
- What's Screen Test?
  - Identification within an apparently normal population of those at risk of disorder (not diagnostic test)

-Difference between screening/Diagnostic test (In general):

<table>
<thead>
<tr>
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<th>Screening Tests</th>
<th>Diagnostic Tests</th>
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<tbody>
<tr>
<td>Benefits</td>
<td>No risk of harm to the fetus.</td>
<td>Gives a diagnostic with 100% accuracy.</td>
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<td>In certain cases, this is a necessary first step that discovers high-risk before diagnostic testing can be performed.</td>
<td>Can test for many diseases (e.g., cystic fibrosis).</td>
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<td>Limitations</td>
<td>Gives the risk a fetus will have a condition(s). Not 100% accurate.</td>
<td>Poses risk of harm to the fetus, possibly leading to miscarriage.</td>
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<td>Can only test for certain conditions (including Down syndrome, Trisomy 18, and spine bifida).</td>
<td>In some instances, a screening test is not available before diagnostic testing can be performed.</td>
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<td>Not every screening test is currently covered by health insurance (Non-Invasive Prenatal Testing - NIPT).</td>
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History of antenatal testing
- 1966- amniocentesis
- 1970’s- age alone
- 1980’s
  - AFP
  - Triple screen- 72% detection 5% False positive
  - Quad screen- 79% detection 5% False positive
  - Penta screen- 83% detection 5% False positive
- 1980’s- CVS
- 1990’s
  - First Trimester screen- 80-85% 5% False positive
  - Sequential screen 90-94% detection 3-5% FP
- 2010’s- Non-invasive prenatal diagnosis (placental fetal DNA)
- **What is NIPT?**

- Non-invasive prenatal testing (NIPT) is a new way to screen pregnant lady to see if her fetus has an increased chance of having a few specific chromosome disorders.

- The chromosome disorders are Down syndrome (tri 21, trisomy 18 and trisomy 13.

- **NIPT:**

  • 1997: Lo and colleagues identified male cell-free fetal DNA in the blood of a pregnant woman.

  • cffDNA – cell free fetal DNA
    – Found in the maternal blood stream
    – >99% is placental in origin

- **NIPT**

  • October 17, 2011 –
    – NIPT became commercially available in the USA
    – Sequenom : MaterniT21 Plus and other like::
-What information can NIPT provide?

• NIPT can find about 98-99% of developing babies with Down syndrome.

• It is sometimes used to tell if a baby has trisomy 18 or trisomy 13; however, NIPT is not as good at finding trisomy 18 or 13 compared to looking for Down syndrome.

-When is NIPT done?

• NIPT is done by taking a blood sample from the mother early in pregnancy, usually around 10 weeks of pregnancy.

• An ultrasound is needed before having NIPT to date the pregnancy accurately and to be sure there is only one baby.

-Who should have NIPT?

• Currently, NIPT has mostly been studied in women who have a higher chance of Down syndrome. (Mother age= to 35 at delivery).

• Singleton pregnancy, cannot be used in women with multiple babies (e.g. twins).

• Previous pregnancy with abnormal baby.

• Couple with translocation carrier.

-What is the risk of NIPT on babies?

- NIPT is a blood test done on the mother.

- It does not hurt the developing baby, so not increase the chance of a miscarriage.

- This is different from other types of testing such as CVS (chorionic villus sampling) and amniocentesis.
- Differences between NIPT and currently available prenatal screening:

- Current prenatal screening tests involve one or two blood samples and usually an ultrasound to measure the thickness of the back of the baby’s neck (nuchal translucency).
- Depending on the type of screen, information about the chance of the baby being born with Down syndrome, trisomy 18 and sometimes trisomy 13 and open neural tube defects (ONTDs) such as spina bifida, is provided.
- Current prenatal screening tests are not as accurate as NIPT for Down syndrome. For example, of every 100 pregnancies where the baby has Down syndrome, current screening tests can identify 80-90 of the affected pregnancies.
- NIPT can find 98-99 of the pregnancies where the baby really has Down syndrome. NIPT does not look for ONTDs.

- Current Application (NIPT):

1- Fetal sex determination
   - Sex linked disorders
   - Congenital Adrenal Hyperplasia

2- Fetal Rhesus D disease typing

3- Detection of aneuploidies
   - Trisomy 21
   - Trisomy 18
   - Trisomy 13
   - Sex chromosome abnormalities
   - Triploidy (Natera only)

- limitation of NIPT:

1- Can’t differentiate between chromosomal changes (Non-dysjunction, translocations, mosaic).
2- Maternal cancer can affect results.
3- Increased maternal weight (and <10 weeks gestation) contribute to fetal cfDNA being low

Maternal Weight

% of patients with >4% cf fetal DNA

- <90 kg
- 90 to 130 kg
- >130 kg

Ariosa data, 2013
- Future Applications:
  - Micro deletions/duplications
  - Twin pregnancies (current!)
  - Monogenic disorders
  - Genome sequencing — NIFWGS
    - Technical challenges
    - Ethical challenges
      - Unanticipated findings

- In Summary:
  1. NIPT Screening test not diagnostic.
  2. Should be done between 10-15 weeks of gestations.
  3. Pre/post test counseling.
  4. NIPT high risk should have invasive test (CVS/Amino).
  5. Use all available resources to help couple make their on informed decisions.
Thank You
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