General information about positive NIPT results

My patient's NIPT is positive for multiple aneuploidies. What does this mean? Your patient's NIPT result suggests the presence of aneuploidy of more than one chromosome. The presences of multiple aneuploidies in a pregnancy is very rare, but can occur. However, NIPT is a screening test and false positives can occur. In addition, there may be other underlying biological explanations for a NIPT result suggesting multiple aneuploidies.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about multiple aneuploidy results.

What is multiple aneuploidy? Multiple aneuploidy refers to the presence of an extra or missing copy of multiple chromosomes.

What are the features of multiple aneuploidy? Most pregnancies with multiple aneuploidies will result in spontaneous miscarriage.[2,3] However, an estimated 0.16% of trisomy 21 cases involve a double aneuploidy with a sex chromosome (XXX, XXY, XYY, or monosomy X).[4] The associated features are dependent upon the exact chromosomes involved.

What is the prevalence of this condition? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Several biological explanations may underlie a multiple aneuploidy result on NIPT. These include, but are not limited to:
  - Multiple aneuploidy in the pregnancy
  - Single aneuploidy in the pregnancy
  - Maternal benign or malignant tumor
  - Maternal aneuploidy or other chromosomal change
- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR and microarray are available to confirm the presence of multiple aneuploidies.
- 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 case of a miscarriage. Sometimes, maternal chromosome testing may be needed to confirm maternal aneuploidy or chromosomal change.
- NIPT results of multiple aneuploidies have been linked to occult maternal benign and malignant tumors.[5-9]
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of multiple aneuploidies, but a normal ultrasound can not exclude this condition.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 1. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 1. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 1 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 1 and additional resources.

What is trisomy 1? Trisomy 1 is a condition that is caused by an extra chromosome number 1 (three copies instead of two).

What are the features of trisomy 1? Most pregnancies with trisomy 1 will miscarry spontaneously. All reported cases of prenatally diagnosed trisomy 1 have resulted in blighted ovum and no cases of full trisomy 1 have been reported in a livebirth. If a developing fetus has mosaic trisomy 1 (where some cells are normal and some cells have trisomy 1), there is an increased chance for the pregnancy to progress and possibly survive to term. However live born infants with mosaic trisomy 1 are expected to have a wide range of medical complications and physical and developmental sequelae, not all of which may be detected by prenatal ultrasound. Confined placental mosaicism ([CPM], when trisomic cells are present in the placenta, but not in the fetus) has not been frequently reported for trisomy 1.

What is the prevalence of this condition? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 1.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 1, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 1:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/1

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Reference:

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Malvestiti F, Agrai 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;35:1117-1127.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 2. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 2. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 2 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 2 and additional resources.

What is trisomy 2? Trisomy 2 is a condition that is caused by an extra chromosome number 2 (three copies instead of two).

What are the features of trisomy 2? Most pregnancies with trisomy 2 will miscarry spontaneously. If a developing fetus has mosaic trisomy 2 (where some cells are normal and some cells have trisomy 2), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 2 are expected to have serious medical problems. Key features include: growth and motor delay, and congenital anomalies. In reported cases of prenatally diagnosed trisomy 2, the outcomes have ranged from normal to livebirths 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. Ultrasound may reveal intrauterine growth restriction, oligohydramnios, or other anomalies.

What is the prevalence of this condition? Trisomy 2 has been reported in 1 in 2000 chorionic villus sampling (CVS) results[2,3] and 1 in 58,000 amniocentesis results.[4] The exact prevalence is unknown, therefore positive predictive value cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 2.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 2, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 2:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/2

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 3. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 3. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 3 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 3 and additional resources.

What is trisomy 3? Trisomy 3 is a condition that is caused by an extra chromosome number 3 (three copies instead of two).

