Trisomy 21 (Down syndrome)

Genetics

-21q22.1-21q22.3 --> DS critical region (but, cases of dup outside this region who manifest DS)

-Mechanism: 1) T21: 47,XX,+21 (~95% of cases; 1% rr; 1.4% rr if mother <30y); 2) Rob Translocation: 46,XX,rob(14;21) (~4%; rr depends on carrier parent: mother carrier: 10-15%; father is carrier: <5%); 3) Mosaic T21: (~2%; may be milder)

Clinical findings/Dysmorphic features

-Upslanting palpebral fissures; excess nuchal skin; auricular dysplasia; flat facial profile; macroglossia; hypodontia; palmar crease; clinodactyly; pelvic changes

-Mild-mod ID; hypotonia; growth delay; joint hyperflexibility; abnormal moro reflex

-Strabismus, adult cataracts, myopia (nearsightedness), conductive HL; hypogenitalism

-CHD: AV canal (hole in the center of the heart; located between atria and ventricles) almost pathognomonic; most common: VSD

-Duodenal atresia; hirschprung disease; thyroid disease; early onset Alzheimers

-Transient myeloproliferation, ALL

Etiology

-Most common and best-known chromosome aneuploidy --> 1 in 800 live births

Pathogenesis

-95% de novo, 5% due to Robertsonian translocation or isochromosome 21

-90% due to maternal meiosis nondisjunction (3⁄4 MI error, 1⁄4 MII error)

Genetic testing/diagnosis

-Prenatal US abnormalities detected in 50%; maternal serum screen: high free beta human choriogonadotropin, low PAPP-A

-Maternal fetal free DNA testing, karyotype is diagnostic

Others

-First described clinically in 1866 by Langdon Down

-Maternal age effect

-Supportive care, overall life expectancy is reduced