

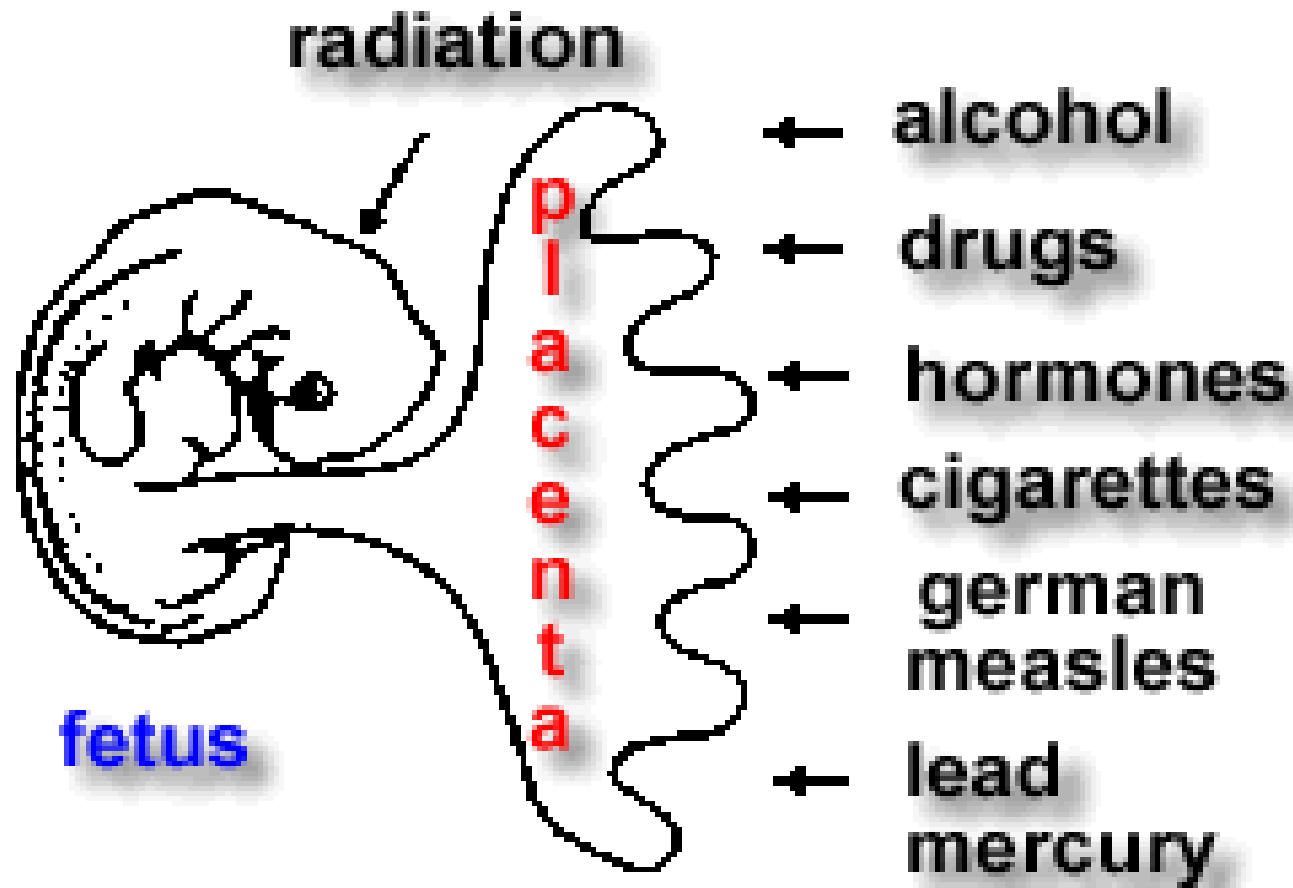
# TERMS

- ▶ *Greek “teras” meaning “malformation”*
- ▶ *Teratogen: Any chemical, substance, or exposure given to the pregnant mother that may cause birth defects to the developing fetus.*
- ▶ *Teratogenesis: The formation of an abnormal embryo.*

# Teratogenicity

- ▶ It refers to capacity of a exogenous agents to cause foetal abnormalities when administered to the mother at any stage of pregnancy.
- ▶ The placenta - not strictly barrier - drugs can cross → effect n fetus.

# COMMON TERATOGENS



# Effects of Teratogens on the Fetus

- *Spontaneous abortion*
- *Malformations (major or minor)*
- *Intrauterine growth retardation*
- *Mental retardation*
- *Carcinogenesis*
- *Mutagenesis (causing genetic mutation)*

# Factors That Determine the Effects of Teratogens

- ▶ *Dose reaching fetus*
- ▶ *Time of pregnancy during which drug exposure occurs*
- ▶ *Duration of exposure*

# Effect of drugs on fetus during pregnancy

▶ Fertilization & implantation

conception to 17 days- Failure of pregnancy

▶ Organogenesis

18 to 55 days- Congenital malformations

▶ Growth & development

56 days onwards-Developmental & functional abnormalities.

