TRISOMY 13 AND 18

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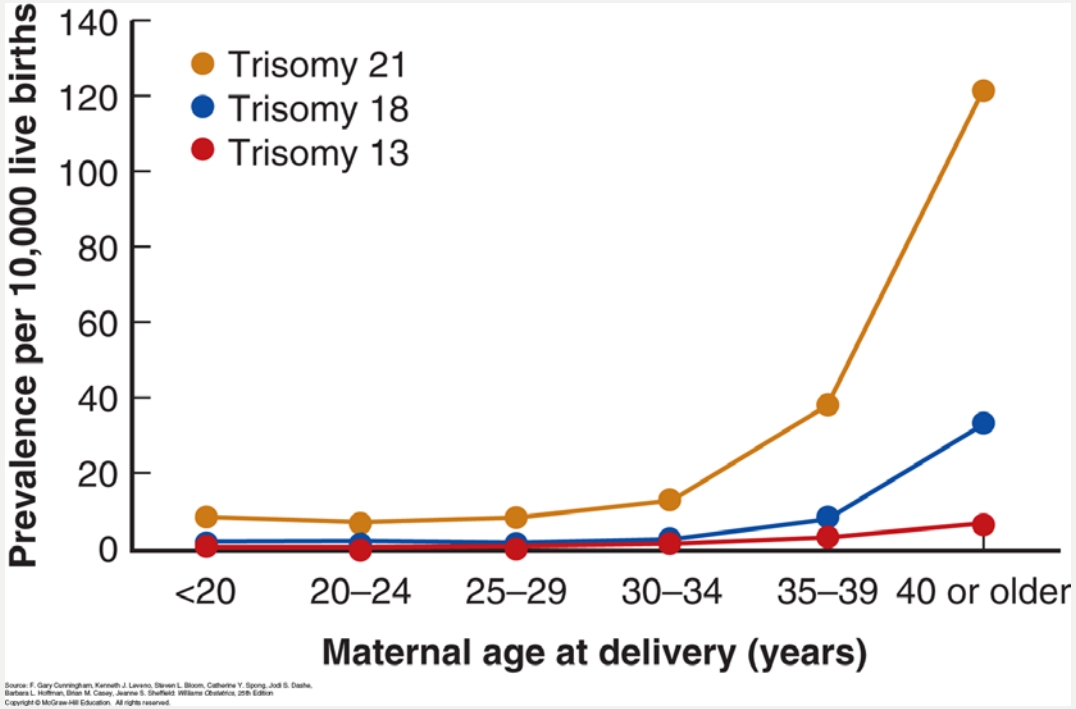
Genetics 2020

