



Teratogens & drugs of abuse

Objectives:

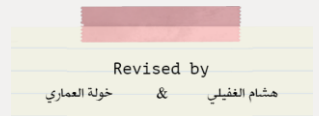
To know:

- > Factors affecting drug **placental transfer**
- > **Harmful effects** of drugs during different stages of development
- > **FDA classifications** of drugs.
- > **Teratogenic** drugs
- > **Adverse effects** of drugs
- > Effects of **drug abuse**

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 - ✓ A big thanks to Shamma Alsaad.

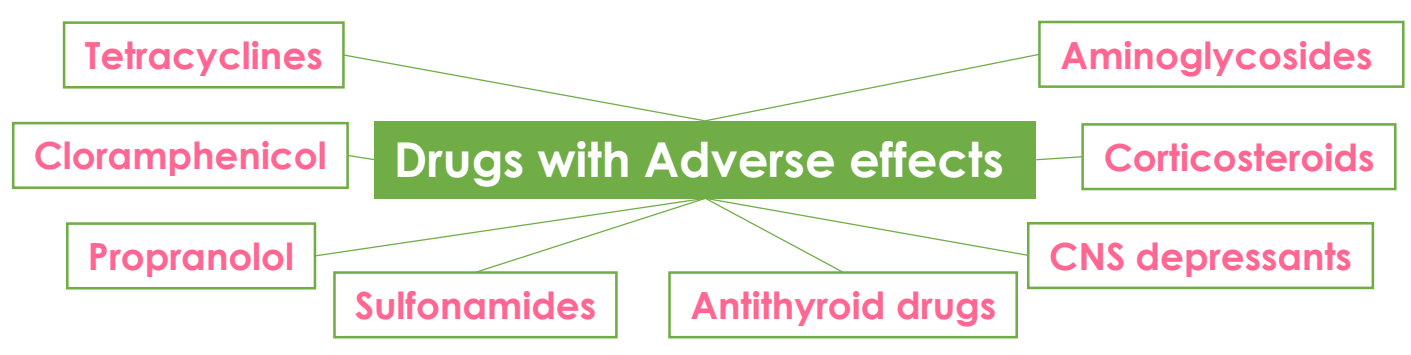
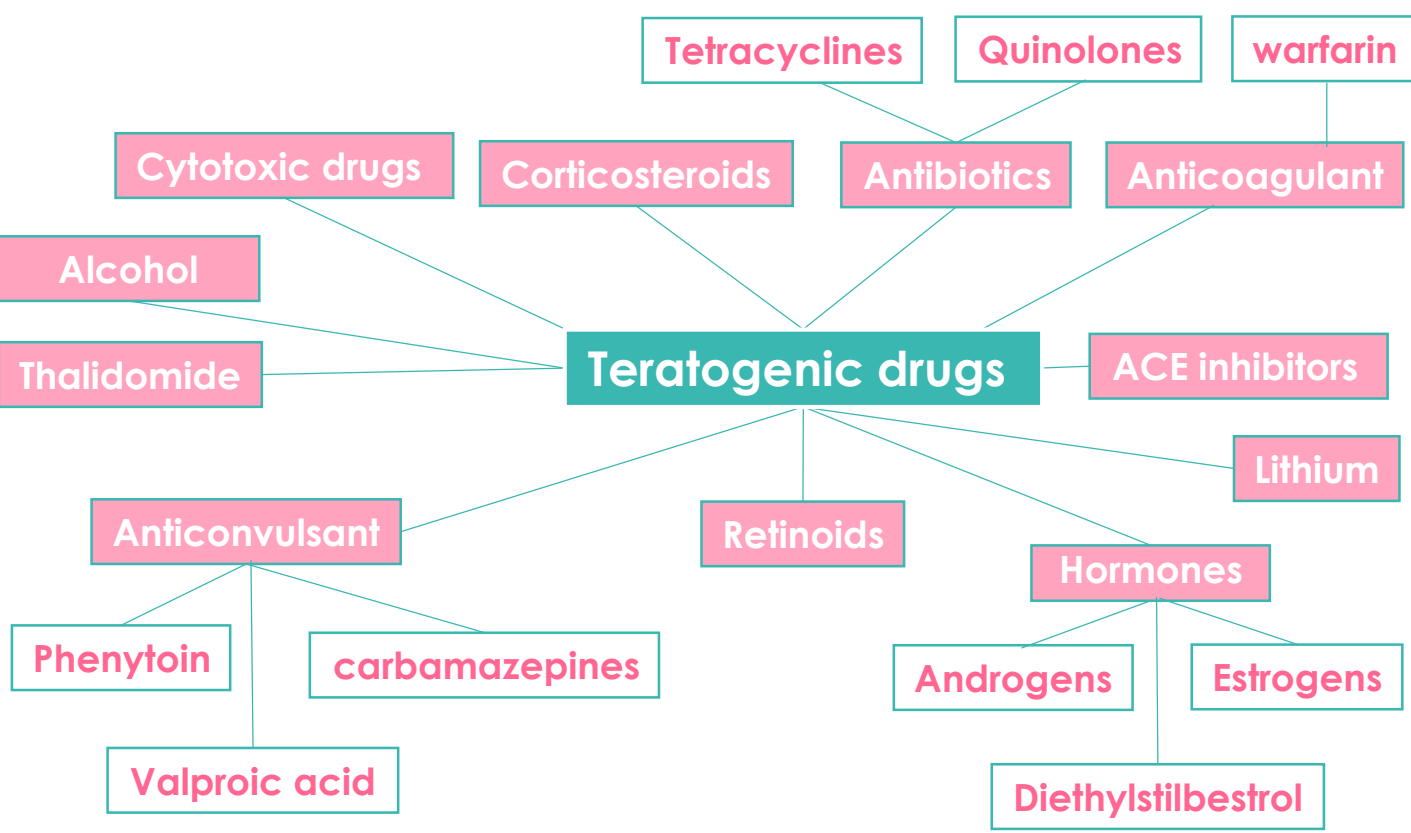