What are the features of trisomy 3? Most pregnancies with trisomy 3 will miscarry spontaneously. Full trisomy 3 is rare and is usually confined to the placenta (CPM). If a developing fetus has mosaic trisomy 3 (where some cells are normal and some cells have trisomy 3), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 3 are expected to have serious medical problems. Key features include: dimorphism, intellectual disability, short stature, congenital anomalies including heart defects, and reduced life expectancy. In reported cases of prenatally diagnosed trisomy 3, the outcomes have ranged from normal to livebirths 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? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 3.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 3, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 3:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/3

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Reference:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 4. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 4. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 4 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 4 and additional resources.

What is trisomy 4? Trisomy 4 is a condition that is caused by an extra chromosome number 4 (three copies instead of two).

What are the features of trisomy 4? Most pregnancies with trisomy 4 will miscarry spontaneously. If a developing fetus has mosaic trisomy 4 (where some cells are normal and some cells have trisomy 4), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 4 are expected to have serious medical problems. Key features include: birth defects and dysmorphism. In reported cases of prenatally diagnosed trisomy 4, the outcomes have ranged from normal to live births with clinical sequelae. The variability in prognosis may 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? Unknown, but extremely rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 4.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 4, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 4:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/4

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Reference:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 5. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 5. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 5 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 5 and additional resources.

What is trisomy 5? Trisomy 5 is a condition that is caused by an extra chromosome number 5 (three copies instead of two).

What are the features of trisomy 5? Most pregnancies with trisomy 5 will miscarry spontaneously. If a developing fetus has mosaic trisomy 5 (where some cells are normal and some cells have trisomy 5), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 5 are expected to have serious medical problems. Key features include: birth defects and intellectual disability. In reported cases of prenatally diagnosed trisomy 5, the outcomes have ranged from normal to live births with clinical sequelae. The variability in prognosis may 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? Unknown, but rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 5.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 5, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 5:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/5

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 6. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 6. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 6 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 6 and additional resources.

What is trisomy 6? Trisomy 6 is a condition that is caused by an extra chromosome number 6 (three copies instead of two).

What are the features of trisomy 6? Most pregnancies with trisomy 6 will miscarry spontaneously. If a developing fetus has mosaic trisomy 6 (where some cells are normal and some cells have trisomy 6), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 6 are expected to have serious medical problems. Key features include: congenital heart defects, minor facial dysmorphism, and hand/feet malformations. Mosaic trisomy 6 is associated with growth anomalies, intellectual disability, birth defects, and reduced lifespan. In reported cases of prenatally diagnosed trisomy 6, 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? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 6.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 6, but a normal ultrasound cannot exclude this condition.

Special Considerations

- CPM can be associated with uniparental disomy ([UPD], when both copies of a chromosome are inherited from the same parent). Paternal UPD 6 has been associated with clinical findings, most commonly transient neonatal diabetes mellitus. Maternal UPD 6 may be associated with congenital anomalies. There may be an increased risk for certain recessive conditions if UPD is present.
- The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients presenting with prenatally detected mosaicism in chromosome 6.[2]

Resources for trisomy 6:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/6

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Malvestiti F, Agrai 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;35:1117-1127.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 7. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 7. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 7 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 7 and additional resources.

What is trisomy 7? Trisomy 7 is a condition that is caused by an extra chromosome number 7 (three copies instead of two).

What are the features of trisomy 7? Most pregnancies with trisomy 7 will miscarry spontaneously. Full trisomy 7 has never been reported in a live birth. If a developing fetus has mosaic trisomy 7 (where some cells are normal and some cells have trisomy 7), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with mosaic trisomy 7 are expected to have serious medical problems. Key features include: skin pigmentary disorders, body asymmetry, renal malformations, facial dysmorphism, and growth retardation. In reported cases of prenatally diagnosed mosaic trisomy 7, 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? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 7.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 7, but a normal ultrasound cannot exclude this condition.

Special Considerations

- CPM can be associated with uniparental disomy ([UPD], when both copies of a chromosome are inherited from the same parent). Maternal UPD 7 leads to Silver-Russell syndrome (SRS), characterized by pre- and postnatal growth retardation, relative macrocephaly, micrognathia, triangular facies, and developmental delay. Paternal UPD 7 is clinically unapparent.
- The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients presenting with prenatally detected mosaicism in chromosome 7.[2]

Resources for trisomy 7:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/7

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 8. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 8. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 8 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 8 and additional resources.

