

## Teratology

Wendy Chung, MD PhD

---

---

---

---

---

---

---

---

## Mrs. B

- 30 year old woman comes to you because her 20 week prenatal ultrasound showed a hole in the heart
- Patient and her husband have many questions:
  - What caused this birth defect?
  - Was it caused by the glass of wine she had before she found out she was pregnant?
  - Will there be other problems for this child?
  - If they have other children, what is the risk of recurrence?

---

---

---

---

---

---

---

---

## Teratology

- The study of abnormal development in embryos and the causes of congenital malformations or birth defects

---

---

---

---

---

---

---

---

## Birth Defects

- Observed in 3% of newborns
- Observed in another 3% of children later
- May or may not be outwardly visible
- Etiology: genetic and environmental

---

---

---

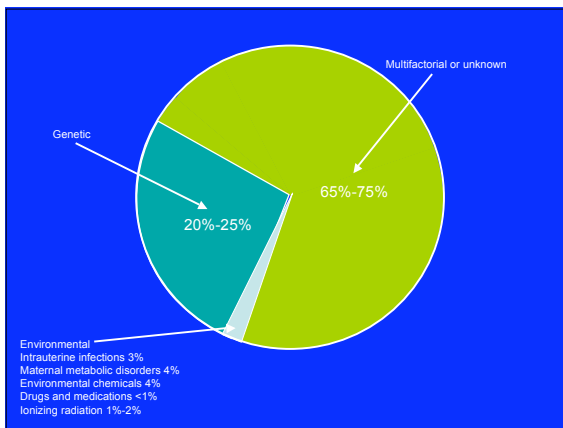
---

---

---

---

---



---

---

---

---

---

---

---

---

## Major and Minor Anomalies

- Major anomalies: life/health threatening
- Minor anomalies: cosmetic
- The greater the number of minor anomalies, the greater the likelihood of a major anomaly
- Certain minor anomalies suggest specific major anomalies

---

---

---

---

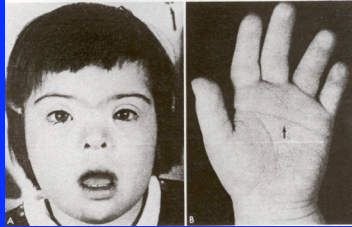
---

---

---

---

## Down Syndrome



---

---

---

---

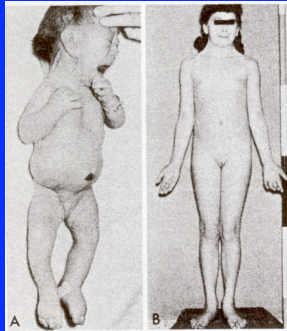
---

---

---

---

## Turner Syndrome



---

---

---

---

---

---

---

---

## Trisomy 13

- Midline defects (cleft lip and cleft palate)
- Central nervous system malformations
- Micro-ophthalmia
- Congenital heart disease
- Poor growth

---

---

---

---

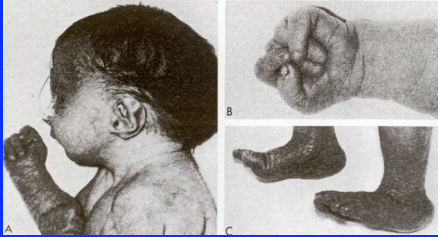
---

---

---

---

## Trisomy 18



---

---

---

---

---

---

---

---

## Mrs. B

- Extensive ultrasound examination does not identify other major anomalies
- Can minor anomalies be excluded?
  
- An amniocentesis is performed and is normal
- Are genetic etiologies excluded?

---

---

---

---

---

---

---

---

## Inborn Errors of Metabolism Causing Birth Defects

- Smith Lemli Opitz
- Congenital disorders of glycosylation
- Fatty acid oxidation disorders

---

---

---

---

---

---

---

---

## Single genes cause developmental disorders

- PAX6: aniridia
- NEUROD1: pancreatic agenesis
- TTF1: thyroid agenesis
- NKX2.5: congenital heart disease
- ZIC3: holoprosencephaly
- Doublecortin: lissencephaly

---

---

---

---

---

---

---

---

## Achondroplasia



---

---

---

---

---

---

---

---

## Teratogens

- A chemical, infectious agent, physical condition, or deficiency that, on fetal exposure, can alter fetal morphology or subsequent function
- Teratogenicity depends upon the ability of the agent to cross the placenta
- The embryo is most susceptible to teratogenic agents during periods of rapid differentiation

---

---

---

---

---

---

---

---



## Effect of Exposure Depends on Timing

- All or none effect early
- Effect of organogenesis during embryonic development
- Effect on size and function during fetal development

