

Primary prevention of congenital disorders

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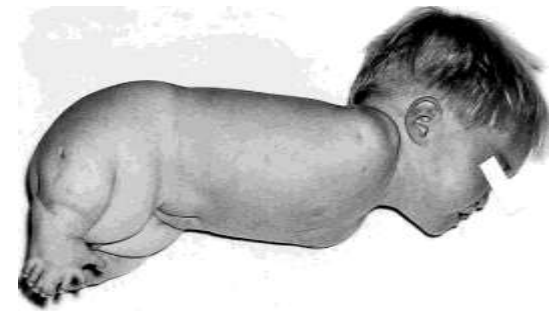
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Birth defects (Congenital Disorders)

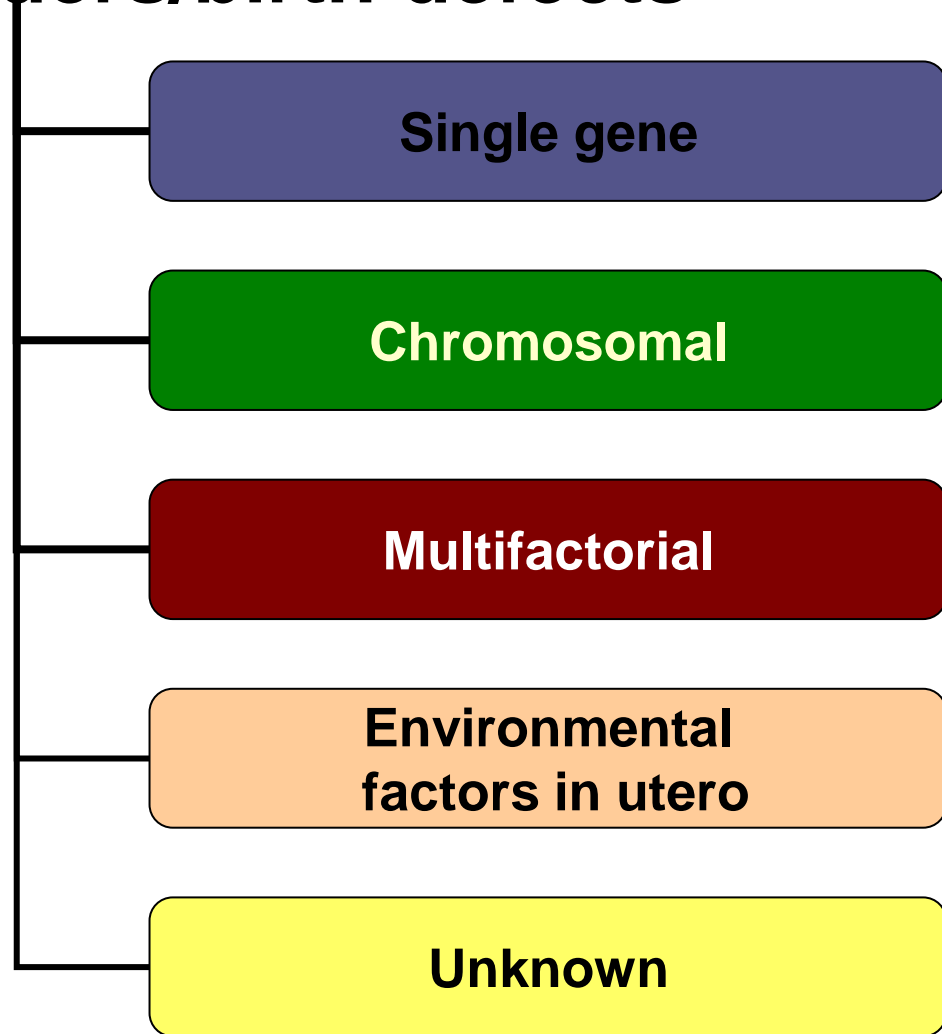
- Congenital disorder or Birth defect includes any morphological (structural), functional and biochemical-molecular defect that may develop in the embryo and fetus from conception until birth, whether detected at birth or later.

