

Drugs & Vaccines in Pregnancy & Lactation

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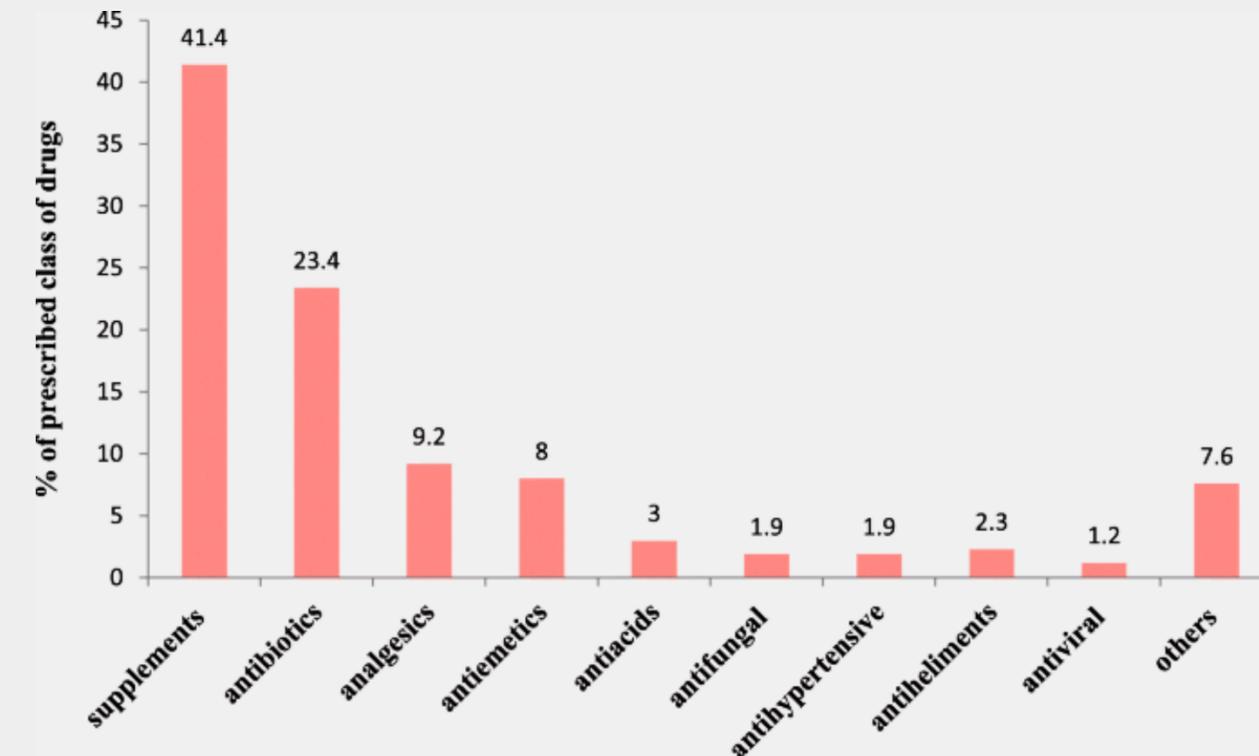
Introduction

Drugs uptake during pregnancy and lactation is of important significance because of its toxic effect on the **developing fetus** .

Using of drugs responsible 3-5% of live births are complicated by a birth defect each year.

65% and 94% of women take at least one prescription drug during pregnancy.

Substances abuse, alcohol, and certain medications during pregnancy can increase risks such as preterm labor, low birth weight , and neonatal withdrawal.



Maternal Physiological Changes in Pregnancy.

Absorption

- **Change:** ↓ GI motility, delayed gastric emptying, ↑ gastric pH
- **Why?** Progesterone relaxes smooth muscle → slower digestion
- **Effect:**
Slower onset of action for many oral drugs
Reduced absorption of **weak acids** (e.g., aspirin) due to ↑ pH
Clinical Tip: Consider **delayed peak effect of oral medications.**

Distribution

- **Change:** ↑ Plasma volume (~30–50%), ↑ body fat, ↓ albumin
- **Why?** Expanding circulatory needs for fetus and placenta
- **Effect:**
↓ plasma concentration of **hydrophilic drugs**
↑ storage of **lipophilic drugs** in fat
↑ free (active) drug levels of **protein-bound drugs** (e.g., phenytoin)
Clinical Tip: **Monitor** free drug levels when protein binding is critical.

Maternal Physiological changes in Pregnancy.

Metabolism

- **Change:** Altered hepatic enzyme activity (CYP450 enzymes)
- **Why?** Hormonal changes affect liver enzyme expression
- **Effect:**
 - ↑ metabolism of some drugs (e.g., phenytoin, caffeine via CYP3A4)
 - ↓ metabolism of others (e.g., theophylline via CYP1A2)

Clinical Tip: **Adjust dosing** based on whether the drug is inactivated or activated by hepatic metabolism

Elimination

- **Change:** ↑ Renal blood flow and glomerular filtration rate (GFR)
- **Why?** Kidneys adapt to increased waste clearance
- **Effect:**
 - ↑ renal clearance → ↓ drug half-life (e.g., lithium, ampicillin, digoxin)

Clinical Tip: May need more **frequent** dosing for renally-cleared drugs.

Increase sensitivity to volatile anesthetics, IV , and local anesthetics., decreased MAC, with faster absorption and Rapid onset of action, he required dose is reduced.

Placental Role

Most drugs cross the placenta by **simple diffusion**; however, Plasma membrane carriers, biotransforming enzymes, and export pumps also play a role.

The placenta functions fully for transport by the **fifth week** of gestation, Before this, diffusion occurs but **capacity is limited**.



Type of drug transfer across the placenta are recognized:

1. Complete transfer (type 1 drugs):

for example, thiopental

Drugs exhibiting this type of transfer will rapidly cross the placenta with pharmacologically significant concentrations **equilibrating** in maternal and fetal blood.

2. Exceeding transfer (type 2 drugs):

for example, ketamine

These drugs cross the placenta to reach **greater concentrations in fetal** compared with maternal blood.

3. Incomplete transfer (type 3 drugs):

for example, succinylcholine

These drugs are **unable** to cross the placenta completely, resulting in **higher concentrations in maternal** compared with fetal blood

Factors affecting placental drug transfer

Lipid solubility:

Lipid soluble drugs **diffuse** readily and enter the fetal circulation, e.g. thiopental

Molecular weight :

Molecular weight (M.W) influences rate of transfer and amount of drug transferred across placenta Drugs

< 500 Dalton → cross easily.

e.g. 1000 Dalton → do not cross (e.g., Heparin, Insulin)

Blood flow:

Increased during pregnancy

For lipophilic drugs, transfer rate is determined largely by placental blood flow.

Protein binding:

During pregnancy, **lower maternal albumin** increases unbound drug levels, allowing more drug to cross the placenta.

E.g. drugs highly protein bound are: propranolol, salicylate, diazepam

Effect of pH:

Fetal blood is **more acid** (pH=7.3) than maternal blood (pH=7.4)

Weakly acidic and weakly basic drugs tend to rapidly diffuse across the placental membrane

Highly ionized drugs e.g. succinylcholine and tubocurarine, cross placenta slowly

Teratogenic effect of drug :

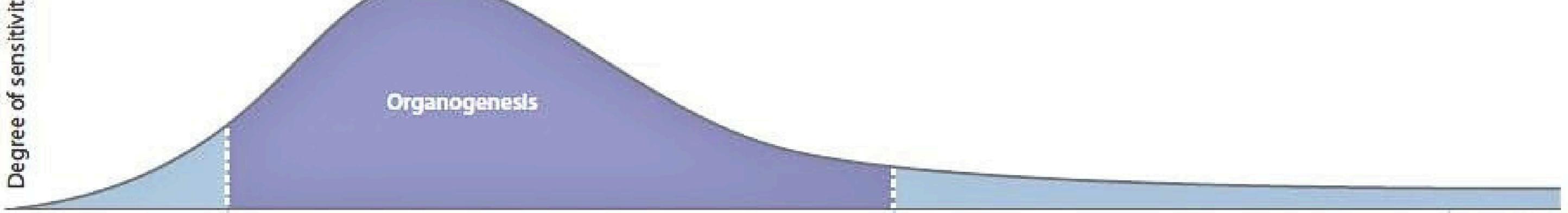
Teratogen : any agent that result in structural or functional abnormalities in the fetus , or in child after birth , as a consequence of maternal exposure during pregnancy.

Teratogenic effects include: loss of pregnancy, structural abnormalities, growth impairment, functional loss and behavioural changes

Teratogenicity risk is determined largely by **TIMING** of drug exposure :

- **first trimester** drugs may produce **congenital or stru abnormalities** (teratogenesis) greatest risk is from **3-12th week**
- **second and third trimesters** drugs may affect **growth and functional development** of the fetus (e.g. brain development)

- Embryo is most vulnerable to teratogens during periods of rapid cell division, especially from 3 to 16 weeks for brain development.
- During the first two weeks of gestation, teratogenic agents usually **kill the embryo** , it is called **All or non period**.
- Embryonic stage 3-8 weeks post-conception so exposure in this time represents the greatest risk of **major birth defect**.
- During organogenesis between days 15 to 60, teratogenic agents are more likely to cause **major congenital malformations**.
- For this reason , women are often advised to avoid or minimize all drug use in the first trimester .
- After 8 weeks , most teratogenicity effect are related to **fetal growth restrictions or functions deficits** such as mental retardation



