

DRUGS USED DURING PREGNANCY & LACTATION



PREGNANCY PHYSIOLOGY AND ITS EFFECTS ON PHARMACOKINETICS

Absorption

1. Gastrointestinal motility is **decreased** but there appears to be **no major** **affect** in drug **absorption** **except** that **reduced** **gastric emptying** **delays** the **appearance** in the **plasma** of orally administered drugs, **especially** **during** **labor**.
بعد الولادة واحدة أقل
=> why? because of gastric emptying
2. **Absorption** from an **intramuscular** site is likely to be **efficient** because tissue perfusion is increased **due** to **vasodilatation**.
why?
⊕ Blood goes higher than before to tissue because of

DISTRIBUTION:

1. Total body water increases by up to 8 Litres, creating a larger space within which water soluble drugs may distribute. →
2. As a result of haemodilution, plasma albumin (normal 33-55 g/l) declines by some 10 g/l. Thus there is scope for increased free concentration of drugs that bind to albumin.
3. Unbound drug, is free to distribute, metabolized and excreted; e.g. the free (and pharmacologically active) concentration of phenytoin is unaltered, although the total plasma concentration is reduced.

خزينة الدواء تصبح أكبر
توزع بشكل أفضل

تخفيف

نسبة ارتباط
تتأثر
بالتخفيف

بسبب زيادة تركيز
البروتينات.

METABOLISM

and blood flow ↓

- **Hepatic** metabolism increases, but not the **blood flow** to **liver**.
- So, **increased clearance** of **drugs** such as **phenytoin** and **theophylline**
(**elimination rate depends on liver enzyme activity**)
- **Drugs** that are so **rapidly metabolized** that their **elimination rate**
depends on their **delivery** to the **liver**, i.e. on **hepatic blood flow**, have
unaltered clearance, e.g. **pethidine**.

ELIMINATION:

- Renal plasma flow almost doubles
- So there is rapid loss of drugs that are excreted by kidney
- e.g. amoxicillin, dose of which should be doubled for systemic infections

Except

(but not for urinary tract infections as penicillins are highly concentrated in urine).

لأنه تركيزه عالي، فلننا ما بعد ذلك
بأكثر من الجوانب.

PLACENTAL TRANSFER OF DRUGS

1. The placenta is not a perfect barrier to drugs and chemicals

administered to mother.

causes mutations in fetus

2. Thalidomide tragedy, showed that placenta was capable of

*سے پھرانی
قہیرہ*

transferring drugs ingested by mother to fetus, with potential for

great harm.

ممکن ہو دیکھ رہے ہیں

when it is beneficial?

3. On other hand, placental transfer of drugs administered to mother

has been used to treat fetal arrhythmias, congestive heart failure, &

other conditions.

All the ^{are} FACTORS AFFECTING PLACENTAL DRUG TRANSFER & FETAL TISSUE, *except?*

(1) Physicochemical properties of drug

(2) Rate at which drug crosses placenta & amount of drug reaching the fetus

كم بوصول وكم عدد؟

(3) Duration of exposure to drug

لأكم يوم؟
كم مدة التمثيل؟

(4) Distribution characteristics in different fetal tissues

توزيع الدواء في أنسجة الجنين؟ =>

(5) Stage of placental & fetal development at time of exposure to the drug

درجته التنموي
placenta

(6) Effects of drugs used in combination

تفاعلها مع بعضها
تفاعلي غيرها للأدوية للحامل

وأي أسبوعين؟

trimester => 3 months

الثلث trimester

بعض المواد للجينات what is Teratogen ?

A teratogen is a chemical substance that can induce a malformation during development.

* Pregnant woman should **NOT** take any drugs, only if she had to!

TERATOGENESIS



Malformations due to maternal **ingestion** of **thalidomide** (Schardein 1982 and Moore 1993).

Q) These are facts about teratogen except?

PRINCIPLES OF TERATOLOGY

دواء محدد

▪ Teratogens act with specificity. A teratogen produces a specific abnormality or constellation of abnormalities. Eg. thalidomide produces phocomelia, and valproic acid produces neural tube defects.

وحدة أو عدة تشوهات

↳ Extremely short limbs

▪ Teratogens demonstrate a dose-effect relationship.

dose \propto effect

▪ Teratogens must reach the developing embryo in sufficient amounts to cause their effects.

