Screening for Fetal Aneuploidy
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Certified Genetic Counselor

Fetal Aneuploidy

• Every woman having a baby has a chance to have a baby with a chromosome difference
• The chance is based on age
• With a history of a previous child with a chromosome condition - risk is greater than age

Risk for chromosome anomalies

<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>Risk for Down Syndrome</th>
<th>Risk for any chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>1 in 256</td>
<td>1 in 141</td>
</tr>
<tr>
<td>36</td>
<td>1 in 200</td>
<td>1 in 111</td>
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<tr>
<td>37</td>
<td>1 in 156</td>
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<tr>
<td>38</td>
<td>1 in 123</td>
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<td>40</td>
<td>1 in 75</td>
<td>1 in 44</td>
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<tr>
<td>41</td>
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<tr>
<td>42</td>
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<td>1 in 38</td>
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<td>46</td>
<td>1 in 17</td>
<td>1 in 11</td>
</tr>
<tr>
<td>47</td>
<td>1 in 13</td>
<td>1 in 9</td>
</tr>
<tr>
<td>48</td>
<td>1 in 11</td>
<td>1 in 7</td>
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</tbody>
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Chromosome conditions

Down syndrome

• Chromosome condition due to the presence of an extra chromosome 21
• Common features include:
  • Congenital heart defects, duodenal atresia, tracheo-esophageal fistula
  • Mild to moderate mental retardation
  • Short neck, flat nasal bridge, low-set posteriorly rotated ears, clinodactyly, relatively short stature, brachycephaly, club feet

Trisomy 18 – “Edwards syndrome”

• Extra chromosome 18
• Multiple fetal anomalies:
  • Growth restriction, heart defects, renal anomalies
  • Clenched hands, rocker bottom feet, abnormally shaped cranium
• Severe mental retardation
• High mortality rate
Trisomy 13 – “Patau syndrome”

- Extra chromosome 13
- Multiple fetal anomalies – midline defects
  - Holoprosencephaly, microcephaly, microphthalmia, cleft lip and palate, heart defects, renal anomalies (cystic dysplasia)
  - Polydactyly, club feet
  - Severe mental retardation
  - High mortality rate

Klinefelter syndrome

- An extra X chromosome in a male (47,XXY)
- Tall stature with long limbs, may have hypogonadism
- May have mild learning difficulties in expressive language, reading and spelling
- May have behavior problems: social adjustment and immaturity
- Infertile

Triple X syndrome

- An extra X chromosome in a female (47,XXX)
- Usually benign consequences, may have taller stature
- Most often normal fertility but may experience menstrual irregularity or increased frequency of miscarriage
- May have mild learning difficulty, but normal IQ

Turner Syndrome

- 45, X or Monosomy X
- Perinatal lethality in 95% of conceptuses
- Congenital lymphedema – may present as cystic hygroma
- Short stature, webbed neck
- Heart defects (coarctation of aorta common)
- Renal anomalies (commonly horseshoe kidney)
- Ovarian dysgenesis
- Mild learning disabilities

Triploidy

- An extra full set of chromosomes, 69 (XXX,XXY or XYY)
- Paternal in origin – large placenta with hydatidiform changes
- Maternal in origin – growth deficiency, abnormal brain, heart defects, renal anomalies, etc.
- Survival to term is very rare in either case
- Can be associated with severe preeclampsia

History of Screening
Screening by Maternal Age

<table>
<thead>
<tr>
<th>Years</th>
<th>Trisomy 21 Risk</th>
<th>Amnio/CVS rate</th>
<th>Detection Rate</th>
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<tbody>
<tr>
<td>20</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>25</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>30</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>35</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>40</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>44</td>
<td>5%</td>
<td>70%</td>
<td>30%</td>
</tr>
</tbody>
</table>

History - Screening
- 1960's – Alpha fetoprotein (AFP) concentrations discovered in cancer research
- 1972 – Brock (England) proposed idea of screening for NTD’s by measuring AFP levels in maternal serum
- 1984 – AFP concentrations in maternal serum were found to be lower in the presence of DS
  - Screening was now available to women <35

