



# Posology 2

By

**Dr. Lamiaa Meghawery**

**Associate professor of pharmacology  
FACULTY OF DENTISTRY  
Mutah university**



# ILOS



Recognize the clinical importance of factors affecting drug dosing.

Rationalize importance of pharmacokinetic changes in hepatic patients.

Identify factors affecting drug dosing in renal patients.

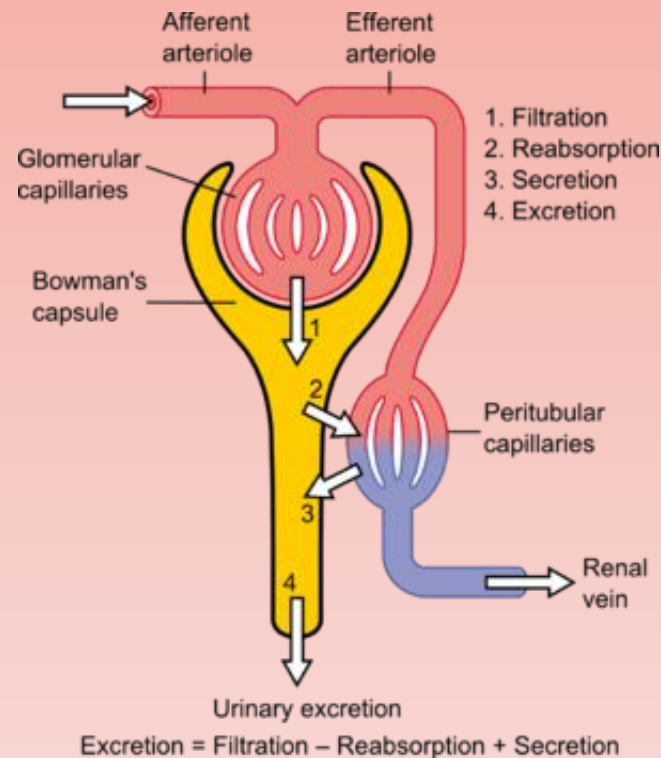
Enumerate teratogenic drugs.

# *Drugs use in patients with renal impairment*



# clearance

- Drugs cleared by renal route often require **adjustment** of **clearance** in **proportion** to **renal function** .
- This can be estimated from the **creatinine clearance** .



# Calculating creatinine clearance



$$\bullet \text{ Cr Cl (ml/min)} = \frac{\text{U cr} \times \text{V urine}}{\text{S cr} \times \text{T}}$$

- **U cr** = the urine creatinine concentration (mg/dl).
- **V urine** = the volume of urine collected (ml).
- **S cr** = the serum creatinine collected at the midpoint of the urine collection (mg/dl).
- **T** = the time of urine collection (minute).

# ***(Cockcroft-Gault Formula)***



**Creatinine Clearance (ml/min) =**

$$\frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}}$$

**N.B. Multiply  $\times 0.85$  in a female patient.**

**Normal creatinine clearance is 100-120 ml/min.**



Are you a new resident?  
Make the most of PGY-1 with our guide.



# Creatinine Clearance (Cockcroft-Gault Equation) ☆

Calculates CrCl according to the Cockcroft-Gault equation.

When to Use ▾	Pearls/Pitfalls ▾	Why Use ▾
---------------	-------------------	-----------

Sex	Female	Male
-----	--------	------

Age	<input type="text"/>	years
-----	----------------------	-------

Weight	Norm: 45 - 113	kg ⇄
--------	----------------	------

Creatinine	Norm: 62 - 115	μmol/L ⇄
------------	----------------	----------

The Cockcroft-Gault Equation may be inaccurate depending on a patient's body weight and BMI; by providing additional height, we can calculate [BMI](#) and provide a modified estimate and range.

## Result:

Please fill out required fields.

# *How to Modify Doses for patients with Renal/Liver impairment*



1- ↓ dose and retain the usual dosage interval.

2- Retain the usual dose and ↑ the dosage interval.

