

Definition of teratogen

Any chemical (drug), infection, physical condition or deficiency that , on fetal exposure, can alter fetal morphology or subsequent function.

Causes of congenital anomalies

Multifactorial or unknown (70 %)

Genetic (20 %)

Environmental(10%)

- Intrauterine infection (2%)

- Maternal metabolic disorders (2%)

- Drugs & chemicals (5%)

- Ionizing radiation (1 %)

Factors determining the effect of the teratogen

Fetal factors :

I Developmental stage :

1. Predifferentiation stage (0-7 days of gestation) :

Death or no effect.

Differentiation stage (7-57 days of gestation) :

Malformation

Post differentiation stage (after 57 days of gestation):

Functional defects

Growth retardation

II Genetic susceptibility :

Species differences.

Individual differences.

The route & length of administration of a teratogen.

Effects of teratogens

Immediate : death & abortion

At birth : malformation

functional defects.

Delayed : carcinogenesis

mutagenesis.

Teratogenic agents

Maternal medical disorders

1. Diabetes mellitus :

Infants of insulin-dependent diabetic mothers have up to 22 % incidence of cardiac , renal, gastrointestinal, CNS & skeletal malformation. Most of the malformations occur between the third & sixth week postconception & are increased if there is hyperglycemia during that stage of gestation.

2.Epilepsy :

3.Phenyl ketonuria.:

Infants have an increased incidence of mental retardation, microcephaly,& low birth weight.

4.Virilizing tumors :

produce pseudohermaphroditic changes in female fetus.

B.Infections

Syphilis :

The incidence of congenital infection is inversely proportional to the duration of maternal infection & degree of spirochetemia.

In utero infection may result in :

PTL or miscarriage

S.B.

Neonatal death in up to 50 % of affected infants

Congenital infection can manifest as :

- hepatosplenomegaly, joint swelling, skin rash, anemia, jaundice, snuffles, metaphyseal dystrophy & periostitis.

Toxoplasmosis :

Active primary infection during pre- ∞ infection.

Rubella virus (German measles)

The congenital rubella syndrome includes: CNS, CV, ocular, ear defects & IUGR.

Cytomegalovirus:

The risk of severe complications is much higher for infants of mothers who had a primary infection in pregnancy compared to those who had recurrent infection.

5. Herpes simplex virus type 2.:

Fetal infection during the first trimester results in miscarriage . In few cases ,fetal anomalies occur.

6.Hyper thermia

Sustained maternal temperature > 38 C between 4 & 14 weeks gestation , rather than spiking fevers , is teratogenic.

Estimate fetal exposure dose

Procedure	Fetal Exposure
Chest radiograph (2 views)	0.02-0.07 mrad
Abdominal film (single view)	100 mrad
Intravenous pyelography	≥ 1 rad*
Hip film (single view)	200 mrad
Mammography	7-20 mrad
Barium enema or small bowel series	2-4 rad
CT scan head or chest	<1 rad
CT scan abdomen and lumbar spine	3.5 rad
CT pelvimetry	250 mrad

C. Ionizing radiation

Dose effect :

< 5 rads & probably < 10 rads : Adverse fetal effects are unlikely

10 - 25 rads : Some adverse fetal effects may occur.

> 25 rads : Classic fetal effects (IUGR, structural malformation, fetal resorption) .Elective abortion should be offered as an option.

The dose of diagnostic radiation to the conceptus should be calculated according to certain tables.

Risks of teratogenicity :

The mutagenic effects are very small

Risk of leukemia for children exposed to X - ray

pelvimetry increases from 1 in 3000 to 1 in 2000.

Radioactive iodine : After the 10 th w of gestation , the fetal thyroid can be retarded in addition to any adverse effects of radiation . Iodine-containing cough preparation , antiseptic solutions or X ray adjuncts should be avoided throughout pregnancy.

Radiation Exposure in Pregnancy

Cumulative dose of 5 rad considered safe

No increase in risk of pregnancy loss

CNS abnormalities

Risk during 10-17 wks gestation

- 10 rad – increased risk for mental retardation, microcephaly
- Should delay non-urgent radiographs > 17wks

Malignancies

Very small increase in malignancies, mostly leukemia

2 rad, malignancy risk increases from 3.6/10,000 (baseline population) to 5/10,000

Gene mutations

Very small increase in incidence of gene mutations

50-100 rad needed to double baseline mutation rate

D. Chemicals

Effects of;

Lead: abortion from embryotoxicity, IUGR

Organic mercury: neurological damage, blindness, deafness

Polychlorinated biphenyls: IUGR, pigmented gums & nails, skull calcification.

Herbicides: congenital malformation

E. Drugs

Food & drug administration classification :

Category A : Controlled studies fail to find a risk to the fetus.

E.g.: prenatal vitamins.

Category B : Animal studies have not demonstrated a fetal risk , but there are no controlled studies in humans.

E.g. penicillins, terbutaline, acetaminophen, cyclizine, antacids, prednisone, insulin, ampicillin, clindamycin, nitrofurantoin, miconazole, spiramycin, .

Category C : Animal studies showed teratogenic effects,
& no human studies.

These drugs should be administered only when their
benefits outweighs the potential fetal harm.

E.g. furosemide, Rifampicin, b-
blockers, phenothiazine, methyl
dopa, nifedipine, heparin, , aminophyllin,
gentamycin, chloroquin, acyclovir, cyclosporin, .

Category D : There is evidence of fetal risk in humans but the benefits may outweigh the risk

These drugs are given only in serious disease because no alternative.

E.g. phenytoin, valporic

acid, diazepam, imipramine, captopril, thiazides, spironolactone,

coumarine, chlorpropamide, progestins, tetracyclin, streptomycin, quinine, methotrexate,

vinblastin, azathioprine,