History - Screening
- Late 1980’s – Discovery of two other markers in maternal serum: beta hCG and unconjugated estriol (uE3)
  - Allowed for Double screen then Triple Screen and then Quad screen
- 1990’s – Fetal nuchal translucency thickness at 11-14 weeks of gestation found to be a marker for trisomies
  - 2012 – cell free Fetal DNA

Biochemical Based screening

Screening tests
- NT Based Screening
  - First trimester screen
  - Integrated screen
  - Sequential Screen
  - Contingent Screen
- Biochemical Only screening
  - Triple Screen
  - Quad screen
  - Serum Integrated Screen

Nuchal Translucency
Nuchal Translucency

- NT increases with increasing gestational age
- Measurement increases 17% each week
- 2.5 mm cut off at 10 weeks: 1.3 false positive
- 2.5 mm cut off at 13 weeks: 13% false positive
- 95th percentile by CRL allows for GA effect
- Use of MoM further reduces false positive

First Trimester Screen

- Ultrasound in late first trimester to measure NT
- CRL between 45-84mm
- Approximately 10-13.9 weeks
- Blood draw to measure free beta hCG and PAPPA
- 91% detection rate for Down syndrome
- 95% detection rate for Trisomy 18 and 13
- 5% FPR (0.3% FPR for Trisomy 18/13)
- Addition of NB assessment increases detection rate for DS 95% (2% FPR)

PAPP-A

- Produced by the placenta
- 60% lower in Trisomy 21 pregnancies
  - Throughout the 8-14 week period
- Median value 0.43 MoM in DS pregnancies
- Most sensitive between 8-11 weeks
- 42% detection rate for DS with PAPP-A alone

First Trimester Screening

- Useful in multiple gestation
- Earlier screening and diagnosis
- Improved confidentiality
- Increased patient safety
- Detailed anatomy scans
- Still need to have AFP only drawn in 2nd trimester to screen for NTD's

Integrated Screen

- Two part screening test
  - Part 1: Late first trimester (10-13.9 wks), measure fetal NT, draw blood – measure PAPP-A
  - Part 2: Blood drawn in early 2nd trimester (15-21.9 wks): measures AFP, hCG, uE3 and DIA
- 92% detection rate for Down syndrome
- 90% detection rate for Trisomy 18
- Also detects NTD's

Sequential Screen

- First trimester screen performed and resulted
  - Reported as "increased risk" or
  - "Proceed to 2nd sample"
- Detection rate of 91% for DS, 95% for T18/13
- Part 2 drawn 15-21.9wks
  - Measures AFP, hCG, uE3, DIA
- Detects 94% of DS, 95% of T18/13
- Screens for ONTD's
Serum Integrated Screen

- For those patients in whom an NT cannot be measured
- Works the same as the integrated screen, but with only biochemical measurements, not NT
- 87% DR for DS
- 90% DR for Trisomy 18
- Screens for ONTD

ACOG - 2004

- 1st Trimester screening using NT should only be offered if:
  - Appropriate ultrasound training and ongoing quality monitoring
  - Resources are available to provide counseling regarding screening options and the limitations of these tests
  - Access to appropriate diagnostic tests if the patient is found to be at elevated risk for aneuploidy

Increased NT – other associations

- Major cardiac malformations
- Body stalk anomalies
- Diaphragmatic hernia
- Omphalocele
- Fetal Akinesia deformation sequence
- Twin twin transfusion syndrome
- Multiple other genetic syndromes

NT and Cardiac Defects

<table>
<thead>
<tr>
<th>NT Thickness and Correlation with Cardiac Defects</th>
<th>% risk of cardiac defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5-3.4 mm</td>
<td>1%</td>
</tr>
<tr>
<td>3.5-4.4 mm</td>
<td>3%</td>
</tr>
<tr>
<td>4.5-5.4 mm</td>
<td>7%</td>
</tr>
<tr>
<td>5.5-6.4 mm</td>
<td>20%</td>
</tr>
<tr>
<td>6.5+ mm</td>
<td>30%</td>
</tr>
</tbody>
</table>

Increased NT – euploid fetus

- Genetic syndromes – the list is growing!
  - Most are sporadic with 1/10,000 prevalence or less
  - Association with Noonan syndrome, Smith Lemli Opitz syndrome, Spinal muscular atrophy and other muscular-skeletal conditions is clear
  - Reassuring results have been reported in long term developmental follow up – when isolated
Increased NT – euploid fetus