What is trisomy 8? Trisomy 8 is a condition that is caused by an extra chromosome number 8 (three copies instead of two).

What are the features of trisomy 8? Most pregnancies with trisomy 8 will miscarry spontaneously. Full trisomy 8 is usually an early lethal disorder in pregnancy. If a developing fetus has mosaic trisomy 8 (where some cells are normal and some cells have trisomy 8), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with mosaic trisomy 8 are expected to have serious medical problems. Key features include: variable growth restriction, intellectual disability, dysmorphism, and organ system anomalies, particularly cardiac and renal. Life expectancy is generally normal for liveborn mosaic cases. In reported cases of prenatally diagnosed trisomy 8, the outcomes have ranged from normal to live births with clinical sequelae. The variability in prognosis may 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? Prevalence is estimated to be 1:25,000 – 1:50,000 live births.[2] Constitutional trisomy 8 mosaicism occurs in ~0.1% of recognized pregnancies. Given the wide range of reported prevalence, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 8.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 8, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 8:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/8

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 9. What does this mean? Your patient's 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 9 and additional resources.

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, live born infants with full trisomy 9 will die shortly after birth. Live born infants with mosaic trisomy 9 are expected to have serious medical problems. Key features include: heart defects, serious intellectual disability, and skeleton 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 live born infants.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), 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 case of a miscarriage.
- 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:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/9

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 10. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 10. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 10 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 10 and additional resources.

What is trisomy 10? Trisomy 10 is a condition that is caused by an extra chromosome number 10 (three copies instead of two).

What are the features of trisomy 10? Most pregnancies with trisomy 10 will miscarry spontaneously. If a developing fetus has mosaic trisomy 10 (where some cells are normal and some cells have trisomy 10), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 10 are expected to have serious medical problems. Key features include: dysmorphism, organ system anomalies, and often neonatal or early infancy death. In reported cases of prenatally diagnosed trisomy 10, 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? Unknown, but rare. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 10.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 10, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 10:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/10

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 11. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 11. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 11 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 11 and additional resources.

What is trisomy 11? Trisomy 11 is a condition that is caused by an extra chromosome number 11 (three copies instead of two).

What are the features of trisomy 11? Full trisomy 11 has not been reported in live births and presumably leads to early pregnancy loss. Almost all reported live births with a prenatal diagnosis of mosaic trisomy 11 have normal prenatal and postnatal outcome, without evidence of trisomy 11 postnatally.

What is the prevalence of this condition? Unknown, but extremely rare. For this reason, positive predictive value cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 11.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 11, but a normal ultrasound cannot exclude this condition.

Special Considerations

- CPM can be associated with uniparental disomy ([UPD], when both copies of a chromosome are inherited from the same parent). There may be an increased risk for certain recessive conditions if UPD is present. Paternal UPD 11 is associated with Beckwith-Wiedemann syndrome. Maternal UPD 11 may be associated with Russell-Silver syndrome.
- The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients presenting with prenatally detected mosaicism in chromosome 11.[2]

Resources for trisomy 11:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/11

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 12. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 12. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 12 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 12 and additional resources.

What is trisomy 12? Trisomy 12 is a condition that is caused by an extra chromosome number 12 (three copies instead of two).

What are the features of trisomy 12? Most pregnancies with trisomy 12 will miscarry spontaneously. Full trisomy 12 has not been reported in livebirths. If a developing fetus has mosaic trisomy 12 (where some cells are normal and some cells have trisomy 12), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with mosaic trisomy 12 are expected to have serious medical problems. Key features include: intellectual disability, dysmorphism, and organ system anomalies, and can lead to fetal or neonatal death. In reported cases of prenatally diagnosed trisomy 12, ~50% represent true fetal mosaicism. The outcomes have ranged from normal to livebirths 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? Unknown, but rare. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 12.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 12, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 12:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/12

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Hahnemann JM, Vejerslev LO. European collaborative research on mosaicism in CVS (EUCROMIC)—fetal and extrafetal cell lineages in 192 gestations with CVS mosaicism involving single autosomal trisomy. *Am J Med Genet.* 1997;70:179-187.

