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
- Account for 20% of perinatal deaths
- May or may not be outwardly visible
- Etiology: genetic and environmental

Major and Minor Anomalies

- Major anomalies: life/health threatening
- Minor anomalies: cosmetic
  - May be seen in 14% of newborns
  - The greater the number of minor anomalies, the greater the likelihood of a major anomaly
- Certain minor anomalies suggest specific major anomalies
Down Syndrome

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

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 - FGFR3

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

How are agents determined to be teratogenic?
- Anecdotal data in humans
- Data from animal studies
- For many drugs there are no definitive data, so we recommend avoiding the use of any medications possible during early pregnancy
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

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

- Caused by the anti-epileptic phenytoin
- Intrauterine growth retardation
- Microcephaly, mental retardation
- Distal phalangeal hypoplasia
- Specific facial features

Retinoic acid

- Extremely teratogenic in the first five weeks of gestation
- Craniofacial dysmorphisms
- Cleft palate
- Thymic aplasia
- Neural tube defects

Thalidomide Syndrome

- Critical exposure is 24-36 days of gestation
- Limbs
- Ears
- Cardiac
- GU anomalies

Congenital Rubella (German measles)

- Cataracts, congenital heart disease, deafness
- Effects are most severe within the first 6 weeks

Congenital CMV

- Most common infection
- Spontaneous termination
- Intrauterine growth retardation
- Micromelia
- Chorioretinitis, blindness
- Microcephaly
- Cerebral calcifications, mental retardation
- Hepatosplenomegaly
Ionizing Radiation

- Affects brain development at 10-18 weeks of gestation at 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
- Tight glycemic control starting prior to conception is critical

Babies of Mothers with PKU

- Mental retardation
- Low birth weight
- Congenital heart disease

Mechanical forces can act as teratogens

Examples: cleft lip, cleft palate, congenital heart disease, neural tube defects

Threshold Effect-Multifactorial

Examples: cleft lip, cleft palate, congenital heart disease, neural tube defects

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?