DRUGS AND VACCINES IN PREGNANCY AND LACTATION

5TH YEAR MEDICAL STUDENTS :

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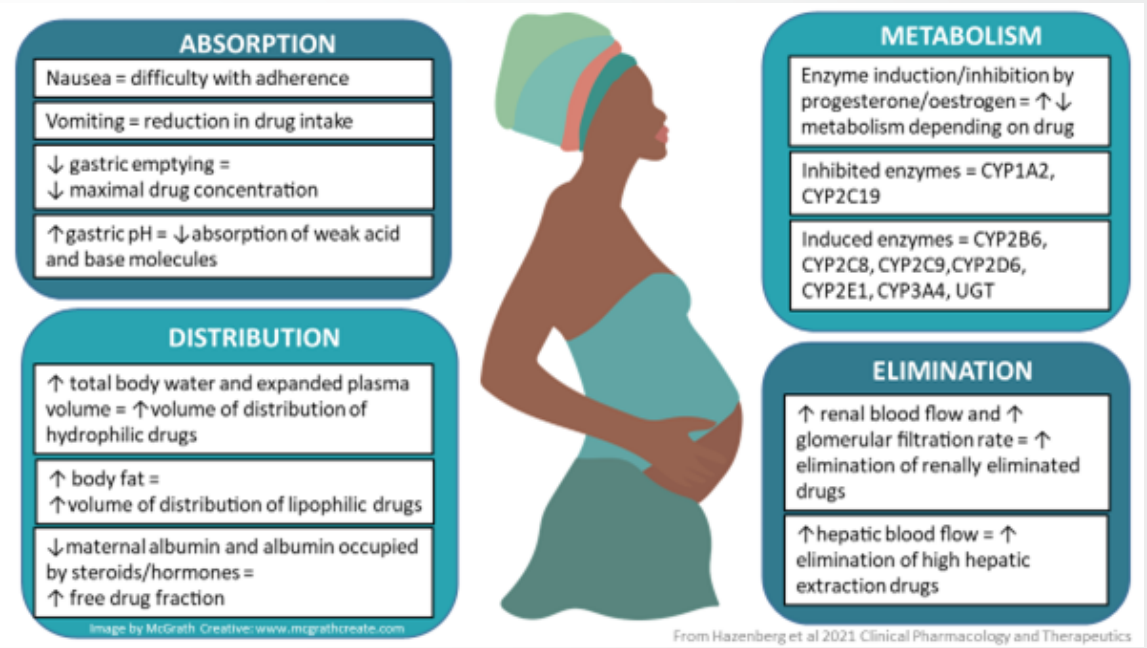
INTRODUCTION

- Drugs uptake during pregnancy and lactation is of important significance because of its **toxic effect on the developing fetus** . Also, the alterations of pharmacokinetics in a pregnant women need careful attention .
- Approximately 3-5% of live births are complicated by a birth defect each year, totaling around 120,000 babies.
- Current evidence suggests that between 65% and 94% of women take at least one prescription drug during pregnancy .

MATERNAL PHARMACOKINETIC IN PREGNANCY :

- Absorption:
- 1- Decreased gastrointestinal motality and tone (progesterone effects& increased acid production) delay absorption of drugs in the small intestines.
- 2-Increased cardiac output affects changes in skin and muscle blood flow, so increasing the absorption of drugs via subcutaneous and intramuscular routes .
- 3- Increased blood flow speeds up the rate of onset of IV drugs .



Maternal pharmacokinetic in pregnancy :

- Distribution :
- three main pharmacokinetic differences:

1. Increased volume of distribution of drugs (due to increased plasma volume and body fluids)
2. Increased tissue deposition of fat-soluble drugs (due to increased body fat)
3. Increased free fraction of the drugs due to decreased protein binding (due to decreased plasma albumin)

MATERNAL PHARMACOKINETIC IN PREGNANCY :

- Metabolism:
- Hormonal changes during pregnancy and the increase of blood flow to the major metabolism site which is the liver contribute to the interaction with drugs metabolism either increasing or decreasing its level.

MATERNAL PHARMACOKINETIC IN PREGNANCY :

- 4-Elimination:
- Renal plasma flow and GFR both increase by 80% and 40-50% , respectively.
- So,there is increase of the elimination of drugs that are normally excreted by kidney . That requires dose modifications .

PLACENTA ROLE

- Most drugs cross the placenta by simple diffusion; however, Plasma membrane carriers, biotransforming enzymes, and export pumps also play a role.
- Three types of drug transfer across the placenta are recognized:

. 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.

. Exceeding transfer (type 2 drugs): for example, ketamine
These drugs cross the placenta to reach greater concentrations in fetal compared with maternal blood.

. 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.

PLACENTA ROLE

- Factors that affect drug transfer include :
- molecular weight, degree of ionization, lipid solubility, protein binding, and fetal and placental blood flow.
- Nonionized, nonprotein-bound, lipid-soluble drugs with molecular weight below 600 Daltons freely cross the placenta .
- While high molecular weight drugs, such as insulin (6000 Daltons), are not transported in significant amounts.

Factors affecting maternal to fetal Drug Transfer

	Increased transfer	Decreased Transfer
1.Size ~molecular weight	<1000 Dalton	>1000 dalton
2.Charge of Molecule	Uncharged	Charged
3.Ph Vs Drug PKa	Higher proportion of unionized drug in maternal plasma	Higher proportion of ionized drug in maternal plasma
4.Placental efflux transporter protein(p-glycoprotein)	Absent	Present
5.Binding protein type	Albumin(lower binding affinity)	Alpha 1 acid glycoprotein
6.Free(Unbound) Drug	High	Low

DRUGS IN PREGNANCY

TERATOGENIC EFFECTS OF DRUGS

- A human teratogen is an agent that alters the growth or structure of the developing embryo or fetus, thereby causing birth defects .
- Factors increasing the prevalence of fetotoxic medication useduring pregnancy:-
- Unplanned pregnancy
- Multiple pregnancy
- Nulliparity, Unemployment
- Age >25 years
- Single status
- Smoking

TERATOGENIC EFFECTS

- loss of pregnancy
- structural abnormalities
- growth impairment
- functional loss
- behavioural changes

- Teratogenicity risk is determined largely by TIMING of drug exposure .