Most  
vulnerable  
period

# THALIDOMIDE

**PHOCOMELIA** : 'seal limbs'

Consists of an absence of development of the long bones of the arms and legs



- ▶ Tetracyclines → staining of teeth
- ▶ Androgens → masculinisation of female fetus
- ▶ Lithium → Ebstein's anomaly
- ▶ Phenytoin → Fetal Hydantoin syndrome
- ▶ Alcohol → Fetal Alcohol syndrome
- ▶ Valproate → Neural tube defects



# PHENYTOIN

- ▶ Cleft lip/palate
- ▶ Microcephaly
- ▶ Mental retardation



# VALPROATE- NEURAL TUBE DEFECTS



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# ISOTRETINOIN

Mental retardation and learning disabilities

Eye & ear deformities

Cleft lip, cleft palate & other facial abnormalities

Heart defects

Microcephaly & Hydrocephaly

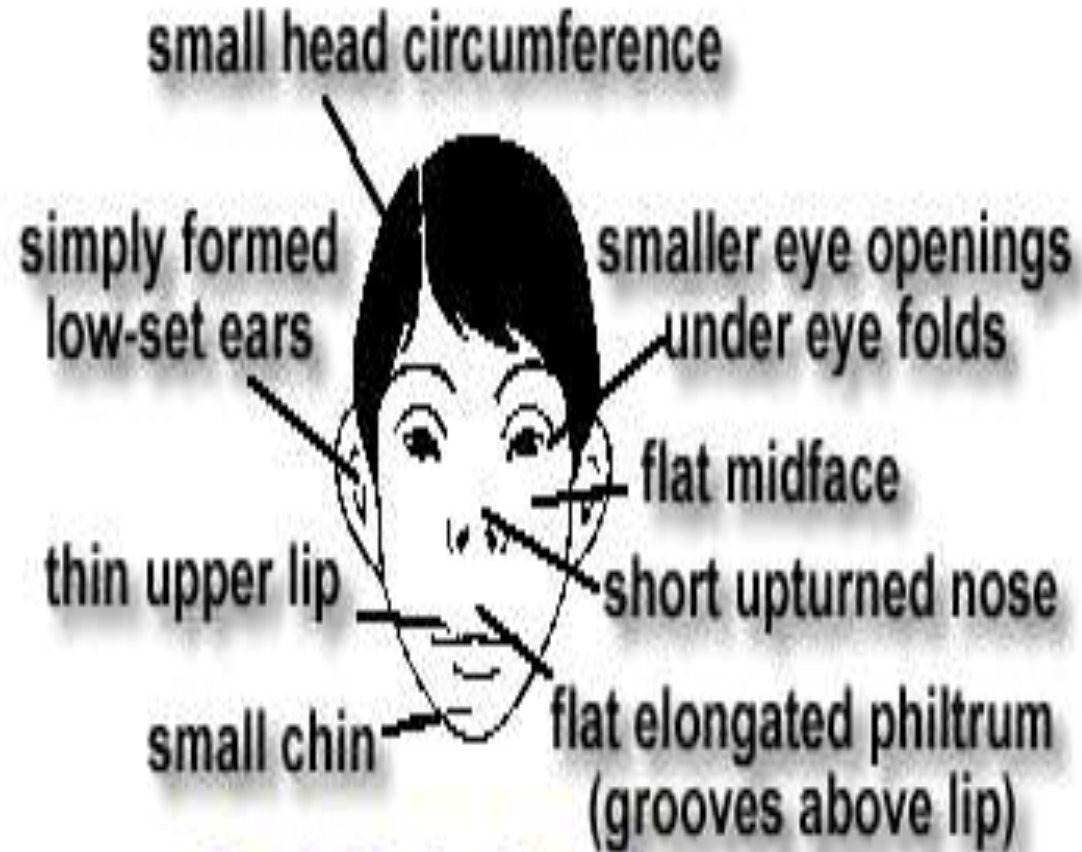


Alterations due to fetal exposure to isotretinoin (Schardein 1993).

# FETAL ALCOHOL SYNDROME



Normal



Fetal Alcohol Syndrome

# FETAL WARFARIN SYNDROME

- Saddle nose
- Retarded growth
- Defects of limbs, eyes and central nervous system



## Tetracycline- Teeth and bone damage

- ▶ Yellow staining
- ▶ Enamel hypoplasia
- ▶ Caries and pigmentation
- ▶ of permanent teeth



# United States FDA

## Pharmaceutical Pregnancy Categories

<i>A</i>	<i>Controlled human studies show no risk</i>	<i>Inj MgSO<sub>4</sub> Thyroxine</i>
<i>B</i>	<i>No confirmatory evidence of risk in humans</i>	<i>Penicillin Paracetamol</i>
<i>C</i>	<i>Risk cannot be ruled out</i>	<i>Morphine codiene</i>
<i>D</i>	<i>Positive evidence of risk</i>	<i>Phenytoin valproate</i>
<i>X</i>	<i>Contraindicated in pregnancy</i>	<i>isotretinoin</i>



## Counseling women about teratogenic risk

- ▶ The baseline teratogenic risk in pregnancy (ie, even in the absence of any known teratogenic exposure) → about 3%.
- ▶ It is also critical to address the maternal-fetal risks of the untreated condition if a medication is avoided.



# Summary

- ▶ Pharmacogenetics is the study of variation in drug response due to genetic variation
- ▶ Genetic variations can lead to decreased drug response or enhanced toxicity
- ▶ So study of Pharmacogenetics is important
- ▶ Teratogenicity- Fetal abnormalities caused by exogenous agents
- ▶ Most vulnerable period- organogenesis
- ▶ Patient education and Proper selection of drugs

# Personalized Medicine

*(Individualized therapy)*

Science concerned with providing medical care based the genomic and molecular profile of the individual patient

Patient requires Treatment

Examination by the Physician

Genomic testing

Traditional investigations

EXPERT SYSTEM

Decision making by Physician, assisted by an Expert System  
(interactive interpretation)

Prescribes individualized drug treatment



Here is my sequence



"Oh! he is a poor metabolizer"



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**Doctors will be able to select the best drug to treat the disease and the appropriate dose based on knowledge of patients specific genetic makeup!**

**Is personalized medicine  
finally arriving?**

# Economic impact on patients...

