Prenatal Genetic Counseling
Wednesdays 9-11am, some until 11:30 or 12
MSB B.612
(multi-D Tuesdays 4-5 when noted)

Course Coordinators:

Jennifer Czerwinski, MS, CGC  Claire Singletary, MS, CGC
Jennifer.L.Sherrill@uth.tmc.edu  Claire.N.Singletary@uth.tmc.edu

Learning Objectives:

1. To demonstrate a working understanding of prenatal genetics to include AMA, abnormal serum screening, NIPT, ultrasound abnormalities and soft signs, and teratogens.
2. To investigate the availability, analytic validity, clinical validity, and clinical utility of prenatal screening and diagnostic tests.
3. To evaluate and critique the primary scientific literature in the prenatal field
4. To synthesize the information learned for use in cases.
5. To work on critical thinking skills which allow effective evaluation of counseling sessions.
6. To gain an appreciation for more complex prenatal issues that have the potential to impact prenatal genetic counseling.

Class Expectations

Each class will, in general, consist of assigned readings, discussion, and assignment(s).

1. Read the chapters/articles assigned by the facilitator(s).
2. Complete assignments.
3. Actively participate in all class discussions and activities.
4. Think outside the box when preparing assignments and develop resources that will be helpful for your future practice.

Attendance

Attendance is mandatory for all assigned classes. Missing more than one class for any reason (excused or unexcused) will result in a reduction in the student’s final letter grade by one full letter grade. Only extreme extenuating circumstances, such as illness with a doctor’s note, will be considered for exceptions to this rule. Make-up work will be required for any missed class. Two tardies (5 minutes late or more) will be considered one unexcused absence. Students should look for clinical correlates when they attend MultiD conference (4-5pm on Tuesdays).
## LECTURE SCHEDULE

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Facilitator(s)</th>
</tr>
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</table>
| 8/15/18 9-12 | **What to Expect When You Are Expecting: Intro to Pregnancy (1 hr)** 1. Murkhoff H (2008) *What to Expect When You Are Expecting*  
Jennifer Czerwinski |

<table>
<thead>
<tr>
<th>Student</th>
<th>Article - DUE 8/22</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wendi</td>
<td>United Kingdom Collaborative Study - Medical Research Council (1978) An Assessment of the Hazards of Amniocentesis.</td>
<td>Amnio</td>
</tr>
<tr>
<td>Brad</td>
<td>Canadian Collaborative Study - Amniocentesis Clinical Trial Group (1989) Multicentre Randomized Clinical Trial of Chorionic Villus Sampling and Amniocentesis <em>Lancet</em>, 333 (8628), 1-6.</td>
<td>CVS</td>
</tr>
<tr>
<td>Date</td>
<td>Time</td>
<td>Topic</td>
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<tr>
<td>8/22/18</td>
<td>9:30 - 12:30</td>
<td>Discuss Primary Literature Assignment (1 hr)</td>
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<td>Student Presentations</td>
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<tr>
<td></td>
<td></td>
<td><strong>Screening Options by Trimester &amp; Clinical Application (2 hr)</strong></td>
</tr>
<tr>
<td>8/29/18</td>
<td>9-12</td>
<td><strong>Non Invasive Prenatal Testing – Part I</strong></td>
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<td>9/05/18</td>
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<td><strong>NIPT – Part II: Microdeletions, NIK, other unusual results</strong></td>
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<tr>
<td>9/12/18</td>
<td>9-11:30</td>
<td><strong>Prenatal Ultrasound – Normal Anatomy (1hr)</strong></td>
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<td><strong>Ultrasound: Soft Signs (1.5 hrs)</strong></td>
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<tr>
<td><em>MultiD 9/11</em></td>
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</table>
1. Review: *Clinical Significance and GC for Common Ultrasound Findings* from NSGC Prenatal SIG

9/19/18
9-11:30

**Ultrasound: Working Up an Ultrasound Case and Head, Heart**


**MultiD 9/18**

9/20/18

**Ultrasound: Abdomen, Renal, Urogenital**


Blair Stevens

Shannon Mulligan


**10/03/18**  
*MultiD 10/2*

**Ultrasound: Skeletal**


**10/10/18**  
*MultiD 10/9*

**Termination of Pregnancy**  
Logistics from GC perspective (2-4)


4. Review the 24 hour Texas law on TOP “A Woman’s Right to Know”: [http://www.dshs.state.tx.us/wrtk](http://www.dshs.state.tx.us/wrtk)