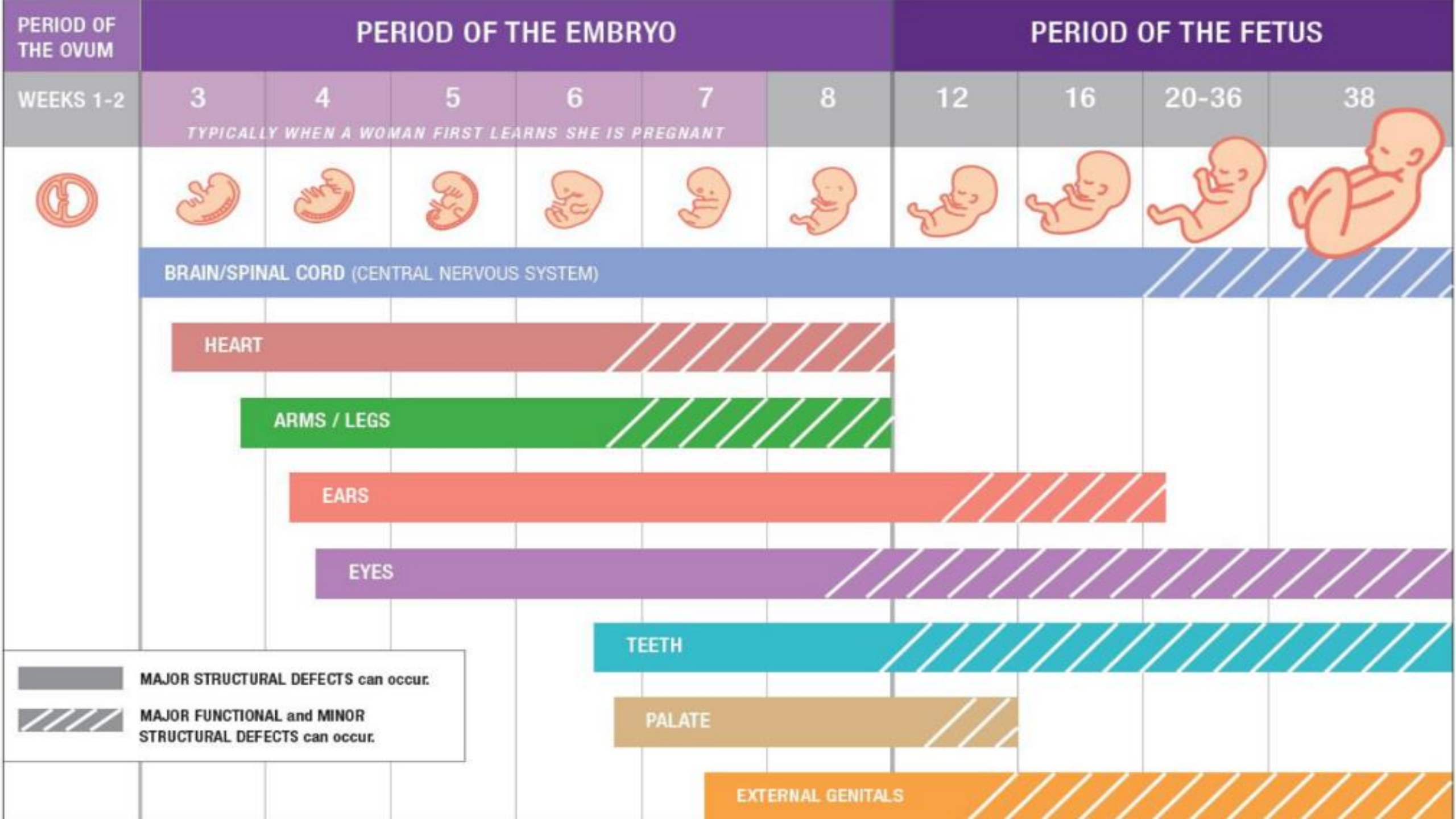
- -During first trimester (T1); drugs may produce congenital (structural) abnormalities (teratogenesis)
  **The period of greatest risk is from 3-12th week .

  -During second and third trimesters (T2,T3) drugs may affect growth and functional development of the fetus (e.g. brain development) .

- During the first two weeks of gestation, teratogenic agents usually kill the embryo rather than cause congenital malformations. It's known to have an " all-or-nothing " response.

- Embryonic stage (weeks 3-8 post-conception) which is the critical time for organogenesis . During organogenesis, teratogenic agents are more likely to cause major congenital (structural) malformations.

- After 8 weeks , most teratogenicity effect are related to fetal growth restrictions or functions deficits (not structural) such as mental retardation .


PERIOD OF THE OVUM
PERIOD OF THE EMBRYO
PERIOD OF THE FETUS
WEEKS 1-2
3
4
5
6
7
8
12
16
20-36
38
TYPICALLY WHEN A WOMAN FIRST LEARNS SHE IS PREGNANT
BRAIN/SPINAL CORD (CENTRAL NERVOUS SYSTEM)
HEART
ARMS / LEGS
EARS
EYES
TEETH
PALATE
EXTERNAL GENITALS
MAJOR STRUCTURAL DEFECTS can occur.
MAJOR FUNCTIONAL and MINOR STRUCTURAL DEFECTS can occur.

FDA CLASSIFICATION

- In general, every medication is classified into one of the Five category (A,B,C,D,X)
- based on how safe or risky to use during pregnancy , And the type and adequacy of studies which is done.

- Category A : Adequate and well-controlled studies in pregnant women fail to detect risk to the fetus in the first trimester and no evidence of risk in later trimesters.

- Category B : Safe on the basis of animal studies , with no controlled study in pregnant women with no evidence of risk

Table 1. FDA classification for medications in relation to teratogenic risk.

Category A	Controlled studies show no risk. Adequate well-controlled studies in pregnant women have failed to demonstrate risk to the fetus
Category B	No evidence of risk in humans. Either animal findings show risk, but human findings do not; or, if no adequate human studies have been done, animal findings are negative
Category C	Risk cannot be ruled out. Human studies are lacking, and animal studies are either positive for fetal risk or lacking as well. However, potential benefits may justify the potential risk
Category D	Positive evidence of risk. Investigational or postmarketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risk
Category X	Contraindicated in pregnancy. Studies in animals or human have shown definite harm to the fetus

FDA: US Food and Drug Administration.

- Category C : Risk not ruled out
- , in which the studies in women and animals are not available
- Benefits outweigh the risks

- 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

- 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.

Drug ratings in pregnancy (US Food and Drug Administration)

Category	Interpretation
A	Controlled human studies show no risk
	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.
B	No evidence of risk in studies
	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.
C	Risk cannot be ruled out
	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.
D	Positive evidence of risk
	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).
X	Contraindicated in pregnancy
	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.

In 2015, the US Food and Drug Administration (FDA) began overseeing the phase-out of pregnancy risk categories (A, B, C, D, and X) from prescription drug labeling and began requiring information from available human and animal studies of (1) known or potential maternal or fetal adverse reactions and (2) dose adjustments needed during pregnancy and the postpartum period. Additional information is available at the FDA website: Pregnancy and Lactation Labeling Final Rule.

