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!

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Outline

- Aneuploidy screening
  - Traditional
  - CFDNA
- 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

Test	What	When
Quad	Four analytes	14-24 wks
Integrated/sequential	Analytes + NT, then analytes	11-13, 15-24 wks

“Traditional” aneuploidy screening

Test	Genetic counseling	Ultrasound	Lab	Total
Quad			$200	$200
Integrated	$125	$325+ $325	$150 + $300	$1225

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

Test	Sensitivity TS 21	Specificity	False positive	Positive predictive value?	Cost
Quad	85%	94%	6%	Pt specific risk- usually <1%	$200
Integrated	85%	99.1%	0.9%	Low	$1275
CFDNA	99.3%	99.8%	0.2%		$100-$1000+

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

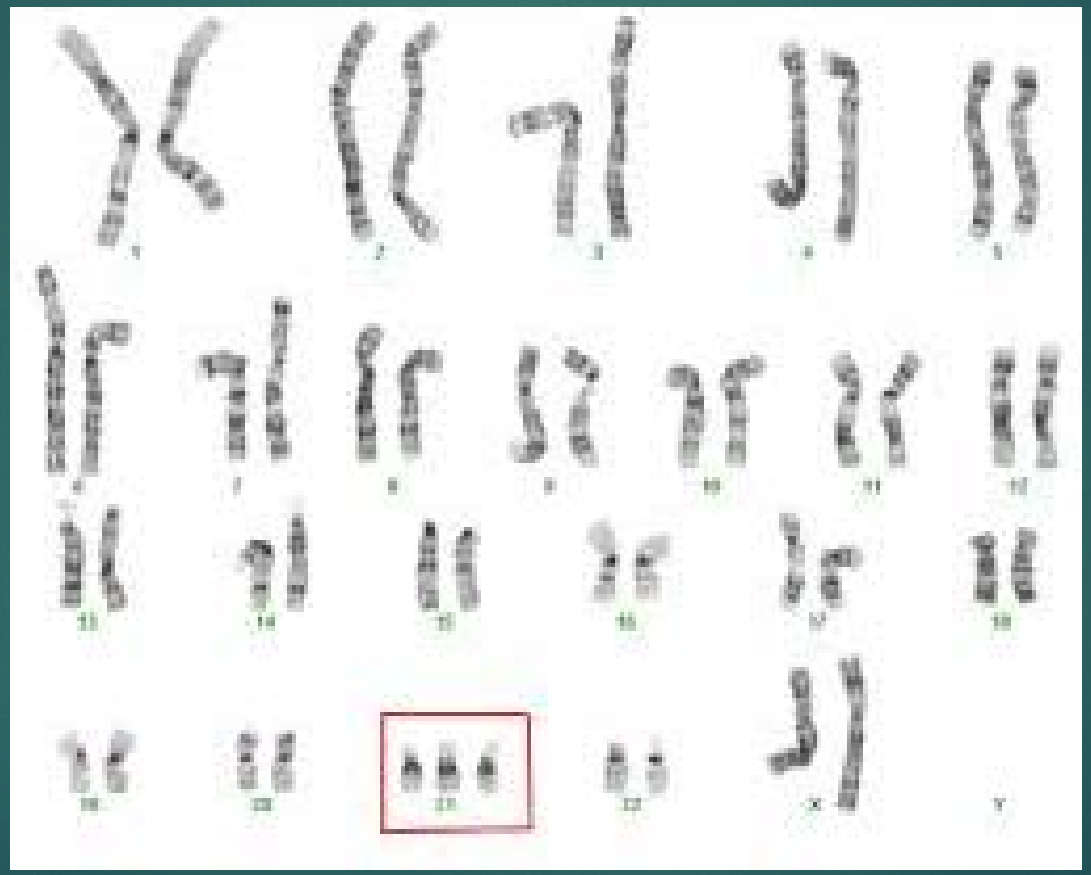
- Bill to insurance company $500-1500
- Many carriers cover, Select Health does not
- Some labs guarantee max out of pocket of $200