**10/16/18***  
*R433*

**Logistics from the MD perspective (4-5)**

**10/17/18**  
*Jen Czerwinski*

**Ultrasound: Multiple Congenital Anomalies**


<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Pages</th>
<th>Reader</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/31/18</td>
<td>Teratogens II</td>
<td>Review readings</td>
<td>Jennifer Lemons</td>
</tr>
<tr>
<td>Date</td>
<td>Time</td>
<td>Location</td>
<td>Event Description</td>
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<tr>
<td>11/20/18</td>
<td>2-5</td>
<td></td>
<td><strong>Prenatal Explanation Role Plays</strong>&lt;br&gt;See assignment section for further details Using rooms B625, B620, B621, B623, B631, B646, B633, B629, B640, B642</td>
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<td>11/21/18</td>
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<td><strong>NO CLASS – Thanksgiving break</strong></td>
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<td>12/5/18</td>
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<td></td>
<td><strong>CMA &amp; WES Results:</strong>&lt;br&gt;Prenatal Microarray Copy Number Variants, VUS</td>
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Assignments

1. **Primary Literature Assignment** - due August 22 to Jen C
   Read your assigned article and consider the following questions: Over what year(s) was the study completed? What type of study is it? (prospective/retrospective, randomized/non-randomized) How many subjects are there? Is there a control group(s)? What is the inclusion/exclusion criteria? How high is the suggested risk of pregnancy complication? How high is the suggested risk of fetal loss? Are the findings significant? Would you feel comfortable quoting this number to a patient? Why or why not? What are the strengths and limitations to this study?

   Bring typed/written answers to be collected at the beginning of class. Bring a second copy to refer back to during the in-class discussion.

2. **Prenatal outline** – due September 19 to Jen C
   Each student is expected to develop an outline from scratch for use in AMA session in the first trimester (38 y/o at 12 weeks for discussion of various screening and diagnostic testing options). Resources for developing an outline:
   - see appendix A1 for example template
   - pg 189 in Uhlmann – table 6-1 on prenatal genetics patients
   - pg 153 in Weil – section on prenatal diagnosis counseling
3. **NIPT Chart** – due September 19 to Claire
Create a chart outlining the differences and similarities between the different NIPT platforms that are available - quantification vs SNP. Use information from the primary literature (do NOT copy and paste only from lecture or websites – use the articles provided and/or search out your own). See Appendix 2 with shell to use as a guide when creating your chart. This is intended to be helpful clinic reference, so design it in such a way that you can easily access the information in clinic.

4. **Twins Chart** – due September 19 to Claire
Create a chart that compares testing options for women with twin gestations: FTS, Quad, NIPT, CVS, and Amniocentesis. Use information from your lectures and the primary literature. Provide detection rates for at least trisomy 21, 13, 18, and sex chromosome aneuploidy. Consider false positive rates, miscarriage risks, and other complications or limitations where applicable. Again, this is designed to be a helpful reference, so create your chart accordingly (see Appendix 2).

5. **Multiple Congenital Anomaly Case Preparation Assignment** – due in class on October 17
Each group/individual will be given a case to work-up. The goal of this assignment is to think about how to approach a case in which more than one ultrasound abnormality is present. Read the case you are assigned (will be handed out October 10) and think about what information you would present to your patient. Things you should consider are the condition(s) you are most concerned about, appropriate testing to offer your patient (be specific – not just amnio but what specific chromosome study, CMA, DNA test, etc) and resources and/or referrals you would make. You will turn in the written part of your assignment at the beginning of class. You should be prepared to discuss your thoughts about your case during class.

6. **Ultrasound Fact Sheet** - due October 24
Complete a one page fact sheet (front only or front and back) on the assigned anomaly. The goal of this assignment is to create a quick reference resource that may be used in clinic when ultrasound abnormalities arise. The fact sheet should contain the most important information on the anomaly. Things you may consider including are a definition of the anomaly, the incidence, the prognosis, the recurrence risks, helpful images (drawings and/or pictures), referral recommendations, testing recommendations and patient resources. Please use the lecture presented in class and the supplemental readings as the source(s) for the information included on your fact sheet. DO NOT cut and paste information from the ultrasound books – use primary literature and synthesize information. If you have more than one finding assigned to you, do one on the front and one of the back of your page. Do not use smaller than 9pt font. Once approved by the coordinators, these fact sheets will be made available to each student so that they may have a collection of fact sheets that can be used in clinic and for case preparation. An example fact sheet is provided in the appendix.

