

PRENATAL CARE: ANEUPLOIDY SCREENING AND DIAGNOSIS

Week 43

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Reading Assignment:

ACOG Practice Bulletin #163, May 2016
Screening For Fetal Aneuploidy

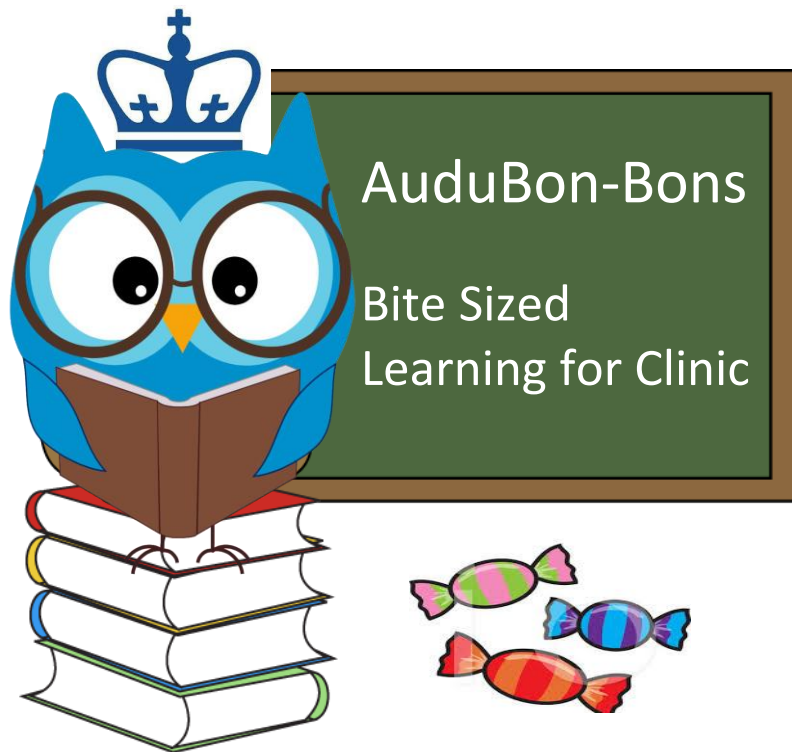
The Ob/Gyn Podcast

Episode 34: Aneuploidy Part 1

Episode 40: Aneuploidy Part 2

<https://www.youtube.com/watch?v=h65Pa2cOhy4>

<https://www.youtube.com/watch?v=F36jEiUqPsk&t=69s>



LEARNING OBJECTIVES



- Gain an understanding of the tests currently available to screen for, and diagnose, aneuploidy
- Be able to identify candidates at increased risk for carrying a fetus with aneuploidy
- Be comfortable initiating a conversation about aneuploidy screening and its limitations
- Be comfortable counseling patients on screening results and options for diagnostic testing



CASE VIGNETTE

- Ms. A. Ma is a 35yo G1 P0 woman who presents at 10 weeks for her second prenatal visit. She is doing well and has no complaints. This is the first child for her and her husband, and they are very excited.
- You have just finished reviewing the lab results from her initial visit, which were all normal. She wants to discuss what kind of testing she should expect to “check if the baby could have chromosomal abnormalities like Down syndrome.”



FOCUSED HISTORY

What will be pertinent in her history?

- **POB:** G0
- **PGYN:** Regular menses
No STI/cysts/fibroids
No abnormal paps
- **PMH:** Denies
- **PSH:** Denies
- **Meds:** PNV
- **All:** NKDA
- **Soc:** Denies toxic habits; works as a teacher; lives with her husband
- **FHx:** **No genetic abnormalities; FOB has no family members with genetic abnormalities**



PERTINENT OBJECTIVE FINDINGS

What will be pertinent in her physical exam?

- **P:** 80 **BP:** 116/70 **Wgt:** 60kg **Hgt:** 160cm **BMI:** 23.4
- **Abd:** Soft, NT/ND
- **FHR:** 145
- **Ext:** NT b/l

What will be pertinent in her prenatal labs?