Nasal Bone screening
- Best performed at 11-14 weeks (12 wks ideal)
- Need to be able to recognize cartilage, skin and nasal bone

Nasal bone screening
- First reported in 1995 by fetal medicine group in France
- Pathologists in Scotland noted malformations or agenesis of NB in 61% of fetuses with Down syndrome at 12-14 weeks
- Another French team reported that 25% of 60 fetuses with Down syndrome had complete absence of ossification of nasal bone regardless of gestational age

Nasal bone screening
- Less attention has been paid to NB screening than NT screening
- Likely due to the difficulty in obtaining the images
- Some estimate that 120 scans are necessary before one is competent in evaluating for presence or absence
- When done correctly it is possible to increase detection and decrease false positive rate when used as part of first trimester screening

Ultrasound as a screening tool
- First Trimester
  - Nuchal translucency screening
  - Nasal bone – presence or absence
  - Combined with biochemical screening
Ultrasound as a screening tool

- Second trimester
- Growth, fluid, placenta
- Fetal anomalies
- Soft markers
  - Not true anomalies, but can be associated with an increased risk for a chromosome condition

2nd Trimester Findings: Trisomy 21

- Major:
  - Cardiac anomalies
  - Duodenal atresia
  - Cystic hygroma/hydrops
  - Hydrocephalus
  - Brachycephaly

- Marker:
  - Increased nuchal fold
  - Hypoplastic or absent nasal bone
  - Echogenic bowel
  - Short humerus/femur
  - Ventriculomegaly
  - Sandal gap toes
  - Pyelectasis
  - Clinodactyly
  - EIF

2nd Trimester Findings: Trisomy 18

- Major:
  - Cardiac (90%)
  - Omphalocele
  - NTD
  - Cystic hygroma
  - Facial clefting
  - Clubbed feet
  - Radial aplasia
  - Esophageal atresia
  - Umbilical cord cyst
  - IUdR w/ polyhydramnios

- Marker:
  - CPCs
  - Clenched hands w/ overlapping digits
  - Enlarged cisterna magna
  - Ventriculomegaly
  - Strawberry shaped head
  - Pyelectasis
  - Short femur/humerus
  - Echogenic bowel
  - Hypoplastic nasal bone

2nd Trimester Findings: Trisomy 13

- Major:
  - Cardiac
  - CNS (holoprosencephaly, agenesis of the corpus callosum, and NTDs)
  - Omphalocele
  - Diaphragmatic hernia
  - Facial clefting
  - Cyclopia
  - Polydactyly
  - Cystic hygroma/hydrops
  - Polycystic kidneys

- Marker:
  - EIF
  - Rocker-bottom feet
  - Enlarged cisterna magna
  - Echogenic bowel
  - Ventriculomegaly
  - Pyelectasis

2nd trimester ultrasound – Fetal well being

- Assessment of:
  - Growth
  - Placenta
  - Fluid

2nd trimester Ultrasound- Anatomy

- Heart
- Kidneys
- Bladder
- Stomach
- Face
- Head/brain
- Limbs
- Spine
Major Sonographic Anomalies and Risk for Aneuploidy

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Aneuploidy Risk</th>
<th>Other Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart (general-unspecified)</td>
<td>15-20%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>AV Canal</td>
<td>60% (smooth 211 and 8p±)</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>VSD</td>
<td>10%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>ASD</td>
<td>10%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>12-50% (includes 22q11 del)</td>
<td>VATER, CHARGE</td>
</tr>
<tr>
<td>Cystic hygroma</td>
<td>50-60%</td>
<td>Noonan syndrome, other single gene</td>
</tr>
<tr>
<td>Omphalocele</td>
<td>30-50%</td>
<td>Beckwith-Wiedemann, OEI</td>
</tr>
<tr>
<td>Holoprosencephaly</td>
<td>30-50%</td>
<td>Single gene, teratogens</td>
</tr>
<tr>
<td>Duodenal Atresia</td>
<td>30%</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Dandy-Walker</td>
<td>10-30%</td>
<td>Viral, other teratogens</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>10-15%</td>
<td>Viral, single gene, multifactorial</td>
</tr>
<tr>
<td>Ventriculomegaly-mild</td>
<td>2-4%</td>
<td>Viral, single gene, multifactorial</td>
</tr>
<tr>
<td>Diaphragmatic hernia</td>
<td>5-10%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>NTDs</td>
<td>1% (other anomalies present)</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Anencephaly</td>
<td>2-10%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>5-10%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>7-11%</td>
<td>Multifactorial, single gene</td>
</tr>
<tr>
<td>Clubfoot</td>
<td>1-4%</td>
<td>Multifactorial, single gene</td>
</tr>
</tbody>
</table>