سلايد ٣ ، ٤ مهم مرة إنكم تفهمونها. في الامتحان حسب كلام البروف: الغالب ما راح يطلع من سلايد ٥ إلى ١٠ (جزئية الأدوية)

Drug's name | **Doctors' notes** | **Important** | **Extra**

« قل سيروا في الأرض فانظروا كيف بدأ الخلق »

Mind Map



To Understand Better

Teratogenesis

Occurrence of congenital defects of the fetus

What is a teratogen?

- It is any **agent** (not a drug only) (medication, street drug, chemicals, disease (e.g. infection), environmental agents) that is able to interfere with fetal development and leads to permanent birth defects.
- This could be more severe during organogenesis which is one of the critical periods of development. (**organogenesis**)

Placental membrane

- The placental membrane is semi-permeable because it is limited by single layer of cells called trophoblast and most of the drugs cross the placenta by passive diffusion.

Factors controlling placental drug transfer

1. Physiochemical properties of the drug.

- A) Lipid solubility
- B) Molecular size
- C) Protein binding

2. The stage of placental and fetal development at the time of exposure to the drug.

3. Duration of exposure to the drug.

If I'm going to prescribe a medication only once for a pregnant woman, will it be dangerous?
Or she has to be exposed for several times to produce effect?
Ans: No! even single dose can cause harm to the fetus

Physiochemical properties of the drug

Lipid solubility of the drug

- **Lipophilic drugs** diffuse readily across the placenta and enter fetal circulation. e.g. (**Thiopental***-anesthesia) crosses placenta & causes **sedation**, **apnea** in newborn infants. *thio=sulfur=high lipid solubility
هذا لا يعني إنه كل دواء cross the placenta يعني إنه ممنوع استخدامه أثناء الحمل
- **Ionized drugs** cross the placenta very slowly so it has very low conc. in the fetus. e.g. **Succinylcholine** & **pancuronium** NMJ blockers, very polar → can't cross the placenta

Molecular size of the drug

MW affects the rate of transfer:
-250 - 500 cross placenta easily.
-500 - 1000 cross placenta with more difficulty.
-Above 1000 → can **not** cross placenta e.g. **Heparin**
لذلك الهيبارين هو المفضل لأن ال MW حقه كبير وهذا ميزة تمنعه من إنه يروح للفتيس

Protein binding

Protein binding in maternal circulation (**delay**) hinders passage of drugs especially **Heparin**, **chloramphenicol** and **propylthiouracil**

يعني لو أنا مخيرة بين دوائين حسب ال p.k حقتهم.. فأختار أيهم؟ الأفضل بصيرون: **Polar** (H₂O solubility), **high MW** & **high protein binding**

The stages of mammalian fetal development

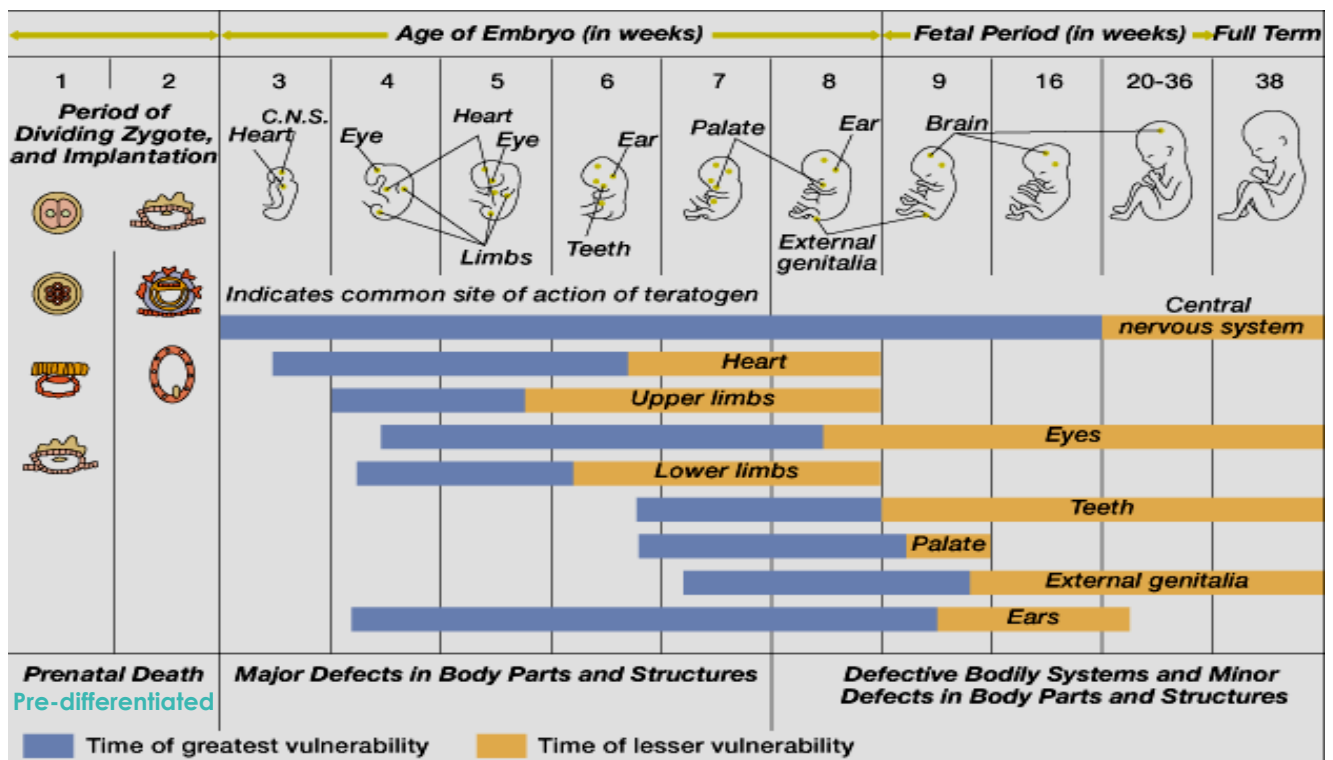
Harmful action of the drug depend upon stage of fetal development at time of drug exposure.

