Clinical Features of Common Aneuploidies

**Trisomy 21: Down syndrome**
- Epicanthal folds of the eye.
- Wide space (sandal gap) between the first and second toes.
- Simian crease (single palmar crease)
- Tongue trusting
- Thick nuchal fold
- Congenital heart defects (75%)
- Low tone

**Trisomy 13: Patau Syndrome**
- Holoprosencephaly
- Microcephaly
- Cleft lip +/- palate
- Polydactyly
- Congenital heart defects

**Trisomy 18: Edward Syndrome**
- Intrauterine Growth Retardation (IUGR)
- Rocker bottom feet
- Overlapping fingers
- Malformed ears
- Congenital heart defects

**Cri du Chat Syndrome (5p−)**
- Microcephaly
- Growth deficiency
- **High pitched cat-cry**
- Congenital heart disease
- Hypotonia

**Prader Willi Syndrome**
- Paternal deletion 15q11
- Obesity, food seeking
- Hypotonia
- Small hands and feet
- Up slanting palpebral fissures
- Infants with failure to thrive.

**Angelman Syndrome**
- Maternal deletion 15q11
- Severe postnatal growth deficiency
- Mental retardation
- “puppet-like gait”
- Paroxysms of inappropriate laughter.
Absent or limited speech.
Seizures

22q11 Deletion Syndrome
- Voice-hyper nasal speech
- Cleft palate
- Congenital heart defect
- Hypocalcemia
- Immune defect due to a T-cell deficit
- Developmental delay/mental retardation

William Syndrome (7q23.2)
- Elfin Facies
- Prominent lips
- Wide spaced teeth
- **Supravalvular aortic stenosis**

Triple Repeat Disorders
- Fragile X CGG >200
- Huntington’s chorea CAG >40

Fragile X Syndrome
- Prominent or large ears
- Long face
- High-arched palate
- Hyper-extensible joints
- Subluxable thumbs
- Macro-orchidism (post pubertal)
- Flat feet
- Soft, velvet-like skin

Mendelian Inherited Disorders

X-linked Recessive

Duchene’s Muscular Dystrophy:
- calf hypertrophy
- toe walking
- progressive weakness
- Dilated Cardiomyopathy
- Gowers sign (difficulty rises from the floor)
Autosomal Dominant

Neurofibromatosis
2 of the following features:
■ >6 café au lait spots
■ 2 or more neurofibromas
■ Lisch nodules
■ Optic gliomas
■ Angiofibromas
■ Axillary or inguinal freckling.

Osteogenesis Imperfecta
■ Bones fracture easily
■ Near normal stature
■ Blue sclera
■ Hearing loss in 20’s to 30’s
■ Most fractures occur before puberty

Lysosomal Storage Diseases

Gaucher Disease
Aut Recessive
1/500 in Ashkenazi Jewish population
Glucocerebrosidase Deficiency
■ Hepatosplenomegally
■ Anemia
■ Bone pain

Fabry’s Disease
X-linked Recessive
α-galactosidase A
■ Renal failure
■ Strokes
■ Myocardial Ischemia
■ Whorl keratopthy (eyes)
■ Angiokeratoma

Hurler Syndrome
Aut Recessive
α-1-Iduronidase deficiency
■ Coarse facial features (upturned nose, thick lips, hirsitism)
■ Gibbus deformity
■ Joint contractures
■ Progressive Mental retardation
■ Cardiac valvular disease
### Hunter Syndrome

X-linked

Iduronidate sulfatase

- *No corneal clouding*
- Coarse facial features

### Pompe Disease

Aut Recessive

Enzyme: Acid Alpha Glucosidase

**Infantile**

- Cardiomyopathy
- Failure to thrive
- Early death

**Adult**

- Muscle weakness
- Respiratory insufficiency

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**Inborn Errors of Metabolism**