- **Normal HbA1c**



DEFINITION

- What is the definition of **aneuploidy**?
 - Gain or loss of one or more chromosomes ☐ unbalanced chromosome number in a cell
- What type of chromosomes are typically affected by aneuploidy?
 - **Autosomes**
- What is the most common autosomal aneuploidy?
 - **Trisomy 21** (Down syndrome)
 - Others: **Trisomy 18** (Edwards syndrome), **Trisomy 13** (Patau syndrome)



PATIENT SELECTION

Which factors (if any) determine which patients should be offered screening and diagnostic testing for aneuploidy?

- Screening and diagnostic testing should be discussed and offered to **ALL** women early in pregnancy, **regardless of maternal age**
- Factors affecting choice of screening tests:
 - Desire for information prior to delivery
 - Prior obstetric history
 - Family history
 - Fetus #
- Counseling for diagnostic testing should include a discussion of the patient's aneuploidy risk



RISK FACTORS

What are factors that increase the risk of having a fetus with aneuploidy?

- Increasing maternal age
- Parental aneuploidy or aneuploidy mosaicism
- Hx prior aneuploid fetus
- Fetal abnormalities
 - Ultrasound
 - Serum screening test



SCREENING TESTS

What are the categories of tests currently available for aneuploidy screening?

- First trimester (10wk – 13w6d)
- Second trimester (15wk – 22w6d)
- Combined
- Cell-Free DNA (10wk)
- Ultrasound



SCREENING TESTS - FTS

What can be used to screen for aneuploidy between **10wk – 13w6d**?

First Trimester Screen (FTS)

- Risk calculation
 - T21, T13, T18
- Factors
 - Nuchal translucency (NT)
 - Analytes – Free beta hCG, PAPP-A
 - Maternal age, prior fetus with aneuploidy, weight, race, # fetuses

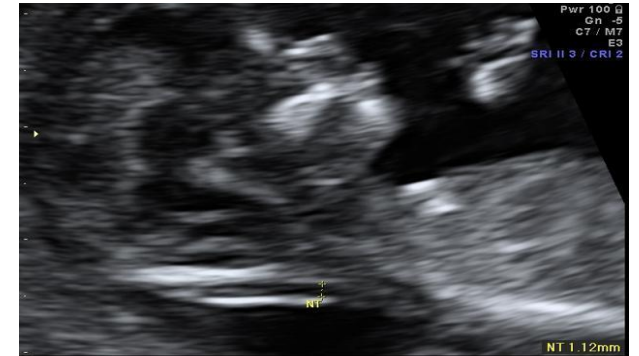
	NT MoM	PAPP-A MoM	Beta hCG MoM
Trisomy 21	↑	↓	↑
Trisomy 18	↑	↓↓	↓↓
Trisomy 13	↑	↓	↓



SCREENING TESTS - FTS

What is **nuchal translucency** and what is considered an increased measurement?

- Fluid-filled space on the dorsal aspect of the fetal neck
- Enlarged NT
 - $\geq 3.0\text{mm}$ above 99th percentile for CRL
 - Independently associated with fetal aneuploidy
 - Also increases risk of other genetic conditions, isolated anomalies (including cardiac and abdominal wall defects) and poor perinatal outcomes



SCREENING TESTS – QUAD SCREEN

What can be used to screen for aneuploidy from **15wk – 22w6d**?

Quadruple screen (Quad screen)

- Risk calculation
 - T21, T18, Open Neural Tube Defects (NTD's)
- Factors
 - AFP
 - Also independently screens for open NTD's
 - Estriol
 - hCG
 - Inhibin A
 - Maternal age, weight, race, presence of DM

	Trisomy 21	Trisomy 18
AFP MoM	↓	↓
Estriol MoM	↓	↓↓
hCG MoM	↑	↓↓
Inhibin A MoM	↑	Equivocal



SCREENING TESTS - COMBINED

What are **combined tests** for aneuploidy screening?