Mammalian fetal development passes through three phases:

1- Blastocyste formation (up to 17 days)	2- <u>Organogenesis</u> (17-60 days) (1 st 2 months)	3- Histogenesis & maturation of function. (60dys – birth)
<ul style="list-style-type: none"> Occurs from (1-16 days) in the first trimester. Period of dividing zygote, implantation Drugs have an all-or-nothing effect. في هذه المرحلة يا إن الدواء يسوي خطر ويحوت وتسقط، أو إنه ما يسوي أي تأثير ويستمر الحمل عادي Exposure to drugs during this period → death of the embryo → abortion 	<ul style="list-style-type: none"> The process by which cells specialize and organize to form the tissues and organs of an organism. Week 2-8. The most sensitive period of pregnancy because major body organs and systems are formed. Exposure to harmful drugs during organogenesis → major birth defect or gross malformation (congenital) (Teratogenesis) 	<ul style="list-style-type: none"> Growth and fetal development occur during this stage. Fetus depends upon nutrients & hormonal supply. Exposure to drugs during (8 weeks onwards) will not induce major malformation but drugs can produce <u>minor morphologic abnormalities</u>, growth retardation and functional defect. → Exposure to drugs can cause “Function problems” rather than “gross malformation” However, <u>CNS is sensitive to toxic effects throughout pregnancy</u> لو حصل وأخذت الحامل دواء خطير في الولادة، ما راح يسبب لي ☹️ teratogenic effect، ليه؟ لأن اتتهينا من مرحلة تصنيع الأعضاء، فاللي بيحصل عندنا بيصير إن العضو موجود، لكن ممكن تتأثر الوظيفة حقتة فقط

إحنا متفقين، إنه أخطر مرحلة للـ 1st trimester, mainly the first 2 months of fetus development الـ organogenesis الـ المرحلة يصير عندنا الـ organogenesis الـ المرحلة التي هو أهم مرحلة في الـ 1st trim ولو أخذت الدواء فيه، بيسبب لي بنسبة كبيرة teratogenic effect !!!! افهموا إن لما نقول له teratogen effect يعني بيحصل في الـ 1st trim

Critical Periods of Human Development



مثلا الكحول، هو C. أثناء الـ 3 شهور الأولى عشان ما يسوي congenital malformation... يعني أقدر أخذ الكحول بعد الـ 1st trim ؟ لا طبعاً!! ليش طيب؟ لأن زي ما نلاحظ إن الـ CNS development & maturation إلى نهاية الحمل، ولو أخذ الكحول راح يأتّر على وظيفة الجهاز العصبي!


Classification & Teratogenesis of drugs

هم قسموها بناء على إيش؟
 عشان أعرف إذا هذا الدواء عمل congenital malformation عندنا نوعين من الدراسات، وحدة على الحيوانات والثانية على الإنسان.. طبعاً أكيد ماراح نجرب على الإنسان؟ إذن كيف عرفوا إنه يسبب ضرر على الإنسان. يصير الطبيب أعطى دواء للحامل (هي تحتاجه وليس بقصد إنه يجرب عليها) وبعدها يصيرون لاحظوا التغير والضرر على الجنين (بالصدفة يعني)