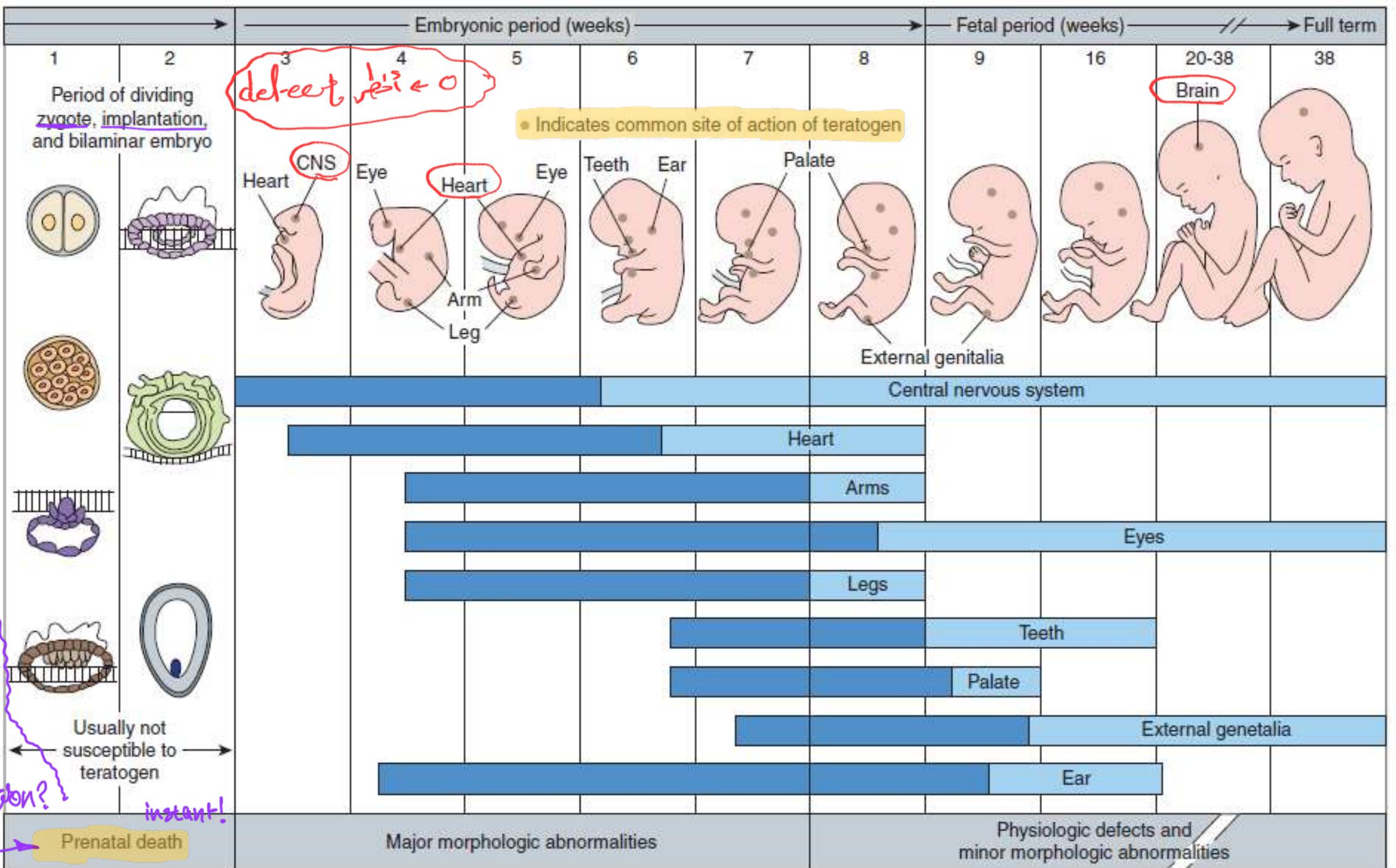
▪ The effect that a teratogenic agent has on a developing fetus depends upon the stage during development when the fetus is exposed.

All of the following are

MECHANISMS OF TERATOGENESIS, except?

کیفہ بصیرت کی آغوش؟

- ① Genetic interference, ② gene mutation, ③ chromosomal breakage, ④ interference with cellular function, ⑤ enzyme inhibition, and ⑥ altered membrane characteristics.
- The response of the developing embryo to these insults is failure of cell-cell interaction crucial for development, interference with cell migration, or mechanical cellular disruption.



EXAMPLES

فقط في الأجنة

Drug	Abnormality
Thalidomide	phocomelia, multiple defects
Anticancer drugs (methotrexate)	cleft palate, hydrocephalus, multiple defects, foetal death
Androgens	virilization; limb, esophageal, cardiac defects
Progestins	virilization of female foetus
Stilboestrol	vaginal carcinoma in teenage female offspring
Tetracyclines	discoloured and deformed teeth, retarded bone growth
Warfarin	depressed nose; eye and hand defects, growth retardation
Phenytoin	hypoplastic phalanges, cleft lip / palate, microcephaly
Phenobarbitone	various malformations
Carbamazepine	neural tube defects, other abnormalities
Valproate sod.	spina bifida and other neural tube defects
Alcohol	low IQ baby, growth retardation, foetal alcohol syndrome
ACE inhibitors	hypoplasia of organs, growth retardation, foetal loss
Lithium → Madness, psychiatry	foetal goiter, cardiac and other abnormalities
Antithyroid drugs	foetal goiter and hypothyroidism
Indomethacin / aspirin	premature closure of ductus arteriosus
Isotretinoin → Acne	craniofacial, heart and CNS defects

in fetus
 ↑
 pulmonary Hypertension
 ↑
 causes

Artery connect Aorta w/ pulmonary artery. should be looked after birth



PRESCRIBING IN PREGNANCY

→ As much as you can!