Categories of Congenital Disorders

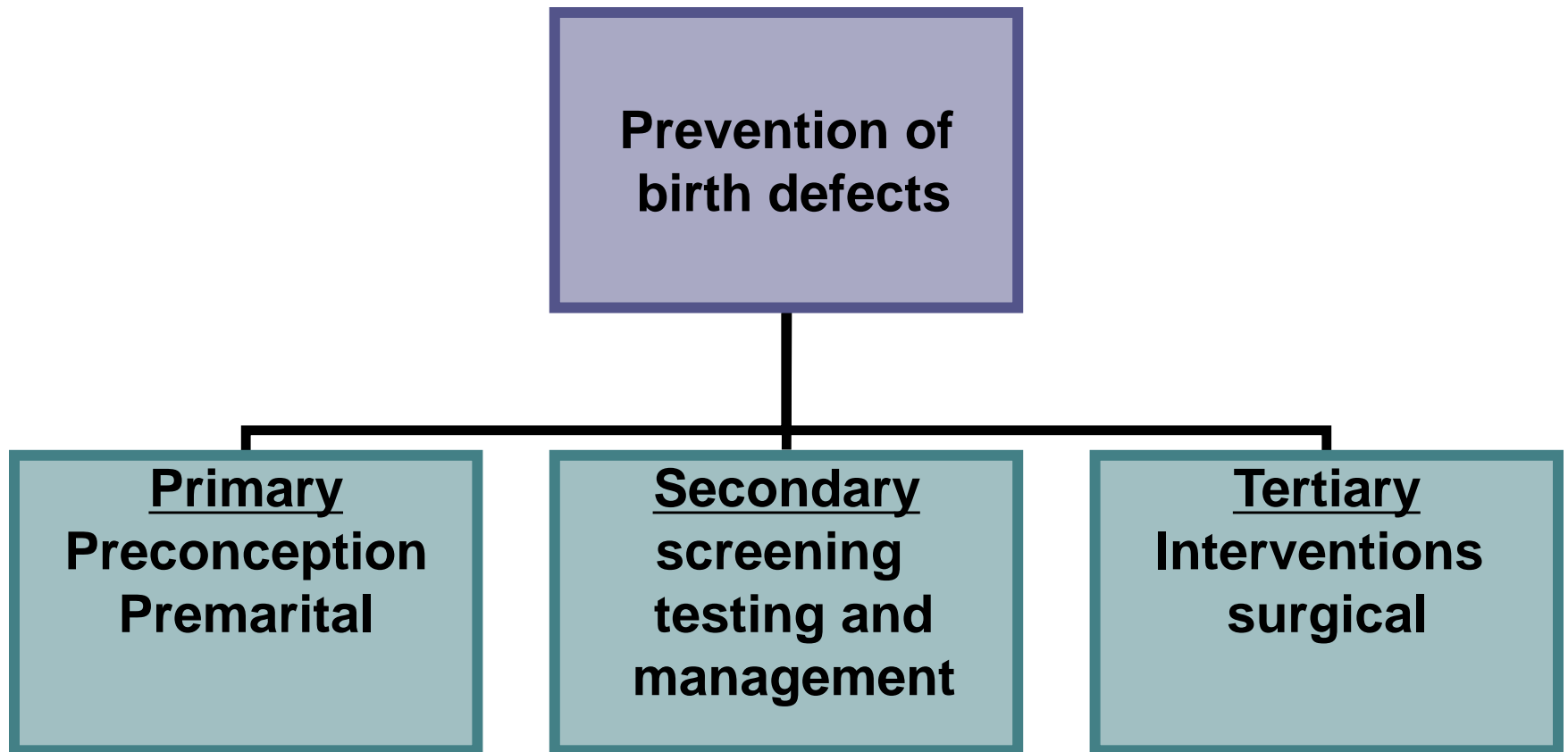
1. Congenital malformations (structural defects).
2. Genetic disease (chromosome or single gene abnormality).
3. Intrauterine infections as toxoplasmosis and exposure to teratogenic drugs.



Underlying etiology of Congenital disorders/birth defects



About 70% of birth defects are preventable



The 4 most serious and prevalent congenital disorders are:

- Hemoglobin disorders (thalassemias and sickle cell anemia) and G6PD deficiency.
- Down syndrome.
- Neural tube defects.
- Congenital heart defects.

Pre and Peri-conception counseling

Includes information that can be given in the preconception period to the couple planning to have a baby.

Objectives of Preconception counseling

- Reducing disorders related to advanced parental age such as Down syndrome, and autosomal dominant disorders due to new dominant mutation.
- Reducing the occurrence of congenital abnormalities such as neural tube defects related to folate deficiency, and mental deficiency due to iodine deficiency, by promoting healthy nutrition for women of reproductive age.
- Reducing the occurrence of hereditary disorders in high risk families through genetic counseling.

Objectives of Preconception counseling

- Providing information on the implications and availability of carrier screening and testing for common disorders such as the hemoglobinopathies and G6PD deficiency.
- Preventing congenital rubella syndrome by immunization.
- Reducing mortality and chronic handicap due to rhesus hemolytic disease through routine prenatal screening.

