TERATOLOGY
Birth Defects and Prenatal Diagnosis

The science that studies birth defects and congenital malformations is called **teratology**. Minor anomalies occur in 15% of newborns

Types of Abnormalities

Malformations - These occur during formation of structures, for example during organogenesis. Most malformations have their origin during the *third to eighth weeks of gestation*. They are caused by environmental or genetic factors, or both.

Disruptions - Disruptions result in *alterations of already formed structures*. Bowel damage due to vascular accidents and amniotic bands is an example of a disruption.

Deformations - Deformations are due to mechanical forces that mold part of the fetus over a prolonged period of time. An example here is clubfeet, due to compression in the amniotic cavity.

Syndrome - This is a group of anomalies occurring together that have a specific common cause.

Environmental Factors

Factors that determine the capacity of an agent to produce birth defects have been defined and set forth as the **principles of teratology**. They include:

1. Susceptibility to Teratogenesis depends on the **genotype of the conceptus** and the manner to which this genetic composition interacts with the environment.
2. Susceptibility to teratogens varies with the **developmental stage at the time of exposure**. The most sensitive period is the *third to eighth weeks*, also know as the *period of embryogenesis* or *organogenesis*.
3. Manifestations of abnormal development depend on **dose and duration of exposure**.
4. Teratogens act in specific ways on developing cells and tissues to initiate abnormal embryogenesis.
5. Manifestations of abnormal development are **death, malformation, growth retardation,** and **functional disorders**.

Infectious Agents

Rubella (German measles) - Cataracts, glaucoma, heart defects, deafness, teeth.
Cytomegalovirus - Microcephaly, blindness, mental retardation, fetal death.
Herpes simplex - Microphthalmia, Microcephaly, retinal dysplasia
Varicella (chickenpox) - Limb hypoplasia, mental retardation, muscle atrophy
Human immunodeficiency viruses (HIV) - Microcephaly, growth retardation
Toxoplasmosis
Syphilis

Other Viral Infections and Hyperthermia

Malformations can occur when infectious agents add further embryonic damage when **hyperthermia** occurs; many infectious agents are **pyrogenic** (cause fever). Defects produced by exposure to elevated temperatures include anencephaly, spina bifida, mental retardation, microcephaly, and facial abnormalities. In addition to febrile illnesses, use of hot tubs and saunas can produce sufficient temperature elevations of cause birth defects.

Radiation

Ionizing radiation kills rapidly proliferating cell. It can produce virtually any kind of birth defect depending on the dose and stage of development of the conceptus.

Chemical Agents

Thalidomide - An antinauseant and sleeping pill. In the early 1960's in Germany it caused increased incidence of **amelia** (complete absence of a limb), **meromelia** (absence of part of a limb), and **phocomelia** (seal limb).

Cocaine - Cocaine has been reported to cause a number of birth defects, possibly due to its action as a vasoconstrictor that causes hypoxia. Cocaine use is associated with premature disruption of the placenta from the uterus (placenta abruptio), although, other things can also cause this problem.

Alcohol - Even moderate alcohol consumption during pregnancy may be deleterious to embryonic development. The incidence of **fetal alcohol syndrome is the leading cause of mental retardation**.

Cigarette smoking - Cigarettes are not linked to major birth defects, but does contribute to intrauterine growth retardation of premature delivery.

Isotretinoin - Retinoic acid is an analogue of **vitamin A** and is prescribed for the treatment of acne and other chronic dermatoses. However, it is highly teratogenic and can produce virtually any type of malformation.

Hormones

Diethylstilbestrol - This hormone was once used to prevent abortions. Of particular interest is vaginal clear cell adenocarcinoma, usually encountered in young girls in their late teens whose mothers took diethylstilbestrol during pregnancy in the mid 1900's.

Maternal Disease

Diabetes - The risk of congenital anomalies in children of diabetic mothers is 3 - 4 times that for the offspring of nondiabetic mothers. Maternal diabetes is associated with high birth weight and stillbirths.

Phenylketonuria - Mothers with phenylketonuria (PKU) have a deficiency of the enzyme **phenylalanine hydroxylase** resulting in elevated serum levels of phenylalanine. Phenylalanine hydroxylase catalyzes the hydroxylation of phenylalanine to tyrosine. Risk for mental retardation and cardiac defects are high in this condition.

Nutritional Deficiencies

With the exception of **endemic cretinism**, related to deficient iodine, no teratogenic defects have been noted. Low thyroid hormone from either the mother or production of it by the fetus will produce **cretinism** associated with retardation. When there is low thyroid hormone production in a child or adult, the result is **myxedema**. Here, there is no retardation. Poor nutrition can lead to **low birth weight**. **Spina bifida** and folic acid will be covered in the section of development of the spine.

Obesity

Prepregnancy obesity is defined as a BMI of greater than 29kg/m^2. This is associated with a 2 - 3 fold increased risk of having a child with neural tube defects.

Prenatal Diagnosis

Ultrasonography - This technique uses high-frequency sound waves to create images from the tissues the waves reflect from. It may be performed transvaginally or transabdominally.

Maternal Serum Screening - One of the first of these screening tests is for **alpha-fetoprotein (AFP)**. This protein is normally produced in the fetal liver at 14 weeks and leaks into the maternal circulation via the placenta. Increased levels of AFP are associated with neural tube defects and abnormalities of the gut. It is not a useful constituent of adult blood.

Amniocentesis - A needle is transabdominally inserted into the amniotic cavity and fluid withdrawn. The fluid is tested for AFP and other biochemical factors. Fetal cells in the fluid can be karyotyped for genetic analysis. This is not done before 14 weeks gestation due to the paucity of amniotic fluid.

Chorion villous sampling - CVS involves the insertion of a needle, either transabdominally or transvaginally, into the placenta. The aspirated cells are analyzed for genetic characteristics. Because even a normal placenta can have chromosomal errors, there may be inaccuracy in interpreting the results if cells are not cultured first. Here, the risk of fetal loss is about twice that of amniocentesis.

Questions

1. Deformed structures that develop during the period of organogenesis is which of the following?
   a. malformation
   b. disruption
   c. deformation
   d. syndrome

2. Cataracts, glaucoma, heart defects, and deafness are seen with infection of _____.
   a. cytomegalovirus
   b. toxoplasmosis
   c. rubella
   d. HIV

3. Which of the following can cause placenta abruptio.
   a. A hot bath.
   b. Cocaine
   c. Too many x-rays.
   d. Alcohol use.

4. Which of the following is a term for complete non-development of a limb.
   a. phocomelia
   b. meromelia
   c. amelia
   d. anencephaly

5. The problem with having phenylketonuria is deficiency of _____.
   a. tyrosinase
   b. tyrosine hydroxylase
   c. insulin
   d. phenylalanine hydroxylase

6. Abnormalities of neural tube development would show elevated levels of _____ in the mother's blood.
   a. insulin
   b. phenylalanine hydroxylase
   c. alpha-fetoprotein
   d. hCG

7. Cretinism is due to lack of _____.
   a. insulin
   b. thyroid hormone
   c. parathyroid hormone
   d. growth hormone