Period of dividing zygote, implantation, and embryo, weeks

Embryonic period, weeks

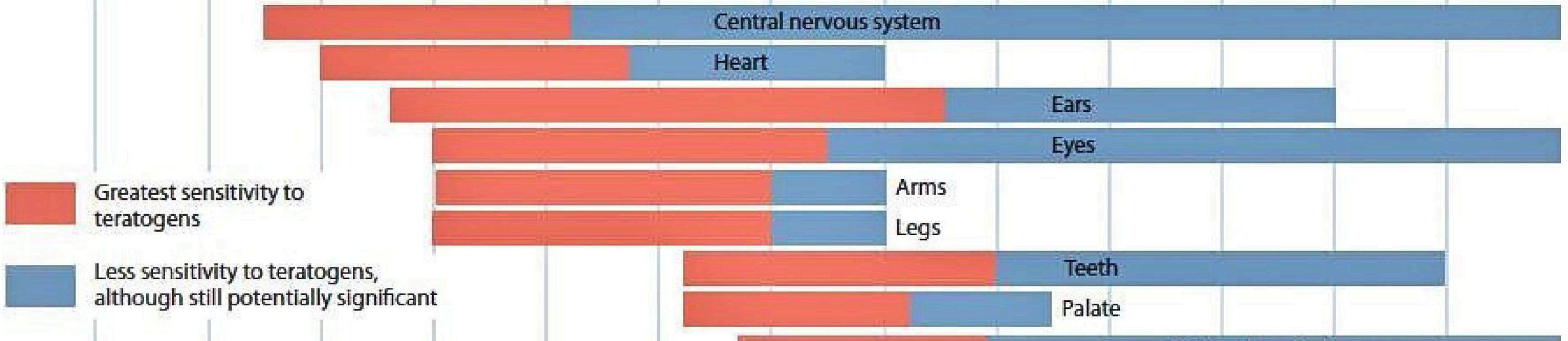
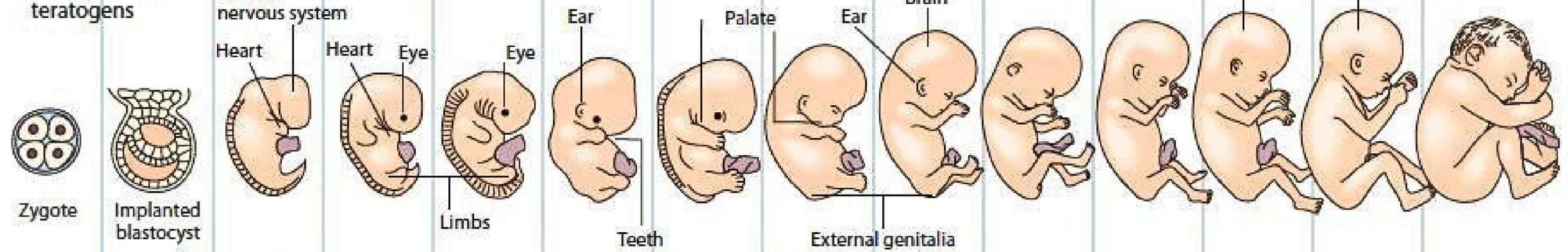
Fetal period, weeks

Full term

1 2 3 4 5 6 7 8 9 10 11 16 20-36 38

Usually not susceptible to teratogens

Common site of action of teratogen



■ Greatest sensitivity to teratogens

■ Less sensitivity to teratogens, although still potentially significant

FDA classifies

The Food and Drug Administration (FDA) classified every medication is into one of the **Five category (A,B,C,D,X)**

Based on how **safe or risk** to use during pregnancy and the **type and adequacy of studies** which is done.

Category A :

- adequate and well controlled studies
- Safe in the first trimester and later trimesters.
- **Levothyroxine, Folic acid**

Category B :

- Generally safe on the basis of animal studies with no controlled study in pregnant women with no evidence of risk

OR

• animal studies have shown an adverse effect which was not confirmed in controlled studies in women in the first trimester and there is no evidence of risk to the fetus in later trimesters

- **Ampicillin, Amoxicillin, Cephalosporins, Prenatal vitamins, Metronidazole, Macrolides, Acyclovir, Paracetamol, Metformin, Insulin**

Category C :

- Studies in women and animals are not available.

OR

- studies in animals have shown adverse effects on the fetus and there is no controlled study in women
- Risk not ruled out benefits outweigh the risks, but use with caution.
- **Fluoroquinolones, Gentamicin, Fluconazole**

Category D :

- There is positive evidence of risk to the human fetus (unsafe)
- Should not be used unless there are no better alternatives in a life- threatening illness
- Benefits outweigh the risks in the serious conditions.
- **Tetracycline, ACE inhibitors, Losartan (ARBs), Sulfa drugs, Anticonvulsants, Warfarin**

Category X :

- Highly unsafe risk of use outweighs any potential benefit .
- Drugs in this category are contraindicated in pregnant women or in a woman who may become pregnant.
- **Isotretinoin, Thalidomide, Ribavirin, Statins**

Drug ratings in pregnancy (US Food and Drug Administration)

Category	Interpretation
A	<p>Controlled human studies show no risk</p> <p>Controlled studies in pregnant women fail to demonstrate a risk to the fetus in the first trimester with no evidence of risk in later trimesters. The possibility of fetal harm appears remote.</p>
B	<p>No evidence of risk in studies</p> <p>Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester and there is no evidence of a risk in later trimesters.</p>
C	<p>Risk cannot be ruled out</p> <p>Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal effects or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus.</p>
D	<p>Positive evidence of risk</p> <p>There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).</p>
X	<p>Contraindicated in pregnancy</p> <p>Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.</p>

ANTIBIOTICS

1- Aminoglycosides (Amikacin, Gentamycin, Kanamycin, , Neomycin, and Streptomycin) : category D

effect: congenital deafness (Ototoxicity) & nephrotoxicity. 2- Penicillin : Category : B

Effects: here is a risk of premature labour & or fetal distress for women taking the drug in the 2nd half of pregnancy (due to Jarisch-Herxheimer reaction)

3-Cephalosporin : Category B 4-Metronidazole : Category B.

5-Macrolides (Azithromycin , Clarithromycin , Erythromycin): Category B.

6 -Fluorquinolones : Category C which Not recommended / May be harmful

7-Tetracyclines : Category D

Readily cross the placenta and are firmly bound by chelation to calcium in developing bone and tooth structures.

This produces cause permanent brown discoloration of the teeth and inhibition of bone growth.

What is a Jarisch-Herxheimer Reaction?

- **Jarisch-Herxheimer Reaction**

- Release of **Endotoxins**, as well as **Inflammatory Cytokines** from reaction to microbial waste & cell death.



- **Potential Symptoms:**

- Flu-like symptoms
- Achiness
- Headache
- Mental Fog
- Skin Rash
- Loose stools
- Fatigue
- Fever
- Sweating
- Chills

Anti fungal

Flucanazole and other azole :

Pregnancy category - C (single dose); D (multiple doses)

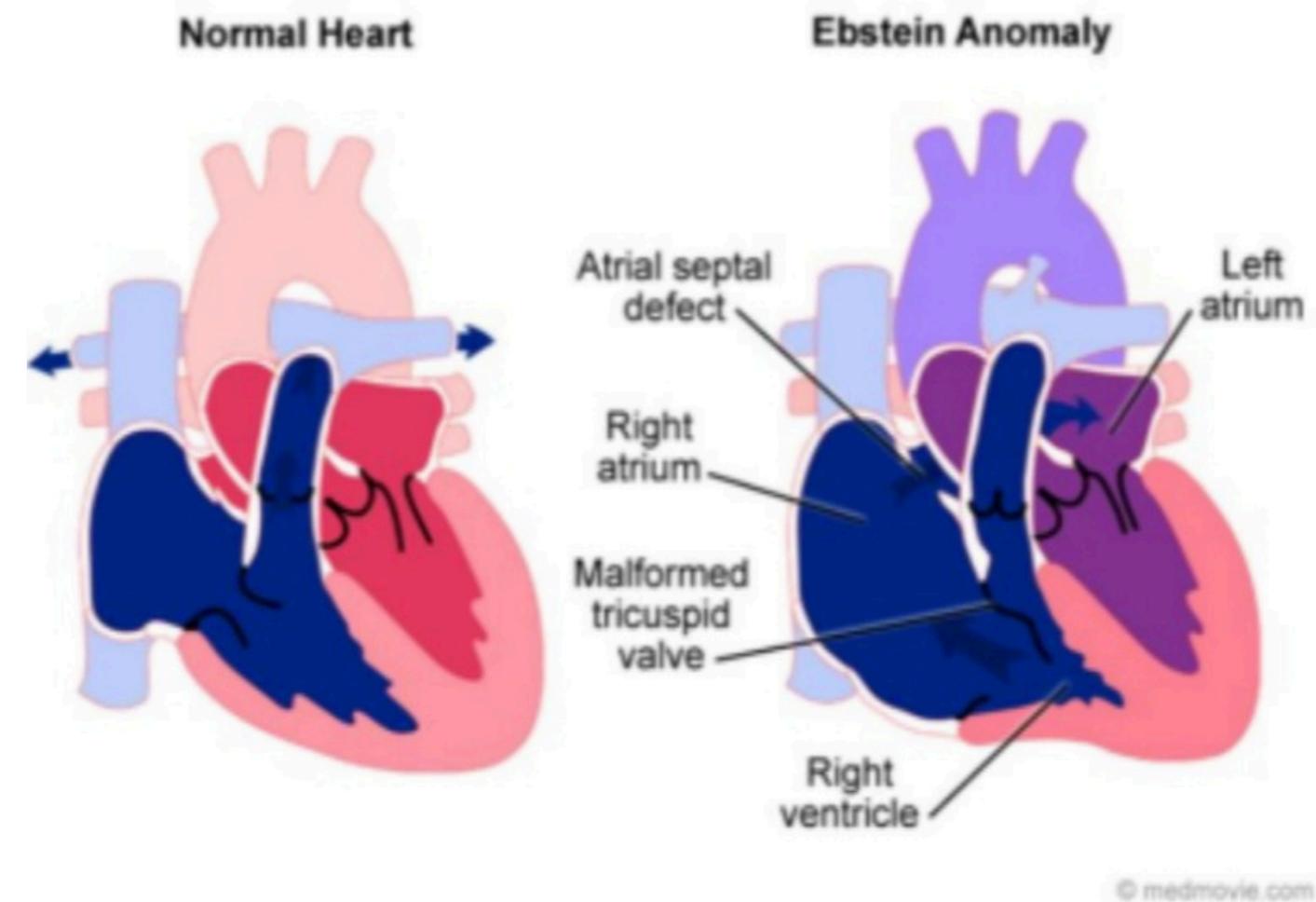
Considerd as a toxic medications, and their use in pregnancy has been limited to life-threatening fungal infections !! As Craniofacial, skeletal, and cardiac defects .