- Heart (ASD, VSD, AV canal) – Autumn
- Heart (Tet, hypoplastic, coarc) – Emily
- Omphalocele and Gastrochisis – Brad
- Diaphragmatic hernia and Duodenal Atresia– Luke
- Cystic hygroma and Increased Nuchal Translucency – Addison
- Cystic kidneys (mulitcystic and polycystic) – Aranza
- Hydrocephalus and agenesis of corpus callosum – Sarah
- Open Neural Tube Defect (anencephaly/neural tube defect) – Wendi
- Holoprosencephaly and encephalocele - Caroline
- Bell shaped chest and <5%long bones - Kaitlyn
7. **TOP Logistics Chart** - due in class on October 31 to Claire

If a patient chooses to terminate a pregnancy, they must then decide which procedure to have performed. Please compare and contrast the two different termination procedures available in the second trimester of pregnancy (patient at 19 weeks gestation). This comparison may be recorded in table format (see example table in appendix). This comparison should include when each procedure can be performed, how long each procedure takes, in what type of facility the procedure takes place, what medications, if any, are administered to the patient and/or fetus, what types of fetal testing are available following each procedure, etc.

8. **Prenatal Explanation Role Plays** – completion/participation grade - November 20

**Patient Scenario 1:** Advanced Maternal Age for Possible Amniocentesis

Name: Janet Smith [husband Chris Smith not present]
DOB: 2/12/1978
LMP: 07/19/18
EDC: 4/25/2019
G1P0
Northern European Caucasian
Occupation: Elementary school teacher
Religion: Protestant

Appointment: Genetic counseling, high resolution ultrasound, and possible amniocentesis

Scenario:
You are meeting with Mrs. Smith to review her age related risk to have a baby with a chromosome problem and discuss her option of amniocentesis for diagnostic testing. Mrs. Smith thinks that she wants the amniocentesis. You need to explain:

1. contracting to determine how she feels about testing
2. age related risk
3. chromosome problems related to age
4. amniocentesis
   a. how the procedure is done
   b. the risks
   c. the benefits
5. explore alternative of NIPT and ultrasound as screens if appropriate based on contracting

You do not need to talk about quadruple marker screening or any other type of serum screening. The patient did not do a first trimester screen or NIPT because she thought she wanted diagnostic testing by amniocentesis after talking to her obstetrician. As the date for the amnio has approached, she has become a little more nervous about the procedure but states from the outset that she ‘wants to know for sure’. You will need to help the patient make a decision about testing. You do not have to take her family history in the interest of time.

**Patient Scenario 2:** average risk patient to discuss first trimester screen vs NIPT screening

Name: Michelle Davis [husband Will Davis not present]
DOB: 8/24/1988
LMP: 08/18/18
EDC: 05/30/19
G2P1
African American
Appointment: Genetic counseling to discuss options for screening in pregnancy (FTS vs NIPT vs ultrasound).

Scenario:
You are meeting with Mrs. Davis to discuss her screening options for aneuploidy in pregnancy. She is low risk, thus focus on comparing and contrasting first trimester screening and NIPT. Mrs. Davis states early on that she doesn’t want to do an amnio or anything invasive unless her screening is abnormal. You need to explain:

1. chromosome conditions screened for
2. FTS
   a. methodology
   b. accuracy
   c. PPV/NPV
   d. pros/cons
3. NIPT
   a. methodology
   b. accuracy
   c. pros/cons
4. what second trimester ultrasound can/cannot tell her about aneuploidy
5. next steps if positive - amniocentesis
6. decision making

Focus on how to explain/compare/contrast the two major screening options, as your patient tells you early on in contracting that she does want to do some type of screening, she just doesn’t want to go straight to a diagnostic test. You will need to explain the options and help the patient make a decision. You do not need to take a family history in the interest of time.

Grading

Students will receive a grade determined by assignments and performance on a midterm and a final exam.

Assignments:
Each student is expected to complete all assignments. Assignments will be reviewed by both course coordinators to help with consistency in scoring.