ANTIBIOTICS

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

effect: congenital deafness (Ototoxicity) & nephrotoxicty.

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 jarish-herixhimer 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 .

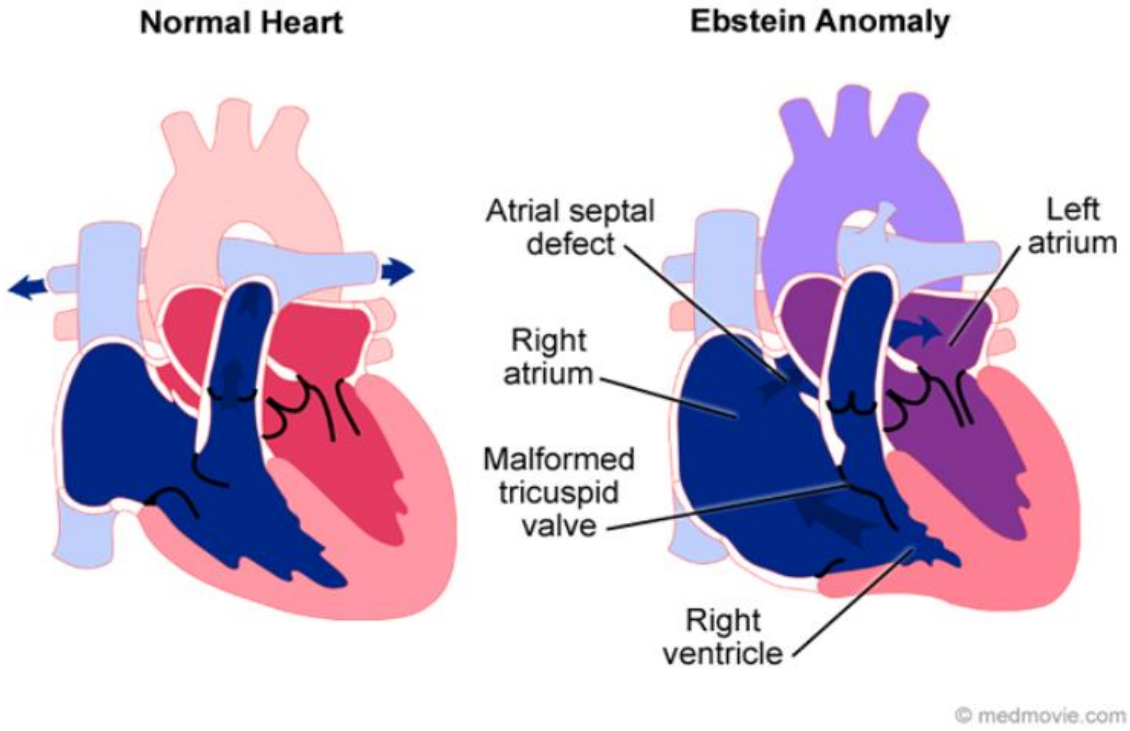
LITHIUM

- Pregnancy category – D.

Effect: cardiac effects, especially Ebstein's anomaly ,

Others include ; Floppy 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)

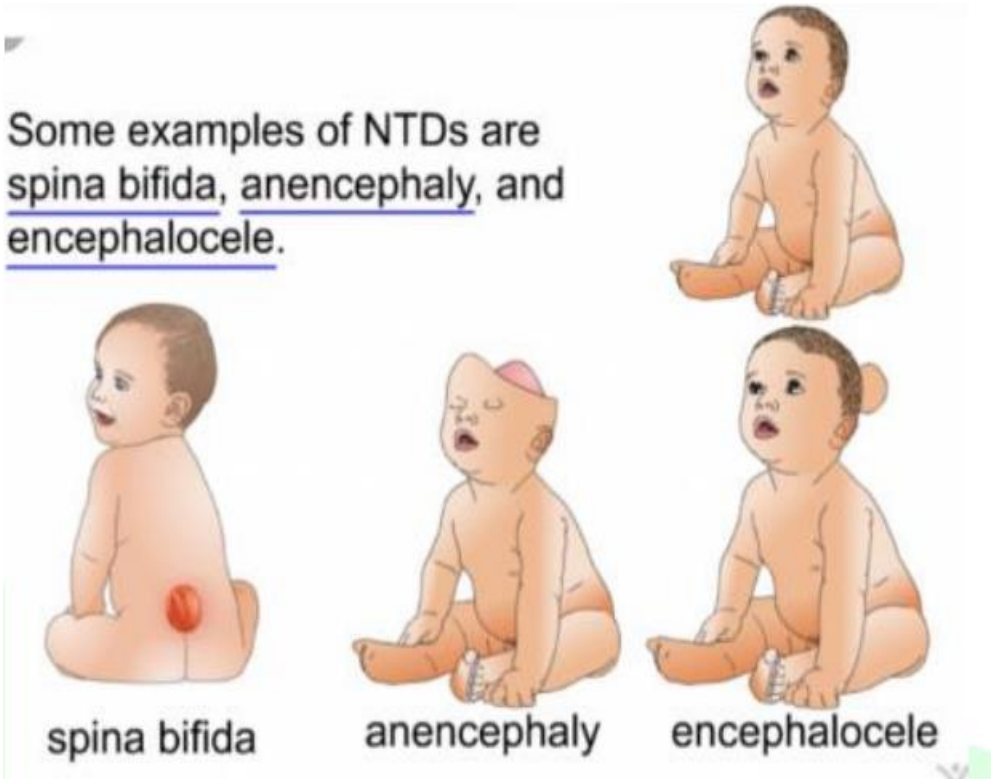
Pregnancy category; D&X

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)

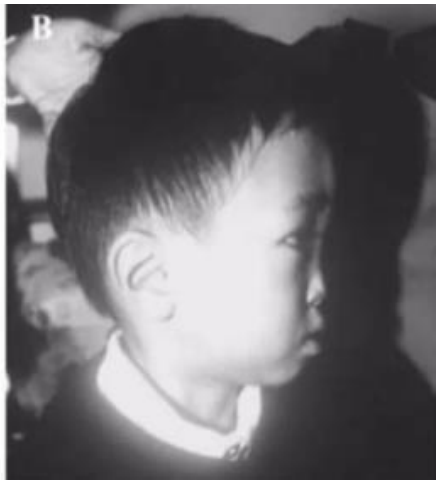
- Category X
- Effect: Methotrexate (MTX) is a folate antagonist with known teratogenicity including abortifacient effects that interfere with DNA synthesis. Also, it is associated with NTDs .



