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 dysmorphology
   - 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

  o **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)

  o **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

2. **Sex chromosomal syndromes**
   
   o **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
1. Dysmorphic Features Syndromes and Sequences

- **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")

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

- **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

- **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
  o 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/

References

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