LITHIUM

- Pregnancy category - D.
Effect: cardiac effects, especially **Ebstein's anomaly**,

Others include; Nappy baby syndrome,, hypoglycemia, cardiac arrhythmias, thyroid dysfunction, and premature delivery

Ebstein anomaly is characterized by a severely malformed and displaced tricuspid valve. This results in regurgitation, or leakage, of blood backwards from the right ventricle into the right atrium. This syndrome also includes an opening in the septum between the atria (ASD). The ASD allows oxygen-poor blood to flow from the right atrium into oxygen-rich blood of the left atrium, causing cyanosis (blueness of the skin).



NSAIDS

- 1- aspirin Full dose Aspirin : category D (avoided)
- Low dose aspirin 75mg : category C (safe)
- Maternal ingestion of aspirin in the Third trimester was related to closure of the ductus arteriosus .
- 2-Acetaminophen category B
- Increased risk of teratogenic effects NOT reported following maternal use of drug during pregnancy.
- 3-Other NSAIDs are considered safe (Ibuprofen, indomethacin, diclofenac , Naproxen) during the first trimester (category B),BUT are contraindicated in the third trimester (category D) , because they promote premature closure of the ductus arteriosus, leading to fetal pulmonary hypertension

Anti-neoplastic

(busulfan, chlorambucil, cyclophosphamide, mechlorethamine)

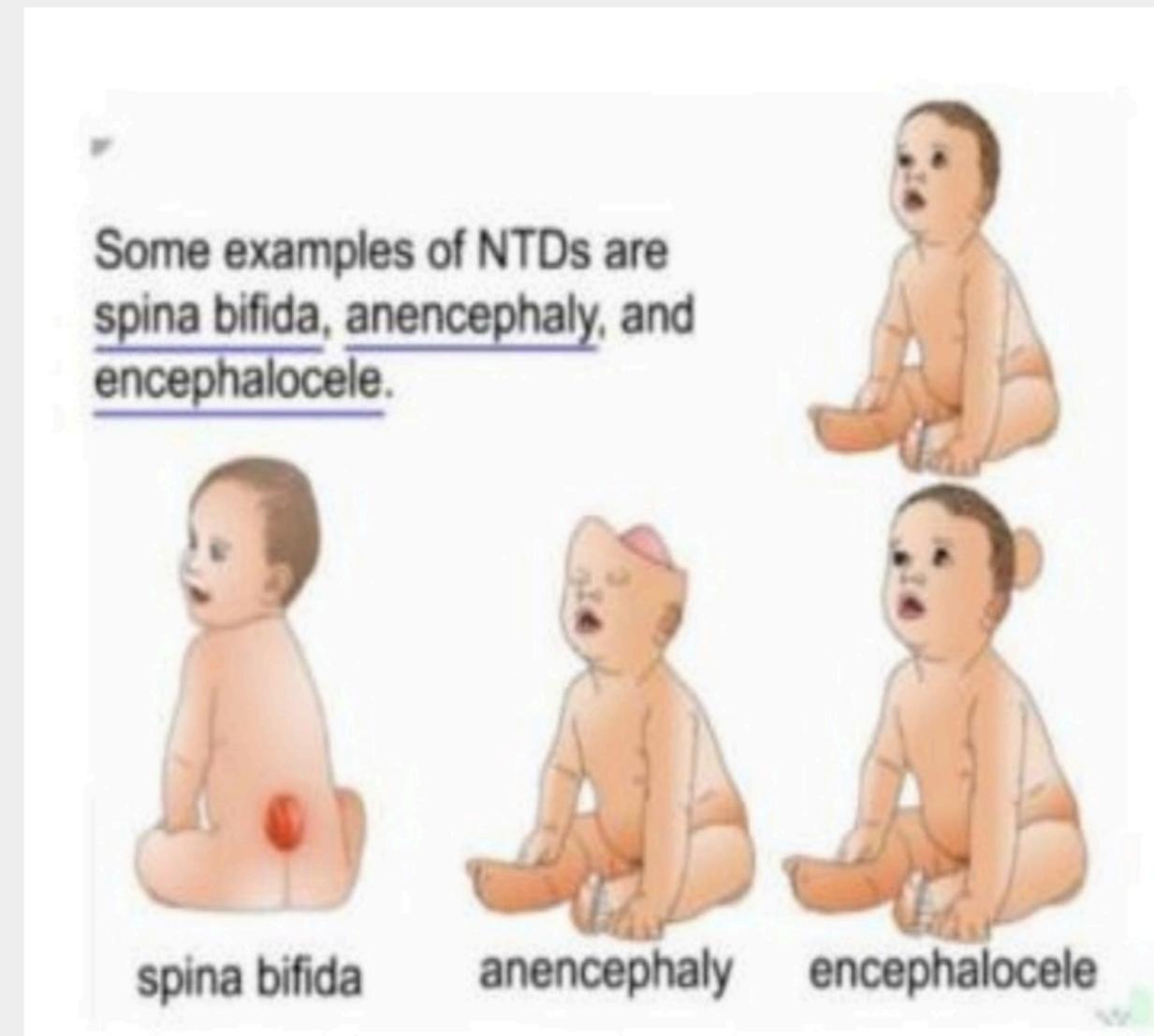
Pregnancy category; D&X

Observed problems included IUGR, cleft palate, renal agenesis, digital malformations, cardiac anomalies, and cloudy corneas. First-trimester exposure to antimetabolites (aminopterin, 5-fluorouracil, methotrexate, methylaminopterin, and cytarabine) produced a risk for cleft lip and palate, low-set ears & NTDs .

- . Cyclosporine : Category C Widely used in organ transplantation, harmful effects on the human fetus But without causing malformations
- . Hydroxychloroquine : safe/can be used once indicated

FOLIC ACID ANTAGONISTS (MTX)

- Category X
- Effect: Methotrexate(MTX) is a folate antagonist with known teratogenicity including abortifacient effects that interfere with DNA synthesis. Also, it is associated with NTDs .



ANTICONVULSANTS

- Phenytoin, Valproic Acid , Carbamazepine ... (Category D)
- Effects : Facial dysmorphism, gingival hyperplasia, neurological hyperexcitability and multiple malformations including (for valproic acid) predominantly temporal atrophy in the left brain hemisphere & NTDs (Lumbosacral spina bifida with meningocele or meningocele, often accompanied by midfacial hypoplasia, deficient orbital ridge, prominent forehead, congenital heart disease, and decreased postnatal growth) .

ANTICOAGULANTS

Warfarin : Pregnancy category - X



Fetal warfarin syndrome (warfarin embryopathy) ; include :
low birth weight , mental retardation, deafness, Microcephaly, Nasal hypoplasia,
malformed bones, cartilage, and joints.

Heparin: **Pregnancy category -B** (does not cross the placenta , because it is a
large molecule with a strong negative charge). So, it's the drug of choice for
patients requiring anticoagulation.

THYROID AND ANTITHYROID DRUG

- 1-Thyroxin (category A): doesn't cross the placenta to any extent (dose), so it not associated with congenital anomalies ,(safe during pregnancy) .
- 2-Propylthiouracil (PTU) and carbimazole : (category D)
- both cross the placenta and may cause fetal hypothyroidism and so some degree of fetal goiter !
- -(PTU) is the preferred antithyroid drug Because treatment with carbimazole during the first trimester has been associated with the occurrence of choanal atresia and aplasia cutis .
- -BUT , Hyperthyroid women who become pregnant while taking carbimazole or PTU should be advised to continue their current drug in pregnancy

CVS MEDICATIONS

- 1- HYPERTENSION
- -ARBs, ACE inhibitors are cat (C/D).
- -Renal dysgenesis or death (if used in 2nd & 3rd trimesters)
- -Increased risk of cardiovascular and CNS malformations when used in the first trimester
- -Diuretics avoided in pregnancy, as they prevent the physiologic volume expansion (prevent increasing in plasma volume)

- 2- Valvular heart diseases:
 - -hydralazine, digoxin, adenosine, and procainamide can be safely used in pregnancy.
 - -Amiodarone cat (D), and nitroprusside cat (C) are contraindicated during pregnancy regardless of the indication.
- 3- Coronary Artery Disease
 - -Low-dose aspirin is safe but prolonged use of 100 mg aspirin can cause increased maternal bleeding complications and low birth weight.
 - -Beta-blockers are safe in pregnancy { Atenolol cat D while Metoprolol, Nadolol, Propranolol and Timolol are cat C (D at term or prolonged use)}
 - -Nitrates and calcium channel blockers should be used with caution to avoid maternal hypotension.

CORTICOSTEROIDS

- Category c: a five-fold increased risk for cleft lip with or without cleft palate in the infant has been reported after exposure to steroids in the first trimester.
- All steroids cross the placenta to some degree, but prednisone and prednisolone are inactivated by the placenta. Therefore, these agents are the drugs of choice for treating medical diseases such as asthma.
- Inhaled corticosteroids also are effective therapy, and little of the drug is absorbed into the placenta.
- When steroid effects are desired in the fetus, for example, to accelerate lung maturity, betamethasone and dexamethasone are preferred.