Midterm and Final Exam:
The exams will be based on the information presented/discussed in class as well as information contained in assigned readings. Each facilitator will be asked to submit questions for the exam. There will be multiple choice, fill in the blank and short answer questions. A significant portion of the questions will be modeled after board-style questions in order to make students more familiar with the format of questions they may see on their boards. Please visit the ABGC website (www.abgc.net) to view some sample board questions. As information on complex anomalies will be included on the final exam, cumulative knowledge from the simple ultrasound anomalies presented in the first part of the course will be needed on the final exam.
The final grade for the course will be determined by the following:

Assignments
1. Primary Literature Review 5
2. AMA Outline 10
3. NIPT Chart 10
4. Twins Chart 5
5. Ultrasound Fact Sheet 10
6. Complex Anomaly 10
7. TOP Chart 5
8. Prenatal Role Play 5
Midterm Exam 20
Final Exam 20
Total 100

90-100 A 80-89 B 70-79 C 60-69 D <60 F

Textbooks:
2. Gardner, Sutherland, and Schaffer (2012) Chromosome Abnormalities and Genetic Counseling
   a. ISBN# 978-0195375336
4. Available from NSGC online: Clinical Significance and GC for Common Ultrasound Findings
### Appendix 1: Prenatal Outline Template for AMA at 12 weeks

**Example Prenatal Outline Template**

- **Introduction**
- **Contracting**
  - ex: what is their understanding of reason for referral (how will you assess this – what questions will you ask?)
- **Information**
  - Rationale for risk of ama
    - Nondisjunction (how will you explain? Always? Certain pts?)
      - Age related risk for that couple
      - Chromosome conditions (what would you highlight? How would you describe what the condition is/what the main features are?)
        - Down syndrome
        - Trisomy 13 and 18
        - Sex chrom abnl
  - Options for screening/testing
    - Diagnostic (fill in much more detail about these – risk of SAB, how procedure is done, other risks and benefits, etc – refer to charts)
      - CVS
      - Amniocentesis
    - Screening (Fill in more details on these too – how do they work? What is the detection rate? False positive rate? How could a ama patient utilize the screen, etc, what happens in the ultrasound part or the lab part – do this for all options)
      - NIPT
      - Ultrasound for anatomy in second trimester
      - Other options that may be relevant (First Trimester Screening, Quadruple Marker Screening depending on when she presents)
- **Decision Making**
- **Family History & Pregnancy History**
  - What specific questions in family history due to the indication, if any? For the pregnancy history?
- **Plan/Wrap-up**
## Appendix 2: NIPT Chart (Guide; please alter as you see fit)

<table>
<thead>
<tr>
<th>Platform</th>
<th>Detection Rate quoted for each chromosome</th>
<th>False positive rate quoted by chromosome</th>
<th>Twins: availability and detection rate by chromosome</th>
<th>Microdeletions (which ones included and detection rates)</th>
<th>Implications of (1) consanguinity (2) egg donor (3) triploidy</th>
<th>Implications of (1) nonreportable (2) low fetal fraction (3) multiple aneuploidy</th>
<th>Possible explanations of false positive</th>
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<tr>
<td>Counting/Quantitative Method</td>
<td>13: 18: 21: 45,X: all sex chrom: Y:</td>
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<tr>
<td>SNP Method</td>
<td>13: 18: 21: 45,X: all sex chrom: Y:</td>
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</tbody>
</table>

### Twin Chart

<table>
<thead>
<tr>
<th>Timing test/screen available</th>
<th>Analytes? Sample type?</th>
<th>Ultrasound used? for what?</th>
<th>detection rate quoted by chromosome condition included on screen/test</th>
<th>false positive rate quoted by condition</th>
<th>Neural Tube Defects tested: y/n and % (or ratio)</th>
<th>Risk of miscarriage: y/n and % (or ratio)</th>
<th>Other complications? (list)</th>
<th>Other differences in twins vs singletons for this screen/test?</th>
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<tbody>
<tr>
<td>FTS</td>
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<td>Quad</td>
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<td>NIPT</td>
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<td>CVS</td>
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<td>Amnio</td>
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Appendix 3: Example Ultrasound Anomaly Fact Sheet: Lower Urinary Tract Obstruction

Lower Urinary Tract Obstruction (LUTO)/Bladder Outlet Obstruction

Blockage of the urinary tract that prevents fetal urination and causes fluid back-up into the urethra, bladder, ureters and kidneys