Hsu LY, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.

Malvestiti F, Agrai 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;35:1117-1127.

Staals JE, Schrander-Stumpel CT, Hamers G, Fryns JP. Prenatal diagnosis of trisomy 12 mosaicism: normal development of a 3 years old female child. *Genet Couns.* 2003;14:233-237.

General information about positive NIPT results

My patient's NIPT is positive for 13 (Patau syndrome). What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 13. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 13 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 13 and additional resources.

What is trisomy 13? Trisomy 13 is a condition that is caused by an extra chromosome number 13 (three copies instead of two).

What are the features of trisomy 13? Although the majority of pregnancies with trisomy 13 result in miscarriage or stillbirth, trisomy 13 can result in live birth. Individuals with trisomy 13 have severe intellectual disability and abnormalities involving multiple organs. Some of the common features of trisomy 13 include heart defects, omphalocele, brain abnormalities such as holoprosencephaly, cleft lip and palate, and other features. Although less than 10% of babies with trisomy 13 will live past 1 year of age, some people with this condition can live years or even decades.

What is the prevalence of this condition? Trisomy 13 occurs in approximately 1 in 12,000 live births. This condition usually happens by chance and is associated with increasing maternal age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 13.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 13, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 13:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/13

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Reference:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.

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Gardner RJM, Sutherland GR, Schaffer LG. *Chromosome Abnormalities and Genetic Counseling.* 4th ed. New York, NY: Oxford University Press; 2012.

Jones KL. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia, PA: W.B. Saunders Company; 1997.

Malvestiti F, Agrai 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;35:1117-1127.

General information about positive NIPT results

My patient's NIPT is positive for trisomy 14. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 14. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 14 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 14 and additional resources.

What is trisomy 14? Trisomy 14 is a condition that is caused by an extra chromosome number 14 (three copies instead of two).

What are the features of trisomy 14? Most pregnancies with trisomy 14 will miscarry spontaneously. Full trisomy 14 has not been reported in live births and there are only a few reports of viability into the late 1st or 2nd trimester. If a developing fetus has mosaic trisomy 14 (where some cells are normal and some cells have trisomy 14), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with mosaic trisomy 14 are expected to have serious medical problems. Key features include: intellectual disability, growth restriction, dysmorphism, and organ system anomalies. In reported cases of prenatally diagnosed trisomy 14, 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? Unknown, but rare. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 14.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 14, but a normal ultrasound cannot exclude this condition.

Special Considerations

- CPM can be associated with uniparental disomy ([UPD], when both copies of a chromosome are inherited from the same parent). Maternal UPD 14 is associated with a somewhat variable phenotype, including an increased risk of growth deficiency, intellectual disability, and dysmorphism. Paternal UPD 14 is associated with intellectual disability, dysmorphism, and a thoracic deformity that can lead to lethal respiratory failure in infancy. There may be an increased risk for certain recessive conditions if UPD is present.
- The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients presenting with prenatally detected mosaicism in chromosome 14.[2]

Resources for trisomy 14:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/14

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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2. Shaffer LG, Agan N, Goldberg JD, Ledbetter DH, Longshore JW, Cassidy SB. American College of Medical Genetics statement on diagnostic testing for uniparental disomy. *Genet Med.* 2001;3:206-211.

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Hsu LY, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 15. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 15. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 15 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 15 and additional resources.

What is trisomy 15? Trisomy 15 is a condition that is caused by an extra chromosome number 15 (three copies instead of two).