Retinoid's (vitamin A related compounds)

- MOST IMPORTANT COMPOUNDS ARE ISOTRETINOIN AND ETRETINATE
ISOTRETINOIDS ARE FIRST GENERATION RETINOIDS AND THEY ARE USED FOR ACNE .
- ETRETINATE ARE SECOND GENERATION RETINOIDS AND THEY ARE USED FOR PSORIASIS
- THEY ARE IN CATEGORY X IN FDA CLASSIFICATION

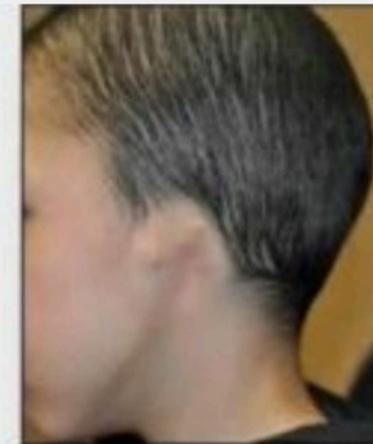
Fetal anomalies reported to be associated with maternal isotretinoin use:

- Microtia/Anotia
- Micrognathia/Cleft palate
- Heart defects
- Eye anomalies
- Brain anomalies/Hydrocephalus
- Thymic agenesis