3- ↓ the dose and ↑ the dosage interval (do both).

# How to calculate the corrected dose?



Normal Creatinine Clearance  $\rightarrow$  Average Dose

Patient Creatinine Clearance  $\rightarrow$  Corrected Dose

$$\text{Corrected Dose} = \frac{\text{Average dose} \times \text{Patient creatinine clearance}}{100\text{ml/min}}$$



Calculate a dose of digoxin for a renal patient if you know that this creatinine clearance is 40 ml/min, (Normal average dose is 120 mg/ day, and normal creatinine clearance is 100 ml/min)

***How to calculate the corrected dose in renal patient?***



Corrected dose=

$$\frac{\text{Average dose} \times \text{Patient creatinine clearance}}{\text{normal creatinine (100ml/min)}}$$

$$\frac{120 \times 40}{100} = 48 \text{ mg / day}$$

# *Drugs in patients with liver impairment*



# *Special considerations in the following situation*



- \*Use of Hepato-toxic drugs.
- \*Use of drugs with high protein binding.
- \*Use of anticoagulants/drugs that cause bleeding.
- \*Presence of liver failure:

# ↓Albumin

# ↑Prothrombin time

**↑Liver enzymes are not always reliable**

# *Special considerations*



- \* The most common way to estimate the ability of liver to metabolize the drugs is to determine the **Child-Pugh score** for a patient.

# *Child-Pugh scores*



<b>Test/symptom</b>	<b>Score 1 point</b>	<b>Score 2 points</b>	<b>Score 3 points</b>
Total bilirubin(mg/dl)	<2.0	2.0-3.0	>3.0
Serum albumin(g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time(seconds prolonged over control)	<4	4-6	>6
Ascites	Absent	Slight	Moderate
Hepatic encephalopathy	None	Moderate	Severe

# *Child-Pugh scores*



- The Child-Pugh score for a patient with normal liver function is 5, whereas for abnormal (hepatic damage) is 15

**5:** the normal usual dose.

**6&7:** No correction still needed.

**8&9:** decrease 25% of the usual dose.

**10 or more:** decrease 50% of the usual dose.



Calculate a dose of propranolol for a hepatic patient if you know that this Child-Pugh score is 9 (Normal average dose is 100 mg/ day).

**5:** the normal usual dose.

**6&7:** No correction still needed.

**8&9:** decrease 25% of the usual dose.

**10 or more:** decrease 50% of the usual dose.

**Normal dose is 100 mg so patient dose is 75 mg**

# Drugs In Pregnancy

**Teratogenic Drug:  
Crosses Placenta  
&  
Causing Fetal  
Malformations**



# Drugs In Pregnancy



- **Five** categories were established suggesting the potentiality of causing birth defects according to FDA.
- Drug categories run from the "**category A**" (safest) to "**category X**" (known danger- never used).
- In general, most drugs are contraindicated **unless the potential benefits** of taking the drug outweigh the risks to the fetus or the infant.

# Table 1. FDA Drug Risk Classification

Category	Description
A	Controlled studies in humans show no risk to the fetus
B	No controlled studies have been conducted in humans; animal studies show no risk to the fetus
C	No controlled studies have been conducted in animals or humans
D	Evidence of human risk to the fetus exists; however, benefits may outweigh risks in certain situations
X	Controlled studies in both animals and humans demonstrate fetal abnormalities; the risk in pregnant women outweighs any possible benefit

*Source: References 4-7.*



- Adequate well controlled studies in in human show no risk to the fetus.

Vitamins  
except vit A

Ampicillin and amoxycillin.



- Animal studies show risk,  
but human findings do not show this risk.
- If no adequate human studies have been  
done and animal studies are negative.



- Risk cannot be ruled out.
- Human studies are lacking and animal studies are either positive for fetal risk or lacking.
- The drug may be used during pregnancy if the potential benefits of the drug outweigh its possible risks.