FDA Classification System

Category	General Info	Examples
A	<ul style="list-style-type: none"> Adequate and well-controlled human studies show with no risk to fetus. ✓ Drugs can be used. 	Folic acid Thyroxine
B	<ul style="list-style-type: none"> No risk in animal studies. No <u>adequate</u> and well-controlled human studies. ✓ Drugs can be used in pregnancy 	Paracetamol Erythromycin
C	<ul style="list-style-type: none"> Adverse effects on the fetus in animals only No <u>adequate</u> and well-controlled studies in humans. * Drug may be used in serious situation despite its potential risk. 	Morphine Diclofenac Tramadol
D	<ul style="list-style-type: none"> Positive evidence of human fetal risk based on adverse reaction data from studies in humans, investigational or marketing experience. * May be used in serious diseases or life threatening situations. 	Antiepileptics: valproic acid, phenytoin, carbamazepines
X	<ul style="list-style-type: none"> Proven fetal abnormalities in animal and <u>human</u> studies. The risks involved in the use of the drug in pregnant women clearly outweigh potential benefits. Drugs are teratogens and contraindicated in pregnant women or planning to conceive. ✗ 	Thalidomide

Proven teratogens & some of their teratogenesis (1st trim)

Teratogen	Teratogenesis	
Thalidomide (Sedative & hypnotic) The most notorious human teratogen	<ul style="list-style-type: none"> It had no teratogenic effects in mice and rats but proved teratogenic when used in pregnant women. Phocomelia (literally meaning seal's extremities) <ul style="list-style-type: none"> Shortened or absent long bones of the limbs. Absence of external ears. 	Phocomelia 
Anticoagulant Warfarin	<ul style="list-style-type: none"> ✓ Hypoplasia of nasal bridge ✓ CNS malformation 	احفظوا أسامي الأدوية (وارفرين) وركزوا على تصنيفها (انتي كواقيلانت)









Teratogens & their teratogenesis (1st trim) (cont.)

Teratogen	Teratogenesis	
<p>Corticosteroids</p>	<ul style="list-style-type: none"> ○ Cleft lip and Palate. من الأشياء المميزة للكورتيكوستيرويد <p>Corticosteroids & phenytoin cause oral cleft so relate both to images on the right</p>	
<p>Anticonvulsant</p>	<ul style="list-style-type: none"> ○ Fetal Hydantoin Syndrome • Nail & Digital hypoplasia • Oral Clefts (cleft lip and palate) • Cardiac Anomalies. 	<p>طبيب لو حامل وجاها نوية الصرع، هل أتركها بدون دواء أو أعطيها الدواء بالرغم من خطورته على الجنين؟ يقولون لك نعطياها الدواء + we monitor the dose ، لأن لو ما أعطيناها مع نوية الصرع راح يصير الليبي ischemia ويموت، في نفس الوقت نعطى مع الدواء folic acid supplements لأن التيراتوجينك افكت حق هذي الأدوية سببها في الفولك أيد (في حال استخدمت phenytoin)</p> 
<p>1- Phenytoin</p>		
<p>2- Valproic acid</p>	<ul style="list-style-type: none"> ○ Neural tube defect (spina bifida) ○ Impair folate absorption 	<p>Valpronate is the most dangerous one of anti-epileptic drugs. Cate. X !</p> 
<p>Antibiotics</p>	<ul style="list-style-type: none"> ○ Permanent teeth staining. ○ Altered growth of teeth and bones. ○ Enamel hypoplasia طبقة المينا للأسنان ○ It likes to deposit in Ca²⁺ rich areas (e.g. bones & teeth) 	
<p>Tetracyclines</p>		
<p>Hormones</p>	<ul style="list-style-type: none"> ○ Serious genital malformation: 1. Testicular atrophy in <u>male</u> (estrogen) 2. Fetal masculinization in <u>female</u> (androgen) 3. Vaginal carcinoma of female offspring (only one use of Dieth. causes carcinoma –late-) 	
<p>1. Estrogens 2. Androgens 3. Diethylstilbestrol</p>		
<p>Lithium</p>	<ul style="list-style-type: none"> ○ Cardiovascular anomalies mainly: ▪ Ebstein's anomaly: valvular heart defect involving <i>tricuspid valve</i>. 	
<p>ACE inhibitors</p>	<ul style="list-style-type: none"> ○ ACEIs + Ang2 blockers disrupt the fetal renin-angiotensin system, which is essential for normal renal development: • Fetal & neonatal anuria (no urine formation) • Renal damage ○ Fetal hypotension, hypoperfusion → growth retardation 	
<p>Captopril Enalapril</p>		
<p>Other drugs</p>	<ul style="list-style-type: none"> ○ Cytotoxic drugs: Cytotoxic → target the proliferative cells (as in cancer), here the fetus is developing → a lot of proliferative cells will be destroyed • Folate antagonists (methotrexate) • Alkylating agents (cyclophosphamide) ○ Alcohols (fetal alcohol syndrome) ○ Retinoids: لازم توقف استخدامهم قبل ما تصير حامل، وأفضل توقف قبل 6 شهور • Vitamin A (should be limited to 700 µg/day) • Isotretinoin (used in treatment of <u>Acne</u>) 	<ul style="list-style-type: none"> ▪ Ionizing radiation: diagnostic X-ray or radiation therapy/Radioactive iodine (I¹³¹) <p>Antibiotics</p> <ul style="list-style-type: none"> ▪ Quinolones

Adverse effects of drugs

❖ During second and third trimesters:

- Some drugs can produce **adverse effects** on the fetus more likely than major malformations due to their pharmacological actions.
- Affect growth & fetal development or toxic effects on fetal tissues.
- ✓ Teratogens = 1st trimester. ADRs = 2nd & 3rd trimesters