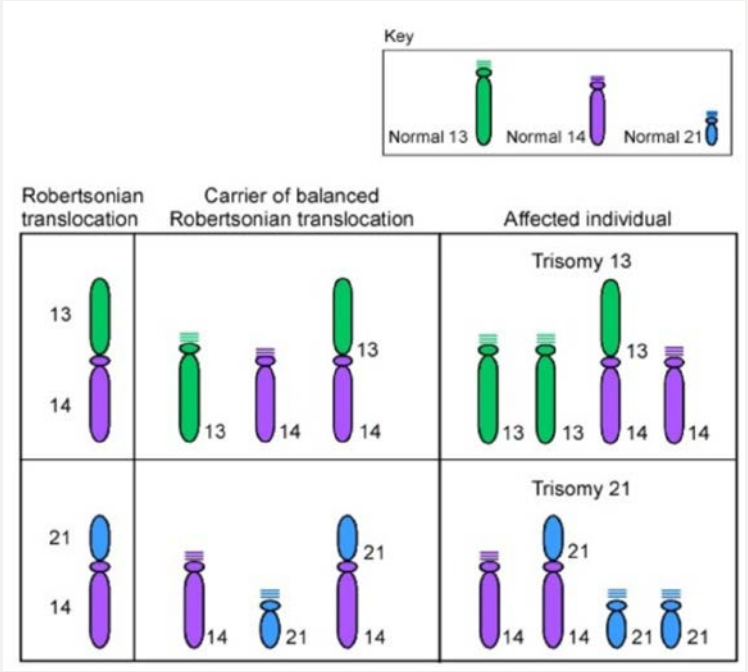
Background information



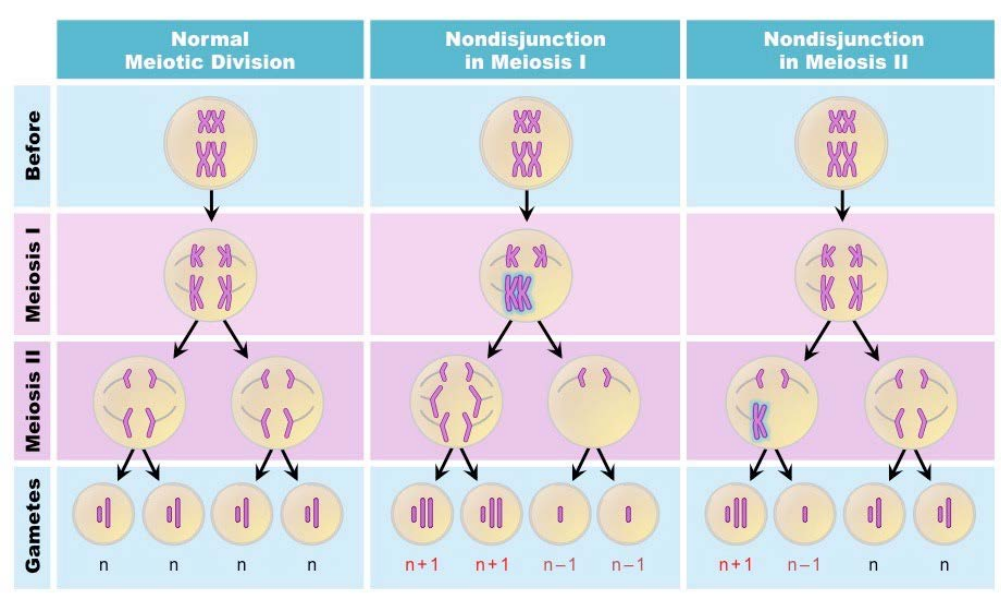
- Epidemiology
  - Actual prevalence in pregnancy is very high, but large numbers lost in early pregnancy due to spontaneous abortion or termination
  - Trisomy 13: 1 in 12,000 live births
  - Trisomy 18: 1 in 4,000 live births
  - 65% of first trimester miscarriages are associated with trisomies
  - Risk of autosomal trisomies increases steeply with age
- Etiology
  - Trisomy 13
    - Full trisomy secondary to meiotic nondisjunction **(95%)**
    - Unbalanced Robertsonian translocation (98-99% end in early embryonic death) **(1%)**
    - Mosaicism secondary to mitotic (somatic) nondisjunction **(5%)**
  - Trisomy 18
    - Full trisomy secondary to meiotic nondisjunction **(95%)**
    - Chromosome 18 translocation (not Robertsonian) **(1%)**
    - Mosaicism secondary to mitotic (somatic) nondisjunction **(5%)**

Genetics

- Robertsonian translocation
  - *Specific type of translocation involving acrocentric chromosomes (centromere closer to one end than the other)*
  - *Acrocentric chromosomes: 13, 14, 15, 21, 22*



Nondisjunction



Prenatal Testing

Test	Timing	Advantages	Disadvantages
1st Trimester Combined Test - PAPP - bHCG - Nuchal translucency	9-13	Early screening Detects ~85% of Down Syndrome Detects ~97% of Trisomy 18	Not diagnostic
Cell-free fetal DNA	>10	High sensitivity and specificity for aneuploidy	Not diagnostic
Chorionic Villis Sampling	10-13	Definitive karyotype diagnosis	Invasive, risk of miscarriage
2nd Trimester Quad Screen - MSAFP - Estriol - bHCG - Inhibin A	15-22	Screens for neural tube defects as well as aneuploidy	Not diagnostic
Amniocentesis	15-20	Definitive karyotype diagnosis	Invasive, risk of membrane rupture, fetal injury, pregnancy loss
2nd Trimester Ultrasound	18-20	Measures growth and anatomy	Cannot identify all anomalies

