing or testing of products of conception (POC); (4) “unconfirmed fetal triploidy” included cases without invasive diagnostic testing but with ultrasound findings consistent with triploidy; (5) “confirmed nontriploid pregnancy” included cases where invasive diagnostic testing ruled out fetal triploidy and there was no evidence of co-twin demise; (6) “pregnancy loss” for cases where patients experienced spontaneous abortion and did not obtain karyotype confirmation; or (7) “no follow-up” where follow-up information was requested but was not received by the time of manuscript submission.

RESULTS

Study participants and samples

In the present cohort of 30,795 cases with an NIPT result, 130 (0.42%) received a report indicating the presence of additional fetal haplotypes. For the whole cohort, the mean maternal age was 33.6 ± 6.1 (range, 13.0—63.0) years (Figure 2, A), and the mean gestational age was 14.5 ± 4.7 (range, 9.0—40.9) weeks (Figure 2, B); maternal age was confirmed for the single case with a maternal age >52 years. For the 130 cases where an additional fetal haplotype was identified by NATUS, the
mean maternal age was 34.3 ± 5.7 (range, 19.0–52.0) years (Figure 2, C), and the mean gestational age was 13.3 ± 4.1 (range, 9.0–38.0) weeks (Figure 2, D). While the majority of NIPT samples were from women at early gestational ages, samples were received up to 40 weeks’ gestation (Figure 3); 2% (658/30,795) of samples were from women in their third trimester.

**Clinical outcomes**

Karyotype or ultrasound confirmation (karyotype for singleton pregnancies, ultrasound for multifetal pregnancies) was available for 76 (58.5%) of the 130 cases identified with additional parental haplotypes. This included 32 (42.1%) vanishing twin, 37 (48.7%) viable twin, 4 (5.3%) triploid pregnancies, and 3 (3.9%) nontriploid pregnancies that lacked evidence of co-twin demise (Table 1). For the 3 nontriploid pregnancies, 2 had euploid karyotypes, and 1 was shown to be a trisomy 18 fetus (Appendix; Supplementary Table).

**Multifetal pregnancies**

Vanishing twin cases had a significantly higher median maternal age than twin cases, 37.5 and 33.0 years, respectively ($P < .001$). The median gestational age was slightly lower in vanishing twin cases than in twin cases, 12.1 and 13.0 weeks, respectively ($P = .018$). There was no significant difference ($P = .686$) between the average fetal fraction of vanished twin (11.0 ± 3.8%) and twin (11.4 ± 4.3%) pregnancies. Of the 32 vanishing twin cases, 25 (78.1%) were in the first trimester and 7 (21.9%) were in the second trimester at the time of NIPT sampling. Five cases reported an estimated date of fetal demise: demise occurred in the first trimester in all 5...
This SNP-based NIPT approach identified previously undetected twin and triploid pregnancies in women undergoing routine prenatal screening. This method was previously validated for detecting fetal trisomy 21, trisomy 18, trisomy 13, monosomy X, and sex chromosome trisomies in singleton pregnancies, as well as additional fetal haplotypes indicating twin or triploid pregnancies. This is the first report detailing the clinical outcomes following NIPT identification of additional fetal haplotypes in a large general screening population.

Because this SNP-based method analyzes polymorphic loci, incorporates genotypic information, and does not require a reference chromosome, it is uniquely able to detect the presence of additional fetal haplotypes associated with dizygotic twins and triploidy. However, this method currently does not distinguish between these possibilities. Ultrasound examination should readily distinguish between an ongoing twin and a singleton pregnancy, and may reveal the presence of a vanished twin. A confirmed ongoing twin pregnancy may warrant close monitoring of the pregnancy, as twin pregnancies involve a unique set of complications; the additional haplotype merely suggests dizygotic twins. In the case of a confirmed singleton pregnancy with NIPT-identified additional haplotypes, options include repeat NIPT, taking a wait-and-see approach, or follow-up diagnostic testing to rule out triploidy; invasive testing should be carefully considered in light of other indications given the inherent risks to mother and baby. Where ultrasound indicates a singleton pregnancy and where triploidy indications are lacking, or where invasive testing ruled out triploidy, the possibility of early and undetected co-twin demise cannot be ruled out. Most vanishings occur in the first trimester, so clinical detection is largely dependent on whether a patient receives an early ultrasound and the time of fetal demise. Thus, for patients electing NIPT, an ultrasound may provide helpful information to assess fetal number and detect the presence of a vanishing twin or fetal triploidy.

FIGURE 3
Graphical representation of time elapsed between estimated fetal demise and detection by NIPT for 5 confirmed vanishing twin cases

Each line indicates an individual confirmed vanishing twin case with a known estimated date of fetal demise. The longest period between fetal demise and NIPT was 8 weeks.

NIPT, noninvasive prenatal testing.