ANTICONVULSANTS

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

ANTICOAGULANTS



- 1- Warfarin : Pregnancy category – X
- -Fetal warfarin syndrome (warfarin embryopathy) ; include : low birth weight , mental retardation, deafness, Microcephaly, Nasal hypoplasia, malformed bones, cartilage, and joints.
- 2-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.

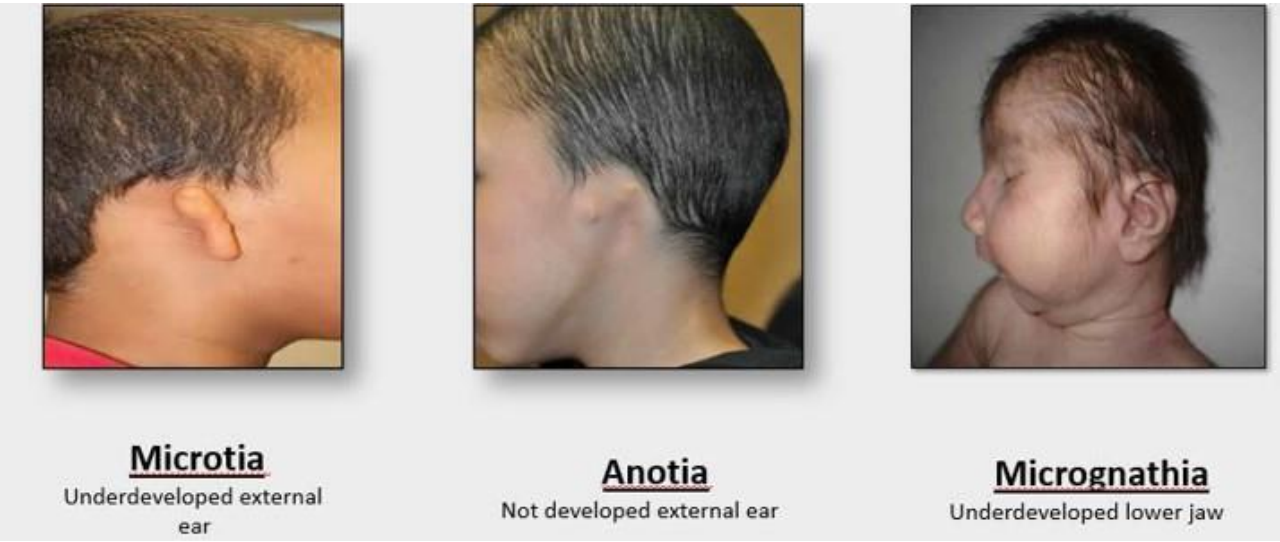
Retinoid's (vitamin A related compounds)

- 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

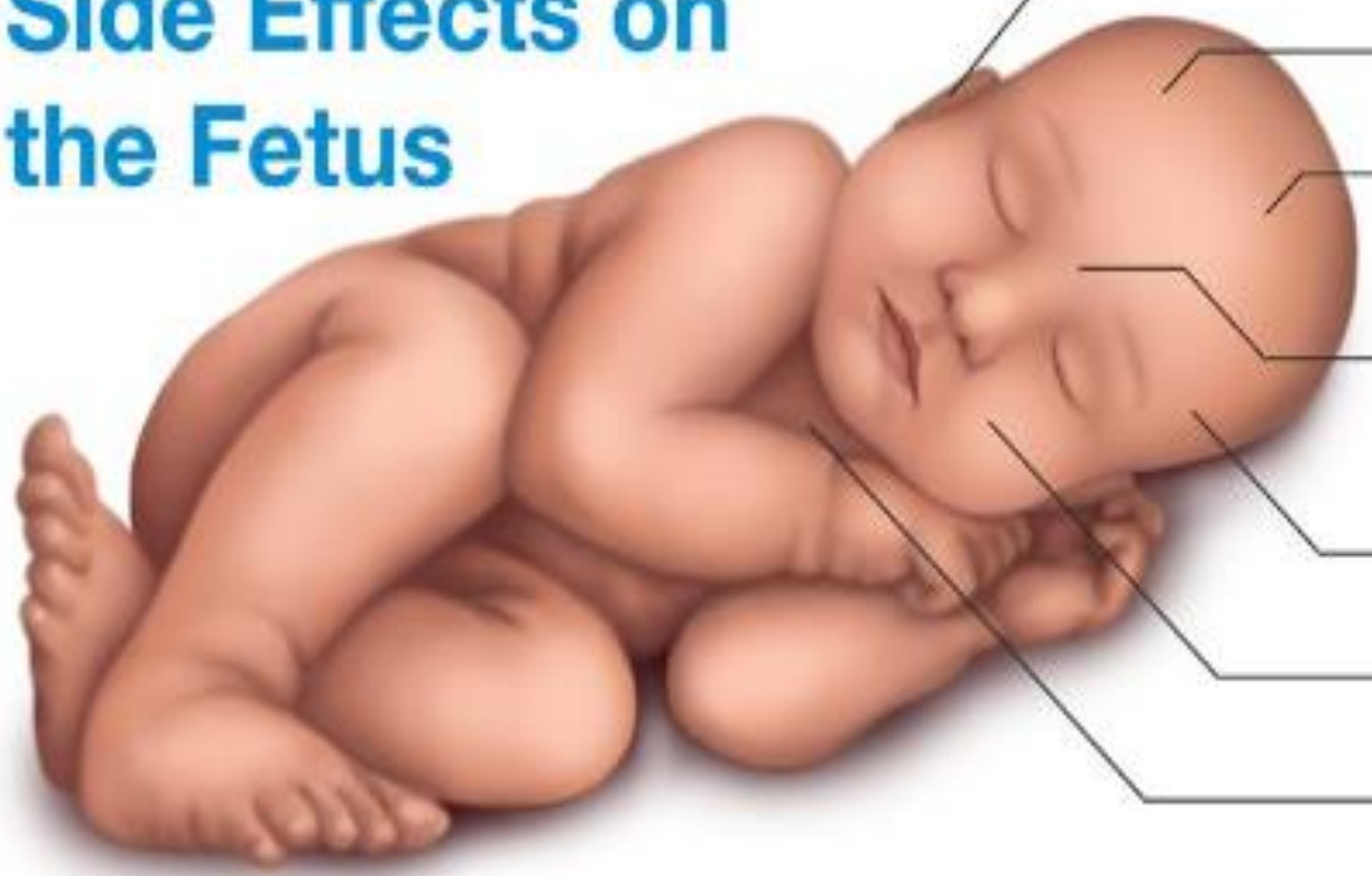
Fetal anomalies reported to be associated with maternal isotretinoin use:

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

May also cause spontaneous abortions

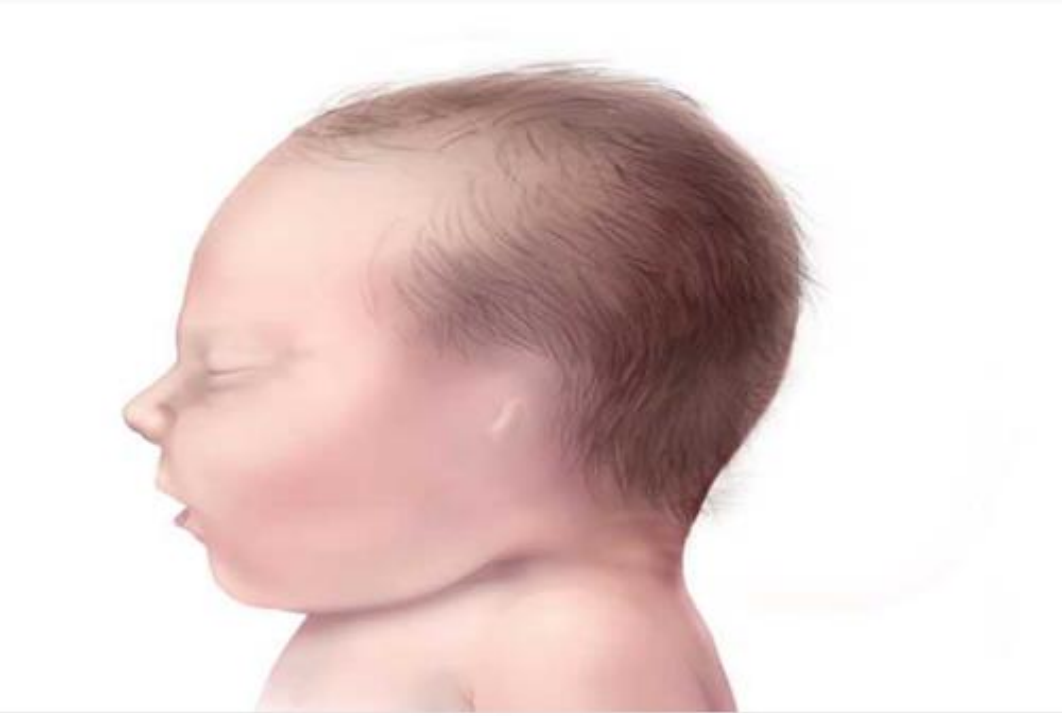


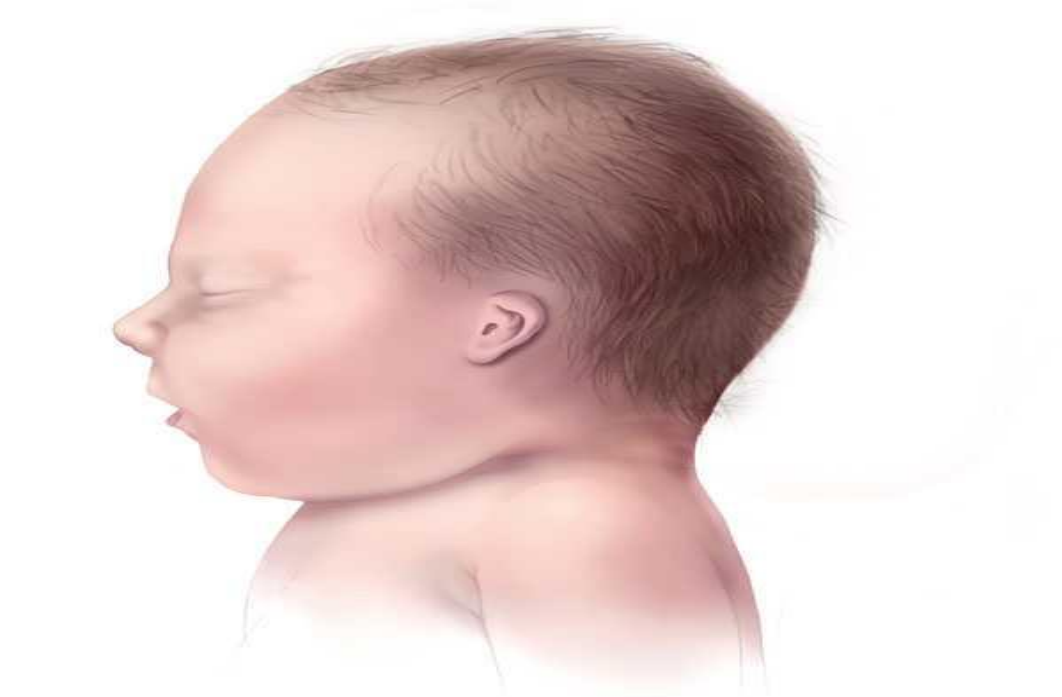
Accutane (isotretinoin) Side Effects on the Fetus

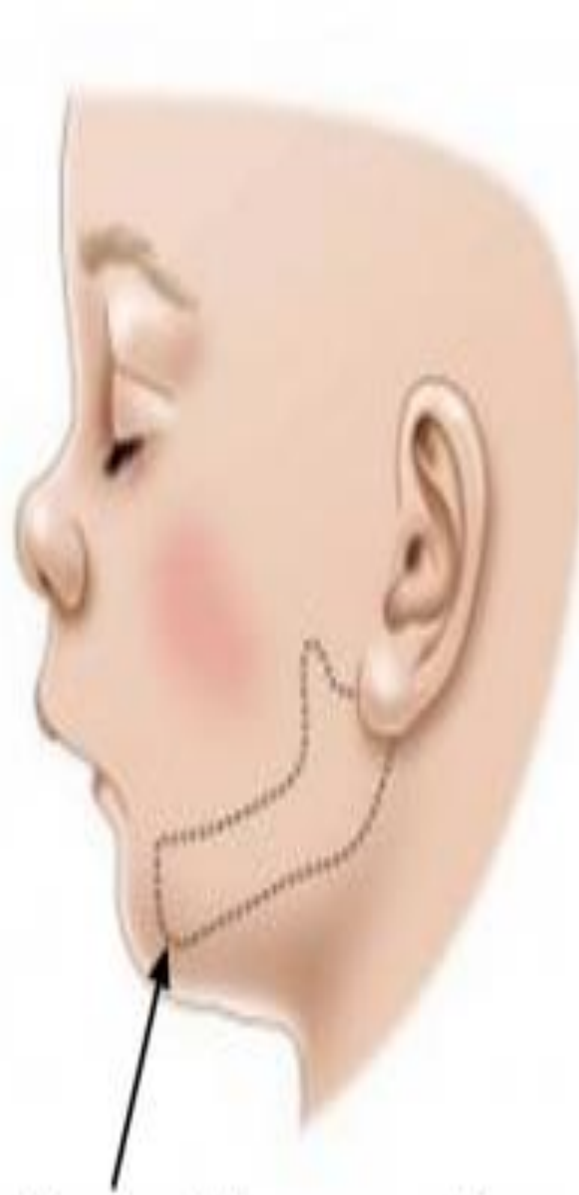


- Ear deformities
- Microcephaly
- Brain fluid accumulation
- Abnormal immune system development
- Learning disabilities
- Facial deformities
- Heart abnormalities