---

---

---

---

---

---

---

---

---

---

Teratogen	Congenital Malformation
Audiogenic Agents Ethanol Norethisterone Tetracycline	Varying degrees of masculinization of female fetuses; ambiguous external genitalia caused by labial fusion and clitoral hypertrophy
Drugs and Chemicals Alcohol	<i>Fetal alcohol syndrome</i> : intrauterine growth retardation (IUGR); mental retardation; microcephaly; ocular anomalies; joint abnormalities; short palpebral fissures
Antimetabolites Bisulfan	Wide range of skeletal defects; IUGR; malformations of the central nervous system, notably microencephaly (a large part of the brain is absent) Stunted growth; skeletal abnormalities; conical opacities; cleft palate; hypoplasia of various organs
Phenytoin (Dilantin)	<i>Fetal Folic acid syndrome</i> : IUGR; microcephaly; mental retardation; ridged scrotop; sparse, more epiphyseal foci; eyelid ptosis; broad depressed nasal bridge; palatal agial hypoplasia
Lithium carbonate Methotrexate	Various malformations, usually involving the heart and great vessels Multiple malformations, especially skeletal, involving the face, skull, limbs, and vertebral column
Large doses of retinoic acid (Vitamin A)	Facial abnormalities; neural tube defects, such as spina bifida cystica (see Fig. 18-14)
Tetracycline Trimethadione	Stained teeth; hypoplasia of enamel Developmental delay; V-shaped eyebrows; low-set ears; cleft lip and/or palate
Infectious Agents Cytomegalovirus	Microcephaly; hydrocephaly; microphthalmia; microgyria; mental retardation; central calcifications
Herpes simplex virus Rubella virus	Microcephaly; microphthalmia; retinal dysplasia Cataracts; glaucoma; chorioretinitis; deafness; microphthalmia; congenital heart defects
Varicella Venezuelan equine encephalitis	Skin scarring; muscle atrophy; mental retardation Cataracts; brain destruction
Toxoplasma gondii	Microcephaly; mental retardation; microphthalmia; hydrocephaly; chorioretinitis; central calcifications
Propionis pallidum High levels of vitamin K	Hydrocephalus; congenital deafness; mental retardation; abnormal teeth and bones Microcephaly; mental retardation; skeletal malformations

---

---

---

---

---

---

---

---

---

---

## Nicotine

- IUGR
- Premature delivery
- Neurocognitive development

---

---

---

---

---

---

---

---

---

---

## Fetal Alcohol Syndrome

- Characteristic facial features
- Congenital heart disease
- Growth deficiency
- Behavioral/neurocognitive deficits

---

---

---

---

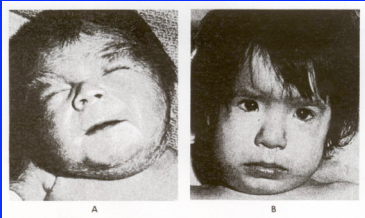
---

---

---

---

## Fetal Alcohol Syndrome



---

---

---

---

---

---

---

---

## Mrs. B

- Do you believe her fetus' congenital heart disease was caused by the glass of wine she drank two weeks after conception?

---

---

---

---

---

---

---

---

## Tetracycline

- Yellow/brown teeth
- Decreased bone growth

---

---

---

---

---

---

---

## Fetal Hydantoin Syndrome

- Intrauterine growth retardation
- Microcephaly, mental retardation
- Distal phalangeal hypoplasia
- Specific facial features

---

---

---

---

---

---

---

## Retinoic acid

- Craniofacial dysmorphisms
- Cleft palate
- Thymic aplasia
- Neural tube defects

---

---

---

---

---

---

---

## Thalidomide Syndrome



---

---

---

---

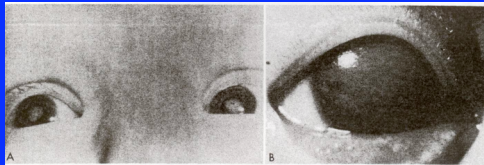
---

---

---

---

## Congenital Rubella



---

---

---

---

---

---

---

---

## Congenital CMV

- Intrauterine growth retardation
- Micromelia
- Chorioretinitis, blindness
- Microcephaly
- Cerebral calcifications, mental retardation
- Hepatosplenomegaly

---

---

---

---

---

---

---

---

## Ionizing Radiation

- Affects brain development at 10-18 weeks of gestation a HIGH dose
- No evidence of effect of exposure associated with typical diagnostic studies

---

---

---

---

---

---

---

---

## Maternal Hyperglycemia

- Congenital heart disease
- Renal, gastrointestinal, and central nervous system malformations such as neural tube defects

---

---

---

---

---

---

---

---

## Babies of Mother's with PKU

- Mental retardation
- Low birth weight
- Congenital heart diseases

---

---

---

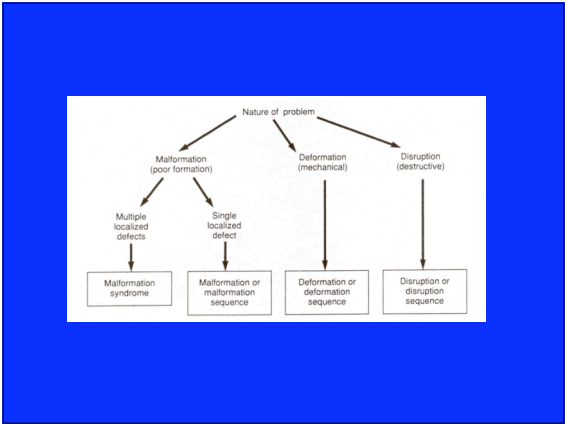
---

---

---

---

---




---

---

---

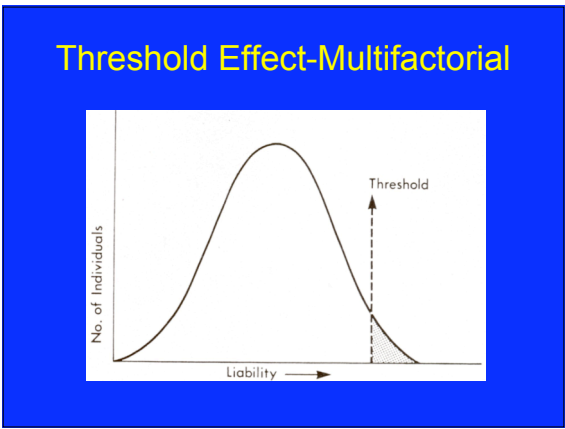
---

---

---

---

---




---

---

---

---

---

---

---

---

### Mrs. B

- After birth, the newborn examination is unremarkable
- The baby's congenital heart disease is repaired
- At age three, the child is growing well and has met all his milestones
  
- What caused his congenital heart disease?
- What is the risk of recurrence for a future sibling?

---

---

---

---

---

---

---

---