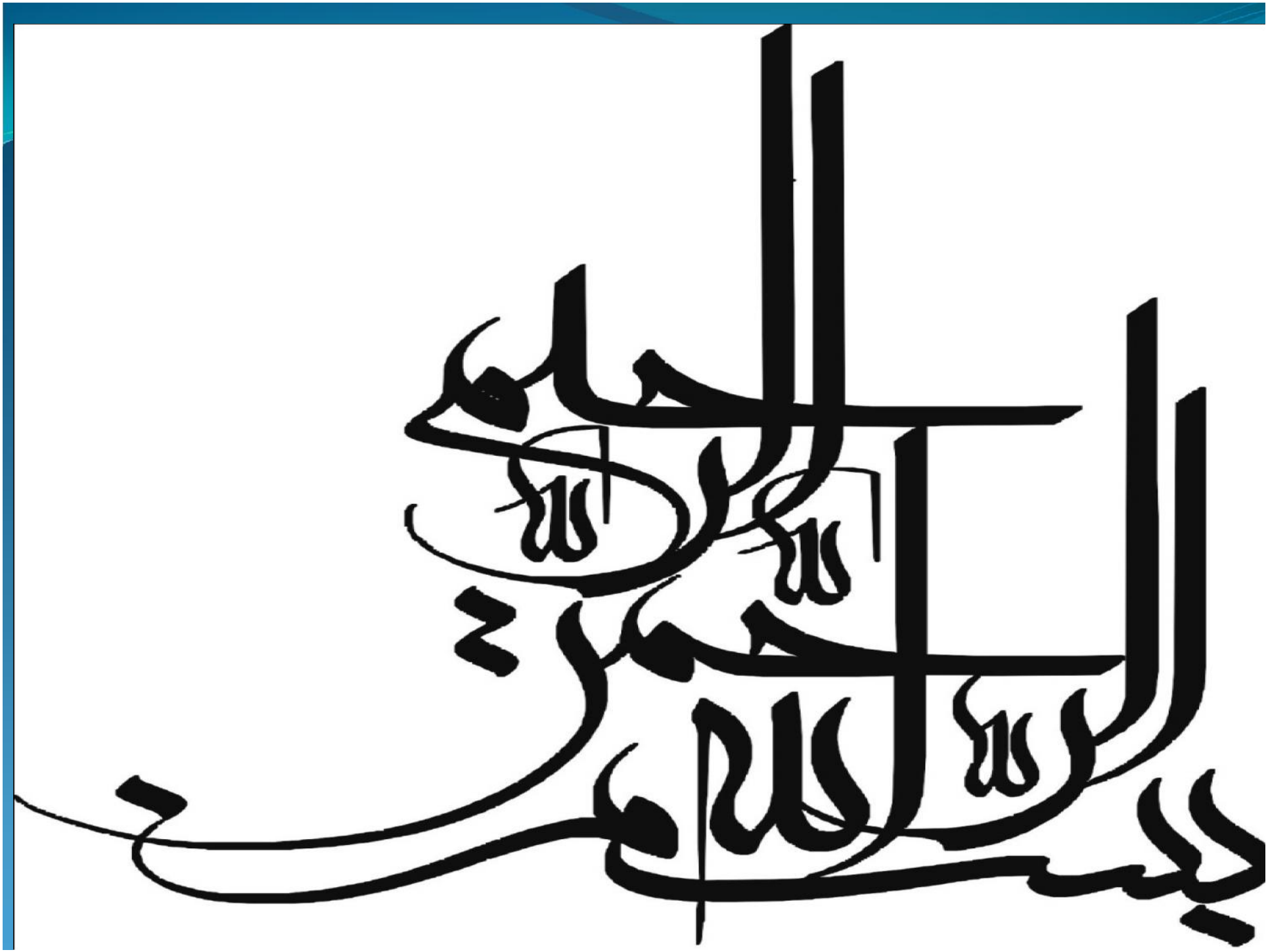

Fetal Aneuploidy Screening

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Prenatal genetic screening and diagnostic testing options should be discussed and offered to **all pregnant patients regardless of maternal age or risk of chromosomal abnormality**.