May also cause spontaneous abortions



Microtia
Underdeveloped external ear

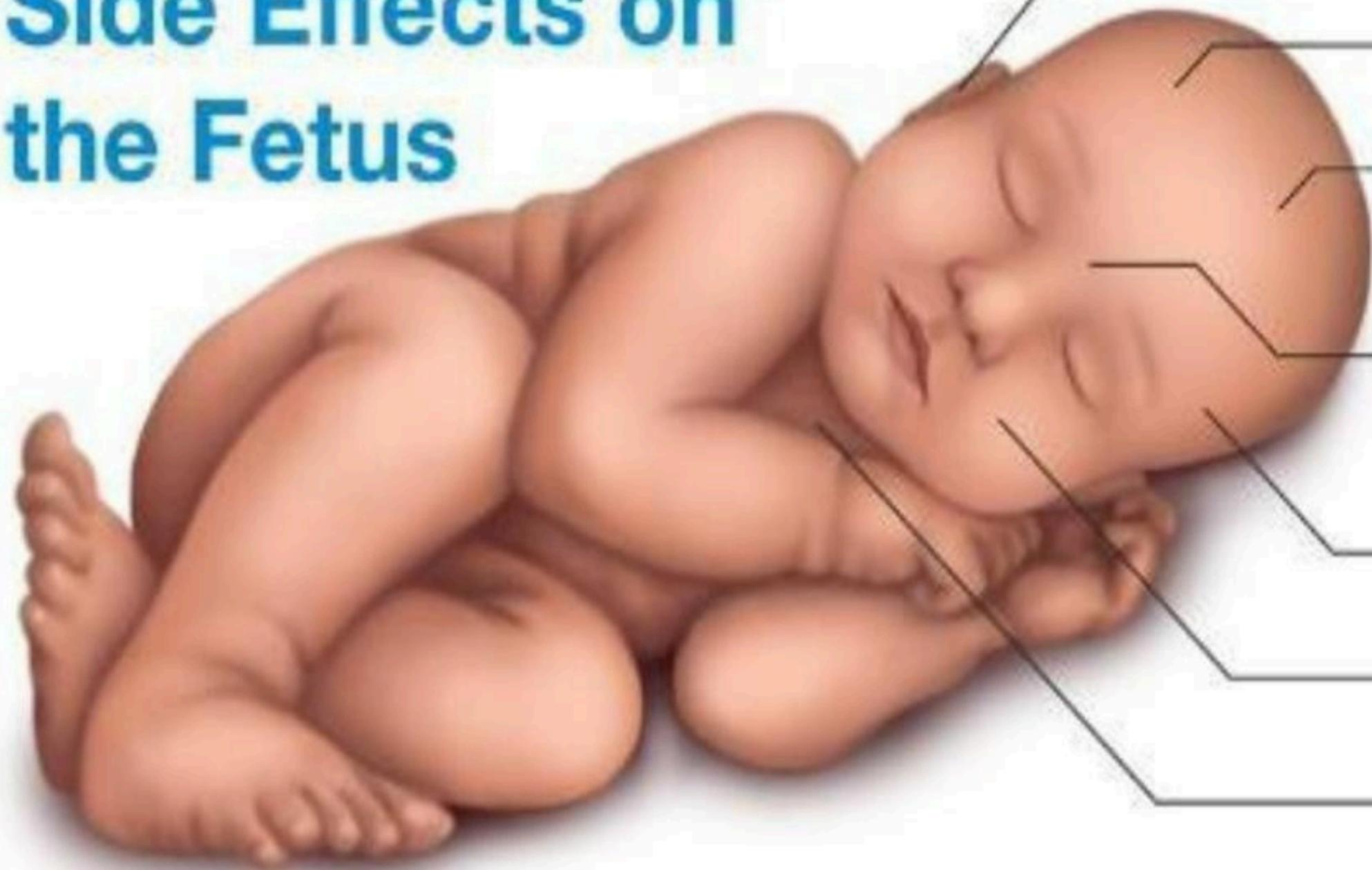


Anotia
Not developed external ear



Micrognathia
Underdeveloped lower jaw

Accutane (isotretinoin) Side Effects on the Fetus



Ear deformities

Microcephaly

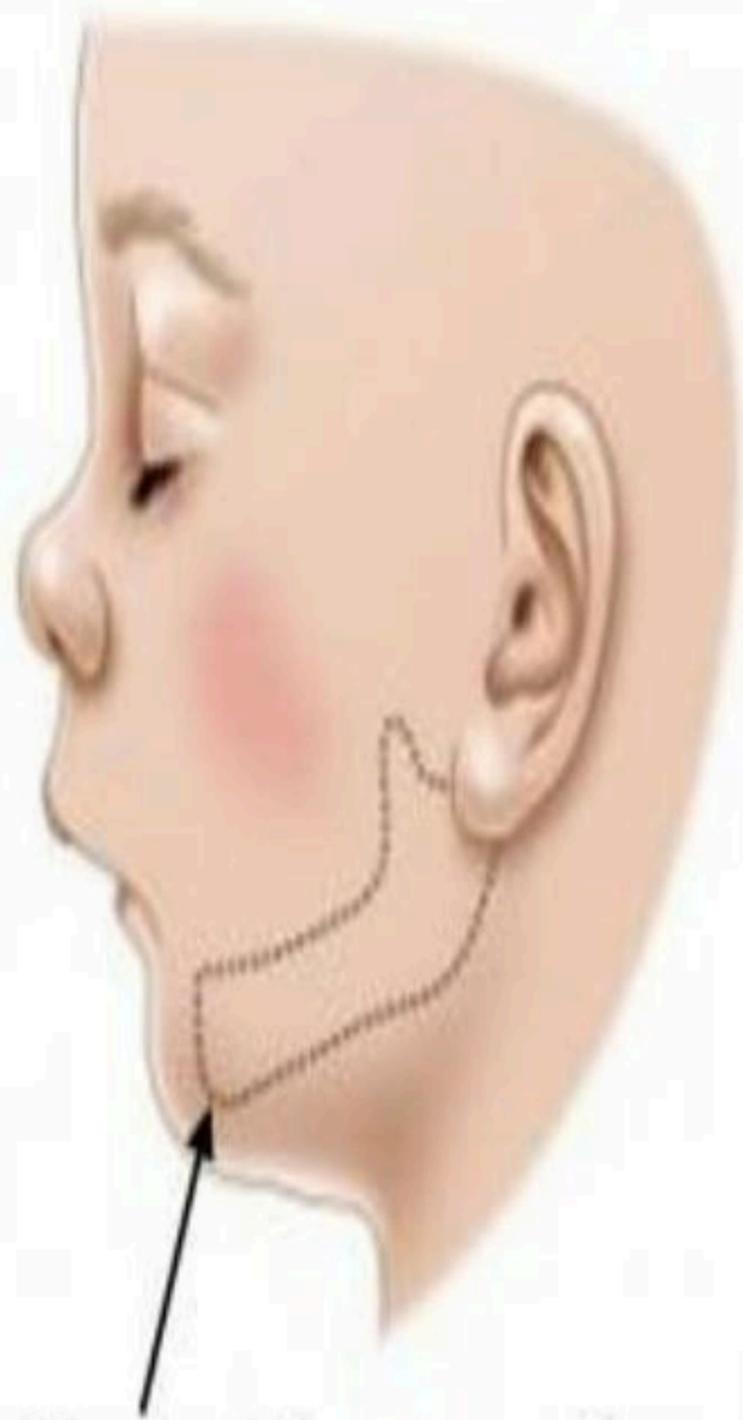
Brain fluid
accumulation

Abnormal immune
system development

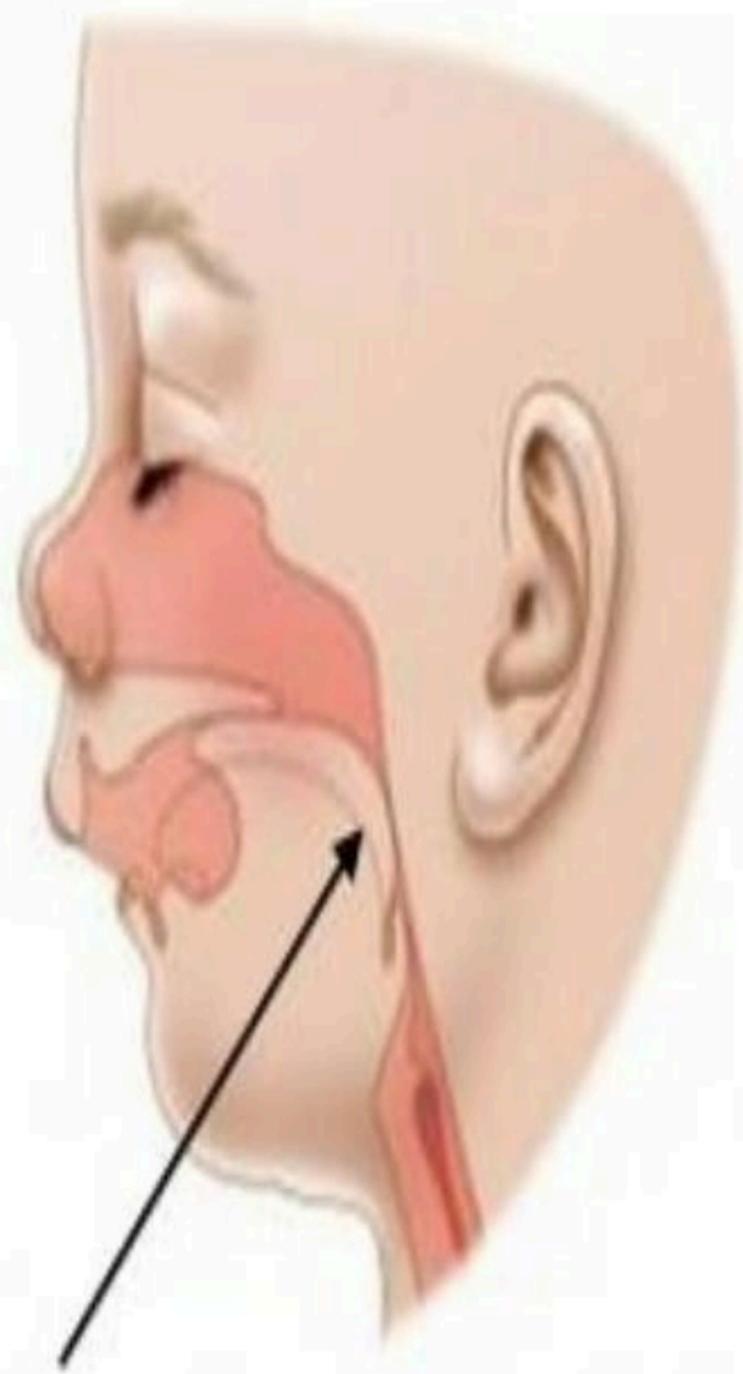
Learning disabilities

Facial deformities

Heart abnormalities



Micrognathia - a small jaw with a receding chin



Tongue that is large compared to the jaw, resulting in airway obstruction

H O R M O N E S

- Maternal androgen therapy (ie. Testosterone) may result virilization of the external genitalia of **female** fetus, including clitoral enlargement and labioscrotal fusion.
- The anti endometriosis drug; danazol can cause same effect as testosterone, Category X.
- DES (diethylstilbestrol): non-steroidal synthetic estrogen is associated with clear cell adenocarcinoma of vagina, reproductive tract abnormalities in the progeny of women exposed to it during late embryogenesis also can cause vaginal adenosis T-shaped uterus, uterine hypoplasia, incomplete cervix
WHILE In male offspring can cause: epididymal cyst, hypoplastic testis
- Clearly DES is contraindicated for pregnancy

SMOKING

- Nicotine-induced vasoconstriction → ↓ placental blood flow
- CO competes with O₂ → ↓ oxyhemoglobin

Effects:

- Spontaneous abortion (1.2 to 1.8 times greater in smokers than in nonsmokers)
- Abruptio placentae, placenta previa, and premature rupture of membranes
- Preterm birth
- Low infant birth weight / IUGR
- Sudden infant death syndrome (SIDS)

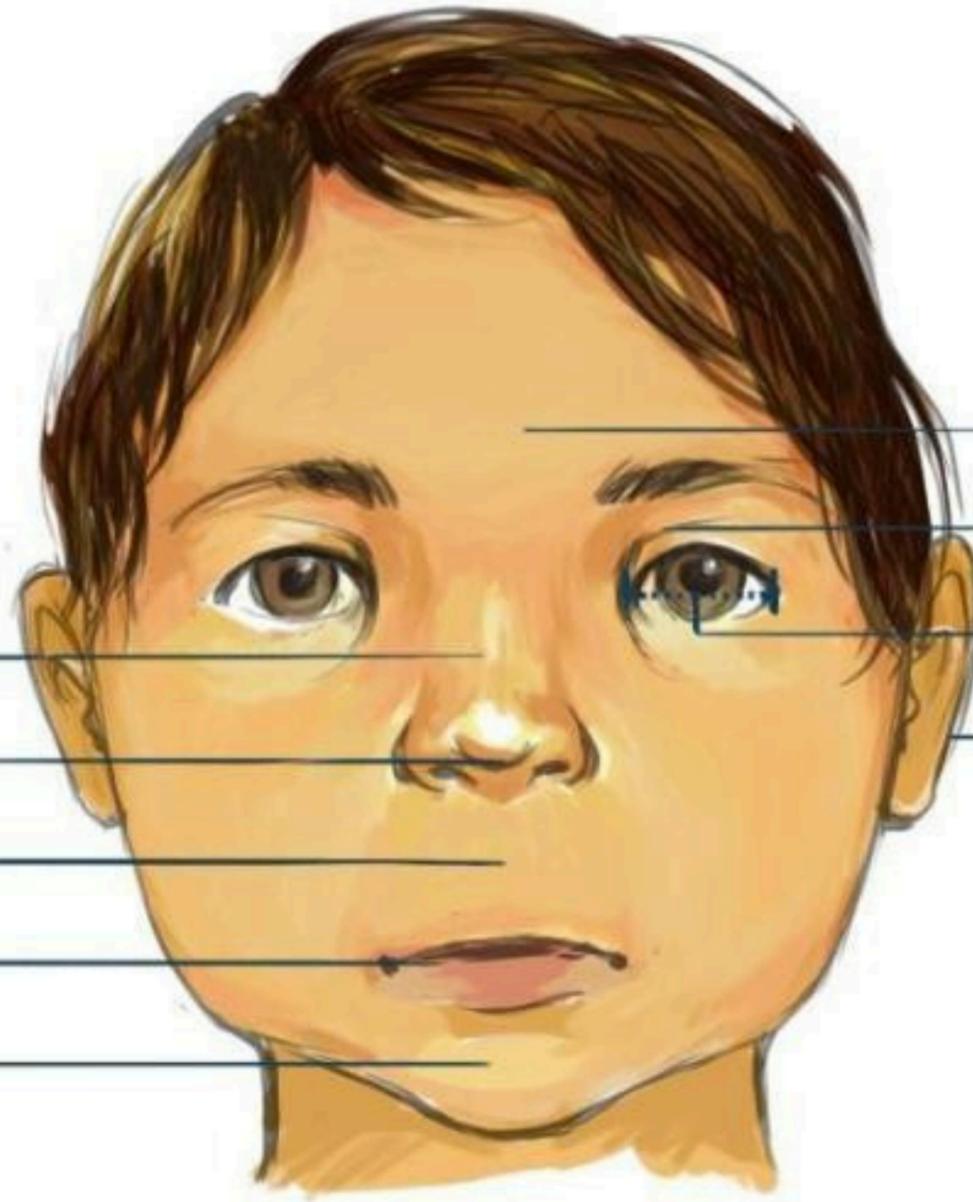
ALCOHOL

Ethanol crosses the placenta and the fetal blood–brain barrier => its toxicity is dose-related but without a defined lower threshold of exposure. No amount is safe.

- The exposure time of greatest risk is the first trimester
- BUT fetal brain development may be affected throughout gestation.
- Effect: **Fetal alcohol syndrome**
 - Facial abnormalities
 - Growth retardation
 - Central nervous system (CNS) dysfunction microcephaly, mental retardation, and behavioral disorders
 - Skeletal abnormalities congenital hip dislocation
 - Structural cardiac defects the most common cardiac structural anomaly is ventricular septal defect

FETAL ALCOHOL SYNDROME

© Lineage



Microcephaly (small forehead)

Epicanthal folds

Short palpebral fissures

Minor ear abnormalities

Low nasal bridge

Short nose and flat midface

Smooth philtrum

Thin upper lip

Micrognathia (small jaw)

COCAINE

Mechanism:

- Potent sympathomimetic causing intense vasoconstriction → reduced uteroplacental blood flow.

1. Maternal Effects:

- Malignant hypertension
- Cardiac ischemia, arrhythmias
- Cerebral infarction, seizures
- Aortic dissection, especially in chronic users
- Cardiotoxicity → risk of sudden death

2. Obstetric Complications:

- Spontaneous abortion
- Fetal demise in utero
- Premature rupture of membranes (PROM)
- Preterm labor
- Abruptio placentae (highly associated)
- Meconium-stained amniotic fluid

COCAINE

3) Fetal Effects:

- Intrauterine Growth Restriction (IUGR)
- Neurodevelopmental delay
- **Cocaine is teratogenic:**
 - Cerebral infarction in utero
 - Microcephaly
 - Limb reduction defects
 - Urogenital anomalies (e.g., renal agenesis)
 - Congenital heart defects

4. Long-term outcomes:

- Impaired cognition
- **Behavioral Effects:**

Issues with attention, impulsivity, and self-regulation. Increased risk of externalizing behaviors (e.g., aggression, conduct problems), especially with additional environmental risk factors.

MARIJUANA (Cannabis)

Mechanism:

- Affects dopamine, serotonin, and acetylcholine systems in fetal brain.

