The Changing Face of Prenatal Genetic Screening

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Disclosure Statement

I have no conflicts of interest to disclose.

Objectives

- Understand the difference between prenatal screening versus prenatal diagnostic testing
- Identify clinical applications/indications for noninvasive prenatal screening (NIPS)
- Recognize various aneuploidy conditions and microdeletion syndromes screened for with NIPS
- Appreciate the limitations of NIPS
Screening vs Diagnostic Testing

- Screening tests
  - Maternal serum screens, ultrasound, carrier screening, NIPS

- Diagnostic tests
  - Chorionic villus sampling, amniocentesis

ACOG and ACMG

- ACOG Committee Opinion (December 2012)
  - Noninvasive Prenatal Testing for Fetal Aneuploidy

- ACMG Policy Statement (February 2013)
  - ACMG Statement on noninvasive prenatal screening for fetal aneuploidy

Indications for NIPS

- AMA
- Abnormal serum screening
- Abnormal ultrasound
- Previous child with aneuploidy/microdeletion
- Parent with balanced Robertsonian translocation*
What does NIPS screen for?

- Aneuploidy (all companies)
  - Trisomy 21
  - Trisomy 18
  - Trisomy 13
- Aneuploidy (some companies)
  - Trisomy 16
  - Trisomy 22
  - Triploidy
  - Sex chromosome abnormalities
- Microdeletions (varies)
  - 1p36
  - 4p
  - 5p
  - 8q
  - 11q
  - 15q11.2
  - 22q11.2

Sensitivity of NIPS

- Aneuploidy
  - 91-99%
- Microdeletions
  - Varies

What NIPS does not screen for..

- Single gene disorders
- Open neural tube defects
- Structural birth defects
Circumstances to consider when offering NIPS

- Multiple gestation
- IVF/Donor egg
- Gestational age

NIPS Options

- Ariosa – Harmony
- illumina - verifi
- Integrated Genetics - informaSeq
- Natera – Panorama
- Sequentom – MaterniT21
- Sequenom – VisibiliT**

Case Example #1

- G1 18 yo
- + mass for Down syndrome
- Normal targeted u/s
- NIPS
  - Screen + trisomy 13
  - Amniocentesis
    - FISH aneuscreen normal
    - Karyotype normal, 46,XX
Case example #2
- G2P1001 32 yo
- +NIPS for X chromosome aneuploidy
  - Unable to determine from NIPS if maternal or fetal origin
- Amniocentesis
  - FISH normal XX
  - Karyotype, 46,XX
- Patient declined maternal testing

Case example #3
- G1 31 yo
- + mss for Down syndrome (1:191)
- Normal targeted u/s
- NIPS
  - Screen + T21
- Amnio
  - FISH confirmed T21
  - Karyotype 47,XX,+21

Case example #4
- G2P1 twin pregnancy
- + mss for Down syndrome
- Targeted u/s
  - Discordant growth
- NIPS
  - Unreportable
  - Call from lab director
  - Follow up u/s
  - Twin B duodenal atresia
  - Declined amnio
- Twin B
  - Postnatal array, 4 abnormalities, including 13q deletion