Drug	Adverse effect
Tetracyclines 	<ul style="list-style-type: none"> ○ Impaired teeth & bone development, yellow-brown discoloration of teeth.
<ul style="list-style-type: none"> ○ Aminoglycosides (Streptomycin, kanamycin)  	<ul style="list-style-type: none"> ○ Ototoxicity = 8th Cranial nerve damage
Cloramphenicol	<ul style="list-style-type: none"> ○ Gray baby syndrome <small>newborn له سمويه gray؟ لأنهم يعملون hypoxia .. هذا حتى ما يصلح أعطيه للـ new born لأن incomplete maturation of liver microsomal enzymes is incomplete + عنده نقص في إنزائم مهم مرة للمتابولزم لهذا الدواء: glucuronyl transferase فيتراكم الدواء في جسم الجنين.</small>
Corticosteroids (orally or systemic injection) 	<ul style="list-style-type: none"> ○ Adrenal atrophy – growth retardation <small>Remember, in the 1st trim → Cleft lip and Palate</small>
Propranolol 	<ul style="list-style-type: none"> ○ Bradycardia, neonatal hypoglycemia, placental insufficiency, reduced uterine blood flow → fetal distress
Antithyroid drugs 	<ul style="list-style-type: none"> ○ Iodide, Methimazole, Carbimazole, propylthiouracil ○ Risk of hypothyroidism and goitre.
<ul style="list-style-type: none"> ○ NSAIDs <ul style="list-style-type: none"> • e.g. Aspirin- indomethacin 	<ul style="list-style-type: none"> ○ Prostaglandin synthesis inhibitors: ○ Constriction of ductus arteriosus (close prematurely) ○ Pulmonary hypertension in newborns ○ Increase in gestation time ○ If taken near delivery: Prolong labor → Bc prostaglandins are important in labor, Neonatal bleeding, Risk of postpartum hemorrhage -antiplatelet activity-.
Benzodiazepines as Diazepam	<ul style="list-style-type: none"> ○ Chronic use → neonatal dependence and withdrawal symptoms <small>طلعت له أعراض الانسحاب، لأنه قبل ما ينولد كان فيه مصدر للبنزو، ولما طلع انقطع عنه المصدر وهو أساساً صار مدمن له</small>
ACEIs 	<ul style="list-style-type: none"> ○ Renal damage
Warfarin 	<ul style="list-style-type: none"> ○ Risk of bleeding.
CNS depressants e.g. diazepam, morphine 	<ul style="list-style-type: none"> ○ Interference with suckling ○ Respiratory depression ○ Reduced blood flow, fetal distress (if taken as chronic use only it will cause these ADRs)
Sulfonamides <small>In general, sulfa containing drugs should not be used</small>	<ul style="list-style-type: none"> ○ Displacement of bilirubin from plasma protein (neonatal hyperbilirubinemia) → Jaundice in the fetus! <small>لو الأم ما لاحظت بعد ولادة طفلها واستمرت فترة، الطفل ممكن develop kernicterus</small>

	Probably safe	Contraindicated	ER Emergency
Hypertension in pregnancy	<ul style="list-style-type: none"> ○ <u>α-methyl dopa</u> ○ Labetalol 	<ul style="list-style-type: none"> ○ ACE inhibitors ○ Angiotensin II receptor blockers ○ Thiazide diuretics ○ Propranolol (not selective) ○ Calcium channel blockers in mild hypertension 	<ul style="list-style-type: none"> ○ Hydralazine ○ Labetalol
Coagulation disorders in pregnancy	<ul style="list-style-type: none"> ○ Heparine <ul style="list-style-type: none"> • Polar, does not cross placenta + high MW ○ Protamine sulphate as <u>antidote</u> for neutralization 	<ul style="list-style-type: none"> ○ Warfarin is contraindicated in all trimesters <ul style="list-style-type: none"> • Cross placenta membrane • <u>1st trimester</u>: teratogenicity • <u>2nd, 3rd</u>: risk of bleeding 	-
Antibiotics in pregnancy	<ul style="list-style-type: none"> ○ Penicillins (ampicillin, amoxicillin) ○ Cephalosporins ○ Erythromycin* and azithromycin* (*macrolides) as alternative in penicillin sensitive individuals, erythromycin estolate should be avoided <ul style="list-style-type: none"> ✓ (risk of hepatic injury to mother) <p>2 groups can be used: beta-lactam antibiotics & macrolides (erythromycin + azithromycin)</p>	<ul style="list-style-type: none"> ○ Aminoglycosides: <u>ototoxicity</u> ○ Tetracyclines: Teeth and bones deformity ○ Sulfonamides: neonatal jaundice-kernicterus ○ Chloramphenicol: Gray baby syndrome ○ Quinolones as ciprofloxacin: bone and cartilage damage (arthropathy) <p>أغلب الأنثبيوتكس عندها مشاكل ☺</p>	-

Anti-thyroid drugs in pregnancy

Used in thyrotoxicosis or Grave's disease

- **Propylthiouracil** (preferable over others) → (**protein-binding**)
- **Methylthiouracil** (Methimazole) - Carbimazol
- **Radioactive Iodine** (I^{131})
- ✓ All can cross placenta
- ✓ All have risk of congenital goiter and hypothyroidism
- ✓ The lowest dose of antithyroid drugs should be used.