Maternal & Fetal Considerations:

- **Tetrahydrocannabinol (THC) is lipid-soluble → accumulates in fetal** tissues and crosses placenta freely
- Remains in maternal fat stores → prolonged fetal exposure for weeks
- Generates 5x more carbon monoxide than tobacco → leads to fetal **hypoxia**

Fetal Effects:

- Possible IUGR
- **Impaired neurodevelopment:**
 - Attention problems
 - Impaired executive function
 - Sleep disturbances in infancy
- **Low birth weight**
- Not considered strongly teratogenic, but long-term data raises concern
- **Note: Often used in conjunction with tobacco or alcohol, complicating isolated effects.**

OPIATES (Heroin, Methadone, Buprenorphine)

Maternal Effects:

- IV drug use → risk of endocarditis, hepatitis B/C, HIV
- Malnutrition, poor prenatal care
- Anemia, infections, preeclampsia

Pregnancy Complications:

- **Increased risk of:**
 - Stillbirth
 - Preterm birth
 - Fetal Growth Restriction (FGR)
 - Placental insufficiency
 - Neonatal mortality

OPIATES (Heroin, Methadone, Buprenorphine)

Fetal Effects:

- **Neonatal Abstinence Syndrome (NAS):**

- Occurs in 50–90% of exposed newborns
- Sx: tremors, seizures, irritability, poor feeding, diarrhea
- Onset: within 24–72 hours (methadone NAS may be delayed up to 5–7 days)

- **Fetal hypoxia, acidosis, IUFD (due to withdrawal-induced fetal distress)**

- No proven teratogenicity, but polysubstance use is common

Management:

- Maintenance therapy with methadone or buprenorphine is preferred over detox in pregnancy

AMPHETAMINES (Methamphetamine, MDMA)

Mechanism:

- Potent central nervous system stimulants
- Cross placenta → direct fetal toxicity

Pregnancy & Fetal Risks:

- Abruptio placentae
- IUGR
- Preterm birth
- Stillbirth
- Decreased fetal head circumference

Teratogenicity:

- No proven teratogenic effects, but neurocognitive deficits and behavioral issues observed

HALLUCINOGENS (LSD, Psilocybin, PCP)

Effects:

- **No confirmed teratogenicity**
- No proven chromosomal abnormalities or malformations
- Can cause acute intoxication, psychosis, trauma risk to mother and fetus due to hallucinations

Pregnancy Considerations:

- May impair maternal judgment → increased injury risk
- **Poor prenatal care common in users**

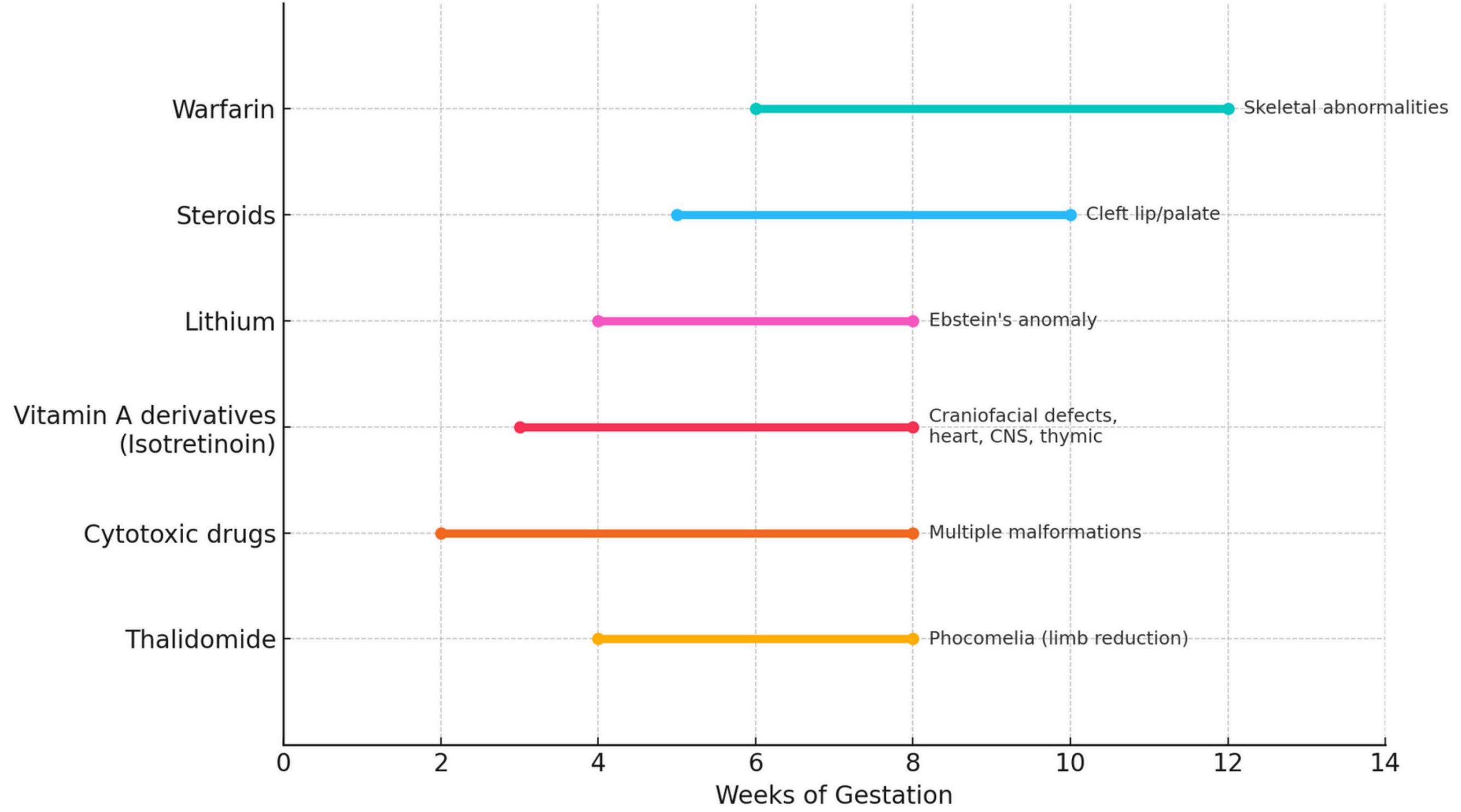
Teratogens in Pregnancy

- **Teratogenicity** = potential of a substance to cause congenital anomalies or functional defects.
- **Timing is critical:**
 - **T1 (1st trimester): organogenesis → structural malformations**
 - **T2 & T3: functional defects, growth restriction, CNS damage**

T1 Teratogens (Organogenesis period)

Drug	Effect	Clinical Note
Thalidomide	Phocomelia (limb reduction)	Classic example of teratogenicity; used in 1950s as antiemetic/sedative
Cytotoxic drugs	Multiple malformations	Affects rapidly dividing cells; includes methotrexate, cyclophosphamide
Vitamin A derivatives (Isotretinoin)	Craniofacial defects , heart, CNS, thymic abnormalities	Strict iPLEDGE program; pregnancy must be avoided
Lithium	Ebstein's anomaly (tricuspid valve displacement)	Especially with 1st trimester use; risk debated, but caution needed
Steroids	Cleft lip and/or palate	Risk with high-dose corticosteroids (controversial in humans)
Warfarin	Skeletal abnormalities (nasal hypoplasia, stippled epiphyses)	Warfarin embryopathy between weeks 6–12; switch to heparin

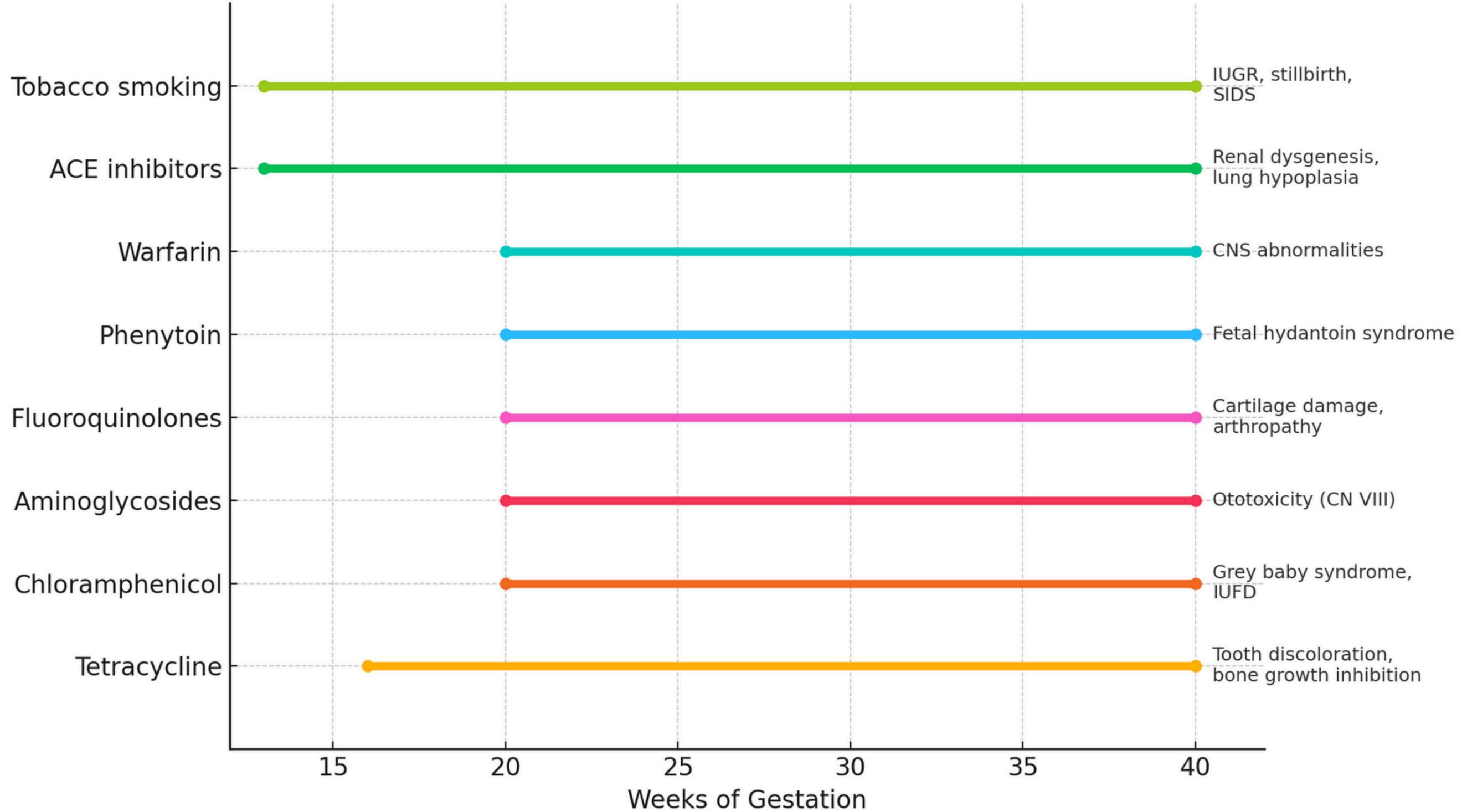
Critical Periods for Teratogenic Risk (Organogenesis)