Integrated

- NT + PAPP-A + Quad screen
- All results sealed until 2nd TM screening results

Sequential

- FTS + Quad released together
- *Exception:* FTS risk $\geq 1:50$? results released early
 - cfDNA or diagnostic testing offered



SCREENING TESTS – CELL-FREE DNA

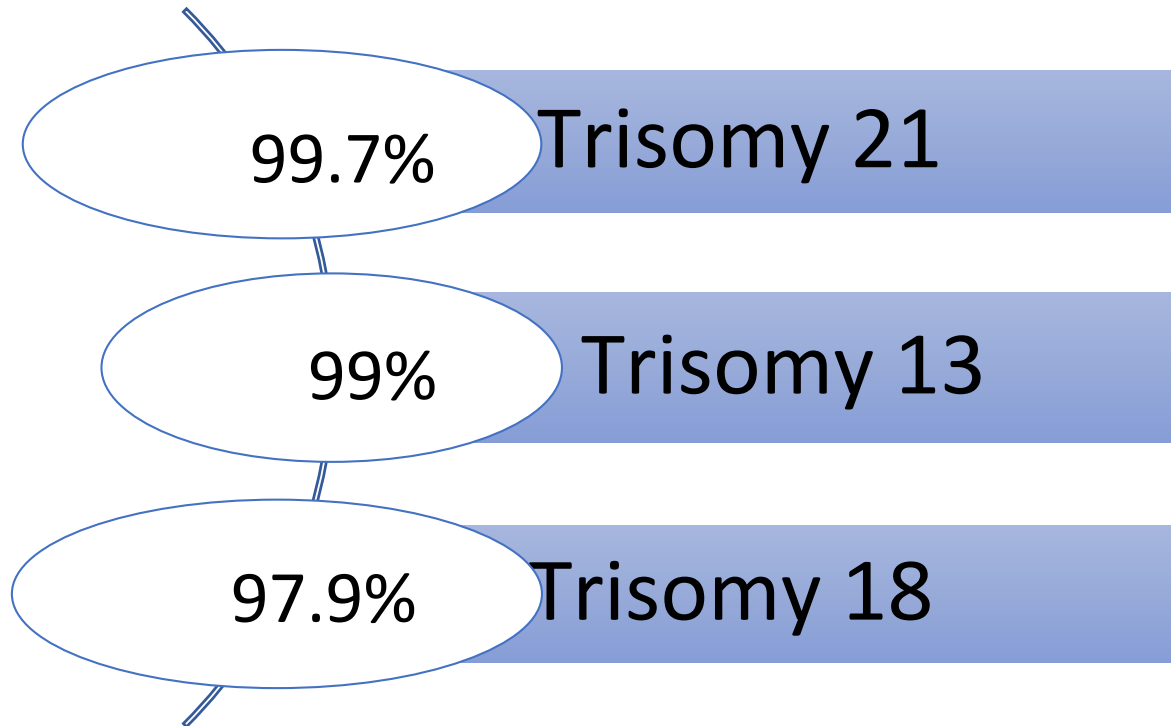
What is **cell-free DNA** and what does it offer?

- Fetal DNA from placental apoptotic debris found circulating in maternal blood
- Risk calculation - **T21, T13, T18**
- Analysis of **sex chromosome DNA**



SCREENING TESTS – CELL-FREE DNA

What are the detection rates for **cell-free DNA**?



Keep in Mind!

- More effective with larger fetal fractions ($\geq 10\%$)
- Low fetal fractions:
 - sampling <10wks,
 - high BMI,
 - fetal aneuploidy
- Irreversible action NOT recommended without diagnostic testing



SCREENING TESTS - ULTRASOUND



What is the role of **ultrasound** in screening for aneuploidy?