Summary of Drugs of choice in pregnancy

Antihypertensive	<ul style="list-style-type: none"> ○ α-methyl dopa ○ Labetalol (α - β Blocker) ○ Hydralazine (emergency only)
Antibiotics	<ul style="list-style-type: none"> ○ penicillin, cephalosporins, erythromycin
Antidiabetics	<ul style="list-style-type: none"> ○ Insulin is safe, <u>avoids oral antidiabetics</u>
Anticoagulants	<ul style="list-style-type: none"> ○ Heparin
Analgesics	<ul style="list-style-type: none"> ○ Acetaminophen
Antithyroid drugs	<ul style="list-style-type: none"> ○ Propylthiouracil (<u>protein-bound</u>)
Anticonvulsants	<ul style="list-style-type: none"> ○ All antiepileptics have potential to cause malformations, carbamazepine may be choice. ○ Avoid valproic acid (<u>highly teratogenic</u>). ○ Folic acid supplementation prevents neural tube defects in women receiving AEDs

Drugs of Abuse in Pregnancy

Definition	<ul style="list-style-type: none"> ○ Habitual use of drugs not for therapeutic purposes but for alteration of one's mood or state of consciousness. ○ Drug abuse may lead to organ damage (teratogens), <u>addiction</u> (in the fetus), and disturbance of behavior.
Most common abused drugs	<ul style="list-style-type: none"> ○ Alcohol; Cocaine; Nicotine; Marijuana; Amphetamines; Barbiturates; Opium Alkaloids, Benzodiazepines.

Drugs of Abuse in Pregnancy

Alcohol

- The use of alcohol is **contraindicated** during **all trimesters of pregnancy**
 - **Fetal Alcohol Syndrome (FAS):**
- Caused by chronic maternal alcohol abuse during early weeks of first trimester of pregnancy.
- **Characters:**
 - Microcephaly
 - Intrauterine growth retardation
 - **Craniofacial abnormalities***
 - CVS abnormalities
 - **CNS abnormalities** (*attention deficits, intellectual disability, mental retardation*)

*صفة مميزة جدًا تعلمك إن
الأم كانت مدمنة للكحول.



Cocaine

- Cocaine is **low MW.**
 - easily passes into fetus through placenta.
- **Inhibits re-uptake of sympathomimetics (epinephrine, NE, dopamine),** → causing **vasoconstriction**, rapid heart rate, hypertension (Vascular disruption).
- It **↓ blood flow to uterus**, fetal oxygenation and intestinal blood flow.
- It **increases uterine contractility.**
- **Characters:**
 - Microcephaly
 - Prematurity
 - Low birth weight.
 - **Abruptio placentae** (separation of placenta from uterus wall **before** delivery) → as a result of hypoxia
 - Growth retardation
 - Mental retardation
 - Withdrawal symptoms



Tobacco

- Tobacco contains nicotine and carbon monoxide that may harm fetus.
- **Tobacco can produce:**
 - ↓ blood flow to placenta
 - **Fetal hypoxia**
 - Retarded fetal growth
 - ↓ birth weight
 - Increased spontaneous abortion → **Preterm labor and stillbirth** (perinatal mortality)

Conclusion

- ✓ The use of drugs during pregnancy should be avoided unless absolutely necessary.
- ✓ Most drugs cross the placenta to some extent.
- ✓ Birth defects are of great concern.
- ✓ Drugs can harm the embryo or fetus depending upon the stage of fetal development.
- ✓ The most critical period of pregnancy is **organogenesis** (17 days – 8 weeks).
- ✓ Alcohol, nicotine and other addicting drugs should be avoided.

Summary-1

Factors controlling placental drug transfer	<ul style="list-style-type: none"> • <u>Physiochemical properties of the drug:</u> <ul style="list-style-type: none"> ○ Lipid solubility or diffusion. <ul style="list-style-type: none"> - Lipophilic ex: Thiopental → cross placenta → sedation and apnea in newborn. - Ionized ex: Succinylcholine & pancuronium cross placenta very slowly → very low concentration in fetus. ○ Molecular size. <ul style="list-style-type: none"> - As much as ↑ in the MW → ↓ the diffusion. Ex: Heparin can't cross placenta ○ Protein binding. <ul style="list-style-type: none"> - Protein binding in maternal circulation hinders passage of drugs especially. Ex: propylthiouracil and chloramphenicol. • <u>The stage of placental and fetal development.</u> <ul style="list-style-type: none"> ○ At the time of exposure to the drug. • <u>Duration of exposure to the drug.</u>
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FDA Classification System	A	<ul style="list-style-type: none"> • Controlled human studies show no risk to fetus • Ex: Folic acid and Thyroxine
	B	<ul style="list-style-type: none"> • Animal studies ok • No human data • Ex: Paracetamol and Erythromycin
	C	<ul style="list-style-type: none"> • Animal studies only are not ok • No human data • Risk can not be ruled out • Ex: Morphine
	D	<ul style="list-style-type: none"> • Positive evidence of risk to human fetus • Benefits outweigh risks • Ex: Antiepileptic
	X	<ul style="list-style-type: none"> • Contraindicated in pregnancy and women how plan to conceive due to poven fetal abnormalmailes • Ex: Thalidomide

