Tools For Instituting Non-Invasive Prenatal Testing in Your Obstetric, Midwifery or Family Practice

Oregon Genetics Program
Public Health Division
March 2014

Oregon Genetics Program

Oregon Health Authority

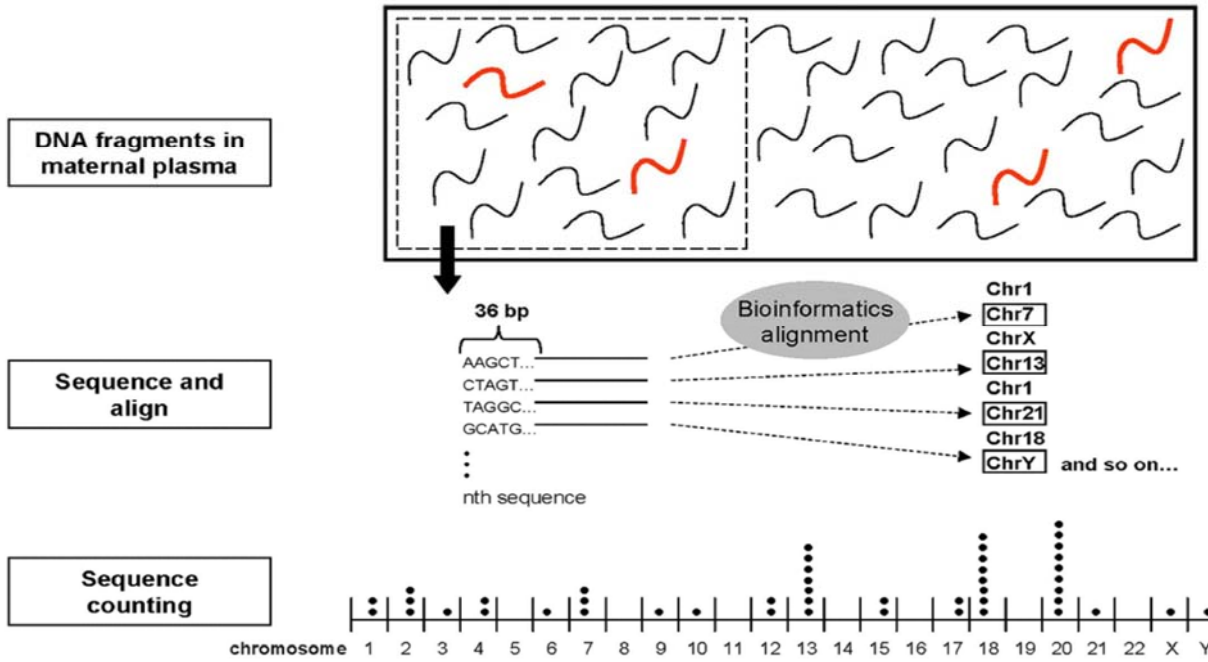
Introduction

NIPT (also referred to as noninvasive prenatal screening, or NIPS) is a screening test that can indicate if there is a strong likelihood that a woman's pregnancy is affected with certain chromosome abnormalities with a low false positive rate.

Education and informed consent are crucial aspects of appropriate NIPT utilization. We recommend this testing be coordinated through a genetic counselor when possible. However, these services may not be accessible to all women who request this test. Thorough counseling by a qualified prenatal provider is essential.

This toolkit is intended to help your office design and implement an NIPT protocol that will allow for excellent patient care.

What is cell free fetal DNA?



Zhong, X. 2009

Maternal and placental cells in the maternal circulation break open, dispersing fragments of DNA. This DNA is sequenced and analyzed to determine the quantity of DNA from specific chromosomes of interest.

Why is NIPT not diagnostic?

- The technology does not visualize chromosomes.
- The DNA is from the placenta, not the fetus (i.e. placental mosaicism).
- The results are dependent on the fetal fraction in the sample.
- We are assuming mom is not mosaic.
- There may have been a vanishing twin who had a chromosome abnormality.
- It may not detect fetal mosaicism.

What conditions are currently screened for with NIPT?