2nd Trimester Ultrasound – Soft Markers

- Not all sonographic markers are created equal
- Most useful markers are those with a high detection rate, but a low false positive rate among normal fetuses
- All studies have been done in HR women
- Combine a priori risk with the likelihood ratios derived from the ultrasound to create an "adjusted risk"

Risk Calculation

- What is a likelihood ratio?
  - Sensitivity/false-positive rate
- Calculating the risk
  - a priori risk x the LR (Nyberg/Bromley method)
  - a priori risk x (+)LR and the (−)LR (Nicolaides method)
  - Maternal age risk
  - Biochemical risk
  - Must make sure that the markers are proven to be independent predictors of aneuploidy
  - Association between
    - Low uE3 and cystic hygroma
    - High uE3, low AFP and EIF
    - High hCG and increased nuchal fold

a priori aneuploidy risk

- Maternal age risk
- Biochemical risk
- Must make sure that the markers are proven to be independent predictors of aneuploidy
- Association between
  - Low uE3 and cystic hygroma
  - High uE3, low AFP and EIF
  - High hCG and increased nuchal fold

Wake Forest Baptist Health
Absent Nasal Bone

- Single most important marker in screening for DS
- Absent in 30-50% of fetuses with Down syndrome
- FPR <1% in Caucasians, but higher among African Americans and Asians
- Sensitivity increases when you include hypoplastic NB
- LR up to 84 in Caucasians; 8.5 in African American

Absent or Hypoplastic Nasal Bone

- Found in 0.5 to 1% of normal fetuses
- Also in 43-70% of fetuses with DS, 55% of fetuses with T18 and 34% with T13
- Nasal bone length increases with gestational age
- Mean at 15wks = 4.7mm; 22wks = 8.2 mm
- Hypoplastic can be defined as <2.5mm
- Or can be derived from MoM value based on GA and use <0.75 MoM

Absent or Hypoplastic Nasal Bone

- LR depends upon ethnicity
- Should be a routine marker surveyed in 2nd trimester and adjust baseline risk for aneuploidy
- Studies have shown range of likelihood ratios from 3.2-84
  - Differences in study populations and design may account for variability
- Reviewed studies show LR of 26-36 in LR Caucasian pop and up to 84 in HR Caucasian

Increased Nuchal fold thickness

- Redundant skin at the back of the neck
- Bencerraf was first to report finding and led to search for other markers
- Normal size varies with GA
  - Cut off 5mm 15-17.9 wks
  - Cut off 6mm from 18-19.9 wks
- Can measure from 15-19.9 weeks
- Also consider single gene conditions (e.g., Noonan)
- LR about 9

Nuchal Fold cont.

- When increased:
  - Adjust baseline risk
  - Offer amnio
  - Offer fetal echo
  - Consider single gene conditions
  - Offer molecular genetic testing if specific syndrome is in question based on other u/s findings or family history

Echogenic bowel

- Non specific, most commonly associated with normal fetus
- Seen in 0.6 – 2.4% of fetuses
- LR of 6
- Associated with bowel atresia, congenital infection, meconium ileus (CF)
- Increased risk IUGR, fetal demise, placental complications
Echogenic Bowel

- Diagnosed in 0.2 – 1.4% of 2nd trimester ultrasounds (*cannot evaluate in the 1st or 3rd trimesters*)
- Can be a normal variant
- EB has been observed in fetuses with: 
  - Chromosome conditions (LR 6), bowel atresia, congenital infection (3% risk) and meconium ileus due to CF (2%)
- First trimester bleeding is a common etiology
- Inc. risk for IUGR, IUFD and placental complications.

