

Dysmorphic Features: **Common Syndromes and Sequences**

Background

1. Dysmorphic features:
 - Abnormal body variations that can be measured or characterized (congenital anomalies or "birth defects")
 - Singular anomalies often diagnostically insignificant
 - Multiples anomalies can aid in diagnosis of a larger syndromes
2. Epidemiology of dysmorphism
 - Incidence of major malformations is approximately 2-3% of live births
 - Congenital malformations account for approximately 20% of infant deaths
3. This summary is limited to common congenital sequences and syndromes

Pathophysiology

1. Etiology is diverse but may include genetic, infectious, chemical or metabolic causes
 - Physical causes may include decreased amniotic fluid, compression, torsion
2. Different organ systems are susceptible to teratogenesis during different stages of development
 - Most major malformations occur in the embryonic period (3 to 8 wks)
 - Functional defects and minor malformations may occur throughout the fetal period (9-38 wks)
 - CNS, sensory organs, teeth, and external genitalia remain susceptible

Common Congenital Sequences and Syndrome

1. Autosomal syndromes
 - General patterns
 - Frequency of chromosomal disorders increases with maternal age
 - Frequency of recurrence depends on whether the cause is a chromosomal translocation (higher recurrence risk, independent of maternal age)
 - Trisomy 21
 - M/c pattern of malformation (approximately 1 in 660 infants)
 - Most cases are full trisomy 21; a minority (approximately 5%) are either mosaic or translocation
 - Clinical findings
 - Mental deficiency
 - Hypotonia, hyperflexibility of joints, flat facial profile, protruding tongue, loose nuchal skin
 - White specks on iris (Brushfield spots)
 - Single transverse palmar crease
 - Pelvic dysplasia
 - Wide gap between first and second toes ("sandal gap")
 - Associated with cardiac defects (approx 40% of cases), immune dysfunction, lymphoma, atlantoaxial dislocation

- Resources for patients and families available at <http://www.ndss.org/>
 - Trisomy 18
 - Approximately 3 in 1000 newborns
 - Ratio 3:1 female:male
 - Almost all cases are full trisomy without translocation; therefore recurrence risk is low (less than 1%)
 - Clinical findings
 - Severe mental deficiency
 - Feeble activity, weak cry, micrognathia
 - With clenched fist, overlapping of index finger over third, fifth finger over fourth
 - Hypoplasia of nails
 - Mild hirsutism of forehead and back
 - Associated with cardiac defects, horseshoe kidney, cleft lip / palate, and many other defects; median survival time is 14.5 days
 - Rarely, may survive into childhood (particularly with mosaic or partial trisomy)
 - Resources for families available at <http://www.trisomy18.org/>
 - Trisomy 13
 - Approximately 1 in 5000 births
 - Clinical findings
 - Severe mental deficiency; holoprosencephaly
 - Microcephaly, microphthalmia, cleft lip / palate, abnormal auricular helices
 - Polydactyly, narrow fingernails, single transverse palmar crease
 - Cryptorchidism, abnormal scrotum in males
 - Associated with cardiac defects, deafness, polycystic kidney; median survival time is 7 days
 - Resources for families available at <http://www.livingwithtrisomy13.org/>
- 2. Sex chromosomal syndromes
 - XXY syndrome (Klinefelter syndrome)
 - Approximately 1 in 660 males
 - Usually diagnosed in adolescence or young adulthood
 - Diagnosis in childhood is helpful in allowing for testosterone replacement
 - Clinical findings
 - Mild mental deficiency (mean IQ between 85 and 90); deficiency particularly in expressive language, processing, and auditory memory
 - Long limbs, slim stature
 - Hypogonadism, hypogenitalism
 - May be associated with severe acne, cryptorchidism, scoliosis, diabetes mellitus (in adulthood), breast cancer, osteoporosis, autoimmune disease
 - Resources for patients and families available at <http://klinefeltersyndrome.org/>

- 45X syndrome (XO syndrome, Turner syndrome)
 - Approximately 1 in 2500 newborn females
 - Most 45X conceptuses die before birth
 - Clinical findings
 - Mild mental deficiency (mean IQ 90)
 - Small stature
 - Prominent ears, webbed posterior neck, low hairline
 - Broad chest ("shield chest")
 - Associated with horseshoe kidney, cardiac defects, ovarian dysgenesis ("streak ovaries")
 - Resources for patients and families available at <http://www.turnersyndrome.org/>
- 3. Genetic syndromes
 - Fragile X syndrome
 - Approximately 1 in 5000 males; rarer in females
 - Generally familial (high rate of recurrence)
 - Clinical findings
 - Mild to profound mental deficiency
 - Macrocephaly, long facies, large ears, epicanthal folds
 - Macrorchidism (post-puberty)
 - Associated with hyperkinetic behavior, emotional instability, autistic features; abnormalities exist on a continuum depending on the number of repeats
 - Resources for patients and families available at <http://www.fragilex.org/>
 - Marfan syndrome
 - Autosomal dominant inheritance
 - Clinical findings
 - Normal intelligence, but may show learning disability or attention deficit disorder
 - Tall stature; long slim limbs; muscular hypotonia
 - Pectus carinatum
 - Wrist and thumb sign
 - Lens subluxation; defect in suspensory ligament
 - Associated with cardiac defects (esp. dilation of ascending aorta), retinal detachment, diaphragmatic hernia
 - Resources for patients and families available at <http://www.marfan.org/>
 - Treacher-Collins
 - Autosomal dominant inheritance
 - Clinical findings
 - Malar hypoplasia
 - Slanting palpebral fissures
 - Mandibular hypoplasia
 - Malformation of auricles; external ear canal defect; conductive hearing loss

- Intelligence is normal
 - Therefore early recognition of deafness is important
 - In order to provide hearing aids or surgery for proper development
 - Plastic surgery in childhood may also offer cosmetic improvement
 - Resources for patients and families available at <http://www.treachercollins.org>
4. Teratogenic syndromes
- Fetal alcohol syndrome
 - Due to exposure of the fetus to alcohol during pregnancy
 - Clinical findings
 - Mental retardation (moderate to profound) and brain malformations (e.g. agenesis of corpus callosum)
 - Smooth philtrum
 - Maxillary hypoplasia
 - Microcephaly
 - Short palpebral fissures
 - Nail hypoplasia
 - Note that there is no "safe" stage during pregnancy to consume alcohol
 - Resources for patients and families available at <http://www.nofas.org/>

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