T2 and T3 Teratogens (Later pregnancy)

Drug/Substance	Effect	Clinical Notes
Tetracycline	Tooth discoloration, bone growth inhibition	Deposits in fetal bone/teeth → avoid after 16 weeks
Chloramphenicol	Grey baby syndrome, IUFD	Due to immature liver enzymes → hypotension, cyanosis
Aminoglycosides	Ototoxicity (CN VIII damage)	Especially streptomycin & gentamicin
Fluoroquinolones	Cartilage damage, arthropathy	Avoid in pregnancy and growing children
Phenytoin	Fetal hydantoin syndrome: craniofacial defects, hypoplasia of nails/distal phalanges, mental deficiency	May include cardiac defects
Warfarin	CNS abnormalities (Dandy-Walker, optic atrophy)	Later exposure affects CNS development
ACE inhibitors	Renal dysgenesis, oligohydramnios, pulmonary hypoplasia, skull ossification defects	Especially dangerous in T2–T3
Tobacco smoking	IUGR, placental insufficiency, stillbirth, SIDS	Nicotine causes vasoconstriction; CO leads to hypoxia

Critical Periods for Teratogenic Risk (T2 & T3)



Summary

- **Key Points:**
- **T1 exposure → structural defects (heart, limbs, face)**
- **T2/T3 exposure → growth restriction, CNS & organ dysfunction**
- **Replace high-risk meds during preconception planning**
- **Use safer alternatives: e.g., heparin instead of warfarin, labetalol instead of ACEi**



Drugs and Lactation

Pharmacokinetics of Drug Transfer to Breast Milk

- **Drug transfer depends on multiple factors:**
 - **Route of administration**
 - **Dose and frequency**
 - **Maternal plasma levels**
 - **Drug half-life and molecular weight**
 - **Lipid solubility, ionization, and protein binding**
 - **Baby's age & maturity (especially renal/hepatic function)**
 - **Milk composition (foremilk vs hindmilk)**

Timing of Drug Intake Matters

- **Ideal strategy:**
- **Take medication 30–60 mins after breastfeeding, and**
- **3–4 hours before the next feeding**
- **↓ Minimizes drug concentration in the milk during peak feeding**

Risk–Benefit Principle

- **Breastfeeding should continue unless:**
- **The drug is proven harmful to the infant**
- **Benefits of drug to mother don't outweigh risks to infant**
- **Weaning is rarely necessary—choose alternatives when possible**

Factors Influencing Drug Excretion into Milk

Factor	Effect
Drug lipophilicity	↑ lipophilic drugs concentrate more in hindmilk
Molecular size	Small molecules (<300 Da) cross more easily
Plasma protein binding	High binding = ↓ milk passage
Milk/plasma pH difference	Milk pH ≈ 7.2, plasma ≈ 7.4
Ion trapping	Basic drugs become ionized in acidic milk → trapped
Milk composition	Hindmilk has more fat → concentrates lipid-soluble drugs

Mnemonic – BREAST (Contraindicated Drugs)

- **B**romocriptine / Benzodiazepines
- **R**adioactive isotopes / Rizatriptan
- **E**rgotamine / Ethosuximide
- **A**miodarone / Amphetamines
- **S**timulant laxatives / Sex hormones
- **T**etracycline / Tretinoin

Vaccines and pregnancy

Protecting maternal and infant health



Introduction

- **Vaccination during pregnancy plays a vital role in protecting both the mother and her unborn child from preventable infectious diseases.**
- **According to UpToDate and other leading health authorities, maternal immunization not only reduces the risk of severe illness in the mother but also provides passive immunity to the newborn during the early months of life .**



Immunization prior to pregnancy:

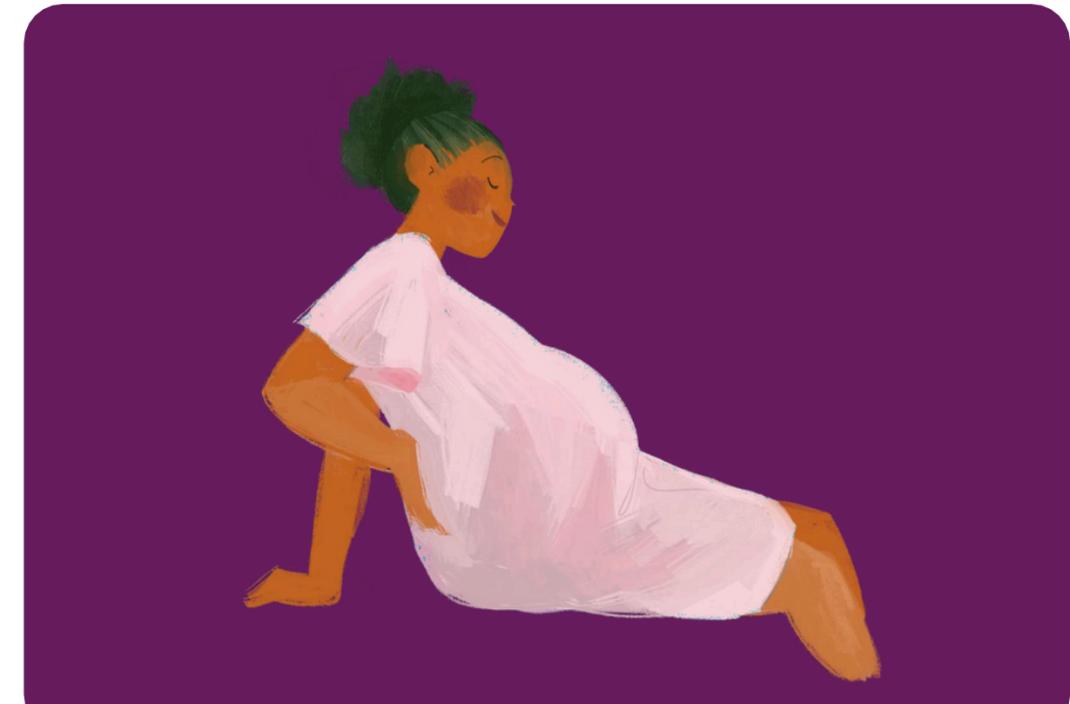
- Ensuring that she is up to date on certain vaccinations before becoming pregnant is crucial
- **MMR, varicella, Hep B, and HPV**
- Non immunized women should receive appropriate vaccinations.
- If live vaccines are administered, advise individuals to avoid conceiving for 1–3 months



Recommended vaccines during pregnancy

For all pregnant individuals, recommend:

- 1. Tdap vaccine once every pregnancy, preferably at 27–36 weeks' gestation**
- 2. RSV vaccine (Abrysvo) between 32–36 weeks' gestation .**
- 3. Inactivated influenza vaccine during flu season (safe in all trimesters)**
- 4. Current COVID-19 vaccination .**



Influenza vaccine :

- All pregnant women **regardless of trimester** during flu season .
- Dose : Injectable form (IM) (inactivated flu vaccine)

COVID-19 vaccine:

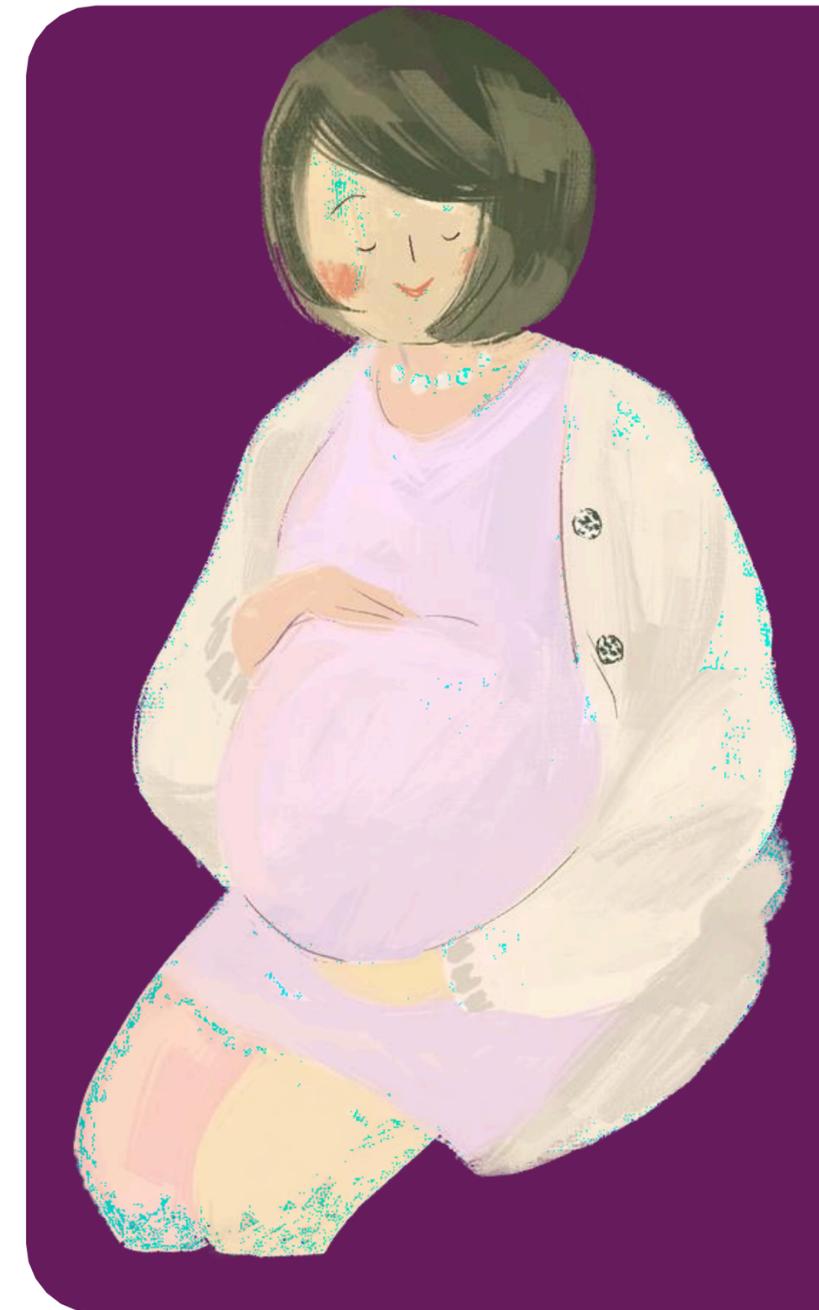
- COVID-19 vaccines authorized for pregnant women are mRNA vaccines (e.g., Moderna and Pfizer), which do not contain live virus
- **Any trimester.**



Tetanus-diphtheria-acellular pertussis (Tdap)

The Tdap vaccine—which protects against **tetanus**, **diphtheria**, and **pertussis** (whooping cough)—is strongly recommended during each pregnancy, regardless of prior immunization history.

