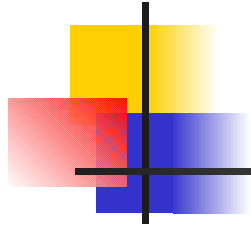


DYSMORPHOLOGY



“There are reckoned up many causes of monsters; the first whereof is the glory of God, this His immense power may be manifested to those that are ignorant of it ... Another cause is that God may punish men’s wickedness ... Monsters are bred and caused by the straightness of the womb ... By the injury of hereditary processes, infants grow monstrous, for crooked back produce crooked back, lame produce lame, flat-nosed their like ... Monsters are also occasioned by the craft and subtlety of the Devil.”

16th century surgeon Ambrose Paré

DYSMORPHOLOGY



Incidence

1. Congenital malformations are defined as “gross structural defects” present at birth.
2. 2 – 3% of all live-born infants show one or more significant malformations
3. By the end of 1 postnatal year, this figure has doubled by the discovery of malformations not identified at birth.

DYSMORPHOLOGY



Environmental factors

1. Until the 1940's, it was assumed that all congenital defects were hereditary.
 - a. 1941 – Gregg – German measles
 - b. 1959, 1961 – Karkany and Kalter – relationship between maternal dietary deficiencies and teratogenic (from the Greek “teratos” – literally “monster”)
2. Despite the rapid development of the field of teratology since the 1960's, knowledge of congenital malformations has increased very little.
 - a. 10% of malformations known to be genetic
 - b. 10% known to be caused by environmental agents
 - c. 80% are presumably due to some blend of genetics and environmental factors

DYSMORPHOLOGY



Infectious agents

1. Rubella (German measles)
2. Cytomegalovirus
3. Herpes simplex virus
4. Other viral infections and hyperthermia
5. Toxoplasmosis
6. Syphilis

DYSMORPHOLOGY



Radiation

1. X-ray effects have been known for years
2. Offspring of Japanese women pregnant at the times of the atomic bombs
3. Indirect effects of low dose exposure on germ cells

DYSMORPHOLOGY



Chemical agents

1. Role of chemical agents in teratology is hard to assess
 - a. Most studies are retrospective
 - b. Pregnant women take a large number of pharmaceutical agents (4/pregnancy)
2. Relatively few drugs have been positively identified as teratogenic
 - a. Thalidomide best known
 - b. Lack of conclusive evidence regarding recreational drugs
 - c. Fetal alcohol syndrome

DYSMORPHOLOGY



Hormones

1. Progestins
2. Diethylstilbesterol (DES)
3. Cortisone
4. Material diabetes

DYSMORPHOLOGY



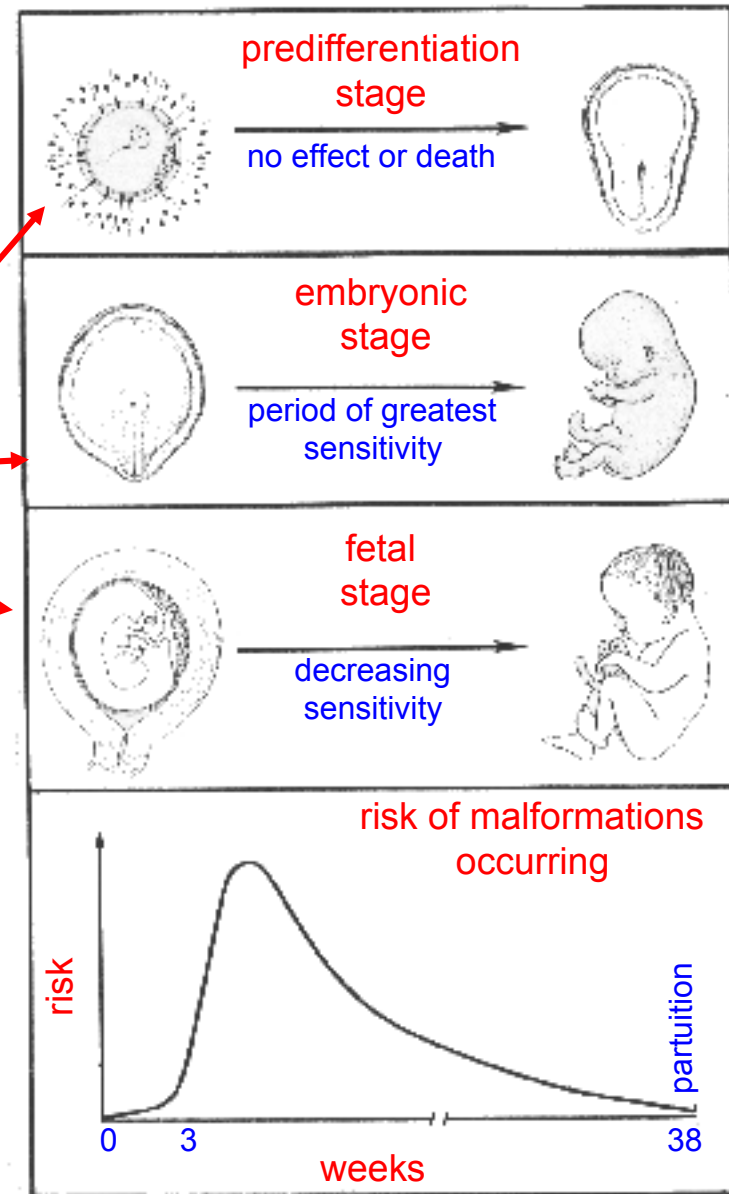
Other factors

1. Nutritional deficiencies
2. Hypoxia
3. Environmental chemicals (think mercury, pesticides, Love Canal)
4. Genetic factors

DYSMORPHOLOGY

Actions of teratogens

1. Stage of development determines susceptibility to teratogenic factors
 - a. 0 – 2 weeks = predifferentiation stage
 - b. 3 – 8 weeks = embryonic stage
 - c. 9 – 38 weeks = fetal stage
1. Effect of a teratogenic factor depends on genotype
2. Teratogenic agent acts in a specific way on a particular aspect of cell metabolism



DYSMORPHOLOGY

Susceptibility to teratogenesis for organ systems

