ANEUPLOIDY SCREENING

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Introductory Case

A 29-year-old G1P0 presents for prenatal care at 11 weeks of gestation. She had an early ultrasound for dating at 7 weeks that showed a single, live intrauterine pregnancy. She has no family history of genetic conditions or mental retardation.

Milestone-Based Focused Questions

LEVEL 1: DEMONSTRATES BASIC KNOWLEDGE ABOUT COMMON AMBULATORY OB/GYN CONDITIONS. DEMONSTRATES KNOWLEDGE OF INDICATIONS AND LIMITATIONS OF COMMON SCREENING TESTS

WHAT IS ANEUPLOIDY? HOW COMMON IS IT? WHAT ARE THE MOST COMMON ANEUPLOIDIES?

- Aneuploidy is the presence of an abnormal number of chromosomes in a cell.
- Overall, aneuploidy is seen in 1/150 live births
    - Downs Syndrome (Trisomy 21) 1/800 live births
    - Klinefelter Syndrome (46 XXY) 1/500 males
    - Turner Syndrome (45 X) 1/2000 female live births, only viable monosomy

WHAT IS THE DIFFERENCE BETWEEN SCREENING AND DIAGNOSTIC TESTS? WHAT ARE OPTIONS FOR ANEUPLOIDY SCREENING?

A **screening test** is a test to *identify individuals at sufficient risk* of a specific disorder to warrant further investigation (i.e., a diagnostic test) or intervention. Prenatal genetic screening is designed to assess whether a patient is at increased risk of having a fetus affected by a genetic disorder.

A **diagnostic test** is a test or procedure performed to *confirm* the presence of disease in an individual suspected of having the disease. Prenatal diagnostic tests for genetic disorders require evaluation for abnormalities in chromosome number or for specific genetic abnormalities. Diagnostic tests are intended to determine, with as much certainty as possible, whether a specific genetic disorder or condition is present in the fetus.

Screening Tests

Test	Gestational Age	Components of Test	Information Ascertained	Other	Detection Rate for Downs
First Trimester Screen	10 0/7 – 13 6/7	Nuchal Translucency (NT) Hcg PAPP-A	Trisomy 21 Trisomy 18 (Other risks with isolated increased NT)	AFP (alpha-fetoprotein) needed after 15 weeks if desired to screen for open neural tube defects	82-87%
Quad Screen	15 07 – 22 6/7	Hcg AFP Inhibin A Estriol	Trisomy 21 Trisomy 18 Open neural tube defects		82%
Cell Free DNA	>10 weeks	Cell free DNA in maternal serum	Trisomy 21 Trisomy 18 Trisomy 13 Sex Chromosomes	AFP needed after 15 weeks if desired to screen for open neural tube defects Allows for fetal sex determination as early as 10w	99%

Diagnostic Tests

Test	Gestational Age	Risk of Pregnancy Loss	Risk if procedure done before 10 weeks
Chorionic villus sampling	10 – 13 weeks	1/400	Limb abnormalities
Aminocentesis	>15 weeks	1/900 (higher with earlier gestational ages)	Club foot

LEVEL 2: DEMONSTRATES KNOWLEDGE OF APPROPRIATE SCREENING GUIDELINES

WHAT ARE THE CURRENT RECOMMENDATIONS FOR ANEUPLOIDY SCREENING?

Aneuploidy screening or diagnostic testing should be discussed and offered to *all* women early in pregnancy, ideally at the first prenatal visit, regardless of maternal age.

WHAT ARE IMPORTANT CONSIDERATIONS WHEN COUNSELING PATIENTS REGARDING ANEUPLOIDY SCREENING?

1. Patient's age-based risk of aneuploidy

Age	Risk of Downs	Risk of Aneuploidy
20	1:480	1:525
35	1:353	1:178
40	1:85	1:62

2. Patient's personal and family history of aneuploidy
3. Presence of multi-fetal gestation (this may decrease the accuracy of screening depending on the screening modality)
4. Patient weight (increased risk of inconclusive cell free DNA with higher body mass index)

WHAT IS THE ROLE OF ALPHA-FETOPROTEIN IN ANEUPLOIDY SCREENING?

AFP is NOT part of the screening for aneuploidy. It is the screening for open neural tube defects. Elevated AFP is also associated with abdominal wall defects (omphalocele, gastroschisis) and pregnancy complications such as growth restriction and pre-eclampsia.

AFP is part of the QUADRUPLE SCREEN. If first trimester screen or cell free DNA is offered for aneuploidy screening, AFP should be offered for screening of neural tube defects between 15- 20 weeks.

WHAT IS THE VALUE OF THE NUCHAL TRANSLUCENCY MEASUREMENT?

- Nuchal translucency is an ultrasound test performed between 10w0d and 13w6d which measures the fluid-filled space along the dorsal aspect of the fetal neck.
- The test requires specialized credentialing to be able to perform.
- An increased nuchal translucency is defined as >3mm OR >99%tile for a given crown rump length and is independently associated with fetal aneuploidy and isolated anomalies (congenital heart defects, abdominal wall defects, and diaphragmatic hernia) in the setting of normal chromosomes.
- If increased nuchal translucency is found, patients should be offered a targeted ultrasound and fetal echocardiogram in the second trimester.

SHOULD PATIENTS WHO HAVE NORMAL PRE-IMPLANTATION GENETIC SCREENING BEFORE IN VITRO FERTILIZATION BE OFFERED ANEUPLOIDY SCREENING?

Yes, because of the risk of false negative results for pre-implantation genetic screening.

REFERENCES

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