# Category D

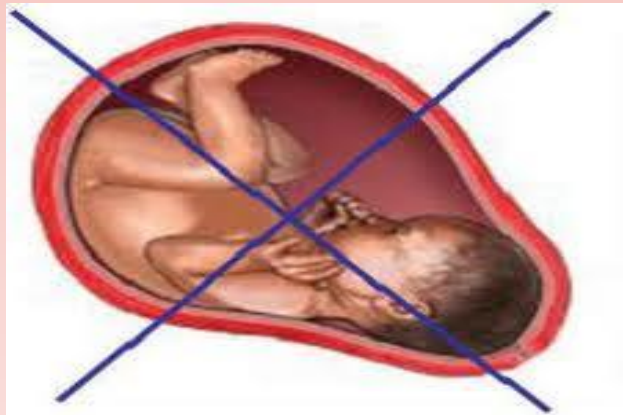


- There is positive evidence of risk to the human fetus.
- Investigational or post-marketing data show risk to the fetus.
- Potential benefits may outweigh the risk to the fetus. If needed in a life threatening situation or a serious disease, the drug may be acceptable if safer drugs cannot be used or are ineffective.

# Category X



- Use of the drug **is contraindicated in pregnancy.**
- Studies in animals or humans or investigational or post-marketing reports have shown fetal risk that clearly outweighs any possible benefit to the patient.



**Methotrexate**

**Warfarin**

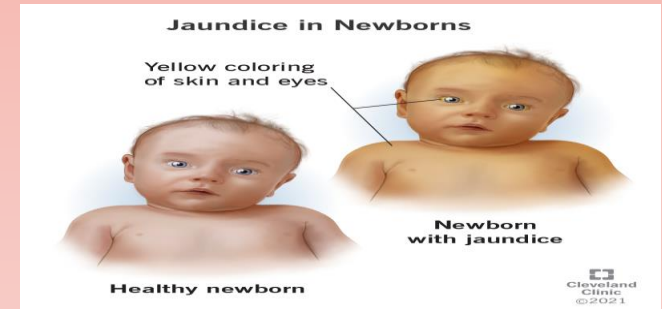
**\*\*Regardless of the pregnancy category or the presumed safety of the drug, no drug should be administered during pregnancy unless it is clearly needed and the potential benefits outweigh potential harm to the fetus**



## COMMON DRUGS TO AVOID DURING PREGNANCY

**Fluroquinolones** → Joint abnormalities & reverse arthropathy.

**Streptomycin** → Deafness.

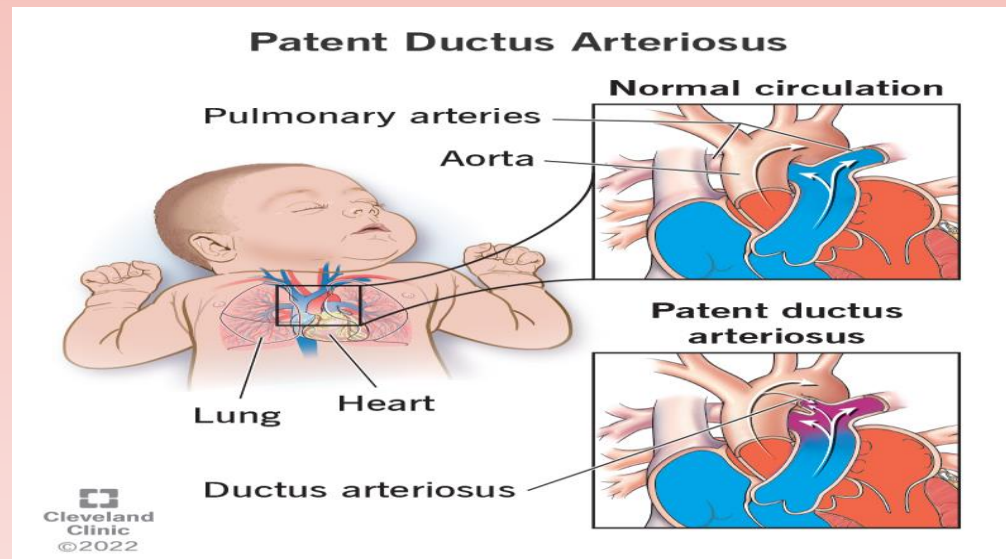


**Sulfonamides** → Jaundice and Kernicterus.

**Tetracyclines** → Permanent yellow brown discolouration and dysplasia in teeth, deformity and inhibition of bone growth.

