Prenatal Diagnosis

Screening and Diagnostic Tools

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KEYWORDS

• Aneuploidy • Genetic screening • Noninvasive prenatal screening • Cell-free DNA • Chorionic villus sampling • Amniocentesis

KEY POINTS

- Aneuploidy screening should be offered to all women at their first prenatal visit.
- Cell-free fetal DNA screening is currently recommended for high-risk populations only and should be considered a screening test rather than a diagnostic test.
- Chorionic villus sampling and amniocentesis carry a small but potential risk of pregnancy loss but remain the only diagnostic methodologies available presently.
- Women should receive thorough pretest counseling regarding the risks and benefits of available options and should receive thorough posttest counseling with individualized interpretation of results.

INTRODUCTION

Approximately 3% to 5% of pregnancies are complicated by birth defects or genetic disorders.[1] Chromosomal abnormalities are present in approximately 1 in 150 live births,[2] and congenital malformations remain the leading cause of infant death and a leading cause of childhood death.[3] These chromosomal abnormalities include aneuploidy (defined as having one or more extra or missing chromosomes), translocations, duplications, and deletions.

The most common chromosomal disorder is trisomy 21 (Down syndrome), with an incidence of 1 per 800 live births.[4] Trisomy 13 and 18 can also result in live births, though with a significantly lower incidence.[2,4] Sex chromosome aneuploidies are less common than autosomal aneuploidies.[4] The only known viable monosomy is monosomy X (Turner syndrome). Incidences are described in **Table 1**.

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Table 1
Incidence of common aneuploidies

Trisomy 21	1 in 800 live births
Trisomy 18	1 in 7500 live births
Trisomy 13	1 in 15,000 live births
Monosomy X (Turner syndrome)	1 in 5000 girls
Trisomy X	1 in 1000 girls
XXY (Klinefelter syndrome)	1 in 1000 boys
XYY	1 in 1000 boys

Data from Nussbaum RL, McInnes RR, Willard HF. Thompson & Thompson genetics in medicine. 7th edition. Philadelphia: Saunders/Elsevier; 2007.

Risk of aneuploidy increases with maternal age (Table 2).[2,4] Other factors also influence patients' risk in any given pregnancy, including the presence of birth defects or soft markers on ultrasound and past obstetric history, particularly if it is notable for a prior pregnancy affected by aneuploidy or another genetic disorder. A past family history of aneuploidy increases current pregnancy risk of aneuploidy, especially if a parent is a balanced robertsonian translocation carrier, though most cases are sporadic and secondary to chromosomal nondisjunction.

Patients report many different motivations for pursuing aneuploidy screening or prenatal diagnosis. Some may choose pregnancy termination if the defect is identified at an early enough gestational age. Others may choose to pursue screening or testing to allow them time to process the diagnosis and seek experienced clinicians who may be able to aid them in preparation for caring for an affected infant and to care for their child after delivery. Some birth defects, such as some neural tube defects, may be eligible for prenatal treatment with subsequently improved neonatal outcomes.[5] All patients choosing to undergo screening or testing should receive counseling regarding risks, benefits, and limitations of their chosen testing plan from their health care provider or genetic counselor. It is important to note that aneuploidy screening and testing decisions are heavily value driven; a frank discussion of the benefits, risks, and limitations of tests is key in ensuring that care is appropriate for each patient's individual goals.

Table 2
Risk of aneuploidy by maternal age

Maternal Age at EDD (y)	Risk of Trisomy 21	Risk of Other Chromosomal Abnormality
20	1:1480	1:525
25	1:1340	1:475
30	1:940	1:384
35	1:353	1:178
40	1:85	1:62
45	1:35	1:18

Abbreviation: EDD, estimated date of delivery.

Adapted from Practice bulletin no. 163: screening for fetal aneuploidy. Obstet Gynecol 2016;127(5):e124.