1. **Chromosomal Etiology**

2. **Chromosomal Syndromes**
   - Syndromes classified as chromosomal if noted on karyotype
   - Most multiple malformations are deviations in chromosomes
   - Abnormal amount or structure = aneuploidy

3. **Types of Aneuploidy**
   - Deletion of entire chromosome
   - Addition of entire chromosome
   - Deletion of parts of chromosomes
   - Addition of parts of chromosome
   - Restructured chromosomes
   - Rearrangement of chromosomes

4. **Monosomy**
   - Deletion of an entire chromosome
   - 45 vs full complement of 46
   - Result from nondisjunction during meiosis
   - Nondisjunction - failure of one or more chromosomes to separate
   - Often lethal

5. **Monosomy**
   - XO - Turner's syndrome
   - YO - Spontaneous abortion

6. **Trisomy**
   - Addition of an entire chromosome
   - 47 vs 46: Typically many anomalies present
   - Also results from nondisjunction
   - Can have trisomy of autosomal or sex chromosomes

7. **Trisomy 21**
   - Most common = Down's syndrome
   - Because of extra chromo, thousands of genes which are present that interfere with normal code
   - Estimate many trisomy 21 spontaneously abort; 20 reach term

8. **Down's Syndrome**
   - MR, short stature, flat nasal bridge, palpebral fissures, protruding tongue, heart defects
   - Severe cardiac malformations lead to mortality in neonatal period

9. **Trisomy 18:** Edwards Syndrome
- Prominent occiput/MR
- malformed ears
- flexed fingers
- rocker-bottom feet/prominent heel
- micrognathia
- limited life expectancy

10 Trisomy 13-15: D Syndrome
- MR, malformed ears, prepalatal cleft (65-75%), holoprosencephaly,
- high mortality: 55% by 1st month, 66% by 6th

11 Trisomy of Sex Chromos
- fairly common
- often not detected at birth
- XXX - MR; poss normal appearance: 1/4000 females
- XXY - Klinefelter's syndrome: small male genitalia, high voice, enlarged breasts, little body hair, MR: 1/1500 male
- XYY - supermales over 6 feet: least impacted

12 Deletion of Parts
- because only part missing, less severe consequences
- two types of deletion
- type based on position within the chromo
- deletions occur at the ends of short (p) or long (q) arm = terminal deletions
- when deletion in middle, interstitial deletion

13 Deletion Syndrome
- 4p- ; Wolf-Hirschhorn syndrome
- severe MR, growth deficiency, hypotonia, seizures, CLCP
- cranial asymmetry, hypertelorism, strabismus, genital anomalies
- many die in infancy

14 Cri Du Chat: 5p-
- cry like cat: small
- facial asymmetry, hypertelorism, epicanthal folds, downslanting eyes, low set ears
- IQ rarely exceeds 30

15 Contiguous Gene Syndromes
- variant of deletion: submicroscopic section is missing
- V-C-F Syndrome: very small segment of the long arm of chromo 22 is deleted
- not usually detectable by karyotyping: requires molecular genetic procedures

16 Mechanical Factors
• developing fetus is normal; abnormality induced by factor extrinsic to fetus
• facial clefts may result from impingement on developing embryo
• account for only small percentage of all clefts

17 □ Extrinsic factors
• intrauterine crowding
  • twins
  • oligohydraminos: small amount of amniotic fluid
• tears in amnion
• presence of uterine tumor
• abnormally small uterus

18 □ Mechanical Deformation

19 □ Sporadic/Unknown Etiology

20 □ Two Types
• recurrent pattern: genesis unknown
  • pattern that has been seen before but not attributable to any known factors: no family history, no chromosomal abnormality, no teratogeneisis
• provisionally unique: genesis unknown

21 □ Recurrent Pattern: Genesis Unknown
• Hemifacial microsomia: Goldenhar Syndrome
  • overwhelmingly number are sporadic
  • etiology remains unknown
• Williams Syndrome
  • characteristic craniofacial pattern-thick lips, large mouth/no CL/CP
  • cognitively impaired with sophisticated language system

22 □ Provisionally unique: genesis unknown
• kids with multiple anomalies/clefts that do not fit any pattern
• scour literature; nothing like it
• researchers anticipate seeing another: therefore “provisional”