Prenatal Genetic Testing in Obstetrics

What's available, what's recommended, and what do patients pay?

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Who can have which genetic diagnostic or screening tests?
Anyone can have any test, regardless of risk status!

ACOG Practice bulletin 162, 2016
Outline

- Aneuploidy screening
  - Traditional
  - CF DNA
-Carrier screening
  - Traditional
  - Expanded panels

- Diagnostic testing
  - How cells obtained (procedures)
  - Standard karyotype
  - FISH
  - Microarray
  - Whole exome sequencing
Disclaimer-

- All costs are approximate
- 2014 numbers
- May vary widely by labs and insurance contracts
"Traditional" aneuploidy screening

<table>
<thead>
<tr>
<th>Test</th>
<th>What</th>
<th>When</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad</td>
<td>Four analytes</td>
<td>14-24 wks</td>
</tr>
<tr>
<td>Integrated/sequential</td>
<td>Analytes + NT, then analytes</td>
<td>11-13, 15-24 wks</td>
</tr>
</tbody>
</table>
“Traditional” aneuploidy screening

<table>
<thead>
<tr>
<th>Test</th>
<th>Genetic counseling</th>
<th>Ultrasound</th>
<th>Lab</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad</td>
<td></td>
<td></td>
<td>$200</td>
<td>$200</td>
</tr>
<tr>
<td>Integrated</td>
<td>$125</td>
<td>$325+$325</td>
<td>$150 + $300</td>
<td>$1225</td>
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</tbody>
</table>
Cell-free DNA testing - widely available since 2011

- Fetal DNA comprises 3–13% of the total cell-free DNA in maternal blood
- TS 21, TS 18, TS 13 and sex chromosome composition
- Can be performed at 10 weeks until delivery
Cost of cell-free DNA aneuploidy screening

• Insurance only covers for high risk—may require preauthorization

• Labs bill insurance $600-$750 if contracted, sometimes > $1000
Cost of cell-free DNA aneuploidy screening (continued)

• Self-pay, insurance denial, out of network, or deductible not met- $100-$350

• Patient assistance program often available

• Medicaid doesn’t cover
# Accuracy vs cost of screening

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity TS 21</th>
<th>Specificity</th>
<th>False positive</th>
<th>Positive predictive value?</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad</td>
<td>85%</td>
<td>94%</td>
<td>6%</td>
<td>Pt specific risk-usually &lt;1%</td>
<td>$200</td>
</tr>
<tr>
<td>Integrated</td>
<td>85%</td>
<td>99.1%</td>
<td>0.9%</td>
<td>Low</td>
<td>$1275</td>
</tr>
<tr>
<td>CF DNA</td>
<td>99.3%</td>
<td>99.8%</td>
<td>0.2%</td>
<td></td>
<td>$100-$1000+</td>
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</tbody>
</table>

CF DNA Sensitivity for T18 - 95%  T13 - 91%
Maternal Carrier Screening for Genetic Conditions

- Historically - based on family history
- Since about 2000
  - Offer all cystic fibrosis screening ($325)
  - “Jewish panel” ($1625)
Carrier Screening

- ACOG now recommends offering pan-ethnic screening for 4 conditions
  - CF ($325)
  - SMA ($575)
  - Fragile X ($325)
  - Hemoglobinopathies ($75)

2017 ACOG Committee Opinion 691 “Carrier screening for genetic conditions”
Expanded carrier screening - ECS

- Screens for many genes simultaneously (200+ conditions in some panels)
  - 25-50% of population screens positive for one or more conditions!
- Similar or lower cost than “a la carte” screening
- Commercial labs developed and offered ECS without guidance by professional organizations
Application of Society Criteria

- Only 20% of conditions on commercial panels meet criteria for inclusion
  - Low carrier prevalence (less than 1/100)
  - Detection rate of less than 70%
  - Uncertain significance / residual risk
  - Many labs don’t meet QA guidelines

- Parental anxiety a big consideration
Cost of expanded carrier screening

- Bill to insurance company $500-1500
- Many carriers cover, Select Health does not
- Some labs guarantee max out of pocket of $200
Diagnostic Testing -
Procedures for procuring tissue

<table>
<thead>
<tr>
<th>Procedure</th>
<th>When</th>
<th>GC</th>
<th>Ultrasound</th>
<th>Procedure</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVS</td>
<td>10-13 wks</td>
<td>$125</td>
<td>$325</td>
<td>$375</td>
<td>$825</td>
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<tr>
<td>Amnio</td>
<td>15-20 wks</td>
<td>$125</td>
<td>$450</td>
<td>$150</td>
<td>$725</td>
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<tr>
<td>Stillbirth/neonate</td>
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<td></td>
<td></td>
<td></td>
<td>$0</td>
</tr>
<tr>
<td>POC’s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$0</td>
</tr>
<tr>
<td>IVF PGS</td>
<td>Pre-implant</td>
<td></td>
<td>$1500</td>
<td></td>
<td>$1500</td>
</tr>
</tbody>
</table>
Standard karyotype
FISH

22q11.2 Del
Microarray

- Measures gains and losses of DNA
- Identifies chromosomal aneuploidy
- Submicroscopic abnormalities not seen with karyotype
Microarray

CNV = “Copy number variants”
Duplicated or deleted sections of DNA

VUS = “Variants of uncertain significance”
Potential for significant patient anxiety!
Microarray vs. Standard karyotype

- Major structural abnormalities
- Fetal death or products of conception
  Microarray recommended
- Structurally normal fetus
  Either test
Cost of diagnostic tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karyotype</td>
<td>$1,200-$1,500</td>
</tr>
<tr>
<td>FISH</td>
<td>+ $1,500</td>
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<tr>
<td>Microarray</td>
<td>$4,800</td>
</tr>
<tr>
<td>Microarray- POC’s</td>
<td>$3,100</td>
</tr>
</tbody>
</table>

- Insurance will pay for most “indicated” tests with prior auth.
- Because microarray is new, insurance may not pay.
Whole-Exome Sequencing

- Looks at all coding genes in human genome
- Commonly used in Pediatric genetic evaluation
- Not yet used for prenatal testing
Bottom line:

- Many more choices
- Much better information available
- Complex counseling
- Not for everyone - I start the discussion with “is it important for you to know…”