Non-invasive testing in pregnancy: update for the perinatal provider
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Objectives
• Describe common screening tests for low-risk pregnancy by trimester.
• Discuss new methods to accomplish genetic screening as part of routine prenatal care.
• Identify abnormal screening results and subsequent follow-up care.

Initial prenatal Assessment
• CBC
• ABO, Rh, antibody screens
• VDRL/ RPR
• HbSag
• Rubella status
• HIV
  • Texas requires initial visit and third trimester or labor HIV
• UA w/culture
• G/C-chlamydia probe

Complete blood count (CBC)
• Can diagnose pre-existing anemia in early pregnancy
  • In pregnancy, anemia is Hgb less than 10
• Gives baseline to evaluate for physiologic drop at 28 weeks
• Elevated WBC can indicate infection
• May also lead to identification of thalassemia or sickle cell disease
• Platelet abnormalities can be diagnosed

Blood type, Rh, Antibody screen
• Possibility of ABO incompatibility with type O mother and type A or B baby
• Rh issues:
  • Rh negative mother does not have Rhesus factor
  • With Rh+ fetus, any mixing of fetal-maternal blood will result in antibodies made by mom
  • Rh+ is foreign tissue
• Type/Rh/Antibody – ex: A+/-

RH and other antibodies
• Rh issues
  • RhoGam prevents formation of maternal antibodies
  • Given at 28 weeks of pregnancy, for any invasive procedures, or SAB/TAB
  • Given whenever Rh negative mother has an Rh+ baby
• Besides Rh there are other rare antibodies
  • Lewis is not a threat to fetus
  • Duffy-b can cause hemolytic disease with hydrops
  • Kell (K or K1) can cause severe anemia, hydrops and death
  • Other, even less common, types exist
Vdrl/rpr - syphilis

- Venereal disease research laboratory/ rapid plasma reagin tests
- These tests screen for antibodies that can be produced with syphilis & other diseases
- Positive result requires further testing
  - FTA-ABS:
    - Fluorescent treponemal antibody absorption
    - not positive in 1st 3-4 wks of infection
  - Darkfield exam: shows actual spirochetes
- In pregnancy: causes stillbirth or congenital syphilis
- Texas law requires a repeat test at delivery

Hepatitis b

- Mother is tested for surface antigen (HepBSag), a sign of chronic infection
- Test required at first visit & at delivery by Texas law
- Fetus at risk when it comes in contact with maternal blood at birth
- 90% of + mothers are chronic carriers; 10% chronically infected
- Hep B + mom: infant care
  - No FSE or IUPC in labor if mom is Hep B +
  - Must bathe baby as soon as possible, before injections or percutaneous tests
  - Give Hep B vaccine + immunoglobulin (HBIG)
  - Giving Hep B at birth to all newborns meant to protect against hidden maternal disease

Rubella

- Rubella titer is drawn
- Titer above level set by the lab shows immunity
- Immunity means no new rubella in pregnancy
- Rubella in pregnancy linked to fetal disease
  - Congenital rubella syndrome 1st trimester
    - Death, mental retardation, heart, eye, brain malformations, other malformations can occur
  - Rarely a problem after 20 weeks pregnancy
- Mothers who are rubella equivocal or non-immune will receive an MMR vaccination postpartum prior to dismissal – usually just before discharge home
  - Women should NOT become pregnant for 3 months after this vaccine, so immediate postpartum is a good time to vaccinate

HIV

- Anytime STD test is positive, offer HIV testing
- ELISA test (enzyme-linked immunosorbent assay) is for HIV antibodies
  - Less specific, so confirm with Western blot if + ELISA
  - Many times this is what is called "reflex" testing
  - It takes from 2 weeks to 6 months for antibodies to be made with HIV (window)

Urine testing

- Urine analysis
  - Test for RBCs, WBCs, urobilinogen, protein, glucose, nitrates, pH, ketone, specific gravity, bilirubin
  - RBCs, WBCs, nitrates, pH with UTI, vag infections
  - Protein: sometimes UTI or vag infection, pre-eclampsia
  - Glucose: possibly diabetes
  - Ketones, elevated specific gravity: dehydration
  - RBCs and WBCs: normal in labor (show)