Interpretation of screening results

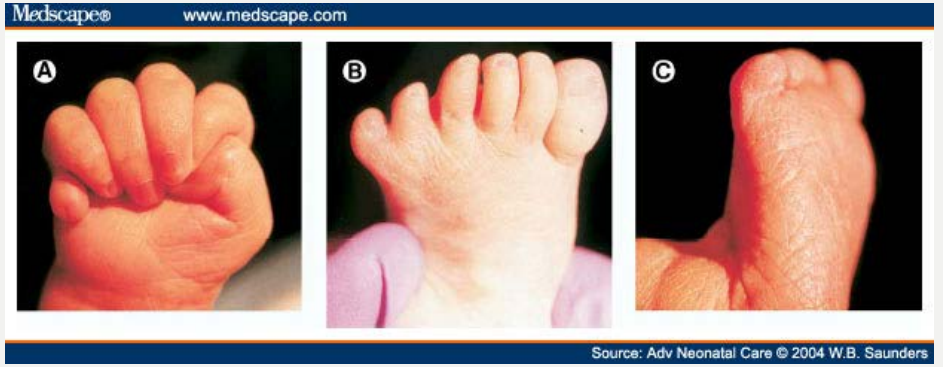
Second trimester Quad screen results

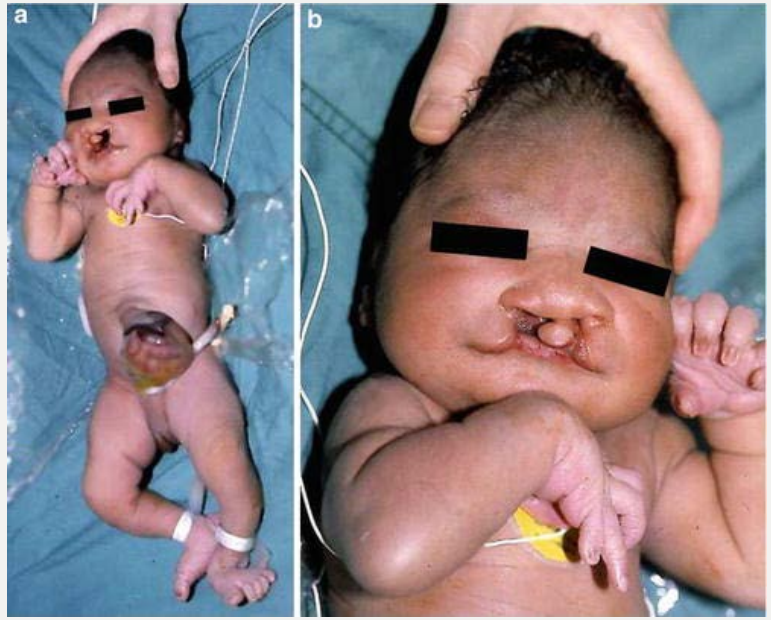
Increased risk for:	hCH	Estriol	AFP	Inhibin A
Open spina bifida	Normal	Normal	High	n/a
Anencephaly	Low	Low	High	n/a
Down syndrome (T21)	High	Low	Low	High
Edwards syndrome (T18)	Low	Low	Low	Normal