Incidence: 1/5,000 – 1/10,000 pregnancies

Ultrasound findings:
- Enlarged urethra
- Thick, distended bladder
- Hydroureter
- Oligohydramnios/anhydramnios (low/no fluid)

Causes:
- Usually sporadic
- Chromosome abnormalities (trisomy 21, 13, 18) in up to 20% of cases
- Posterior urethral valves (only occurs in males) – thickened valves in the posterior urethra
- Other urethral abnormalities (atresia, stenosis, other blockage)
  - Females - consider cloacal syndrome (oligo) or megacystis microcolon syndrome (normal AFI) (rare)

Prognosis:
- Occurs early in pregnancy and/or there is minimal/no renal function
  - 95% IUFD/SAE/neonatal death without intervention
- Occurs late in pregnancy and there is remaining renal function
  - Variable, survivors at risk for complications including chronic/acute renal failure and incontinence

Testing/Fetal Intervention/Monitoring:
- Oligohydramnios/Anhydramnios
  - Placental biopsy
  - FISH/Karyotype/CMA
    - May consider vesicoamniosentesis (bladder tap/fluid sample from fetal bladder)
    - Possible electrolyte studies (not always predictive of renal function)
    - Repeat ultrasound in a few days to assess refil of bladder
    - Consider shunt placement (Only if: male, renal function present, LUTO is isolated, normal genetic testing)
      - risks for infection and prematurity
      - may have to be repeated
  - Normal AFI (amniotic fluid index)
    - Amniocentesis (karyotype/CMA)
    - Usually no intervention
    - Ultrasound every 2-3 weeks to monitor AFI

Consults:
- Pediatric urology, nephrology, neonatology
- Consider delivery at a tertiary care center
  - Respiratory distress/pulmonary hypoplasia 2ndary to oligohydramnios
  - Postnatal renal assessment
  - Dialysis/renal transplant
  - Surgery (resection of PUV, if present)

Patient Resources:
http://childrens.memorialhermann.org/services/urinary-tract-obstruction/
http://auvs.org/

http://childrens.memorialhermann.org/services/urinary-tract-obstruction/
### Appendix 4: TOP Chart

<table>
<thead>
<tr>
<th>TOP Options</th>
<th>D&amp;E</th>
<th>Induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing of procedure</td>
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<tr>
<td># of visits</td>
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</tr>
<tr>
<td>Length of process</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td></td>
<td></td>
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<tr>
<td>Facility</td>
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<tr>
<td>Medications (patient)</td>
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<td></td>
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<tr>
<td>Medications (fetus)</td>
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<tr>
<td>Frequency of complications</td>
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<td></td>
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<tr>
<td>Risks to the mother</td>
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<td></td>
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<tr>
<td>Contraindications</td>
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<tr>
<td>Types of fetal testing available</td>
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<tr>
<td>Other considerations</td>
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</tbody>
</table>
### Appendix 5: Additional Readings for Reference:

#### AMA and Diagnostic Testing

#### Prenatal Screening

#### NIPT


12. Ariosa PPV slide


**NIPT II:**


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### Unusual Results

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### Web Based Resources:

- Chad’s Webtool (Baylor)
  - [https://galton.imgen.bcm.tmc.edu:8443/cgh/browsecases.jsp](https://galton.imgen.bcm.tmc.edu:8443/cgh/browsecases.jsp)
  - [https://www.bcm.edu/geneticlabs](https://www.bcm.edu/geneticlabs)
- UCSC: [http://genome.ucsc.edu/cgi-bin/hgGateway](http://genome.ucsc.edu/cgi-bin/hgGateway)
- Ensembl: [http://www.ensembl.org/Homo_sapiens/Info/Index](http://www.ensembl.org/Homo_sapiens/Info/Index)
- DatabasE of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources: [https://decipher.sanger.ac.uk/application](https://decipher.sanger.ac.uk/application)
- Database of Genomic Variants: [http://projects.tcag.ca/variation](http://projects.tcag.ca/variation)
- The Copy Number Variation project: [http://cnv.chop.edu/](http://cnv.chop.edu/)

### ART

Optional Readings:


Additional references:


2. ACOG Committee on Obstetric Practice; ACOG Committee on Gynecologic Practice; ACOG Committee on Genetics. ACOG Committee Opinion #324: Perinatal risks associated with assisted reproductive technology. Obstet Gynecol. 2005 Nov;106(5 Pt 1):1143-6.


Maternal Conditions