- Urine culture
  - Many women have no s/s or altered s/s with UTI in pregnancy
  - UTI in pregnancy has been linked to preterm labor and birth
  - All women get a starting urine culture to identify asymptomatic bacteriuria

Reportable diseases

- Conditions that are contagious and can have serious public health consequences are reported to the state department of health
- Each state has some variation
  - http://www.dshs.state.tx.us/dcu/investigation/forms/101A.pdf
  - Common STIs are reportable in Texas: HIV, Hepatitis, syphilis, chlamydia, gonorrhea
  - Herpes is not reportable
Gonorrhea & chlamydia

- Women often asymptomatic with gonorrhea
  - Linked to salpingitis, PPROM, preterm birth, chorioamnionitis, neonatal sepsis, IUGR in pg
  - Can cause ophthalmia neonatorum/blindness in NB
- Gonorrhea is reportable disease
- Women often asymptomatic with chlamydia
  - Linked to salpingitis, PID and infertility in men
  - Linked to PPROM, PTL, chorioamnionitis in pg
  - Neonatal pneumonia, conjunctivitis in NB
- Chlamydia is reportable disease
- Cultures required by the state in early pregnancy

Sickle cell disease/trait

- Sickle cell affects 72,000 Americans, primarily those of African heritage, but also those of Arabian, Asian, Caribbean, Indian, Mediterranean, and South and Central American descent.
- Red blood cells become rigid, sticky and sickle-shaped and are more fragile.
- This results in periodic plugging of blood vessels, thereby preventing the delivery of oxygen to tissues and organs

Sickle cell disease/trait

Why does sickle cell or thalassemia matter?

- With the disease, the pregnancy is higher risk
- With the trait, there is inheritance
  - Women with sickle cell trait are more prone to UTI in pregnancy

Subsequent labs

- Targeted (Level II) ultrasound scan for women at high risk at 16-20 weeks
- Hbg/Hct ~ 28 weeks
- Glucose screening 26-28 weeks
- Antibody screen and RhoGAM for Rh negative women at 28 weeks
- Vaginal / rectal culture for Group B Strep ~35 weeks

Diabetes screening

- Diabetes screening at 24-28 weeks
- One hour Glucose Tolerance Test (GTT):
  - 50 gm glucose load w/ one hour lab draw post dose; may draw fasting level pre-dose also
  - Results >140-200 indicates need for 3 hour GTT
- 200 or > is diagnostic for gestational diabetes
- Repeat Hgb/Hct w/ this screen

GBS testing

- Group Beta Strep (GBS) swab of perineum and rectum ~ 35 weeks
- Swab introitus, and through the anal sphincter for best sample
- Mothers who are positive for GBS must be treated in labor
- Must deliver at least 4 hours after first dose of antibiotic to ensure antibiotic in amniotic fluid
Tests for fetal well-being

• Kick counts
• NST
• BPP
• AFI

Kick counts

• Evaluated by mother
  • Many different methods
  • In the third trimester all mothers should be monitoring their babies movement

Kick counts

• Put a penny in a cup every time the baby moves in the morning; if 10 are not there by lunch, call clinic.
• Monitor movement for a 30 minute period
• Count 10 movements and chart how long it takes
• Mother should call clinic if eating or taking juice or sugar doesn’t “wake up” the baby
• Decreased fetal movement is often the first sign that a baby has a problem

Intimate partner violence

• Screen all women – at initial visit and once/trimester
• Always screen women alone
• Posters, business cards in bathrooms for hotlines
• Domestic violence may start in pregnancy or increase
• Up to 23% of women in prenatal care are battered
• Assess safety (i.e., weapons in home, type of previous assaults)
• Discuss exit plans with woman if possible

NST/BPP

• Non-stress test:
  • 20 min FHR tracing
  • ≥2 accelerations = Reactive NST
  • If non-reactive:
    • Continue for additional 20 min, provide drink/snack
    • If still not reactive – complete BPP
• Biophysical Profile:
  • Components: fetal movement, fetal tone, fetal breathing, and AFI
  • Scored 0 (absent) or 2 (present)

AFI Assessment

• Amniotic Fluid Index measured via ultrasound
• Oligohydramnios: <5cm
• Polyhydramnios: single pocket >8cm
• Other assessments:
  • Fundal height measurement
  • Hydration status
  • Fetal anatomy assessment
  • Presence of fetal anomalies
Ongoing assessment