TABLE 1
Follow-up information on twins/triploidy calls

<table>
<thead>
<tr>
<th>All cases (n = 130)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multifetal pregnancies</td>
<td></td>
</tr>
<tr>
<td>Ongoing twin</td>
<td>37</td>
</tr>
<tr>
<td>Vanishing twin</td>
<td>32</td>
</tr>
<tr>
<td>Singleton pregnancies</td>
<td></td>
</tr>
<tr>
<td>Confirmed triploid</td>
<td>4</td>
</tr>
<tr>
<td>Unconfirmed triploid</td>
<td>1</td>
</tr>
<tr>
<td>Confirmed nontriploid</td>
<td>3</td>
</tr>
<tr>
<td>Unknown fetal no.</td>
<td></td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td>3</td>
</tr>
<tr>
<td>No follow-up</td>
<td>50</td>
</tr>
</tbody>
</table>

a Total no. of cases with “additional fetal haplotypes (twins/triploidy) result at ≥ 9 wk of gestation; Confirmed by ultrasound detection of multifetal pregnancy; Confirmed by karyotype; Patient had ultrasound findings that were consistent with triploid fetus, amniocentesis was not possible because of oligohydramnios; Invasive testing revealed single euploid fetus in 2 pregnancies and single trisomy 18 fetus in 1 pregnancy; Patient experienced spontaneous abortion and did not obtain karyotype confirmation, ultrasound was suggestive of singleton pregnancy; Follow-up information was not available.

The ability to detect vanished twins is clinically important. Specifically, chromosomal abnormalities, which are common in vanished twins, are likely to generate false-positive results when using methods that can only assess total DNA and are unable to detect additional haplotypes. Indeed, 2 recent studies using counting-based methods attributed a significant proportion of false positives to vanished twins: in one, 15% of NIPT false-positive results were shown to involve vanished twins,14 and in a second study 33% (1/3) of trisomy 21 false positives were attributed to vanishing twins.20 Additionally, a vanished twin with discordant fetal sex may lead to the incorrect NIPT-based identification of fetal sex when compared to ultrasound (eg, a female fetus where there is a male vanished twin may be identified as male via NIPT). Both circumstances lead to parental anxiety and may escalate to unnecessary invasive testing, which carries with it a small but real risk of harm to mother and fetus.18

Similarly, identification of triploid pregnancies is beneficial because of the substantial clinical implications for patients. Triploidy results in severe fetal abnormalities and elevated risks for spontaneous abortion, preeclampsia, excessive postdelivery bleeding, and gestational trophoblastic neoplasia.21,22 As such, timely detection of triploid cases may alter clinical management. The incorporation of parental genotypic information allowed for determination of parental origin; all cases in this study were diandric triploidy. Clinically, these cases would likely present as partial molar pregnancies, which would be at risk for gestational trophoblastic neoplasia and choriocarcinoma, a malignant trophoblastic cancer.23-25 Diganic triploidy should also be detectable with this SNP-based method. However, these pregnancies present with very small, nonmolar placenta,26 which is correlated with decreased fetal cfDNA fractions and complicates detection using NIPT.10 However, previous studies showed that an “extremely low fetal fraction” per se increased the risk of fetal chromosomal aneuploidy, including digync triploidy.10,12

The prevalence of twin pregnancies is approximately 1 in 30 births,27,28 with vanishing twins occurring in approximately 30% of early diagnosed twin pregnancies.29-33 This is substantially higher than for triploid pregnancies, which occur in approximately 1 in 2000 pregnancies at 12 weeks of gestation, when many women undergo NIPT.34,35 Thus, the substantially greater possibility of a vanishing twin pregnancy (or unrecognized multiple gestation) should not be overlooked upon a screen-positive result.

The increased incidence of twinning in developed countries, a reflection of the progressive rise in the average maternal age at the time of conception36,37 and increasing utilization of assisted reproductive technology (ART),27 has important clinical implications for prenatal screening. Specifically, twinning rates are higher in women using ART, so the proportion of vanishing twin pregnancies is also likely higher. Indeed, 9% of conceptions using intracytoplasmic sperm injection resulted in vanishing twin pregnancies.18 However, it is unclear how many women in this cohort used ART; the number of cases found to involve a vanishing twin was 0.18% (additional fetal haplotypes were identified in 0.42% of the 30,795 cases, and of those cases with clinical follow-up, 42.7% were

### TABLE 2
Case details for confirmed vanishing twin cases

<table>
<thead>
<tr>
<th>Case</th>
<th>GA at demise, wk</th>
<th>GA at NIPT, wk</th>
<th>Time from demise to NIPT, wk</th>
<th>Fetal fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.0</td>
<td>10.3</td>
<td>2.3</td>
<td>11.7%</td>
</tr>
<tr>
<td>2</td>
<td>7.1</td>
<td>10.4</td>
<td>3.3</td>
<td>4.6%</td>
</tr>
<tr>
<td>3</td>
<td>8.6</td>
<td>12.6</td>
<td>4.0</td>
<td>12.8%</td>
</tr>
<tr>
<td>4</td>
<td>8.0</td>
<td>14.7</td>
<td>6.7</td>
<td>11.8%</td>
</tr>
<tr>
<td>5</td>
<td>7.0</td>
<td>15.0</td>
<td>8.0</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

GA at estimated date of co-twin demise and at time of sample collection for NIPT, elaps time between estimated demise and NIPT sampling, and fetal fraction for confirmed vanishing twin cases where clinical follow-up provided estimated date of fetal demise.

