

Drugs use in pediatric

"المهم من المحاضرة"

هذا الجدول فقط لمعرفة المصطلحات

Terms	Definition
Gestational age	Time from the mother's last menstrual period to the time the baby is born
Postnatal age	Age since birth
Postconceptional age	Age since conception, i.e., gestational plus postnatal age
Neonate	First 4 weeks or first month of life
Premature neonates	Born at less than 37-weeks gestation
Fullterm neonates	Born between 37- and 42-weeks gestation
Postterm neonates	Born after 42-weeks gestation
Infant	1 month to 1 year of age
Child	1 year up to puberty

1) Absorption :

***oral**

1- PH \rightarrow more alkaline \rightarrow weak base \rightarrow increase absorption .
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 Weak acid \rightarrow decrease absorption.

2- gastric emptying delayed .

3- decrease enzyme secretion by the intestine.

4- decrease bile acid secretion → decrease absorption of lipid soluble vitamins (as vitamin K).

5-delayed bacterial colonization of gastrointestinal tract → decrease systemic levels of drugs that enter enterohepatic circulation.

In children enterohepatic circulation occurs 8 times/day > Decreased systemic levels of drugs with enterohepatic circulation

* **percutaneous** → increase absorption .

* **IM administration** → decrease absorption due to less muscle mass.

2) Distribution:

* **Degree of protein binding**: decrease because

1\ Lower concentrations of plasma protein. (Children has low concentration of albumin & α_1 acid glycoprotein = The fraction of the free form of the drug increases = The response increases & maybe toxicity.)

2\ Reduced affinity of many drugs to these proteins.

3\ Endogenous or exogenous substances may compete with drugs for binding proteins (e.g., bilirubin). (Children have endogenous or exogenous substance may compete with drugs for binding to plasma proteins: = The fraction of the free form of the drug increases = The response increases & maybe toxicity.)

* $\uparrow V_d$ and \uparrow dose requirements (for hydrophilic drugs).

* $\downarrow V_d$ and \downarrow dose requirements (for lipophilic drugs).

3) metabolism :

Enzymes in neonate / infant :

- Most of the cytochrome P450 enzyme activity decrease EXCEPT (cyp3A4 , cyp3A7).

Sulfation is active in the new born so we have to increase the dose .

"في الاختبار فقط القانون بدون ارقام وحسابات"

Calculation of the dose based on age

Young's rule (adjustment of dose based on age of the child)

$$\text{Pediatric dose} = \frac{\text{Age} \times \text{adult dose}}{\text{Age} + 12}$$

Age = age of the child in years

Fried's rule (adjustment of dose based on age of the infant)

$$\text{Infant dose} = \frac{\text{Age} \times \text{adult dose}}{150}$$

Age = age of the infant in months

Calculation of the dose based on weight

$$\text{Dose} = \frac{\text{Weight} \times \text{adult dose}}{70}$$

Weight = weight of the child in kg

Dose adjustment according to weight or body surface area (BSA)

$$\text{Pediatric dose} = \frac{\text{Adult dose}}{\text{Adult weight}} \times \text{Pediatric weight}$$

$$\text{Pediatric dose} = \frac{\text{Adult dose}}{\text{Adult BSA}} \times \text{Pediatric BSA}$$

Calculation of BSA

$$BSA (m^2) = \frac{Ht (cm) \times wt (kg)}{3600}$$

$$BSA (m^2) = \frac{(4 \times wt) + 7}{90 + wt}$$

Ht = height in cm

Wt = weight in kg

Common Pediatric Dosage Forms

1-Elixirs: Are alcoholic solutions in which the drug molecules are dissolved and evenly distributed

No shaking is required, the first dose from the bottle and the last dose should contain equivalent amounts of drug.

2-Suspensions: Contain undissolved particles of drug that must be distributed throughout the vehicle by **shaking(important)**.

If shaking is not thorough each time a dose is given, the first doses from the bottle may contain less drug than the last doses.

Special adverse drug **reactions** in infants and children

Tetracyclines (before 8 years old)	Enamel hypoplasia and permanent discoloration of teeth
Corticosteroids (long-term administration to prepubertal children)	Growth suppression
Phenobarbital	Paradoxical hyperactivity
Sodium Valproate	Increased hepatotoxicity
Salicylates (administration to children with mild viral infection)	Reye's syndrome (hepatic encephalopathy)

"Explain whys"

:

1- Young children are subjected to Vitamin K deficiency?

Because they have bile acid & enzyme deficiency because the liver is not well developed.

2-Dose of carbamazepine (as mg/kg body weight) and its side effects are greater in children than adults?

The CYP3 A4 enzyme activity which is responsible for metabolism of carbamazepine is higher in children → increased metabolism of carbamazepine and overproduction of its metabolite carbamazepine epoxide. This leads to increased dosing requirements of carbamazepine in children, and the increased carbamazepine epoxide may be responsible for some of the observed adverse drug reactions.

3- in spite of the TP "T half life " of (Rephimpacin) is short, it's action is prolonged ?

Because it enters the enterohepatic circulation

4-flare of action of "degecsin" ?

Due to insufficient of bacteria flora

5-plasma protein decreased .

-the amount of protein synthesis from liver is less .

-Affinity of drug to plasma protein is less > plasma protein is not well formed .

-exogenous and endogenous substances may compete with drugs for binding protein .

6-drugs that metabolite by (cyp3A7) and (cyp3A4) must decrease their dose in neonate .

CYP3A7 and CYP3A4 level is increased .

7-Benzylalcohol is more toxic in neonate\infants\young children than adult .

They have lower than activity of conjugation with glycine than adult .

8-Aspirin Prohibited for children up to age 12 years .

If the child has viral infection, Aspirin cause Rays Syndrome in the brain (encephalopathy)

9-although concentration of drug in the blood is constant , the dug is toxic .

Due to decrease in plasma protein .