لا زهر ياكونه صخره و معروف!

- minimize prescribing;
- use 'tried and tested' drugs whenever possible in preference to new agents; ↗
- use the smallest effective dose;
- remember that the fetus is most sensitive in the first trimester;
- consider pregnancy in all women of childbearing potential;
- discuss the potential risks of taking or withholding therapy with the patient; ↗
- seek guidance on the use of drugs in pregnancy in the British National Formulary, Drug Information Services, National Teratology Information Service (NTIS);
- warn the patient about the risks of smoking, alcohol, over-the-counter drugs and drugs of abuse.

↗ when? ↘

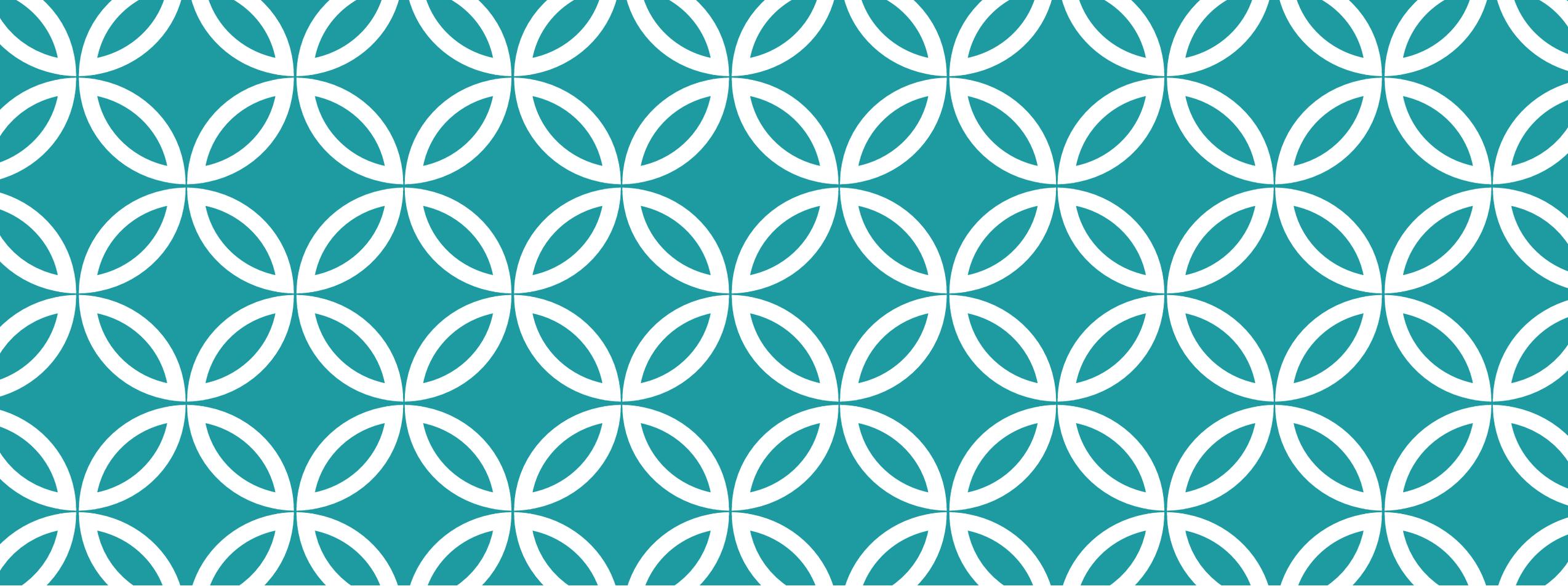
↗ to make sure that the patient don't take it on their own.

↘ Needs prescription

↘ drugs may cause addiction

DRUG USE DURING LACTATION

- Most drugs administered to lactating women are detectable in breast milk. Fortunately, the concentration of drugs achieved in breast milk is usually low.
- Infant would receive in a day is substantially less than what would be considered a "therapeutic dose." => in breast milk. => No toxicity is reached!
- If the nursing mother must take medications and the drug is a relatively safe one, she should optimally take it 30–60 minutes after nursing and 3–4 hours before the next feeding.
في وقتها وراحة
- Caution: Sedative-Hypnotics, Lithium Tetracyclines
لا يوجد



THANK YOU |

Syringe \Rightarrow for Blood draw, IV, IM, ... etc injections.

capsule \Rightarrow coated \Rightarrow protect from gastric acidity

Ointment \Rightarrow route? topical, direct on skin

Suppository \Rightarrow high temp, resist orally drug?

so we give \rightarrow ^{! ~~edges~~} Run - Hattler