GA, gestational age; NIPT, noninvasive prenatal testing.


### TABLE 3
Case details for triploidy cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Fetal fraction</th>
<th>Parent of origin</th>
<th>Predicted sex</th>
<th>Clinical outcomes</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.1%</td>
<td>Diandric</td>
<td>XXX</td>
<td>Triploidy</td>
<td>69,XXX</td>
</tr>
<tr>
<td>2</td>
<td>11.4%</td>
<td>Diandric</td>
<td>XXY</td>
<td>Triploidy</td>
<td>69,XXY</td>
</tr>
<tr>
<td>3</td>
<td>22.6%</td>
<td>Diandric</td>
<td>XXY</td>
<td>Triploidy</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>12.2%</td>
<td>Diandric</td>
<td>XXY</td>
<td>Triploidy</td>
<td>69,XXY</td>
</tr>
<tr>
<td>5</td>
<td>6.4%</td>
<td>Diandric</td>
<td>XXX</td>
<td>Unconfirmed triploidy</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Parent of origin of extra fetal haplotype, as determined by NIPT; 1 Detailed karyotype findings were not communicated during clinical follow-up; 2 Amniocentesis was not possible because of oligohydramnios, but ultrasound findings were consistent with triploid fetus.

N/A, not available; NIPT, noninvasive prenatal testing.

Abnormal spontaneous abortions with a normal karyotype. As such, it is quite possible that in a multifetal pregnancy there may be a similarly increased cfDNA contribution from a vanished twin immediately following the loss, thus compromising cfDNA screening results for the viable twin. In the results reported here, fetal cfDNA from a vanished twin was detectable for up to 8 weeks following co-twin demise. Thus, there is the potential for vanished twins to influence NIPT results long after co-twin demise.

A limitation of this study was incomplete follow-up, reflecting the reality that many patients do not receive a first-trimester ultrasound or may transfer care. Nevertheless, where data were reported, the presence of additional fetal haplotypes determined by NIPT was confirmed in the vast majority of cases by ultrasound detection of a multifetal pregnancy or karyotype confirmation of fetal triploidy.

This SNP-based NIPT identified vanishing twin, unrecognized ongoing twin, and triploid pregnancies. Identification of partial (triploidy) and complete molar pregnancies is important because of the substantial clinical implications for patients, including the risk for gestational trophoblastic neoplasia and choriocarcinoma. As vestigial placental tissue from a lost twin can contribute fetal cfDNA to maternal circulation for weeks post-dimise, identification of vanishing twin pregnancies is critical to avoid incorrect NIPT results and subsequent unnecessary invasive procedures when non-SNP-based NIPT methods are used.

Conclusion

The principal finding of this study was that SNP-based NIPT can uniquely detect triploidy and unrecognized multifetal pregnancies, including vanishing twins, within a general screening population. Clinical outcomes revealed that the majority of these cases were unrecognized multifetal pregnancies, ongoing or vanishing twins, with a small number of triploid pregnancies also detected. The ability to detect vanishing twin pregnancies is clinically important as it will reduce the number of false-positive results and thereby reduce unnecessary invasive diagnostic procedures. Future longitudinal studies, designed to evaluate the typical time period for which residual fetal cfDNA from vanishing twins remains detectable, may provide greater insight into appropriate clinical care in these patients.

REFERENCES

Kuller JA, Patil S, Williamson RA. Risk of
mosome aneuploidies from maternal blood
somies 21, 18, 13 and the common sex chro-
18.


## Appendix

### Supplementary Table

<table>
<thead>
<tr>
<th>Case</th>
<th>Outcome</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Triploidy</td>
<td>CVS</td>
</tr>
<tr>
<td>2, 3, 4</td>
<td>Triploidy</td>
<td>POC</td>
</tr>
<tr>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Euploid</td>
<td>Amniocentesis</td>
</tr>
<tr>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Euploid</td>
<td>CVS</td>
</tr>
<tr>
<td>7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Trisomy 18</td>
<td>CVS</td>
</tr>
</tbody>
</table>

CVS, chorionic villus sampling; POC, products of conception testing.

<sup>a</sup> Three nontriploid pregnancies that lacked evidence of co-twin demise.