- Approximately 35% of fetuses with EB will have some underlying pathology
- Management of isolated EB
  - Assess for history of bleeding
  - Calculate new risk for DS (prior risk x LR)
  - Offer amniocentesis
  - Chromosomes, CF (if possible/indicated), Infections
  - Maternal infection titers (Toxo, CMV, Parvo, HSV)
  - CF risk – offer carrier testing to parents
  - Only 80-90% of carriers test positive, but need to have parents mutations to test fetus
  - Growth scan for risk of IUGR at 28-32 wks

Shortened long bones

- More pronounced difference in humerus than in femur in fetuses with Down syndrome
- Cut off used – observed to expected limb lengths
- Finding of short humerus AND short femur increases risk for Down syndrome 11 fold
- LR for short humerus 5.1-7.5
- LR for short femur 1.8-2.7

- More common in males
- Whether there is an increased risk for aneuploidy with isolated pyelectasis is debated
- Most commonly described as AP diameter of the renal pelvis ≥4mm
- Isolated pyelectasis is uncommon finding in aneuploidy
- Smith-Bindman reported likelihood ratio of 1.9 but because CI crosses 1 isolated pyelectasis may actually reduce risk of DS
- Pyelectasis has been associated with increased risk of hydronephrosis and postnatal urinary reflux – but risk with "mild" pyelectasis is very low
- Almost all cases at 4-7mm in 2nd trimester need no surgery postnatally

Pyelectasis

- Cut off values vary in the literature
  - 4mm <20 wks
  - 6mm 20-30 wks
  - 8mm >30 wks
- Using cut off of 4mm, seen in 3% of normal fetuses
- Although increased LR in all studies, may not increase risk when pyelectasis isolated
- LR 1.6
- More common in males

Short FL and HL

- Definition
  - <5th %tile
- Associated with an increased risk for:
  - Aneuploidy
  - Skeletal dysplasias
  - IUGR (placental etiology)
Pyelectasis Cont.

- Recommendations for management of isolated pyelectasis
- Notify pt of need for 3rd trimester ultrasound to evaluate for progression to hydronephrosis – 32 weeks
- No need to discuss aneuploidy as the likelihood ratio crosses 1 unless additional markers are observed

Echogenic Intracardiac Focus

- Most often seen in LV
- Observed in 3-4% of normal fetuses
- 10-15% of Asian fetuses
- Single most common finding in DS and normal fetuses
- If isolated finding (young, normal screening, no other markers) not associated with increased risk
- LR of 2

Echogenic Intracardiac Focus

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- Observed in 3-4% of normal fetuses
- 10-15% of Asian fetuses
- Single most common finding in DS and normal fetuses
- If isolated finding (young, normal screening, no other markers) not associated with increased risk
- LR of 2

EIF

- In low risk populations, EIF does not increase the risk of aneuploidy and should be considered a benign variant
- Do we tell the patient?
- In a high risk population (AMA w/out screening or pt with an abnl screen) patient has 2-2.6x increase in risk for aneuploidy-specifically DS

Choroid Plexus cysts

- Common transient finding seen in 1% of normal fetuses (14-24 wks)
- Always resolve
- 50% of babies with Trisomy 18 have CPC’s
- Less than 10% of fetuses with T18 have no other features except CPC’s
- LR 9 for T18
- No increased risk when isolated finding

Choroid Plexus cysts

- Common transient finding seen in 1% of normal fetuses (14-24 wks)
- Always resolve
- 50% of babies with Trisomy 18 have CPC’s
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- LR 9 for T18
- No increased risk when isolated finding

Ventriculomegaly

- Atrial width of 10-15mm is mild VM -isolated if there are no other ultrasound abnormalities
- Frequently associated with CNS and extra-CNS anomalies -careful evaluation of fetal anatomy should be performed by expert ultrasound exam
- Where available and experienced, fetal MRI is also indicated, but no consensus on optimal timing

Ventriculomegaly cont.

- Likelihood ratio for chromosome abn is 9
- Maternal serum CMV and Toxo should be considered
- Rate of neurodevelopmental delay with isolated mild VM is 11% - unclear if this is increased over GP
- Most important prognostic factors are the association with other abnormalities not detected at time of initial dx (about 13%) and progression of the ventricular dilatation (about 16%)
- Follow up sonograms and or MRI in third trimester should be considered

Ventriculomegaly cont.

