A. Drug therapy during pregnancy:

During pregnancy, major physiological and anatomical changes occur that can alter the pharmacokinetics and pharmacodynamics of administered drugs:

1. **Absorption: ↑ed due to**
   - Gastric emptying time is delayed & gut motility reduced because of ↑ed progesterone.
   - pressure of the expanding uterus on the blood supply to abdominal organs affect the absorption of drugs.
2. **Distribution: ↑ed due to**
   - Total body water increases i.e. hemodilution
   - Plasma albumin conc. ↓**ed** so ↑**ed** free drug conc.
   - Increased body fat, reservoir of lipid soluble drug
3. **Drug metabolism** is significantly **altered during pregnancy** and ↑**ed** for certain drugs. Ex: anticonvulsants such as carbamazepine (Tegretol), phenytoin (Dilantin)**.**
4. **Excretion:** - Renal blood flow doubles, so rapid elimination of drugs excreted by kidney (↑**ed).**

❖ Placental Drug Transfer

Multiple factors affect the transfer of drugs across the placenta include:

- The plasma drug level in the mother
- Lipid solubility characteristic of the drug
- The drug's molecular size
- Drug protein binding capability
- Drug ionization
- Blood flow to the placenta.

❖ Fetal effects from drugs depend on several factors:

1. Time of exposure to drug during pregnancy
   Ex:
   a) 0-2 weeks >>> prenatal death (antimetabolites drug).
   b) Embryonic period-3-8 weeks>>> gross malformations (thalidomide cause missing limb)
   c) Fetal period-9-40 weeks>>> Functional defects (learning deficit)
2. Dose of drug.

❖ **Teratogenesis**: -

means *to produce a monster*. *It means* birth defects in terms of gross malformations, such as cleft palate, clubfoot, and hydrocephalus. Or defects appeared in a time after birth that are not limited to distortions of gross anatomy; they also include neurobehavioral and metabolic anomalies.

❖ **FDA Pregnancy Risk Categories**

In 1979, the FDA established a system for classifying drugs according to their probable risks to the fetus:

Category	Description
A	Remote risk of fetal harm
B	Slightly more risk than A
C	Greater risk than B
D	Proven risk of fetal harm (WARNING)
X	Proven risk of fetal harm (CONTRAINDICATED)

❖ **Some Examples of drugs safe during pregnancy:**

Disease condition	Drug
Nausea & vomiting	Pyridoxine, meclizine, cyclizine
Bacterial Infections	ampicillin, amoxycillin, cephalexin, cefadroxil, cefuroxime, cloxacillin, cefuroxime, ceftriaxone) , azithromycin), gentamycin & tobramycin only if serious infection
Fungal infections	miconazole, clotrimazole & nystatin
Hypertension	α-methyl dopa oral & hydralazine in emergency. β blocker like labetolo
Headache & Inflammation	paracetamol, codeine preparation

❖ **DRUG THERAPY DURING BREAST-FEEDING**

Drugs taken by lactating patients can be excreted in breast milk. If drug concentrations in milk are high enough, a pharmacologic effect can occur in the infant.

drugs that are lipid soluble enter breast milk readily, whereas drugs that are ionized, highly polar, or protein bound tend to be excluded.

when drugs *must* be used by nursing patient, steps should be taken to minimize risk. These include:

- ✓ Dosing immediately *after* breast-feeding (to minimize drug concentrations in milk at the next feeding)
- ✓ Avoiding drugs that have a long half-life
- ✓ Avoiding sustained-release formulations
- ✓ Choosing drugs that tend to be excluded from milk
- ✓ Choosing drugs that are least likely to affect the infant
- ✓ Avoiding drugs that are known to be hazardous.
- ✓ Using the lowest effective dosage for the shortest possible time