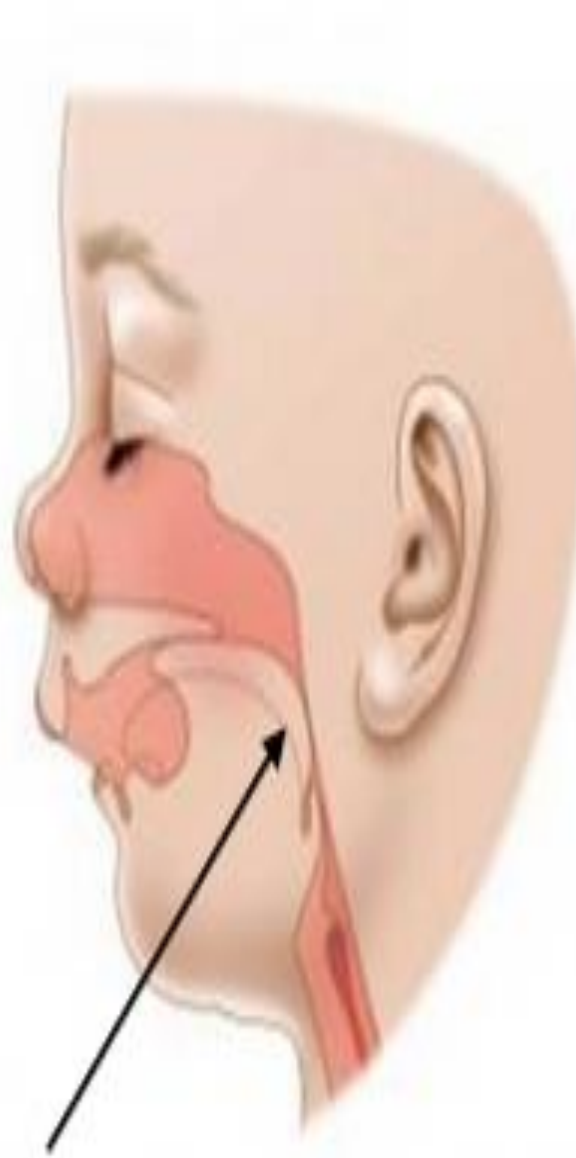
acne.org







Micrognathia - a small jaw with a receding chin



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

HORMONES

- Maternal androgen therapy (ie. Testosterone) may result virilization of the external genitelia of female fetus, including clitorial 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 embrogenesis 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

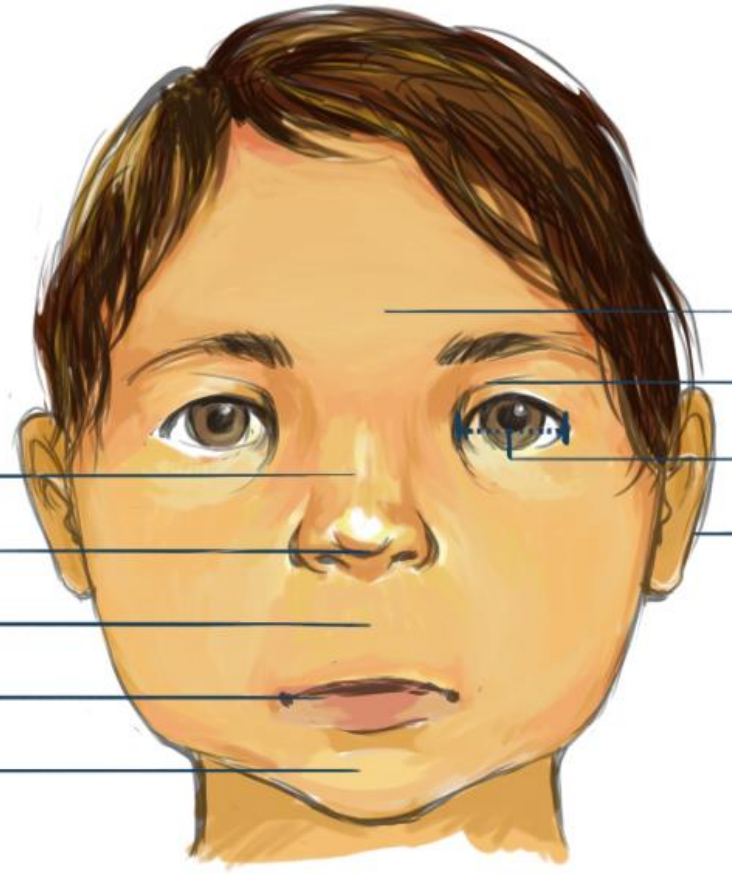
Ethanol crosses the placenta and the fetal blood–brain barrier => its toxicity is dose-related but without a defined lower threshold of exposure. No amount is safe.

- The exposure time of greatest risk is the first trimester
- BUT fetal brain development may be affected throughout gestation.
- Effect: Fetal alcohol syndrome

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



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

Also causes vasoconstriction

Complications in pregnancy:
- Spontaneous abortion
- Fetal death in utero
- Premature rupture of membranes
- Preterm labor
- IUGR
- Meconium staining
- Abruptio placenta

Effects:

- Cocaine is teratogenic, associated with in utero fetal cerebral infarction, microcephaly, and limb reduction defects.
- Genitourinary malformations
- Neurobehavioral abnormalities

Marijuana:

Alter brain neurotransmitters so the brain chemistry. remain in the body for up to 30 days, thus prolonging fetal exposure. produces as much as five times the amount of carbon monoxide as does cigarette smoking .

Opiates:

Increased rates of stillbirth, fetal growth restriction, prematurity, and neonatal mortality,

Amphetamines:

A potent stimulant that is inhaled, injected, or snorted, associated with decreased fetal head circumference and increased risk of abruptio placentae, IUGR, and fetal death in utero. However, no proven teratogenicity exists.