After review and discussion, every patient has the right to pursue or decline prenatal genetic screening and diagnostic testing.

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Table 1. Chromosomal Abnormalities in Second-Trimester Pregnancies Based on Maternal Age at Term

	Trisomy 21	Trisomy 18	Trisomy 13	Sex Chromosome Aneuploidy (XXX, XY, XYY, 45, X)	Microarray or Rare Chromosomal Abnormality	All Chromosomal Abnormalities
Age 20	8 per 10,000 1 in 1,250	2 per 10,000 1 in 5,000	1 per 10,000 1 in 10,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	82 per 10,000 1 in 122
Age 25	10 per 10,000 1 in 1,000	2 per 10,000 1 in 5,000	1 per 10,000 1 in 10,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	84 per 10,000 1 in 119
Age 30	14 per 10,000 1 in 714	4 per 10,000 1 in 2,500	2 per 10,000 1 in 5,000	34 per 10,000 1 in 294	37 per 10,000 1 in 270	91 per 10,000 1 in 110
Age 35	34 per 10,000 1 in 294	9 per 10,000 1 in 1,111	4 per 10,000 1 in 2,500	35 per 10,000 1 in 285	37 per 10,000 1 in 270	119 per 10,000 1 in 84
Age 40	116 per 10,000 1 in 86	30 per 10,000 1 in 333	14 per 10,000 1 in 714	51 per 10,000 1 in 196	37 per 10,000 1 in 270	248 per 10,000 1 in 40

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There are a variety of screening test options, each offering varying levels of information and accuracy.

Obstetric care providers are expected to discuss not only the risk of aneuploidy but also the benefits, risks, and limitations of available screening tests .

If screening is accepted, **patients should have one prenatal screening approach**, and should not have multiple screening tests performed simultaneously.

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Recommendations for patients who desire aneuploidy screening:

- Regardless of the patient's baseline risk, all patients should be offered screening for chromosomal anomalies, including NT measurement, serum screening and cfDNA, in addition to offering diagnostic testing.

-Test characteristics, advantages and disadvantages of screening options should be counseled.

- High risk patients based on ultrasound findings or screening test results should be counseled about advantages and disadvantages of advanced screening options vs diagnostic testing .

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Table 2. Characteristics, Advantages, and Disadvantages of Common Screening Tests for Chromosomal Abnormalities

Screening Approach	Approximate Gestational Age Range for Screening (Weeks)	Detection Rate (DR) for Trisomy 21 (%)	Screen Positive Rate* (%)	Advantages	Disadvantages	Method
Cell-free DNA†	9–10 to term	99	2–4% Includes inability to obtain results, which is associated with increased risk†	1. Highest DR 2. Can be performed at any gestational age after 9–10 weeks 3. Lowest false-positive rate	Results may reflect underlying maternal aneuploidy or maternal disease	Several molecular methods
First trimester‡	10–13 6/7§	82–87‖	5	1. Early screening 2. Single time point test	Lower DR than tests with first and second trimester component NT required	NT+PAPP-A, free beta hCG, +/− AFP¶
Quad screen‡	15–22	81	5	1. Single time point test 2. No specialized US required	Lower DR than first trimester and first and second trimester combined tests	hCG, AFP, uE3, DIA
Integrated‡	10–13 6/7§, then 15–22	96	5	High DR	Two samples needed No first-trimester results NT required	NT+PAPP-A, then quad screen
Serum integrated‡	10–13 6/7§, then 15–22	88	5	1. DR compares favorably with first-trimester screening 2. No specialized US required	Two samples needed No first-trimester results	PAPP-A + quad screen

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Aneuploidy screening in multiple gestations

- Screens that include a serum sample will be less accurate in twin gestations as compared to singleton gestations.
  - o No data available for higher order multiple gestations
- Consider obtaining genetic counseling to allow a more detailed discussion of the options listed below
- The decision regarding the appropriate screening option for patients with twin gestations is complex, and patients should be counseled prior to any screening or testing.