## COMMON DRUGS TO AVOID DURING PREGNANCY

**Salicylates , Ibuprofen → Bleeding to mother during the delivery and if taken in late pregnancy causing premature closure of ductus arteriosus.**

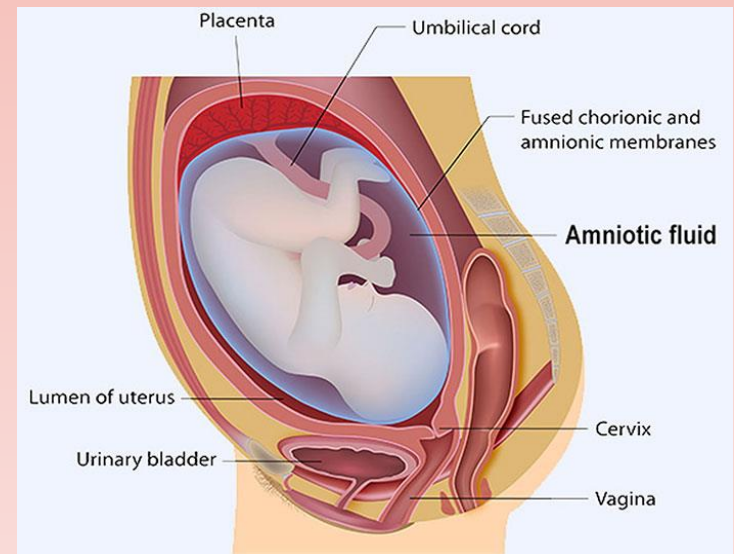


# Examples of drugs that may cause teratogenicity :

**ACE inhibitors** → Renal failure and oligohydramnios.

**Beta blocker** → Decrease heart rate and hypoglycemia in fetus.

**Thiazide diuretics** → ↓ in  $O_2$ , Na, K and the number of platelets in fetus.



# Examples of drugs that may cause teratogenicity :

**Warfarin** → abnormal bone formation, cutaneous necrosis , haemorrhage in fetus.

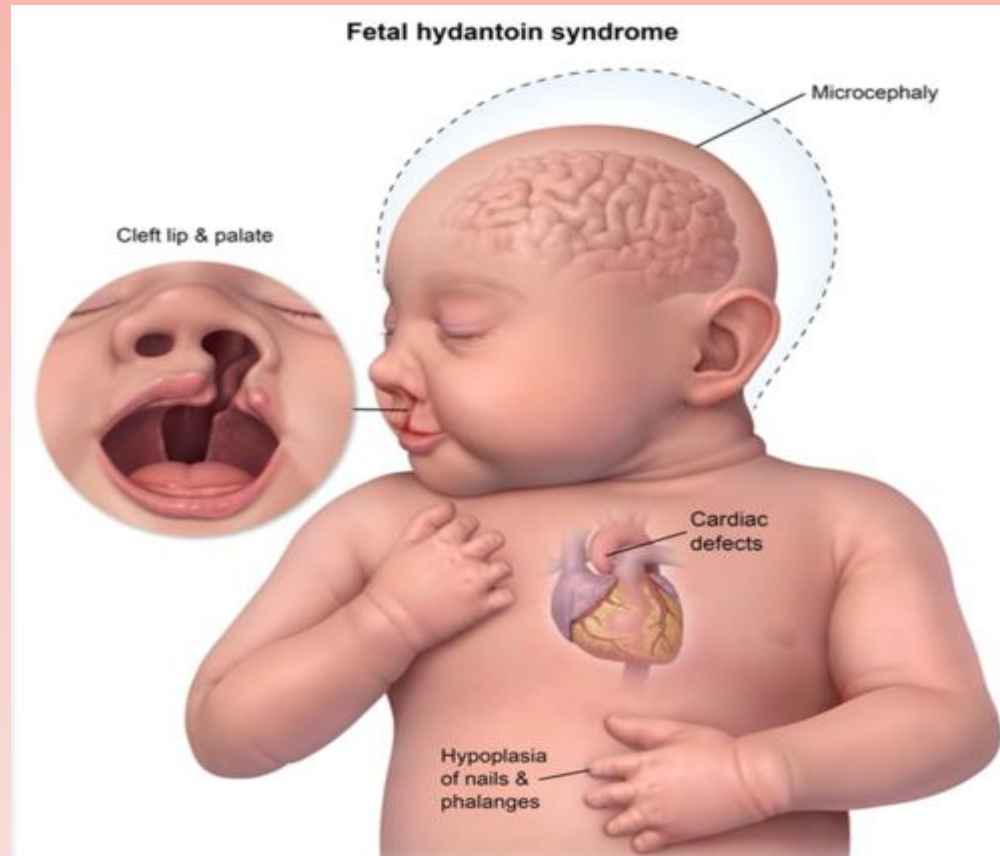
**Anticoagulant  
(Warfarin and coumadin)**