- Patients who did not previously have aneuploidy screening
 - Offer screening if isolated soft markers are identified
- Patients who have received negative screening or diagnostic result
 - Don't use u/s as an additional aneuploidy screen
 - No further evaluation for **EICF** or **CPC** seen as sole markers
 - Recommend further counseling for:
 - Hypoplastic/absent NB
 - Echogenic bowel
 - Thickened nuchal fold



SCREENING RESULTS

What is the next step for patients with a positive screen?

- First step, verify gestational age to ensure accuracy of results
- cfDNA+  Genetic counseling + diagnostic testing
- FTS/Quad/Combined+  Genetic counseling + cfDNA and/or diagnostic testing
- *NB: cfDNA is reasonable for patients looking to avoid invasive testing, otherwise, may create a delay in diagnosis and management*

What is the residual risk of aneuploidy with a normal cfDNA screen after abnormal traditional screen?

- 2%



SPECIAL POPULATIONS

- Patients who have conceived with **IVF after PGS**
 - Offer aneuploidy screening and diagnosis as false-negative tests can occur
- Patients with **multifetal gestations**
 - NT can screen each fetus independently
 - Analyte screening should be limited to twin gestations
 - cfDNA is not recommended



COUNSELING

What are the key components when counseling patients about screening/diagnostic tests and results?

- Clear, objective, nondirective fashion
 - Allow time to understand information and make informed decisions
- **Pretest**
 - Include information on types of potential results, and risks/limitations/benefits of testing
- **Posttest**
 - Timely communication of results to optimize options for evaluation and management
 - Be prepared to discuss all reproductive management options with patients, including, but not limited to prenatal surgery, adoption, neonatal palliative care, or termination of pregnancy
 - **Genetics referral** for all abnormal results to optimize counseling



CODING AND BILLING

- ICD-10

- **Z36.0** - Encounter for antenatal screening for chromosomal anomalies
- **Z36.82** - Encounter for antenatal screening for nuchal translucency
- **O28.5** - Abnormal chromosomal and genetic finding on antenatal screening of mother

- CPT

- **81420** - Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
- **81507** - Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy



SOCIAL DETERMINANTS OF HEALTH

Northwestern 2015

Likelihood of pursuing diagnostic testing after a positive screening test for aneuploidy
Patients with private insurance – 57%
Patients with Medicaid – 35%

- The institution conducting the study had no direct financial and systems barriers for having genetic counseling or after a positive screen result because these services were covered
- The disparity in uptake of prenatal diagnosis based on insurance status persisted after adjusting for differences in sociodemographic characteristics
- Based on their data and that of prior studies, the authors concluded their results likely reflect disparities in patient–physician communication about this complex and nuanced topic

-As this study was performed in 2015, NIPT was not introduced as another testing option at this institution until the end of the study period.

-There is a paucity of studies investigating the SDH impact on uptake of diagnostic testing after positive aneuploidy screening results with NIPT.

-Similar studies need to be done accounting for the time since NIPT was introduced to gain a better understanding of factors influencing patients' decisions. This will help ensure that there is not only sufficient provision of information, but a thorough understanding of the information that is provided.



EVIDENCE

References

- Wong, A.E., Dungan, J., Feinglass, J. and Grobman, W.A., 2015. Socioeconomic disparities in diagnostic testing after positive aneuploidy screening. *Obstetrical & Gynecological Survey*, 70(11), pp.673-675.



EPIC Phrase

- . BBonNIPTresults
- Description: NIPT Results Counseling
- The patient was informed of her NIPT results

***We discussed that this is a screening test and the negative result should be interpreted as a low risk of Trisomies 13, 18, and 21, as well as an abnormal number of sex-chromosome. I reviewed with the patient that while NIPT offers very high detection rates for the above aneuploidies, it is still a screening test, and should not be viewed as equivalent to diagnostic testing.

***We discussed that this is a screening test, and the positive result should be interpreted as an elevated risk of ***. We discussed that a definitive diagnosis could only be obtained with diagnostic testing. The patient was offered a referral for genetic counseling to receive further information and counseling about diagnostic testing, and to schedule the testing if she desires.



EVIDENCE

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