What are the features of trisomy 15? Most pregnancies with trisomy 15 will miscarry spontaneously. If a developing fetus has mosaic trisomy 15 (where some cells are normal and some cells have trisomy 15), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 15 are expected to have serious medical problems. Full trisomy 15 has been reported in association with multiple congenital anomalies and neonatal death. Mosaic trisomy 15 can be associated with growth restriction, intellectual disability (sometimes mild), and birth defects. In reported cases of prenatally diagnosed trisomy 15, the outcomes have ranged from normal to livebirths 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? Unknown, but rare. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 15.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 15, but a normal ultrasound cannot exclude this condition.

Special Considerations

- CPM can be associated with uniparental disomy ([UPD], when both copies of a chromosome are inherited from the same parent). Maternal UPD 15 is associated with Prader-Willi syndrome. Paternal UPD 15 is associated with Angelman syndrome. There may be an increased risk for certain recessive conditions if UPD is present.
- The American College of Medical Genetics and Genomics (ACMG) states that specialized UPD testing should be considered for patients presenting with prenatally detected mosaicism in chromosome 15. [2]

Resources for trisomy 15:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/15

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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References:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.
2. Shaffer LG, Agan N, Goldberg JD, Ledbetter DH, Longshore JW, Cassidy SB. American College of Medical Genetics statement on diagnostic testing for uniparental disomy. *Genet Med.* 2001;3:206-211.

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 16. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 16. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 1 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 16 and additional resources.

What is trisomy 16? Trisomy 16 is a condition that is caused by an extra chromosome number 16 (three copies instead of two).

What are the features of trisomy 16? Pregnancies with full trisomy 16 will end in spontaneous miscarriage. If a developing fetus has mosaic trisomy 16, some of the cells in the fetus have the usual number of chromosomes. These pregnancies may survive to birth, but infants born with mosaic trisomy 16 may have growth issues and other serious medical concerns.

What is the prevalence of this condition? Trisomy 16 occurs in approximately 1 in 100 pregnancies. It is the most common cause for miscarriage early in pregnancy, accounting for approximately 12% of chromosomally abnormal miscarriages. This condition is very rare in live born infants and the exact prevalence is not known. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 16.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 16, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 16:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/16

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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General information about positive NIPT results

My patient's NIPT is positive for trisomy 17. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 17. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 17 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 17 and additional resources.

What is trisomy 17? Trisomy 17 is a condition that is caused by an extra chromosome number 17 (three copies instead of two).

What are the features of trisomy 17? Most pregnancies with trisomy 17 will miscarry spontaneously. Full trisomy 17 has not been reported in live births and presumable leads to early pregnancy loss. If a developing fetus has mosaic trisomy 17 (where some cells are normal and some cells have trisomy 17), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with mosaic trisomy 17 are expected to have serious medical problems. Key features include: intellectual disability, growth restriction, and organ system anomalies. In reported cases of prenatally diagnosed trisomy 17, 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? Unknown, but very rare. For this reason, positive predictive value (PPV) cannot be calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 17.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 17, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 17:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/1

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Hsu LY, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.

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Utermann B, Riegel M, Leistritz D, et al. Pre- and postnatal findings in trisomy 17 mosaicism. *Am J Med Genet A.* 2006;140:1628-1636.

General information about positive NIPT results

My patient's NIPT is positive for trisomy 18 (Edwards syndrome). What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 18. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 18 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 18 and additional resources.

What is trisomy 18? Trisomy 18 is a condition that is caused by an extra chromosome number 18 (three copies instead of two).

What are the features of trisomy 18? Although many pregnancies with trisomy 18 result in miscarriage or stillbirth, trisomy 18 can result in live birth. Individuals with trisomy 18 have severe intellectual disability and abnormalities involving multiple organs. Some of the common features of trisomy 18 include heart defects, brain abnormalities, musculoskeletal problems, cleft lip and palate, and low birth weight. Although less than 10% of babies with trisomy 18 will live past 1 year of age, some people with this condition can live years or even decades.

What is the prevalence of this condition? Trisomy 18 occurs in 1 in 6000 to 8000 live births. This condition usually happens by chance and is associated with increasing maternal age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 18.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 18, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 18:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/18

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Reference:

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Additional Sources:

Gardner RJM, Sutherland GR, Schaffer LG. *Chromosome Abnormalities and Genetic Counseling.* 4th ed. New York, NY: Oxford University Press; 2012.