❖ Drugs that are contraindicated during breast-feeding

- ❖ **CONTROLLED SUBSTANCES**
- ❖ Amphetamine
- ❖ Cocaine
- ❖ Heroin
- ❖ Marijuana
- ❖ Phencyclidine
- ❖ **ANTICANCER AGENTS/IMMUNOSUPPRESSANTS**
- ❖ Cyclophosphamide
- ❖ Cyclosporine
- ❖ Doxorubicin
- ❖ Methotrexate
- ❖ **OTHERS**
- ❖ Atenolol
- ❖ Bromocriptine
- ❖ Ergotamine
- ❖ Lithium
- ❖ Nicotine
- ❖ Radioactive compounds (temporary cessation)

Drug Therapy in Pediatric Patients

The pediatric population is subdivided into six groups:

- Premature infants (less than 36 weeks' gestational age)
- Full-term infants (36 to 40 weeks' gestational age)
- Neonates (first 4 postnatal weeks)
- Infants (weeks 5 to 52 postnatal)
- Children (1 to 12 years)
- Adolescents (12 to 16 years)

❖ Pharmacokinetics in children:

- Because of organ system immaturity, very young patients are highly sensitive to drugs.
- **Absorption: -** ↑ed from **skin** due to better hydration, **GIT absorption**: altered, low acidity, ↑ed gastric emptying time, **IM absorption** in the *neonate* is *slow* and Delayed absorption is due to low blood flow through muscle during the first days of postnatal life.

- **Distribution:** - altered in neonates due to:
  a. low serum albumen level lead to higher free drug and more toxicity.
  b. fatty acids, bilirubin) compete with drugs for available binding sites.
  C. B.B.B not well developed at birth so that make the CNS more sensitive to drug affect the CNS.

- **Metabolism:** - drug-metabolizing capacity of newborns is low>>> more sensitive to drug metabolized and eliminated by liver.
  Ex: chloramphenicol causing grey baby syndrome in newborns.

- **Excretion: -** Renal drug excretion is significantly reduced at birth and infancy.
  - Normal clearance achieved at the age of 1 year.

Calculating Drug Dosages for the Pediatric Client: -

Drug dosage calculation for pediatric clients should be individualized, and nurses should take into consideration the child's age, height, weight, maturational state, and body surface area.

** Two common procedures for calculating pediatric dosages: -

A. body weight method : requires a calculation of the number of milligrams of drug, based on the child's weight in kilograms (mg/kg) for example, gentamicin (Garamycin) 5 mg/kg/24h.

$$\text{Child dose} = \frac{\text{Body weight (kg)}}{70} \times \textit{adult dose}$$

B. body surface area (BSA) method:
(Child's BSA × Adult dosage) ÷1.73m^2 = **Pediatric dosage**

Note: Child`s body surface area obtained from nomogram (reference) that determine body surface area using the height (cm or in) and weight (kg or lb) of the child.

Drug Use in Geriatric Patients

Physiologic changes that can affect pharmacokinetics in older adults:

- **ABSORPTION OF DRUGS**

Increased gastric pH
Decreased absorptive surface area
Decreased splanchnic blood flow
Decreased GI motility
Delayed gastric emptying

- **DISTRIBUTION OF DRUGS**

Increased body fat
Decreased lean body mass
Decreased total body water
Decreased serum albumin
Decreased cardiac output