- All labs provide a risk estimate for Down syndrome, trisomy 18 and trisomy 13.
- Some labs automatically screen for sex chromosome abnormalities, other labs allow the ability to opt in or out.
- Some labs also screen for subchromosomal microdeletions or tripoloidy.

ACOG Committee Opinion

- Noninvasive Prenatal Testing for Fetal Aneuploidy (Number 545, December 2012)
  - Patients at increased risk based on the following criteria for aneuploidy can be offered this testing:
    - Maternal age 35 or older at delivery
    - Ultrasound findings
    - History of a prior pregnancy with a trisomy
    - Other positive screening test
    - Parental balanced translocation increasing risk for tested aneuploidy

2012 ACOG Committee Opinion

- NIPT should not be part of routine prenatal labs.
- NIPT should not currently be offered to low-risk women or women with multiple gestations as it has not been sufficiently evaluated.
- Pretest counseling should explain that this screening test has high sensitivity and specificity. It tests for common chromosome abnormalities and cannot test for all chromosome abnormalities or genetic disease.
- A detailed family history should be obtained.
- Invasive testing should be offered for structural anomalies.
- Negative NIPT results do not ensure an unaffected pregnancy.
- Genetic counseling is recommended for positive results along with invasive testing for confirmation.
- NIPT does not replace CVS or amniocentesis.

NIPT Fact Sheet

- Please review this NIPT Fact Sheet developed by the National Coalition for Health Professional Education in Genetics and the National Society of Genetic Counselors:

  http://www.nchpeg.org/index.php?option=com_content&view=article&id=384&Itemid=255

- This document will be modified over time as more conditions are added to this testing platform
- You will need to review this document often as technology is rapidly changing

Choosing a Lab

- NIPT technologies are relatively new, four labs are currently offering testing.
- Not all laboratories offer the same screening with the same accuracy.
- When choosing a lab, please consider the following:
  - Technology used by lab
  - Eligibility requirements
  - Validation data/peer reviewed publications
  - How results near the cut-off are reported
  - Availability of sample reports
  - Patient information brochures
  - Cost
  - Financial support for patients
  - Customer service
  - Availability of genetic counseling services

Labs currently offering NIPT

- Ariosa- Harmony™
- Natera- Panorama™
- Sequenom- MaterniT21plus™
- Verinata- Verifi™

NIPT Protocol

- We recommend that in your practice setting, the group should agree on specific indications for testing, who will be responsible for obtaining informed consent, how blood samples will be drawn and sent, and how disclosure of results will be communicated.
- Ultrasound is recommended prior to blood draw to establish a viable pregnancy, gestational age and singleton pregnancy.
- All individuals involved in the process should have formal education regarding the technology and office policies.

If you plan to offer NIPT in your office, you will need to:

- have an account with one (or more) companies
- maintain a supply of kits
- decide where blood will be collected
- decide who will be responsible for shipping kits
- understand billing/insurance issues

Patient Education Materials

- To inform patients about the availability of this test, most practices will provide educational flyers or brochures
  - In the waiting room
  - As part of a pregnancy packet
  - At the first intake visit
- Patient informed consent should not rely on the brochure alone
  - face-to-face counseling is necessary

Pretest Counseling

- As part of informed consent, the following should be discussed with all patients:
  - Screening & diagnostic testing is *optional*
  - The purpose of screening
  - Current screening & diagnostic testing options including the sensitivity and specificity of each test
  - An accurate, unbiased, up-to-date description of the conditions for which screening is performed
  - Additional or expanded NIPT test panels (if applicable depending on lab)
  - Alternatives to NIPT

For more information regarding sensitivity and specificity please see the NIPT factsheet

Questions For Your Patient To Consider

- What will I do if I have a screen positive result?
- What will I do if I have an abnormal CVS or amniocentesis result?
- What will I do if I have a false negative result?
- How do I feel about having a child with a chromosome difference or birth defect?