- Fetal warfarin syndrome:
  - Nasal hypoplasia (bones appears small)
  - Bone stippling
  - Mental retardation
- Respiratory distress syndrome
- Fetal and maternal hemorrhage



# Examples of drugs that may cause teratogenicity :

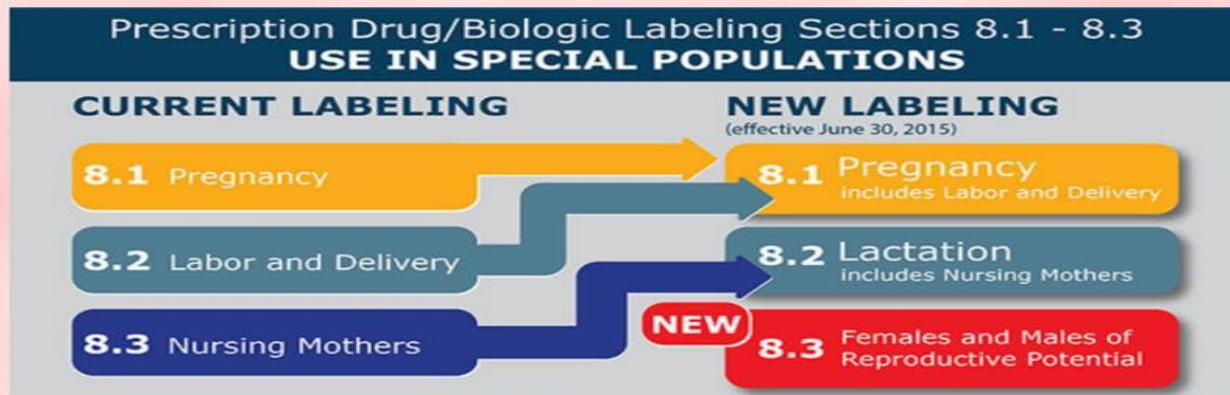
**Phenytoin → Fetal Hydantoin Syndrome (Hare lip & cleft palate).**



# The pregnancy & lactation labelling rule(PLLR)

## The Pregnancy & Lactation Labelling Rule (PLLR) - Part 1

- Dec 2014 - Published by FDA to improve the current pregnancy category labelling system.
- Pregnancy category will be gradually phased out for affected drugs.
- Applicable to prescription drugs and biological products (to include in product information)



Source: [fda.gov](http://fda.gov)

# Questions



## **Explain:**

Warfarin is contraindicated in pregnancy.

Penicillins are classified as category A in pregnancy.