Jones KL. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia, PA: W.B. Saunders Company; 1997.

Malvestiti F, Agrai 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;35:1117-1127.

General information about positive NIPT results

My patient's NIPT is positive for trisomy 19. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 19. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 19 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 19 and additional resources.

What is trisomy 19? Trisomy 19 is a condition that is caused by an extra chromosome number 19 (three copies instead of two).

What are the features of trisomy 19? There has been one reported case of prenatally-diagnosed mosaic trisomy 19 (where some cells are normal and some cells have trisomy 19) by amniocentesis. This case resulted in a normal live birth and the trisomy 19 cells were most likely confined to the placenta and were not present in the fetus. Full trisomy 19 has not been reported in live births and presumably leads to early pregnancy loss.

What is the prevalence of this condition? Unknown, but extremely rare. For this reason, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 19.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 19, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 19:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/19

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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Additional Sources:

Dighe M, Cheng E, Dubinsky T. Ultrasound manifestations of unusual trisomies-excluding trisomy 13, 18, and 21: a literature review. *Ultrasound Q.* 2009;25:15-24.

Gardner RJ, Sutherland GR, Shaffer LG. *Chromosome Abnormalities and Genetic Counseling.* 4th ed. New York, NY: Oxford University Press; 2012.

Hsu LY1, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.

Malvestiti F, Agrai 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;35:1117-1127.

General information about positive NIPT results

My patient's NIPT is positive for trisomy 20. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 20. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 20 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 20 and additional resources.

What is trisomy 20? Trisomy 20 is a condition that is caused by an extra chromosome number 20 (three copies instead of two).

What are the features of trisomy 20? Most pregnancies with trisomy 20 will miscarry spontaneously. If a developing fetus has mosaic trisomy 20 (where some cells are normal and some cells have trisomy 20), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 20 are expected to have serious medical problems. Full trisomy 20 is rarely reported in livebirths and is associated with anomalies often involving the central nervous system and heart. Mosaic trisomy 20 is associated with an increased risk of organ system anomalies (most commonly cardiac and renal anomalies), growth restriction, intellectual disability, and dysmorphism. In reported cases of prenatally diagnosed trisomy 20, the outcomes have ranged from normal to livebirths 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? Unknown, but rare. For this reason, positive predictive value cannot be accurately calculated. Mosaic trisomy 20 is detected in 1 in 5,000 amniocentesis samples.[2]

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 20.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 20, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 20:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/20

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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References:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-e137.
2. Forabosco A, Percesepe A, Santucci S. Incidence of non-age-dependent chromosomal abnormalities: a population-based study on 88965 amniocenteses. *Eur J Hum Genet.* 2009;17(7):897-903.

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Bianca S, Boemi G, Barrano B, et al. Mosaic trisomy 20: considerations for genetic counseling. *Am J Med Genet A.* 2008;146A:1897-1898.

Chen CP, Chang SD, Chueh HY, et al. Discrepancy in the trisomy mosaicism level between cultured amniocytes and uncultured amniocytes in prenatally detected mosaic trisomy 20. *Taiwan J Obstet Gynecol.* 2013;52:145-146.

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Hsu LY, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.

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Malvestiti F, Agrai 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;35:1117-1127.

Mavromatidis G, Dinas K, Delkos D, Vosnakis C, Mamopoulos A, Rousso D. Case of prenatally diagnosed non-mosaic trisomy 20 with minor abnormalities. *J Obstet Gynaecol Res.* 2010;36:866-868.

Morales C, Cuatrecasas E, Mademont-Soler I, et al. Non-mosaic trisomy 20 of paternal origin in chorionic villus and amniotic fluid also detected in fetal blood and other tissues. *Eur J Med Genet.* 2010;53:197-200.

Willis MJ, Bird LM, Dell'Aquilla M, Jones MC. Expanding the phenotype of mosaic trisomy 20. *Am J Med Genet A.* 2008;146A:330-336.