Objectives of Preconception counseling

- Reducing congenital abnormalities and stillbirths by better control of maternal diabetes prior to and during pregnancy.
- Reducing the risk of miscarriage, congenital abnormality and fetal growth retardation through avoidance of smoking during pregnancy.
- Avoiding congenital abnormalities caused by certain infections such as syphilis and toxoplasmosis, through prevention, early detection and prompt treatment.
- Minimizing exposure to industrial and domestic teratogens before and during pregnancy.

Preconception counseling to maximize the chances of a couple to have a healthy baby would include

1. Preconception nutritional supplementation for example proper intake of folic acid can minimize the risks for neural tube and other defects.
2. Prevention and treatment of maternal infections (Rubella, TORCH, Syphilis).
3. Diagnosis of maternal Rh status.
4. Information on risks of advanced maternal age at conception.
5. Avoidance of teratogenic drugs and chemicals.
6. Cessation of smoking and alcohol intake.
7. Family planning.
8. Monitoring of maternal health before and during pregnancy (diabetes, hypertension, epilepsy, hyperthermia).

Folic acid has been a major success story. Food fortification with folic acid is one of very few modalities that can actually prevent a serious birth defect. Much more needs to be learned about the other benefits and risks associated with food fortification with folic acid.

Premarital screening and counseling

- Premarital counseling for consanguinity.
- Premarital screening for carriers of common autosomal recessive disorders in the population, for example beta thalassemia.

Premarital counseling for consanguinity

Detailed family history
and specific questions

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graph TD; A[Detailed family history and specific questions] --> B[No genetic disease]; A --> C[Genetic disease present]; B --> D[Risk of congenital malformations about 2% higher than the population risk]; C --> E[Refer to specialist counselor];
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No genetic
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Risk of congenital
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Genetic disease
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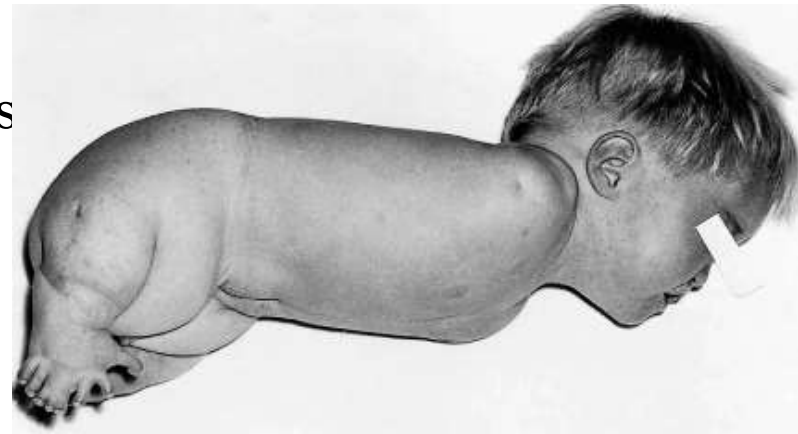
Refer to
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Teratogens

A teratogen is an environmental agent affecting the fetus in utero and may cause a birth defect by interfering with normal embryonic or fetal development.

Thalidomide

- Thalidomide was used widely in Europe during the years 1958 to 1962 as a sedative. In 1961 an association with severe limb anomalies in babies whose mothers had taken the drug during the first trimester was recognized and the drug was subsequently withdrawn from use. It has been estimated that during this short period over 10 000 babies were damaged by this drug. Review of these babies' records indicated that the critical period for fetal damage was between 20 and 35 days from conception, i.e. 34-50 days after the beginning of the last menstrual period.



Anticonvulsant drugs

Potential fetal effects of anticonvulsant drugs could include:

- Major malformations: The range of effects has been a doubling (for drugs like carbamazepine, phenytoin and lamotrigine) to a 4- to 6-fold increase (for phenobarbital and valproate) in congenital malformations.
- Specific malformations that are more common include cleft lip, cleft palate, heart defects, and spina bifida.

Fetal Alcohol syndrome

- Children born to mothers who have consistently consumed large quantities of alcohol during pregnancy tend to show a distinctive facial appearance, with short palpebral fissures (eye apertures) and a long smooth philtrum (upper lip). They also show mild developmental delay and are often hyperactive and clumsy in later childhood. This condition is referred to as the fetal alcohol syndrome. There is uncertainty about the level of alcohol consumption that is 'safe' in pregnancy and there is evidence that even mild-to-moderate ingestion can be harmful. Generally, it is advised that all women should try to abstain from alcohol intake completely throughout pregnancy.