Drugs abuse	Definition	Habitual use of drugs not for therapeutic purposes but for alteration of one's mood or state of consciousness.		
	Alcohol	Contraindicated in all trimesters because of Fetal alcohol syndrome FAS: Microcephaly, Craniofacial abnormalities , Intrauterine growth retardation, CVS abnormalities, CNS abnormalities (attention deficits, intellectual disability, mental retardation)		
	Cocaine	P.K	Low molecular weight, easily passes into fetus through placenta.	
		MOA	Inhibits re-uptake of sympathomimetic (epinephrine, NE, dopamine) → vasoconstriction , rapid heart rate, hypertension (Vascular disruption).	
		Effects	It ↓ blood flow to uterus and fetal oxygenation (Hypoxia). It increases uterine contractility , Microcephaly, Prematurity. Intrauterine growth retardation. Placental abruption (separation of placenta from uterus wall before delivery) Growth and Mental retardation.	
Tobacco	Contains nicotine and carbon monoxide that may harm fetus → ↑ risk : Spontaneous abortion, Prematurity, ↓ blood flow to placenta, Fetal hypoxia , Retarded fetal growth, Low birth weight, Perinatal mortality .			

Summary-2

Class	Drug	Teratogenic effects	Adverse effects during 2 nd & 3 rd trimester
Thalidomide	-	Phocomelia , Shortened or absent long bones of the limbs	-
Anticonvulsant	phenytoin	Fetal Hydantoin Syndrome: Nail & Digital hypoplasia, Oral Clefts (cleft lip and palate), Cardiac Anomalies	-
Anticoagulants	Warfarin	Hypoplasia of nasal bridge, CNS malformation.	Risk of bleeding
Antiepileptic	Valproic acid	Neural tube defect (spina bifida). Impairs folate absorption.	-
	Carbamazepines	-	-
Antibiotics	Tetracyclines	Altered growth of teeth and bones. Permanent teeth staining. Enamel hypoplasia.	Impaired teeth and bone development, yellow-brown discoloration of teeth
	Quinolones	-	-
	Aminoglycoside Ex: Streptomycin, kanamycin	-	Ototoxicity → 8th Cranial nerve damage
	Chloramphenicol	-	Gray baby syndrome
Corticosteroids	-	Cleft lip and Palate.	Adrenal atrophy and growth retardation
Hormones → Serious genital malformation	Estrogens	Testicular atrophy in male fetus	-
	Androgens	Fetal masculinization in female fetus	-
	Diethylstilbestrol	Vaginal carcinoma of female offspring	-
-	Lithium	Ebstein's anomaly: Cardiovascular anomalies mainly valvular heart defect involving tricuspid valve.	-
ACEI	Captopril	ACE inhibitors disrupt the fetal renin-angiotensin system → - Renal damage, - Fetal & neonatal anuria, - Hypotension, hypoperfusion → growth retardation	-
	Enalapril		
Cytotoxic drugs	Folate antagonists Ex: Methotrexate	-	-
	Alkylating agents: Cyclophosphamide	-	-

Summary-3

Class	Drug	Adverse effects during 2 nd & 3 rd trimester
β Blocker	Propranolol	Bradycardia, neonatal hypoglycemia , placental insufficiency, reduced uterine blood flow → fetal distress
Antithyroid	Iodide	risk of neonatal hypothyroidism and goiter
	methimazole	
	carbimazole	
	propylthiouracil	
Benzodiazepine	Diazepam	In chronic use → neonatal dependence and withdrawal
NSAIDs	Aspirin-indomethacin which is Prostaglandin synthesis inhibitors	Leading to Constriction of ductus arteriosus (close prematurely), pulmonary hypertension in newborns, ↑ in gestation time, prolong labor, neonatal bleeding and risk of postpartum hemorrhage

Drugs effectiveness near labor

Drug	Effects
CNS depressants	Ex: Diazepam, Morphine. → Interference with suckling, respiratory depression, ↓ blood flow and fetal distress.
Sulfonamides	Can displace bilirubin from albumin (neonatal hyperbilirubinemia)

Medical conditions at pregnancy

Contraindicated	Probably safe	Emergency
Hypertension		
<ul style="list-style-type: none"> • ACEI. • Angiotensin II receptor blockers. • Thiazide diuretics. • Propranolol. • Ca⁺⁺ channel blockers in mild hypertension. 	<ul style="list-style-type: none"> • α- Methyl Dopa • Labetalol 	<ul style="list-style-type: none"> • Hydralazine • Labetalol

Coagulation disorders

Warfarin in all trimester because it cross placenta→: <ul style="list-style-type: none"> • 1st → teratogenicity (chondroplasia) • 2nd & 3rd → risk for bleeding. 	<ul style="list-style-type: none"> • Heparin because it is polar→ doesn't cross placenta • Antidote which potent sulphate. 	-
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Antithyroid drugs in pregnancy

<ul style="list-style-type: none"> • Propylthiouracil • ¹³¹I 	<ul style="list-style-type: none"> • Methylthiouracil • Carbimazol 	Propylthiouracil with lowest dose due to protein binding	-
→ congenital goiter ,hypothyroidism			