General information about positive NIPT results

My patient's NIPT is positive for trisomy 22. What does this mean? Your patient's NIPT result suggests the presence of an extra copy of chromosome 22. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have trisomy 22 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about trisomy 22 and additional resources.

What is trisomy 22? Trisomy 22 is a condition that is caused by an extra chromosome number 22 (three copies instead of two).

What are the features of trisomy 22? Most pregnancies with trisomy 22 will miscarry spontaneously. If a developing fetus has mosaic trisomy 22 (where some cells are normal and some cells have trisomy 22), there is an increased chance for the pregnancy to progress and possibly survive to term. However, live born infants with full or mosaic trisomy 22 are expected to have serious medical problems. Key features include: intrauterine growth restriction, dysmorphism, and organ system anomalies. In reported cases of prenatally diagnosed trisomy 22, 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. Full trisomy 22 is rarely reported in live births and is usually associated with a poor, typically fatal, prognosis. Most live borns with mosaic trisomy 22 do not survive past the first few months. When mosaic trisomy 22 is detected by amniocentesis, the risk for abnormal outcome is >60%.[2,3]

What is the prevalence of this condition? Full trisomy 22 is rare and may be about 1 in 30,000 to 50,000 live births.[4] Since the prevalence is not clearly known, positive predictive value cannot be accurately calculated.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR, and microarray are available to confirm the presence of trisomy 22.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of trisomy 22, but a normal ultrasound cannot exclude this condition.

Resources for trisomy 22:

Genetics Home Reference http://ghr.nlm.nih.gov/chromosome/22

Unique, The Rare Chromosome Disorder Support Group http://www.rarechromo.org/

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References:

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2. Gardner RJ, Sutherland GR, Shaffer LG. *Chromosome Abnormalities and Genetic Counseling.* 4th ed. New York, NY: Oxford University Press; 2012.
3. Hsu LY, Yu MT, Neu RL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. *Prenat Diagn.* 1997;17:201-242.
4. Dighe M, Cheng E, Dubinsky T. Ultrasound manifestations of unusual trisomies-excluding trisomy 13, 18, and 21: a literature review. *Ultrasound Q.* 2009;25:15-24.

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General information about positive NIPT results

My patient's NIPT is positive for XXX syndrome (triple X syndrome). What does this mean? Your patient's NIPT result suggests the presence of an extra copy of the X chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have XXX syndrome 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about XXX syndrome and additional resources.

What is XXX syndrome? XXX syndrome is a condition that is caused by a female having an extra copy of the X sex chromosome (three copies of the X chromosome instead of the usual two copies).

What are the features of XXX syndrome? XXX syndrome is likely to result in livebirth. XXX syndrome is usually not associated with intellectual disability or severe birth defects. Some of the common features of XXX syndrome include delayed speech and motor development. Females with XXX syndrome can be taller than average height. Pubertal development and fertility is usually normal.

What is the prevalence of this condition? Approximately 1 in 1000 females are born with XXX syndrome. This condition usually happens by chance and can be associated with advanced maternal age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR and microarray are available to confirm the presence of XXX syndrome.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with prenatal diagnosis, but a normal ultrasound cannot exclude this condition. Ultrasound is usually normal with XXX.

Resources for XXX Syndrome

Genetics Home Reference
http://ghr.nlm.nih.gov/condition/triple-x-syndrome

National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/trisomy-x/

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Jones KL. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia, PA: W.B. Saunders Company; 1997.

General information about positive NIPT results

My patient's NIPT is positive for XXY syndrome (Klinefelter syndrome). What does this mean? Your patient's NIPT result suggests the presence of an extra copy of the X chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have XXY syndrome 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about XXY syndrome and additional resources.

What is XXY syndrome? XXY syndrome is a condition that is caused by a male having an extra copy of the X sex chromosome (two copies of the X chromosome and one copy of the Y chromosome rather than the usual one copy of each).