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Single Umbilical Artery

- SUA is associated with chromosomal defects when major anomalies are also present.
- Isolated SUA is NOT associated with chromosomal defects.
- The evidence supporting the association between isolated SUA and poor pregnancy outcomes is contradictory.

SUA-Recommendations

- Detailed u/s is warranted.
- If seen with anomalies:
  - Offer genetic counseling and amnio
  - Explain aneuploidy risk based on other u/s findings
- If isolated:
  - Counsel on u/s limitations
  - Potential for preterm delivery and low birth weight
  - Decision of fetal echo based on institution

What else?

- Widened pelvic angle
- Shortened frontal lobes
- Small ears
- Clinodactyly
- Pericardial effusion
- Right – Left disproportion of the heart
- Hypoplastic nasal bone
- Unfused amnion and chorion after 14 weeks

Efficacy of 2nd trimester Ultrasound for detection of Down syndrome

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
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<tbody>
<tr>
<td>Ultrasound Marker</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nuchal Thickening</td>
<td>87% [60/69]</td>
<td>90.4% [4371/4836]</td>
<td>11.4% [60/535]</td>
<td>99.8% [4371/4380]</td>
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<tr>
<td>Short Humerus</td>
<td>7.94 [6.7-9.25]</td>
<td>6.77 [5.16-8.8]</td>
<td>0.62 [0.56-0.67]</td>
<td>1.6</td>
</tr>
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<td>Pyelectasis</td>
<td>6.77 [5.16-8.8]</td>
<td>7.94 [6.7-9.25]</td>
<td>0.62 [0.56-0.67]</td>
<td>1.6</td>
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<td>EIF</td>
<td>6.41 [5.15-7.9]</td>
<td>6.77 [5.16-8.8]</td>
<td>0.75 [0.69-0.8]</td>
<td>1.1</td>
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<tr>
<td>Echogenic Bowel</td>
<td>21.17 [14.34-31.06]</td>
<td>6.41 [5.15-7.9]</td>
<td>0.75 [0.69-0.8]</td>
<td>1.1</td>
</tr>
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<td>Major Defect</td>
<td>32.96 [23.9-43.28]</td>
<td>6.77 [5.16-8.8]</td>
<td>0.89 [0.74-0.93]</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Overall LR proposed by Nicolaides

<table>
<thead>
<tr>
<th>Ultrasound Marker</th>
<th>Positive LR [95% CI]</th>
<th>Negative LR [95% CI]</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuchal Thickening</td>
<td>53.05 [39.37-71.26]</td>
<td>0.67 [0.61-0.72]</td>
<td>9.8</td>
</tr>
<tr>
<td>Short Humerus</td>
<td>22.76 [18.04-28.56]</td>
<td>0.60 [0.62-0.73]</td>
<td>4.1</td>
</tr>
<tr>
<td>Short Femur</td>
<td>7.94 [6.7-9.25]</td>
<td>0.62 [0.56-0.67]</td>
<td>1.6</td>
</tr>
<tr>
<td>Pyelectasis</td>
<td>6.77 [5.16-8.8]</td>
<td>0.85</td>
<td>1</td>
</tr>
<tr>
<td>EIF</td>
<td>6.41 [5.15-7.9]</td>
<td>0.75 [0.69-0.8]</td>
<td>1.1</td>
</tr>
<tr>
<td>Echogenic Bowel</td>
<td>21.17 [14.34-31.06]</td>
<td>0.87 [0.83-0.91]</td>
<td>3</td>
</tr>
<tr>
<td>Major Defect</td>
<td>32.96 [23.9-43.28]</td>
<td>0.89 [0.74-0.93]</td>
<td>5.2</td>
</tr>
</tbody>
</table>
Reduction of Risk

- Ultrasound markers are not considered equally but weighted by the strength of the individual finding
- Absence of markers will reduce risk
- May be applied to all women but most useful for those women 34-40 or those with intermediate risk based on maternal serum screen
- Degree of risk reduction depends on a variety of factors including number and type of criteria used, individual threshold, gestational age of scan

Commonly used references

- Choroid Plexus Cysts and Trisomy 18: Risk modification based on maternal age and multiple-marker screening
- Bedside Estimate of Down syndrome risk during first-trimester ultrasound screening