Antibiotics in pregnancy

<ul style="list-style-type: none"> • Tetracyclines→ Teeth and bone deformity. • Quinolone Ex: Ciprofloxacin → arthropathy which is bone and cartilage damage. • Aminoglycosides→ Ototoxicity • Sulfonamides→ Neonatal jaundice – kernicterus • Chloramphenicol→ Gray baby syndrome 	<ul style="list-style-type: none"> • Penicillin Ex: ampicillin and amoxicillin. • Cephalosporins • Erythromycin and azithromycin use in case of penicillin-sensitive individuals but Erythromycin estolate should be avoid→ risk of hepatic injury to mother. 	-
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Summary-4

Drugs of choice in pregnancy

Class	Drugs
Antihypertensive	<ul style="list-style-type: none">• α Methyl dopa• Labetalol which is α and β blocker• Hydralazine for emergency only
Antibiotics	<ul style="list-style-type: none">• Penicillin• Cephalosporins• Erythromycin
Antidiabetics	<ul style="list-style-type: none">• Insulin• Avoids oral antidiabetics
Anticoagulants	<ul style="list-style-type: none">• Heparin
Analgesics	<ul style="list-style-type: none">• Acetaminophen
Antithyroid	<ul style="list-style-type: none">• Propylthiouracil because of protein-bound
Anticonvulsants	<ul style="list-style-type: none">• All Antiepileptics have potential to cause malformations• Avoid valproic acid because of highly teratogenic• Folic acid supplementation prevents neural tube defects in women receiving AEDs

MCQs

1- Which one of the following period is the most sensitive to the drug during pregnancy:

- A. blastocytes
- B. organogenesis
- C. Histogenesis & maturation function

2- Molecular size of 250-500 cross placenta with more difficulty:

- A. True
- B. False

3- In FDA's drug classification system, category C represents:

- A. Evidence of human fetal risk, May be used in serious diseases.
- B. Adverse effects on animal studies only, few studies indicate some risk to fetus, can't be used till new evidence confirm otherwise.
- C. Adverse effects on animal studies only, human studies not showing similar results, can be used.
- D. Adverse effects on animal studies only, No human studies, human fetal risk is unknown, may be used in serious situation.

4- A mother comes with her baby to the dental clinic after discovering that her growing teeth were stained, after further investigations, her dentist found out that she has enamel hypoplasia, which one of the following drugs is probably been used by the mother during her pregnancy with this baby?

- A. Valproic acid
- B. Quinolones
- C. Tetracyclines
- D. Lithium

5- Prolong in labor is one of the adverse effects of which of the following:

- A. Indomethacin
- B. Sulfonamide
- C. ACEIs
- D. Tetracycline

6- Which of the following antibiotics is probably safe in pregnancy:

- A. Erythromycin estolate
- B. Chloramphenicol
- C. erythromycin
- D. All antibiotics are contraindicated

7- A 33-year-old pregnant woman begins taking a new drug, Drug X, for morning sickness. Drug X has not been found to have adverse maternal or fetal effects in animal models, but no human studies have been done. Under which FDA Pregnancy Category would Drug X fall?

- A. A
- B. B
- C. C
- D. X

8- A woman in the 28th week of pregnancy has developed pregnancy induced hypertension with a blood pressure reading of 150/100 mm Hg. Select the most appropriate antihypertensive drug for her:

- A. Lisinopril
- B. Losartan
- C. Hydrochlorothiazide
- D. Methyldopa

9- A 26-year-old woman at 33 weeks gestation presents to the emergency department with pain and swelling in her right calf. A duplex of the right calf confirms the presence of a deep vein thrombosis (DVT). What is the most appropriate treatment for the rest of her pregnancy?

- A. Warfarin
- B. Aspirin
- C. Heparin
- D. Streptokinase

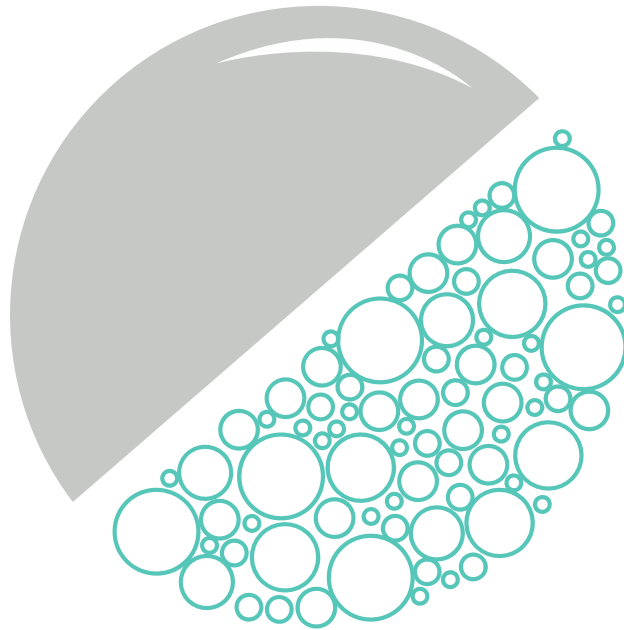
10- Which of the following agents would likely produce a newborn with the lowest intelligence quotient (IQ)?

- A. Carbamazepine
- B. Lamotrigine
- C. Phenytoin
- D. Valproic acid

11- Aspirin is contraindicated in pregnant women near term because:

- A. Labor may be delayed and prolonged
- B. Blood loss during delivery may be more
- C. Fetus may suffer premature closure of ductus arteriosus
- D. All of the above

Thank you for checking our team!



Pharmacology 435

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Source:

1. 435's slides.