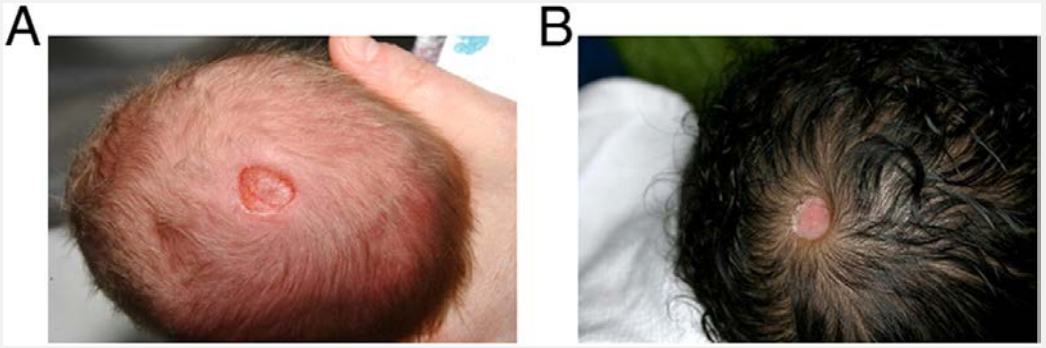
- First trimester combined screen findings suggestive of Trisomy 18
  - Low PAPP-A and low b-hCG
- Trisomy 13 screening
  - Quad screen not useful, but would have low PAPP-A and low b-hCG in first trimester

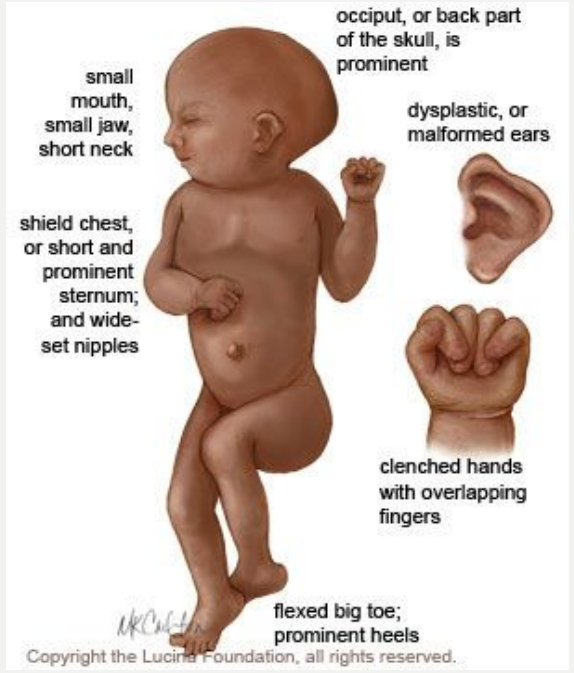
Trisomy 13

- AKA Patau Syndrome
- Associated with hyperplacentosis and preeclampsia in pregnancy
- Features
  - Characteristic findings
    - Holoprosencephaly
    - Cephalocele and omphalocele
    - Cleft lip/palate
    - Polydactyly
    - Rocker bottom feed
    - Cutis aplasia
    - Cystic renal disease
  - Any other organ system can be involved, but other common findings include:
    - CHD (VSD, PDA, ASD)
    - Extreme delays and intellectual disability
    - Microcephaly









Trisomy 18

- Features
  - *Characteristic findings*
    - IUGR
    - Horseshoe kidney
    - Overlapping digits
    - Radial aplasia
    - Rockerbottom feet
  - Other findings include
    - Hypertonia
    - Micrognathia
    - CHD (VSD and PDA most common)
    - Meckel diverticulum and malrotation
    - Extreme delays and intellectual disability

Prognosis

- Nearly all cases of Trisomy 13 and 18 are lethal in the first year of life
- Those that do survive past one year have severe delays and many other health conditions requiring extensive interventions
- A ‘noninterventional paradigm’ and withdrawal of extensive measures would be appropriate in these cases, though many parents choose to pursue life extending measures

	Trisomy 13	Trisomy 18
Mean life expectancy	130-180 days	60 days
Median life expectancy	7-10 days	4 days
(40-48 days if no major cardiac/GI malformations)		
Death by 1 month	45%	
Death by 6 months	70%	
Death by 1 year	82%-90%	90%

References

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- Meeks NL, Saenz M, Tsai A, Elias ER. Genetics & Dysmorphology. In: Hay, Jr. WW, Levin MJ, Deterding RR, Abzug MJ. eds. *Current Diagnosis & Treatment: Pediatrics, 24e* New York, NY: McGraw-Hill; . http://accessmedicine.mhmedical.com/content.aspx?bookid=2390&sectionid=189084922. Accessed April 08, 2020.
- Up to Date: Congenital cytogenic abnormalities