Hallucinogens:

No evidence proves that lysergic acid diethylamide (LSD) or other hallucinogens cause chromosomal damage, No proven teratogenicity to LSD exists

T1 :

- Thalidomide: phocomelia
- Cytotoxic drugs: multiple congenital malformations
- Vitamin A derivates (isotretinoin): craniofacial defects
- Lithium: ebstein anomaly of tricuspid valve
- Steroids: cleft lip and or cleft palate
- Warfarin: skeletal abnormalities

T2 and T3:

- Tetracycline: tooth and bone defects
- Chloramphenicol: Grey baby syndrome, intra-uterine foetal death
- Aminoglycoside: ototoxicity
- Fluoroquinolone: interference with cartilage growth
- Phenytoin: craniofacial defect, mental deficiency
- warfarin: CNS malformations
- ACE inhibitors: irreversible renal damage
- Tobacco smoking: retarded fetal growth

DRUGS IN LACTATION

- The route of maternal drug administration, dose, pharmacokinetics, the type of medication, the baby's age and maturity level, the frequency and volume of feeding have influence on breast milk drug concentration
- A drug taken 30-60 minutes after breast feeding, and 3-4 hours before next feeding, reduced the amount of drug in baby blood
- Benefits of breastfeeding are well known, so doctors should recommend a mother wean only when there is scientific documentation that a drug will be harmful to her infant physician should always look at the situation from a risk/benefit perspective .

- Factors:

- Medication enters the breast mainly via passive diffusion or sometimes via active transport. The passage of drugs to milk is directly proportional to its maternal plasma concentration
- The pH of breast milk is slightly more acid (pH=7.2) than plasma (pH=7.4) .
- Therefore, basic drugs are more un-ionizable (more lipid soluble) in blood than in milk. Lipophilic drugs that pass to breast milk get more ionized (due to higher acidity of milk) and trapped in milk.
- Hind-milk is released in the last few minutes of nursing, fore-milk is released from beginning until the last few minutes of the nursing Drugs which are more lipophilic tends to concentrate in the hind-milk than in the fore-milk which has less lipid content.

Breastfeeding and Drugs

Table 25. Drug Safety During Breastfeeding

Safe During Breastfeeding	Contraindicated When Breastfeeding
Analgesics (e.g. acetaminophen, NSAIDs)	Chloramphenicol (bone marrow suppression)
Anticoagulants (e.g. heparin)	Cyclophosphamide (immune system suppression)
Antidepressants (e.g. sertraline, fluoxetine, TCAs)	Sulphonamides (in G6PD deficiency, can lead to hemolysis)
Antiepileptics (e.g. phenytoin, carbamazepine, valproic acid)	Nitrofurantoin (in G6PD deficiency, can lead to hemolysis)
Antihistamines	Tetracycline
Antimicrobials (e.g. penicillins, aminoglycosides, cephalosporins)	Lithium
β-adrenergics (e.g. propanolol, labetalol)	Cocaine
Insulin	Phenindione
Steroids	Bromocriptine
OCP (low dose) – although may decrease breast milk production	Anti-neoplastics and immunosuppresants
	Psychotropic drugs (relative contraindication)

Breastfeeding: Contraindicated Drugs

BREAST

Bromocriptine/**B**enzodiazepines
Radioactive isotopes/**R**izatriptan
Ergotamine/**E**thosuximide
Amiodarone/**A**mphetamines
Stimulant laxatives/**S**ex hormones
Tetracycline/**T**retinoin

Drug/Class	Possible Adverse Effects in Infant
Antineoplastic agents	Fetal death, congenital anomalies, organ system toxicity
Immunosuppressants	Potential suppression of the immune system
Lithium	High potential for toxicity
Chloramphenicol	Blood dyscrasias, aplastic anemia
Ergot alkaloids	Ergotism poisoning
Radiopharmaceuticals	Potential toxicity; brief to full interruption of breastfeeding recommended
Bromocriptine	Suppresses prolactin secretion; hyperprolactinemic mothers taking drug can breastfeed successfully
Iodides	Thyroid suppression

VACCINES IN PREGNANCY

INTRODUCTON

- In general, inactivated immunizations present a low risk for adverse outcomes in pregnant women and their offspring.
- With the exception of yellow fever and smallpox(absolute), live vaccines are relatively contraindicated in pregnancy. All live vaccines should be avoided during pregnancy unless the risk of disease exposure exceeds the potential risk of immunization.
- Maternal immunization has been demonstrated to be a safe and effective strategy for protecting both pregnant women and their infants from severe vaccine-preventable disease, including influenza and pertussis.

PRECONCEPTION

- BEFORE PREGNANCY
  Women should be vaccinated against preventable diseases in their environment according to the recommended adult immunization schedule
  Ensuring immunity against -Measles -Mumps -Rubella -Varicella is important (also given postpartum if not taken before / during pregnancy)
  Pregnancy should be avoided for 28 days following administration of a live vaccine

DURING PREGNANCY

- Benefits of vaccinating of pregnant women usually outweigh potential risks :

1- when the likelihood of disease exposure is high

2- when infection would pose a risk to the mother or fetus

3- when the vaccine is unlikely to cause harm.

- Goals :

1- Diminish the severity of infections

2- Passive protection against vaccine-preventable infections

3- Improved birth outcomes.

- Antenatal screening during each pregnancy:

-Rubella

-HBsAg

- Timing of immunization during pregnancy :

-If its medically indicated : at any gestational age

-If not : delay until the second trimester ; as the possibility of risk to fetal development cannot be definitively excluded . Or Between weeks 28 to 32 of gestation which may optimize the transfer of antibodies to the fetus .

VACCINES CONTRAINDICATED DURING PREGNANCY

1- Measles, mumps and rubella

These vaccines should not be administered to women known to be pregnant because of the possible risk of teratogenic effects of the vaccine on the fetus Women should be counselled to avoid becoming pregnant for 28 days after vaccination with MMR .

2- Varicella

Pregnant women should not be vaccinated against Varicella zoster (chicken pox) because of the known adverse effects of the varicella virus on the fetus Where nonpregnant women are vaccinated they should be advised to avoid becoming pregnant for 4 weeks after completing the two-dose vaccine schedule.