Diagnostic Testing-

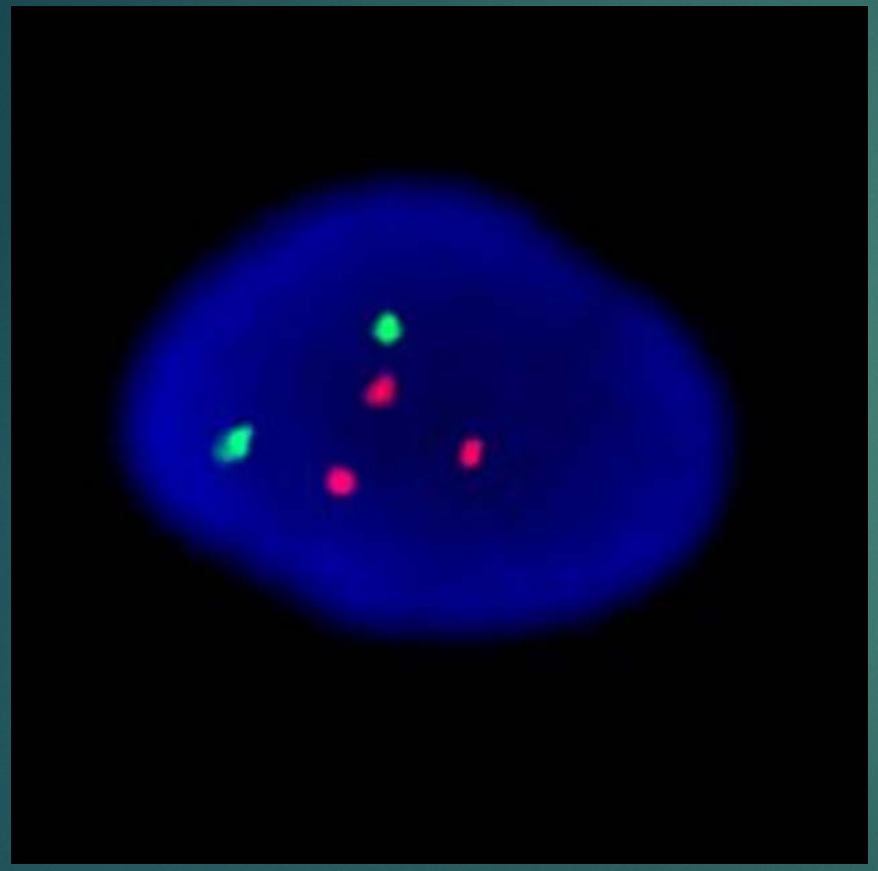
Procedures for procuring tissue

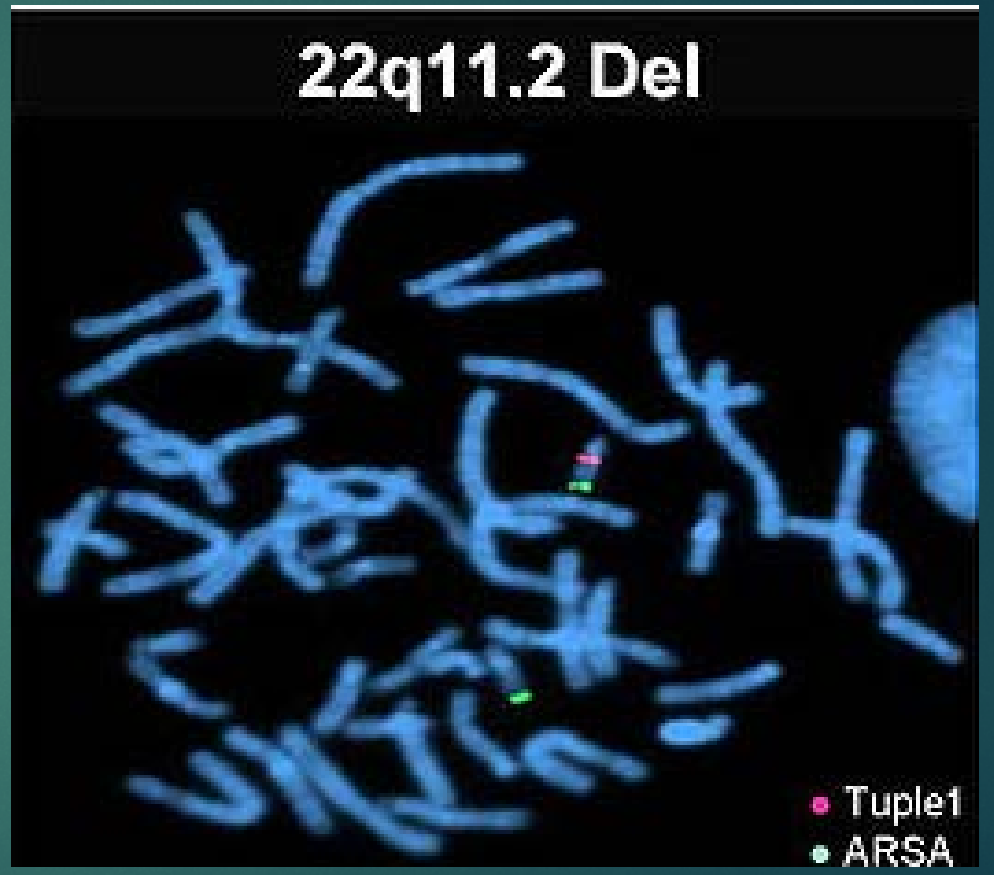
Procedure	When	GC	Ultrasound	Procedure	Total
CVS	10-13 wks	$125	$325	$375	$825
Amnio	15-20 wks	$125	$450	$150	$725
Stillbirth/neonate					$0
POC's					$0
IVF PGS	Pre-implant			$1500	$1500