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Options for aneuploidy screening in twins include the following:

- **Combined first trimester screen**
  - NT measurement directly evaluates each of the individual twins
  - DR for T21 75-89% with 5% FFR.
  - DR for T18 66.7%

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Quad screen:

If patients present after first trimester, serum Quad screening can be used in twin gestations:

DR 60% for T21 with 5% FFR.

CfDNA testing can be performed in twin gestations

DR for T21 screening may be similar to singleton gestations (98-99%).

Accurate DR for T13 or T18 is not definitely determined but appears to be >90% based on limited numbers.

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- Obtaining an ultrasound at 11-13 weeks for all twin gestations may be reasonable regardless of desires for genetic screening.

This can allow determination of chorionicity and can serve as an early screen for certain twin related complications.

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- Patients with a positive screening test result for fetal aneuploidy should be offered further detailed counseling and testing.
-All patients should be offered second-trimester ultrasound to screen for fetal structural defects, ideally performed between 18-22 weeks, **with or without second trimester MSAFP.**

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- - CfDNA is the most sensitive and specific screening test for common aneuploidy.
- CfDNA should not be used as a substitute for diagnostic testing.
- - CfDNA testing is only recommended for T21, T18, T13 and sex chromosome anomalies.
- Testing of other forms of aneuploidy, microdeletion syndromes or genome-wide copy number variants is not recommended in all-comers due to insufficient data, but these screens may be performed in a select population following appropriate counseling.
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POSTTEST FOLLOW-UP

Screen positive NIPT

Invasive diagnostic testing must be offered to patients in order to confirm the fetal karyotype.

A conventional G-banded karyotype is critical to obtain in these cases.

Screen negative NIPT

Screen-negative patients are not usually offered invasive diagnostic testing.

But if screen-negative patients develop an indication for invasive diagnostic testing, such as a fetal anatomic anomaly on ultrasound examination, should be offered invasive diagnostic testing.

Uptodate , Nov 23, 2021

No call result

The rates generally occur in <5% of samples.

ACOG currently recommends genetic counseling and diagnostic testing in these cases because of an increased risk for fetal aneuploidy.

Although, a repeat test is acceptable if the No call result is due to a low FF.

In such cases, the test should always be repeated using the same laboratory that evaluated the initial sample.

If an enlarged NT or an anomaly is identified on ultrasound examination, the patient should be offered genetic counseling and diagnostic testing for genetic conditions and a comprehensive ultrasound evaluation including detailed ultrasonography at 18–22 weeks of gestation to assess for structural abnormalities.

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The use of cell-free DNA screening as follow-up for patients with a screen positive serum analyte screening test result is an option for patients who want to avoid a diagnostic test. However, patients should be informed that this approach may delay definitive diagnosis and will fail to identify some fetuses with chromosomal abnormalities.

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In clinical situations of an isolated soft ultrasonographic marker (such as ECF, CPC, pyelectasis, short humerus or femur length) where aneuploidy screening has not been performed, the patient should be counseled regarding the risk of aneuploidy associated with the finding and cell-free DNA, quad screen testing, or amniocentesis should be offered.

If aneuploidy testing is performed and is low risk, then no further risk assessment is needed.

If more than one marker is identified, then genetic counseling, maternal–fetal medicine consultation, or both are recommended.

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Because preimplantation genetic testing is not uniformly accurate, **prenatal screening and prenatal diagnosis should be offered to all patients regardless of previous preimplantation genetic testing.**

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The use of multiple serum screening approaches performed independently (eg, a first-trimester screening test followed by a quad screen as an unlinked test) is not recommended because it will result in an unacceptably high positive screening rate and could deliver contradictory risk estimates.

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In multifetal gestations, if a fetal demise, vanishing twin, or anomaly is identified in one fetus, there is a significant risk of an inaccurate test result if serum-based aneuploidy screening or cell-free DNA is used.

This information should be reviewed with the patient and diagnostic testing should be offered.

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Patients with unusual or multiple aneuploidies detected by cell-free DNA **should be referred for genetic counseling and maternal–fetal medicine consultation.**

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Thank you for your attention