Every visit:
- BP, P
- Weight
- Urinalysis for glucose, protein, s/s dehydration or infection
- Fetal Heart Rate by Doppler after 12 weeks
- After 20 weeks, fundal heights for fetal growth
- Evaluation for HA, visual changes, edema as s/s pre-eclampsia
- Surveillance for common discomforts of pregnancy

Maternal serum screening options

- Integrated Screening vs Sequential Screening
- Available Tests
- Follow-Up for high risk patients

First trimester screen

- This test is done between 10 and 13 6/7 weeks after a woman’s LMP.
- Can show if a baby is at increased risk for trisomy 13, 18 or 21
- Women who have the first-trimester screening test for Down syndrome should be screened for NTDs in the second trimester by checking MSAFP levels or having an ultrasound exam

First trimester screen

- Blood test for free-beta hCG (a specific form of hCG) and pregnancy-associated protein A (PAPP-A).
  - Levels of PAPP-A tend to be decreased, and hCG increased, with Down syndrome.
- Ultrasound exam for nuchal translucency
- Positive results should be followed up with either chorionic villi sampling or second trimester amniocentesis
- Combined test is more accurate for Down’s, so is helpful if woman has other risk factors

Nuchal translucency

- Refers to the normal subcutaneous fluid-filled space between the back of the fetal neck and the overlying skin.
- In the fetus, fluid collects behind the neck, much like it does in dependent ankle edema in later life.
- This fluid can represent the end point of several pathological processes, including heart failure.
- The more fluid that has accumulated, the greater the risk of abnormality

Nuchal translucency – U/s

- Used to measure fetal size
- Estimate due dates
- Specific exams for anomalies: Level 2 US
- Nuchal translucency
  - Normal translucency measures 3 mm (.3cm) or less
  - Locate fetus, cord or placenta for diagnostic procedures

Quad screen

- At 15-19 weeks offer quad screen
  - Earlier is better in case of abnormalities
  - Alpha-fetoprotein (AFP) -- a protein produced by the fetus’ liver
  - Unconjugated Estriol (UE) -- a protein produced in the placenta and in the fetus’ liver
  - Human Chorionic Gonadotrophin (hCG) -- a hormone produced by the placenta
  - Inhibin A -- a hormone produced by the placenta
  - Without inhibin-A, called triple screen
  - If first trimester screen done, only need MSAFP

Quad Screen Results at 15-18 weeks

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amniocentesis

- Used to obtain amniotic fluid and fetal cells for karyotyping or other tests
- Follow up for suspected genetic anomalies
- Near term-fluid is used for fetal lung maturity (FLM)

Chorionic villus sampling

- Priority if the woman will want to terminate the pregnancy
- Amniocentesis cannot be done until 15-16 weeks of pregnancy
- Chorionic villus sampling (CVS) is an option
- Can be done from 10+1 to 12+6 weeks
Preventing early-onset GBS disease
CDC, 2010 Guidelines

**Indications**  |  **Non-indications**
--- | ---
Previous infant with invasive GBS disease  | GBS colonization in previous pg
GBS bacteriuria during any trimester of the current pregnancy  | GBS bacteriuria during previous pregnancy
Positive GBS screening culture during current pregnancy (except elective C/S prior to ROM, labor)  | Cesarean delivery performed before onset of labor on women without ROM
Unknown GBS status at the onset of labor & any of the following:  | Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors
• Delivery at <37 weeks' gestation  |
• Ruptured membranes (ROM) >18 hours  |• Cesarean delivery performed before onset of labor on women without ROM
Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors

GBS Prophylaxis

**Figure 4. Recommended regimen for intrapartum antibiotic prophylaxis for prevention of early-onset GBS disease**

- **Patient allergic to penicillin?**
  - Yes
  - No

- **Penicillin G, 5 million units IV initial dose, then 2.5 to 4 million units every 4 hours until delivery or Amoxicillin, 2g IV initial dose, then 1 g IV every 4 hours until delivery**
  - Yes
  - No

- **Cefazolin, 2g IV initial dose, then 1 g IV every 6 hours until delivery**
  - Yes
  - No