3- Human papillomavirus

not recommended for use during pregnancy as their safety has not been evaluated in pregnant women woman is found to be pregnant after initiating the vaccination series, the remainder of the three dose regimen should be delayed until completion of the pregnancy

- **Vaccines Recommended in Pregnancy:**

1- Influenza vaccine

2- tetanus vaccine

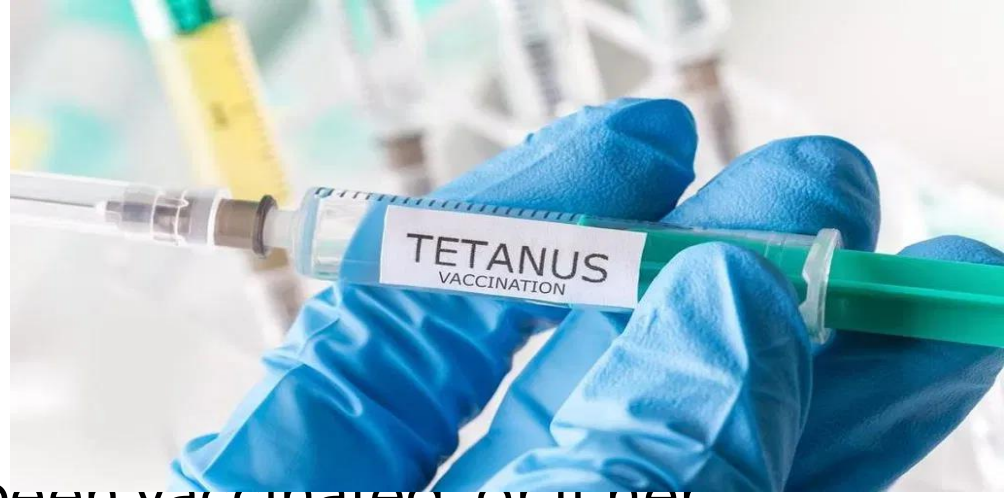
3- Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine

4- Respiratory syncytial virus (RSV) vaccine

INFLUENZA VACCINE

- The flu shot is recommended for women who are pregnant during flu season at any trimester. The flu shot is made from an inactivated virus, so it's safe for both mother& baby.
- Avoid the influenza nasal spray vaccine, which is made from a live virus.
- pregnant women should be vaccinated even if they received an influenza vaccine during a previous pregnancy.

TETANUS VACCINE

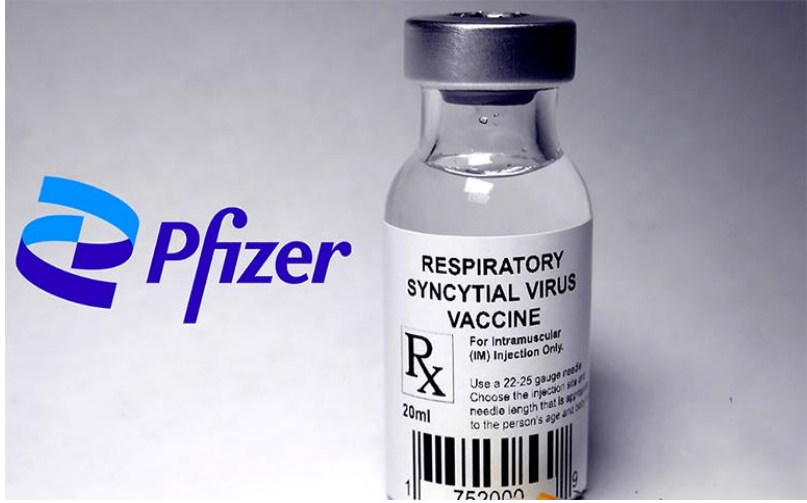


- If a pregnant woman has NOT previously been vaccinated, or if her immunization status is unknown, she should receive two doses of a tetanus toxoid-containing vaccine (TT- CV) one month apart.
- Second dose given at least two weeks before delivery.
- A third dose is recommended six months after the second dose, which should extend protection to at least five years.
- Another dose for each subsequent pregnancy

TETANUS TOXOID, REDUCED DIPHTHERIA TOXOID AND ACELLULAR PERTUSSIS (TDAP) VACCINE

- Given during each pregnancy ,to all pregnant women , irrespective of the patient's prior history of receiving Ideally, the vaccine should be given between 27 and 36 weeks of pregnancy ,but can be given at any time
- Common side effects:
- Erythema, swelling, pain, and tenderness at the injection site.
- Fatigue.
- Fever.

RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINE



- The FDA approved active immunization of pregnant individuals at 32 through 36 weeks' gestational age with RSV vaccine (Abrysvo) for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by RSV in infants from birth through 6 months of age.

VACCINES FOR SPECIAL CIRCUMSTANCES

- These vaccines are generally safe during pregnancy, but they are only given if there is a medical indication like Pregnant women with comorbidities or exposures that place them at high risk. Including:
- Hepatitis A vaccine, Hepatitis B vaccine ,Meningococcal vaccine, Pneumococcal conjugated vaccine ,Typhoid vaccine, Rabies vaccine & Yellow fever vaccine .

VACCINES IN LACTATION

- The two vaccines that are generally not recommended for breastfeeding mothers are smallpox vaccine and yellow fever vaccine.
- All other vaccines, both inactivated and live-attenuated, can be administered safely to lactating women without interruption in infant feeding patterns. Inactivated vaccines pose no risk to the infant as they cannot cause infection in either the lactating woman or her child. Live vaccines are capable of replication; however, mumps, measles, and varicella virus have not been identified in breast milk. Although rubella vaccine virus has been found in breastmilk, the virus has not been found to infect the infant and breastfeeding is not a contraindication to postpartum immunization. The advise is that recombinant, subunit, polysaccharide and conjugate vaccines pose no risk to breastfeeding mothers or their infants

Routine (common) vaccinations	Recommended before pregnancy	Recommended during pregnancy
Flu shot	Yes	Yes, if you didn't get it before pregnancy
Hepatitis A	Maybe	Maybe
Hepatitis B	Maybe	Maybe
Hib	Maybe	Maybe
HPV	Maybe, through age 26	No
MMR	Maybe	No
Meningococcal	Maybe	Maybe
Pneumococcal	Maybe	Maybe
Td	Maybe	Maybe (better to get Tdap)
Tdap	Maybe (better to get during pregnancy)	Yes, during every pregnancy (if you don't get it during pregnancy, get it right after giving birth)
Varicella	Maybe	No
Zoster	No	No

RESOURCES

- 1. Medscape :

A. https://emedicine.medscape.com/article/260725-overview

B. https://emedicine.medscape.com/article/2500098-overview#a18

- 2. Uptodate :

A. https://uptodatefree.ir/image.htm?imageKey=DRUG%2F50021

B. https://pro.uptodatefree.ir/show/442

3. Pubmed (NIH): https://pubmed.ncbi.nlm.nih.gov

THANK YOU