Genetic Screening in pregnancy and what to do about it

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Objectives

Why do we screen

What do we screen for

What happens if the screen is positive

Post natal resources

What are the common things we screen for?

Abnormal number of chromosomes

Genetic diseases- Tay sachs SMA etc

Types of test

Screening test

- Positive- chance of disease state
- Negative- low/minimal chance of disease state

Diagnostic testing

- Confirmation testing
  - Positive- have the disease
  - Negative do not have the disease

Types of screening tests

- Carrier screening- done on parents blood or tissue, single gene conditions- CF, sickle cell, SMA- lifetime test
- Prenatal genetic screening- mom's blood and US
  - Abnormal number - T21, XO
    - cfDNA/NIPT- 10 weeks
    - Serum screening- protein levels- sequential screen, quad screen, 1T serum- 11 weeks
  - Physical abnormalities
    - NT- thickened likely to have abnormal # and heart malformations 11-14 weeks
    - AFP- increased AFP associated with abdome, face or spine abnormalities 15-22 weeks
    - Quad screen 15-22 weeks measures 4 markers in the blood associated with abnormalities
    - Anatomy scan- US to look at anatomy of baby 18-20 weeks
    - Level 2 scan- more in depth anatomy scan for high risk pregnancies

First trimester screening

- **Combined- blood and ultrasound 10-13 weeks**
  - **Blood measures 2 substances - hCG and PAPP-A**
  - **ultrasound - NT screening**
- cfDNA
  - As early as 10 weeks
  - Looks at DNA outside cells
- Carrier screening
  - Any point in pregnancy or any other point outside pregnancy
  - Single gene conditions

2nd trimester screening

Quad screen
- Checking blood for 4 substances- MS-AFP, Estriol, hCG, inhibin-A
- Down's, Edwards, NTDs
- 15-22 weeks

Fetal anatomy scan
- ~20 weeks
- Full anatomy ultrasound

Fetal echo
- Done for high risk for heart abnormalities or concerns on anatomy scan

Combined trimester screening

Can combine multiple test form different trimesters for more information

Cell Free DNA

Small amounts of DNA are released form the placenta into maternal circulation.

a. Screens for T21, T13, T18, XO,XXY, XYY,XXX
b. Results ~ 1 week
c. Low risk no further testing needed
d. Positive send for diagnostic testing

Carrier screening

Testing mom to look for carrier status of single mutation diseases

- If genetic conditions run in the family
- Certain ethnic backgrounds

All women should be offered CF and SMA screening

Women should also be offered hemoglobinopathies and thalassemias

If positive other parent should be screened if possible

Screening for physical abnormalities

- If positive screens highly suspicious for physical abnormalities
  - Ultrasound is our best tool
    - Level 2 ultrasound

Diagnostic tests

- **Screening positive or high risk for condition**
  - **Cells are sampled**
    - **Amniocentesis**
      - **16-20 weeks**
    - **CVS**
      - **11-13 weeks**
    - **Samples sent to lab**
      - **FISH**
      - **Karyotyping**
      - **Microarray**
      - **Panels**
    - **Results in 3d-multiple weeks**
  - **Invasive**
  - **Costly**
  - **Risky**

Level 2 ultrasound

High resolution

- Better detail
- Look at more structures
- 18-22 weeks
- Usually done by MFM

CVS

- Provider collects a small amount of the placenta the chorionic villus
  - 10-12 weeks
- Risks
  - Bleeding, cramping, LOF
  - Infection
  - SAB
  - PTL
  - Limb defects
  - Allergic rxn to supplies
- If multiple placenta needs multiple sampling
- CI
  - Infection
  - Abnormal uterine anatomy
  - Abnormal AFI

CVS prep

Informed consent

If mom Rh-, rhogam

Show up with full bladder, depending on position

Procedure

US- to find fetal heart, placenta, fetus and umbilical cord

Transcervical approach

Speculum placement, clean, US guided tube placement, suctioning of CV, removal

https://www.merckmanuals.com/home/women-s-health-issues/detection-of-genetic-disorders-before-and-during-pregnancy/prenatal-diagnostic-testing