- **METABOLISM OF DRUGS**

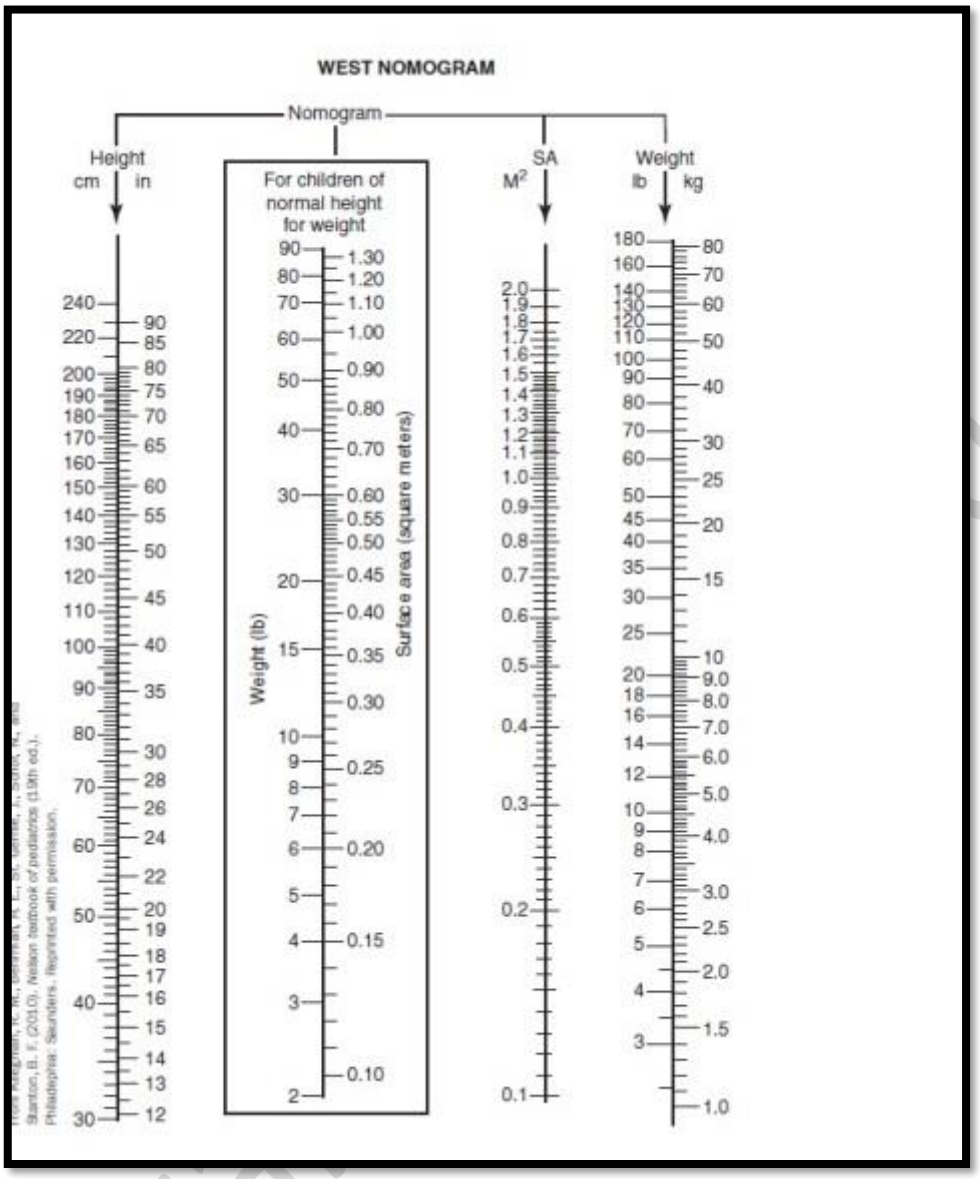
Decreased hepatic blood flow
Decreased hepatic mass
Decreased activity of hepatic enzymes