- **Vancocin, 1 g IV every 12 hours until delivery**
  - Yes
  - No

- **Clindamycin, 600 mg IV every 8 hours until delivery**
  - Yes
  - No

- **Patient with a history of any of the following after receiving penicillin or a cephalosporin?**
  - Yes
  - No

- **-Anaphylaxis -Urgent delivery -Respiratory distress -Chorioamnionitis**

- **Isolate sensitive to clindamycin and erythromycin?**
  - Yes
  - No

Biophysical profile

Combination of NST and ultrasound exam
• US looks for
  • Fetal breathing
  • Fetal movements
  • Fetal tone
  • Amniotic fluid index (AFI)

Biophysical profile scoring

- 2 points for reactive NST
- 2 points each for
  • Fetal breathing
  • Fetal movement
  • Fetal tone
  • Amniotic fluid volume
- Can be done in 4-8 minutes or up to 30” (breathing)

Assessment of bpp score

• Score of 8 or higher with normal fluid: risk of asphyxia rare or normal fetus.
• Score of 8 with low AFI: Induce
• Score of 6; low AFI: Induce
• Score of 6; normal fluid but >36 weeks, cervix favorable: Induce
• If repeat < or = 6, Induce
• If repeat > 6, continue to monitor

Amniotic fluid index (AFI)

• Ultrasound assessment of amniotic fluid
  • Each quadrant of the uterus is assessed for the largest pocket of fluid in cm- total is AFI
  • Normal range for AFI is 5-25
  • <5 is oligohydramnios
    • Think about poor placential flow, poor urine output of fetus, maternal dehydration or poor diet.
  • >25 is polyhydramnios
    • Think about diabetes (elevated maternal glucose leads to polyuria in fetus)
    • Consider GI or renal problems-can’t swallow or process fluid
Genetic and carrier testing

Screening vs. diagnostic

- Maternal Serum Screening Test
- Invasive Diagnostic Test

Testing by week

- Not Pregnant
- 2-13 Weeks
- 14-21 Weeks
- 22+ Weeks

Preconception testing

- Carrier Testing
  - Ashkenazi Jewish
  - Cystic Fibrosis (CF)
  - Fragile X
  - Spinal Muscular Atrophy (SMA)

First Trimester testing

- Carrier Testing
  - Ashkenazi Jewish
  - CF
  - Fragile X
  - SMA
  - Chorionic Villus Sampling (CVS)
- First Screen® - maternal serum screening for T21 and T18
- Harmony Prenatal Test – serum screening for T13, T18, T21 – measures the relative amount of chromosomes in maternal blood

First trimester

- Integrated Screen SM - MSS that combines 1st & 2nd trimester results to screen for T13, T18, T21, & ONTD. (2-part)
- Sequential Screen – MSS for T21, T18, and ONTD. (2-part)
- Serum Integrated Screen SM – MSS that combines results from 1st & 2nd trimester results to screen for T18, T21, ONTD. (2-part)
- Ultrasound
Second trimester (14-21 weeks)

- Amniocentesis
- Carrier Testing (CF, Ashkenazi Jewish, SMA, Fragile X)
- MSS Tests (Harmony, Integrated Screen, Sequential Screen, Serum Integrated Screen)
- Afp4® Screening – MSS that measures proteins to screen for T21, T18, and ONTD.
- Ultrasound

Second trimester (22+ weeks)

- Amniocentesis
- Carrier Testing
- Ultrasound

Non-invasive prenatal testing

How testing happens?

- cfDNA – cell-free DNA
- Fetal Fraction
- SNP vs. Counting Method
- SNP Technology

How testing happens?

- Simple blood test from mom.
- Results as early as 9 weeks.
- Takes about 10 days to get results.
- Access to/contact from Genetic Counselors with high risk results.
Results reporting

Results suggest high risk of Trisomy 21. Follow-up counseling and testing is recommended.

Follow up for high risk patients

• Positive Carrier Screening:
  • Testing father of baby for carrier status
  • If both positive, IVF pregnancy with preimplantation testing, donor egg or sperm, or adoption

• High Risk Chromosomal Screening:
  • CVS
  • Amniocentesis
  • Cytogenetics/FISH/etc