Transabdominal approach

Clean, local anesthesia, us guided tube placement, suction, bandage

After either approach reassess give rhogam if applicable

Monitor for ~1 hour

Amniocentesis

Collect amniotic fluid and test protein levels @ 15-18 weeks

AFP and AChE, look for infection, can be therapeutic in polyhydramnios, fetal maturity testing, genetic testing

Procedure

Us guided needle insertion

Risks

Infection, bleeding, SAB, PTL

https://www.youtube.com/watch?v=bZcGpjyOXt0

Who should have genetic testing

- While everyone should be offered this population is at higher risk
  a. Family hx or personal hx of genetic conditions
  b. AMA
  c. Hx of SAB or stillbirth

Do pts have to get testing? How to advise pts

- Benefits
  - Plan for care of child
  - If termination would be desired
  - Can find out gender early
- Risks
  - Unwanted information
  - The risks of a blood draw
  - MAy involve further more invasive testing
- Alternatives
  - Wait until anatomy scan

Other risks

Screening test means false positives

False negatives also exist

Undue stress

Timeline

- In Illinois abortion cannot be performed after 24 weeks
  - Some patients may want to terminate based on the results of the amniocentesis but be outside the window
    - Anatomy scan ~20 weeks
    - ~1 week for results
    - Amniocentesis at ~21-22 weeks(best case)
    - ~2 weeks for results(~23-24 weeks)
  - Patients may also request to see a genetic counselor in there
  - Time to think

Cost of testing

Covered by insurance if medically indicated

- Many labs have deals if not covered by insurance

Guiding parents

Parents maybe thrown down a very different path then they were expecting

May require emotional and psychological support

- Having information on counseling
- Support groups
- I also like to have resources planned before I tell patients the possibly bad news

Treatments

Fastly growing field

Prenatal parenteral treatments to target underlying drug mutations

New ones coming out as we speak

Postpartum

Can pick a pediatrician with knowledge of disorder or allow the FM to learn more about disorder

Get very early referral to EI and other specialists that are needed

Have procedures that may need done early

Find a community to support the family

Q1

Which pt should be offered genetic screening?

A. 35 YO G1
B. 22 YO G2P1 with older child with T21
C. 27 YO G1 with family hx of SMA
D. 19 YO G1 with no PMhx or family hx
E. 22 YO G4P1030
F. All of the above

Q2

At what gestational age can cfDNA be done?

A. 4 weeks

B. 10 weeks

c . 20 weeks

Q3

Which diagnostic testing can be done transvagianlly?

A. CVS
B. Amniocentesis

Q4

If a patient elects for termination what is the lastest GA they can have a termination in Illinois?

A. First heart beat
B. Not legal in Illinois ever
C. Viability
D. End of first trimester
E. Third trimester

Q5

Which screening can be done prior to pregnancy?

A cfDNA

B Amniocentesis

C Quad screen

D Level 2 Ultrasound

E Carrier screening

Resources

https://www.acog.org/womens-health/faqs/prenatal-genetic-screening-tests

https://my.clevelandclinic.org/health/diagnostics/24136-pregnancy-genetic-testing

https://www.cdc.gov/ncbddd/birthdefects/diagnosis.html#:~:text=Cells%20in%20the%20amniotic%20fluid,might%20be%20at%20higher%20risk.

https://www.cdc.gov/nchhstp/pregnancy/screening/index.html

https://www.cdc.gov/genomics/famhistory/famhist_plan_pregnancy.htm

https://www.cdc.gov/genomics/famhistory/famhist_during_pregnancy.htm

https://www.acog.org/womens-health/videos/prenatal-genetic-testing

https://www.youtube.com/watch?v=fHnaSFQThsk

https://www.youtube.com/watch?v=wCpg54vuEqA

https://www.michiganmedicine.org/health-lab/what-moms-be-should-know-about-prenatal-genetic-testing

https://www.mayoclinic.org/tests-procedures/amniocentesis/about/pac-20392914

https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/chorionic-villus-sampling-cvs