- **EXCRETION OF DRUGS**

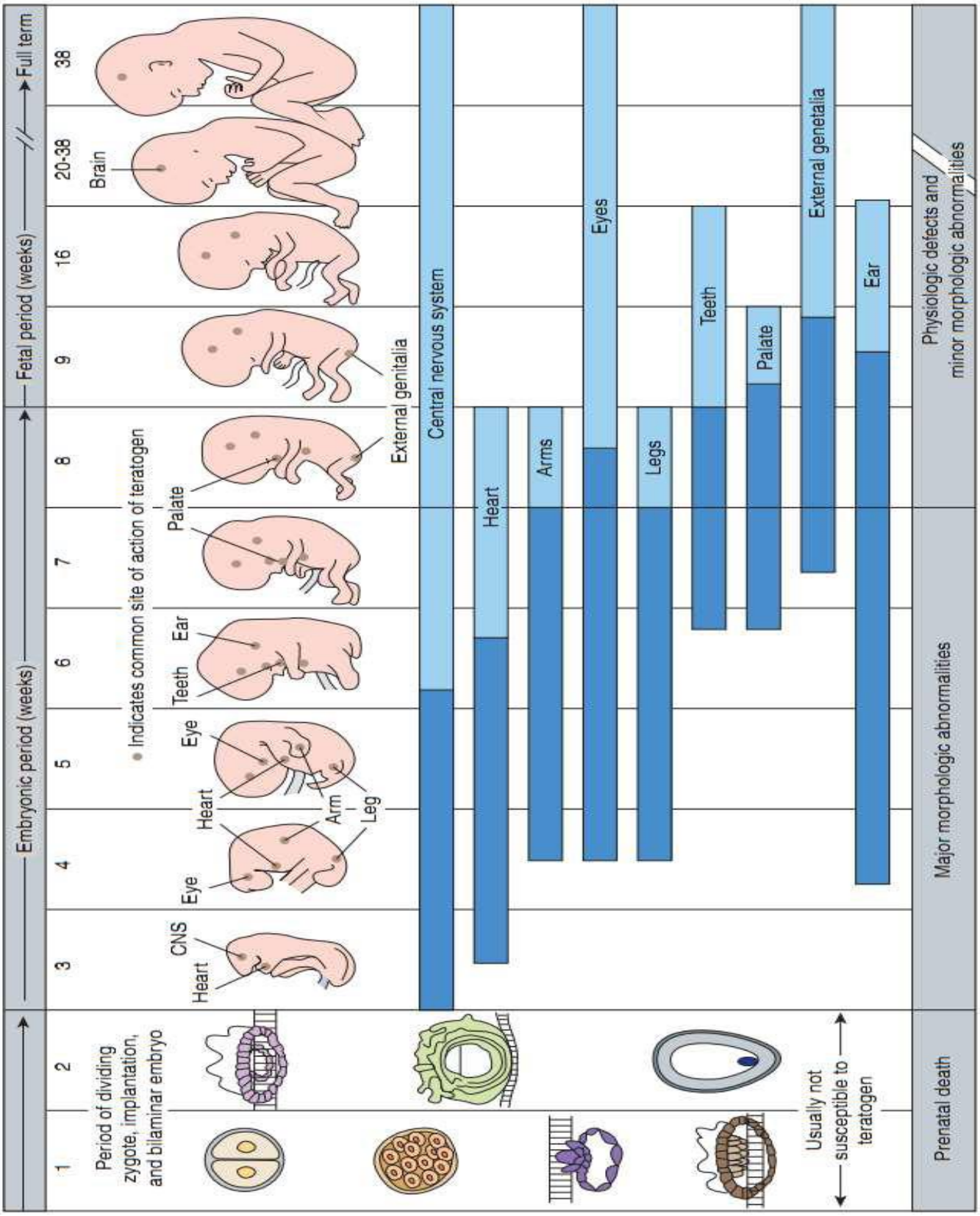
Decreased renal blood flow
Decreased glomerular filtration rate
Decreased tubular secretion
Decreased number of nephrons

❖ **Geriatric (>65 years) patients have more chances of drug interactions & ADRs: -**

1. Presence of multiple disease
2. Sluggishness of various body functions
3. Reduced healthcare finance
4. Nutritional problem
5. Poor patient compliance due to poor understanding, confusion, forgetfulness, poor hearing, poor vision, physical disability
7. Pharmacological changes due to ageing.



Nomogram for estimation of surface areas.


Embryonic period (weeks)
Fetal period (weeks)
Full term
1
2
3
4
5
6
7
8
9
16
20-38
38
Period of dividing zygote, implantation, and bilaminar embryo
Indicates common site of action of teratogen
CNS
Heart
Eye
Heart
Arm
Leg
Eye
Teeth
Ear
Palate
Brain
External genitalia
Central nervous system
Heart
Arms
Eyes
Legs
Teeth
Palate
External genetalia
Ear
Usually not susceptible to teratogen
Prenatal death
Major morphologic abnormalities
Physiologic defects and minor morphologic abnormalities