

Factors Responsible For Congenital Anomalies



Congenital abnormality

Congenital anomaly is defined as structural, behavioral, functional and metabolic disorders present at birth. There are many synonymous terms used like congenital malformations, birth defects, etc.

In 40 to 60% of persons with birth defects, the cause is unknown.

Genetic factors, such as chromosome abnormalities and mutant genes, account for approximately 15%

Environmental factors produce approximately 10%

Combination of genetic and environmental influences (multifactorial inheritance) produces 20 to 25%; and twinning causes 0.5 to 1%.

Congenital anomalies can be of various types:

- 1.Structural: Where external form or structure is abnormal.
- 2.Functional: Where the function of the organ is affected. In functional anomaly the defect can be at cellular level, where a particular enzyme may not be formed normally, e.g. in hemophilia a particular factor essential for clotting is absent.
- 3.Metabolic: Where there can be defect in metabolism because of absence or defect in one or more enzymes.

VARIATIONS

1. Malformations > intrinsic abnormal developmental process i.e. in organogenesis. Most malformations have their origin during the **third to eighth weeks of gestation**.
2. Disruptions > morphological alterations of already formed structures and are due to destructive processes. E.g. Vascular accidents leading to bowel atresias
3. Deformations > mechanical forces that mold a part of the fetus over a prolonged period. oligohydramnios producing club foot
4. Dysplasia > abnormal tissue formation e.g. congenital ectodermal dysplasia

Principles Of Teratology

1. Genotype of the conceptus and the manner in which this genetic composition interacts with the environment.
2. Developmental stage at the time of exposure. The most sensitive period for inducing birth defects is the third to eighth weeks of gestation, the period of embryogenesis. For example, cleft palate can be induced at the blastocyst stage (day 6), during gastrulation (day 14), at the early limb bud stage (fifth week), or when the palatal shelves are forming (seventh week).
3. Dose and duration of exposure to a teratogen.
4. Teratogens act in specific ways (mechanisms) on developing cells and tissues to initiate abnormal embryogenesis (pathogenesis).
5. Manifestations of abnormal development are death, malformation, growth retardation, and functional disorders.

Causes of congenital anomalies

Genetic factors

Chromosomal anomalies

1. Numerical: change in chromosomal number

I. Aneuploidy- e.g. trisomy, monosomy.

e.g. Turner syndrome (45,X) , trisomy 21 or Down syndrome

I. Polyploidy- e.g. triploidy, tetraploidy etc.

2. Structural:

I. Translocation > between non-homologous chr.

II. Deletion > e.g. chr. 5 – cri du chat syndrome

III. Duplication > within a chr.

IV. Inversion > segment of chr. is reversed

V. Isochromosomes > centromere divide transversely i.e. 1 arm missing & other duplicated

- **Environmental Factors**

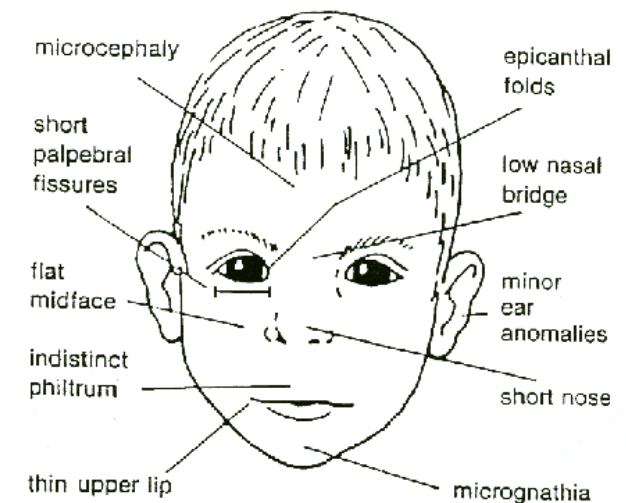
- Drugs

- 1. Thalidomide

- Given to women in the 60s to alleviate morning sickness (Europe, Canada, & South America).
- Babies were born with deformed legs & arms, damage to the ears, heart, kidneys, and genitals.