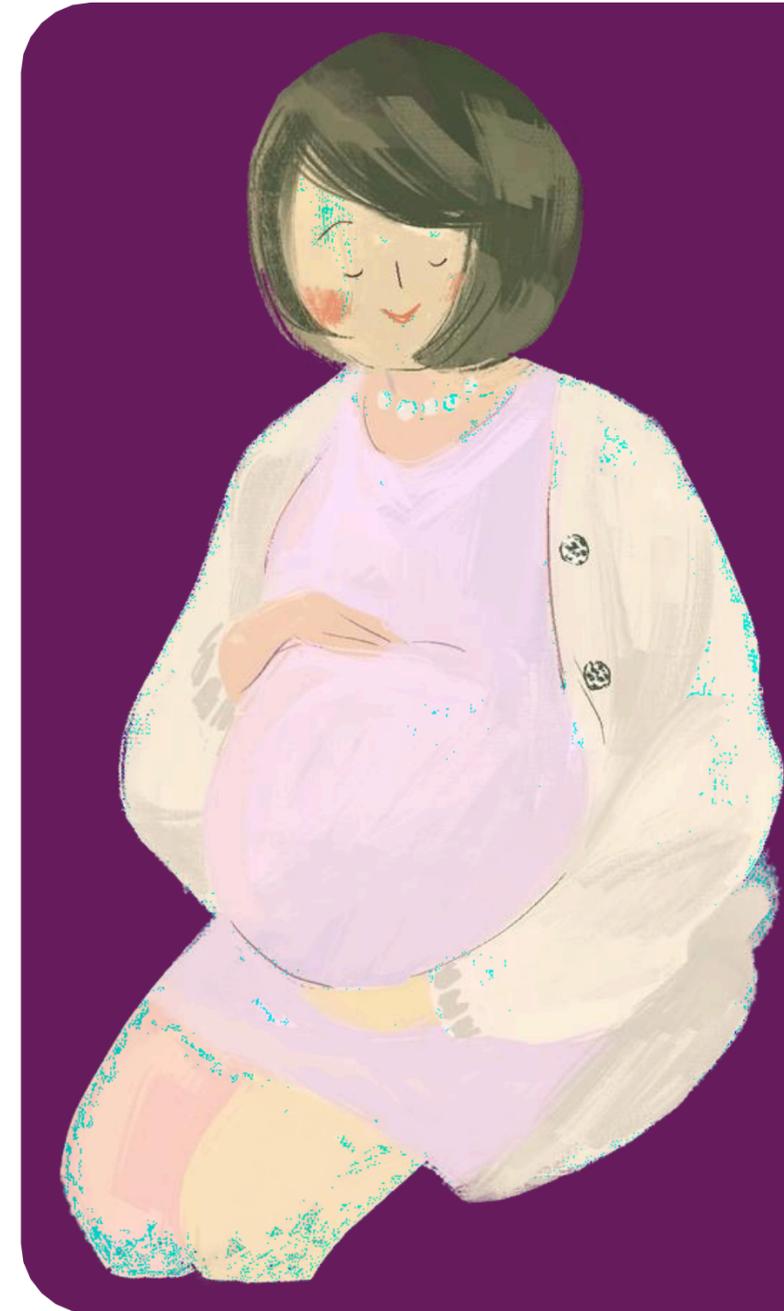
- **Optimal Timing:** The vaccine should be administered **between 27 and 36 weeks of gestation**.
- **Dosage:** A single intramuscular injection of 0.5 mL.



Respiratory Syncytial Virus (RSV) vaccine :

- **Abrysvo (RSVpreF) vaccine.**
- **Timing: Single dose during weeks 32 - 36 of pregnancy.**
- **Benefits:**

Infant Protection: Maternal vaccination during this window allows for the transfer of protective antibodies to the fetus, significantly reducing the risk of severe RSV-related lower respiratory tract infections in infants during their first months of life.



Additional vaccines:

Beyond routine vaccinations, certain risk factors may necessitate additional vaccines

Hepatitis A (HepA) Vaccine:

- Risk Factors:

1. Travel to countries with high or intermediate Hepatitis A virus prevalence.
2. Chronic liver disease

Meningococcal Vaccines:

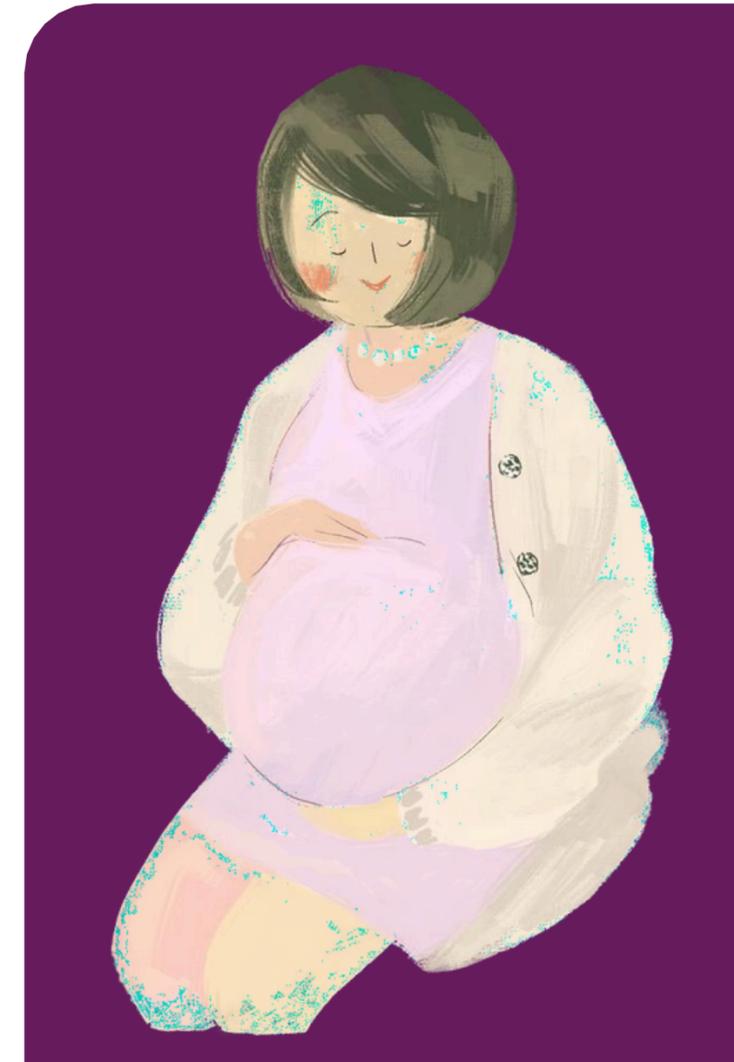
- Risk Factor:

Travelers to areas where meningococcal disease is common, such as the meningitis belt in sub-Saharan Africa.

Hepatitis B (HepB) Vaccine:

- Risk Factors:

1. Multiple sex partners
2. Being evaluated or treated for a sexually transmitted infection.



Contraindicated :

Contraindicated vaccines :

Live attenuated vaccines are contraindicated as they carry a risk of fetal infection (e.g., congenital rubella syndrome, congenital varicella syndrome).

- Examples are **vaccines against varicella-zoster, measles, mumps, rubella, polio, chickenpox, and yellow fever.**
- Moreover, **1 month or longer** should ideally pass between vaccination and conception attempts.



Vaccines and lactation:

- According to (CDC), **most vaccines are safe** for breastfeeding women and do not adversely affect lactation or the breastfed child.
- Vaccines Requiring Caution:
 - i. **Smallpox Vaccine**
 - ii. **Yellow Fever Vaccine**



Vaccine	Before pregnancy	During pregnancy	After pregnancy	Type of Vaccine
Hepatitis A	Yes, if indicated	Yes, if indicated	Yes, if indicated	Inactivated
Hepatitis B	Yes, if indicated	Yes, if indicated	Yes, if indicated	Inactivated
Human Papillomavirus (HPV)	Yes, if indicated, through 26 years of age	No, under study	Yes, if indicated, through 26 years of age	Inactivated
Influenza IIV	Yes	Yes	Yes	Inactivated
Influenza LAIV	Yes, if less than 50 years of age and healthy; avoid conception for 4 weeks	No	Yes, if less than 50 years of age and healthy; avoid conception for 4 weeks	Live
MMR	Yes, if indicated, avoid conception for 4 weeks	No	Yes, if indicated, give immediately postpartum if susceptible to rubella	Live
Meningococcal: • polysaccharide • conjugate	If indicated	If indicated	If indicated	Inactivated Inactivated
Pneumococcal Polysaccharide	If indicated	If indicated	If indicated	Inactivated
Tdap	Yes, if indicated	Yes, vaccinate during each pregnancy ideally between 27 and 36 weeks of gestation	Yes, immediately postpartum, if not received previously	Toxoid/ inactivated
Tetanus/Diphtheria Td	Yes, if indicated	Yes, if indicated, Tdap preferred	Yes, if indicated	Toxoid
Varicella	Yes, if indicated, avoid conception for 4 weeks	No	Yes, if indicated, give immediately postpartum if susceptible	Live

**Thank you
Pray for Gaza**