What are the features of XXY syndrome? XXY syndrome is likely to result in livebirth. Males with XXY syndrome have variable phenotypes. Some of the common features of XXY syndrome include learning disabilities, delayed speech and language development, taller stature, hypogonadism, and risk of infertility.

What is the prevalence of this condition? Approximately 1 in 600 males are born with XXY syndrome. This condition usually happens by chance and can be associated with advanced maternal age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR and microarray are available to confirm the presence of XXY syndrome.
- 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 case of a miscarriage.
- Ultrasound evaluation is not expected to be useful in aiding with a prenatal diagnosis of XXY syndrome, as ultrasound is usually normal. A normal ultrasound cannot exclude this condition.

Resources for XXY syndrome

Genetics Home Reference -
http://ghr.nlm.nih.gov/condition/klinefelter-syndrome

National Organization for Rare Disorders -
https://rarediseases.org/rare-diseases/klinefelter-syndrome/

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Jones KL. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia, PA: W.B. Saunders Company; 1997.

General information about positive NIPT results

My patient's NIPT is positive for XYY syndrome (Jacobs syndrome). What does this mean? Your patient's NIPT result suggests the presence of an extra copy of the Y chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have XYY syndrome depends on many factor, 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about XYY syndrome and additional resources.

What is XYY syndrome? XYY syndrome is a condition that is caused by a male having an extra copy of the Y sex chromosome (one copy of the X chromosome and two copies of the Y chromosome rather than the usual one copy of each).

What are the features of XYY syndrome? XYY syndrome is likely to result in live birth. Males with XYY syndrome have variable phenotypes. Some of the common features of XYY syndrome include delayed speech and language development and taller stature. There is a slightly increased risk for males with XYY syndrome to have an autism spectrum disorder or learning disability.

What is the prevalence of this condition? Approximately 1 in 1000 males are born with XYY syndrome. This condition usually happens by chance and is not associated with advanced parental age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR and microarray are available to confirm the presence of XYY syndrome.
- 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 case of a miscarriage.
- Ultrasound evaluation is not expected to be useful in aiding with a prenatal diagnosis of XYY syndrome, as ultrasound is usually normal. A normal ultrasound cannot exclude this condition.

Resources for XYY syndrome

Genetics Home Reference
http://ghr.nlm.nih.gov/condition/47xyy-syndrome

National Organization for Rare Disorders
http://rarediseases.org/rare-diseases/xyy-syndrome/

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Jones KL. *Smith's Recognizable Patterns of Human Malformation.* 5th ed. Philadelphia, PA: W.B. Saunders Company; 1997.

General information about positive NIPT results

My patient's NIPT is positive for monosomy X (Turner syndrome). What does this mean? Your patient's NIPT result suggests the presence of one X sex chromosome and the absence of a second sex chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have monosomy X 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. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for more information about monosomy X and additional resources.

What is monosomy X? Monosomy X is a condition that is caused by having one X sex chromosome and an absent second sex chromosome (one sex chromosome instead of two sex chromosomes).

What are the features of monosomy X? Many pregnancies with monosomy X will result in a pregnancy loss; however, monosomy X is compatible with continued survival and live birth. Females with monosomy X have variable phenotypes. Typically, females with monosomy X have normal intelligence; however, learning disabilities are possible and variable. Some of the common features of monosomy X include heart defects, kidney abnormalities, short stature, congenital lymphedema, and primary amenorrhea.

What is the prevalence of these conditions? Approximately 1 in 2500 females are born with monosomy X. This condition usually happens by chance and is not typically associated with advanced parental age.

What testing could be considered?

- Specialized genetic tests such as karyotyping, fluorescence in situ hybridization (FISH), qPCR and microarray are available to confirm the presence of monosomy X.
- 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 case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of monosomy X, but a normal ultrasound cannot exclude this condition.

Resources for monosomy X

Turner Syndrome Society of the United States
http://www.turnersyndrome.org/

Turner Syndrome Resource List
http://www.kumc.edu/gec/support/chromoso.html#xo

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