- 2. Alcohol

- Extreme alcohol use or even one binge drinking episode during pregnancy may cause the infant to develop Fetal Alcohol Syndrome (FAS).
- Mental retardation
- Impaired motor coordination
- Poor attention, memory & language abilities
- Facial abnormalities (widely spaced eyes, short eyelid openings, thin lips)



- *Tobacco* > Low birth weight, Increased chance of miscarriage, SIDS (Sudden Infant Death Syndrome), Behavioral problems (ADHD), Short attention spans, Poor scores on mental tasks
- *Aminopterin* > 1st trimester > Anencephaly, hydrocephaly, cleft lip and palate
- *Diphenylhydantoin* (phenytoin) > Fetal hydantoin syndrome: facial defects, mental retardation
- *Valproic acid* > Neural tube defects, heart, craniofacial, and limb anomalies
- *Trimethadione* > Cleft palate, heart defects, urogenital and skeletal abnormalities
- *Lithium* > early pregnancy > Heart malformations
- *Amphetamines* > Cleft lip and palate, heart defects
- Tetracycline > 3rd month > yellow teeth's , 4-10 months > dec. growth of long bones

- *Warfarin* > 6-12 weeks > Chondrodysplasia, microcephaly
- *ACE inhibitors* > Growth retardation, fetal death, hyoplasia of cranial vault
- *Cocaine* > Growth retardation, microcephaly, behavioral abnormalities, gastroschisis
- *Isotretinoin (vitaminA)* > 3rd week – 5 months > Vitamin A embryopathy: small, abnormally shaped ears, mandibular hypoplasia, cleft palate, heart defects
- *Industrial solvents* > Low birth weight, craniofacial and neural tube defects
- *Organic mercury* > Neurological symptoms similar to those of cerebral palsy
- *Lead* > Growth retardation, neurological disorders

Maternal infections

- *Rubella virus* > Cataracts, glaucoma, heart defects, deafness, tooth abnormalities
- *Cytomegalovirus* > Microcephaly, blindness, mental retardation, fetal death
- *Herpes simplex virus* > Microphthalmia, microcephaly, retinal dysplasia
- *Varicella virus* > Limb hypoplasia, mental retardation, muscle atrophy
- *HIV* > Microcephaly, growth retardation
- *Toxoplasmosis* > Hydrocephalus, cerebral calcifications, microphthalmia
- *Syphilis* > Mental retardation, deafness

Hormones

- *Androgenic agents* (ethisterone norethisterone) > Masculinization of female genitalia: fused labia, clitoral hypertrophy
- *Diethylstilbestrol* (DES) > Malformation of the uterus, uterine tubes, and upper vagina; vaginal cancer; malformed testes
- *Maternal diabetes* > Variety of malformations; heart and neural tube defects most common

Physical agents

- *X-rays* > Microcephaly, spina bifida, cleft palate, limb defects
- *Hyperthermia* > Anencephaly, spina bifida, mental retardation, facial defects
- *Isotopes*

Maternal Obesity Heart defects, omphalocele

- i. Parental age > age less than 17 and more than 35 years
- ii. Order of pregnancy > 1st preg. Cong. Pyloric stenosis, PDA
- iii. Season of birth
- iv. Geographical location
- v. Social class > anencephaly
- vi. Psychological factors > hormonal – thyroxine, cortisol
- vii. Blood incompatibilities (rh factor)
- viii. maternal diabetes and pre-diabetes
- ix. Immunity > thrombocytopenia, myasthenia gravis

Regional Factors

- 1. Faulty implantation
- 2. Ectopic pregnancy
- 3. Twinning > acardiac monster
- 4. Amniotic bands > fetal amputation
- 5. Abnormal uterine position of fetus

Maternal dietary deficiencies

- 1. Starvation > Vit. B, C, D, Ca, Fe
- 2. Trace deficiencies > Iodine, antisterility – vit E

Ultrasound can accurately determine fetal age and growth parameters and detect many malformations.

Maternal serum screening for alpha-fetoprotein can indicate the presence of a neural tube defect or other abnormalities.

Amniocentesis is a procedure in which a needle is placed into the amniotic cavity and a fluid sample is withdrawn. This fluid can be analyzed biochemically and also provides cells for culture and genetic analysis.

Chorionic villus sampling (CVS) involves aspirating a tissue sample directly from the placenta to obtain cells for genetic analysis. Because many of these procedures involve a potential risk to the fetus and mother, they are generally only used for higher risk pregnancies (the exception is ultrasound).

These risk factors include advanced maternal **age** (35 years and older); a **history** of neural tube defects in the family; previous gestation with a chromosome abnormality; chromosome abnormalities in either parent; and a mother who is a carrier for an X-linked disorder