Standard karyotype



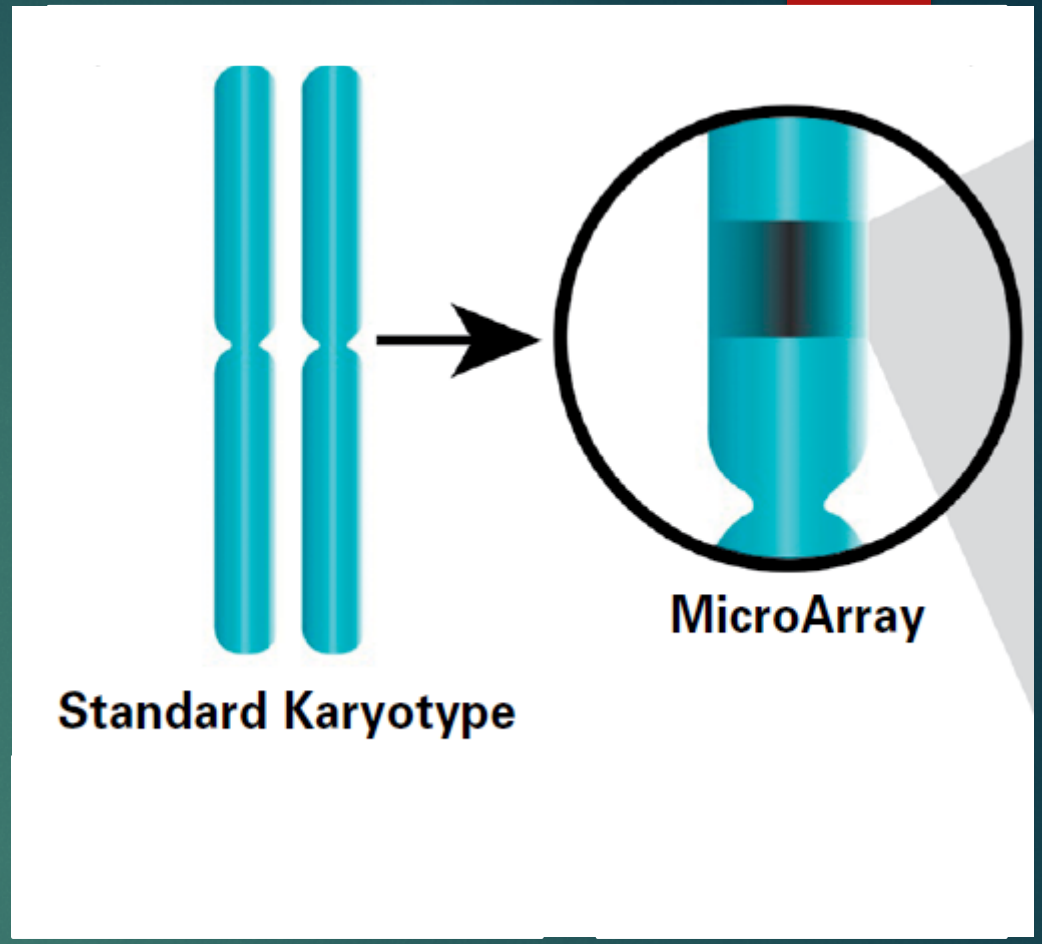
FISH





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

Test	Cost
Karyotype	$1,200-$1,500
FISH	+ $1,500
Microarray	$4,800
Microarray- POC's	$3,100

- 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…”