Examples of agents with a proven teratogenic effect in humans

Agent	Effect
• ACE inhibitors	Renal dysplasia
• Alcohol	Cardiac defects, microcephaly, characteristic facies
• Chloroquine	Chorioretinitis, deafness
• Diethylstilbestrol	Uterine malformations, vaginal adenocarcinoma
• Lithium	Cardiac defects (Ebstein's anomaly)
• Phenytoin	Cardiac defects, cleft palate, digital hypoplasia
• Retinoids	Ear and eye defects, hydrocephalus
• Streptomycin	Deafness
• Tetracycline	Dental enamel hypoplasia
• Thalidomide	Phocomelia, cardiac and ear abnormalities
• Valproic acid	Neural tube defects, characteristic facies
• Warfarin	Nasal hypoplasia, stippled epiphyses

Maternal Infections

Several infectious agents can interfere with embryogenesis and fetal development. The developing brain, eyes and ears are particularly susceptible to damage by infection.

Teratogenic infections

- Most infections that a woman contracts during pregnancy do not harm the developing embryo or fetus. However, a few infectious diseases can kill an embryo, fetus, or newborn, cause birth defects, trigger a premature delivery, or inhibit fetal growth.
- Only eight infectious agents are generally considered to increase the risk of birth defects in humans.
- These include six viruses: **the rubella virus, Venezuelan equine encephalitis virus, cytomegalovirus, varicella zoster virus, herpes simplex viruses, and lymphocytic choriomeningitis virus;**
- one bacterium, **Treponema pallidum;**
- one protozoal parasite, **Toxoplasma gondii.**

Infectious teratogenic agents

Viruses

- Cytomegalovirus: The risk of abnormality is greatest if infection occurs during the first trimester. Overall this virus causes damage in only 5% of infected pregnancies. Effects include chorioretinitis, deafness, microcephaly.
- Herpes simplex teratogenic effect could include microcephaly, microphthalmia.

Infectious teratogenic agents

Viruses

- Varicella zoster teratogenic effects could be microcephaly, chorioretinitis, skin defects.
- The rubella virus, which damages between 15% and 25% of all babies infected during the first trimester, also causes cardiovascular malformations such as patent ductus arteriosus and peripheral pulmonary artery stenosis. Congenital rubella infection can be prevented by the widespread use of immunization programs based on administration of either the measles, mumps, rubella (MMR) vaccine in early childhood or the rubella vaccine alone to young adult women.

Infectious teratogenic agents

Bacteria

- Syphilis: congenital syphilis may include hydrocephalus, osteitis, rhinitis

Parasites

- Toxoplasmosis teratogenic effects may include hydrocephalus, microcephaly, cataracts, chorioretinitis, deafness. The highest risk for severe effects occurs with maternal infection between 10 and 24 weeks of gestation. Up to 40 percent of fetuses infected during the first trimester of pregnancy develop severe effects.

Teratogenic Physical agents

Ionizing radiation

- Diagnostic radiological studies (less than 0.1 Gy, or 10 rad) that do not expose the embryo (on the head, neck, chest or extremities) will not increase the risk for birth defects or miscarriage above the background risk of 3% for birth defects and 15% for miscarriage (Teratology Primer 2010).
- Exposure of human fetus to high doses (1–2 Gy) of ionizing radiation can result in mental retardation and microcephaly. The most vulnerable stage for the induction of mental retardation and severe microcephaly is reported to be from the 8th to 15th week of human gestation.

Teratogenic Physical agents

Prolonged hyperthermia

There is evidence that prolonged hyperthermia in early pregnancy can cause microcephaly and microphthalmia as well as neuronal migration defects. Consequently it is recommended that care should be taken to avoid excessive use of hot baths and saunas during the first trimester.

Maternal Illness

Diabetes mellitus

Maternal insulin-dependent diabetes mellitus is associated with a two- to threefold increase in the incidence of congenital abnormalities in offspring. Malformations which occur most commonly in such infants include congenital heart disease, neural tube defects, sacral agenesis, femoral hypoplasia, holoprosencephaly and sirenomelia ('mermaidism'). The likelihood of an abnormality is inversely related to the quality of the control of the mother's blood glucose levels during early pregnancy. This can be assessed by regular monitoring of blood glucose and glycosylated hemoglobin levels. Non-insulin-dependent diabetes and gestational diabetes do not convey an increased risk for congenital malformations in offspring.

Population screening programs for the prevention of congenital disorders



- Newborn screening for hypothyroidism, phenylketonuria, G6PD deficiency and other disorders.
- Prenatal screening for Down syndrome, neural tube defects and major malformations.

Conclusions

Community genetic services should be integrated into primary health care systems

- Preconception counseling and care
- Screening programmes
- Management for affected children