Educating Yourself About Aneuploidy

www.ndss.org

www.nwdsa.org

www.trisomy.org

www.turnersyndrome.org

www.genetic.org (47,XXY; 47,XXX; 47, XYY)

Consent Document

- A formal consent process that includes a signature may help reduce accidental and undesired screening

Disclosing Results

- Having a consistent communication plan may be the most important part of an NIPT program
- Given the complexity of the testing and results, even normal results should be disclosed by a medical professional designated to review this information
- Abnormal or 'no call' results should be disclosed by the primary prenatal provider

Normal Results

- Attempt to speak with the patient personally rather than leaving a message
- Review that normal results "reduce" but do not "eliminate" risk for tested conditions
- Have contact information for a genetic counselor on hand in case the patient desires more information

Other Recommended Tests

- Nuchal translucency (NT) ultrasound can be considered to screen for chromosome abnormalities and other birth defects.
- MSAFP should be considered for open neural tube defect screening.
- Anatomy ultrasound should be offered.
- CVS and amniocentesis should be available to high-risk patients with normal NIPT, especially if there are other concerns later in pregnancy (i.e. ultrasound findings).
- If a family is at high risk for hereditary conditions or other aneuploidies not screened for with NIPT, they should have access to genetic counseling for a comprehensive risk assessment.

‘No Call’ Results

- Be aware of the ‘unreportable’ and ‘no call’ specifications of your chosen laboratory
- As many as 5% of women who choose NIPT will receive a ‘no call’ result, typically due to a low fetal fraction of DNA. This may be more common in patients with a higher BMI
- Each laboratory has their own recommendations regarding redraws
- Be prepared to discuss alternate screening or diagnostic testing options

Aneuploidy Suspected

- Some laboratories may report a result as 'aneuploidy suspected' if a value falls near the z-score cut off.
- There is currently not enough data to predict the risk for aneuploidy in this category, but it should be presumed to be increased.
- This result should be treated as a "screen positive" with an increased chance for aneuploidy.

Abnormal Results

- The chance for a true positive can vary widely and results should always be interpreted in the clinical context of the pregnancy
- Review the condition in order to provide up-to-date information about the result
- Think about wording/vocabulary ahead of time
- Speak with patient directly on telephone
- Offer to meet in person to review
- Recommend CVS or amniocentesis to confirm diagnosis
- Referral to genetic counseling and/or MFM is strongly recommended

NSGC Recommendations For Disclosing Abnormal Results (1)

- Tell the parents about the diagnosis as soon as possible, even if the diagnosis is suspected but not yet confirmed.
- The family should be informed of the diagnosis in their preferred language. If possible, a professional medical interpreter should be present at the time of disclosure.
- Discuss the diagnosis in a private, comfortable setting, free from interruptions. Allow time for questions and make plans for a follow-up conversation.
- Parents should be provided with accurate and up-to-date information. Information should be given with a balanced perspective, including both positive aspects and challenges related to the diagnosis.
- Provide the information in a sensitive and caring, yet confident and straightforward manner, using understandable language that is clear and concise.

From: Sheets et al. J Genet Couns (2011)

NSGC Recommendations For Disclosing Abnormal Results (2)

- Use neutral language and avoid using value judgments when starting the conversation, such as "I'm sorry" or "Unfortunately, I have bad news".
- Use sensitive language and avoid outdated or offensive terminology. Use person-centric language, emphasizing that this is a baby who has Down syndrome, rather than a "Downs baby" or a "Down syndrome child."
- Allow time for silence and time for tears. Do not feel that you need to talk to "fill the silence". Offer the family time alone.
- Informational resources should be provided, including contact information for local and national support groups, up-to-date printed information or fact sheets, and books. The opportunity to meet with families who are raising a child with Down syndrome, those who have chosen to create an adoption plan, and/or those who have terminated a pregnancy should be offered. When appropriate, referrals to other specialists may also be helpful (e.g., medical geneticists, genetic counselors, cardiologists, neonatologists, etc.).

From: Sheets et al. J Genet Couns (2011)

Resources For Patients

www.ndss.org

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www.turnersyndrome.org

www.genetic.org (47,XXY, 47,XXX and 47, XYY)

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