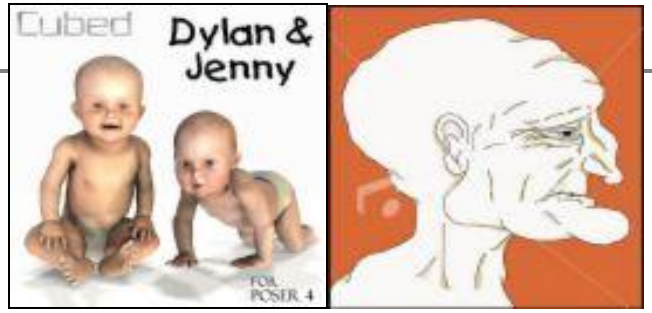
Drugs Prescribing in Infants, Children and Elderly



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Less doses are needed in young children and elderly than in adult due to changes in:

- Drug pharmacokinetics
- Sometimes pharmacodynamics

Children should not be regarded as small adults when prescribing for them, particularly in the first few months of life. They differ in:

- Body composition
- Elimination of drugs

Infants (1-12 months) and children:

Drugs responses may differ from adults due to:

1. **Surface area /body weight** ratio is less in neonates (under 1month)
2. **Pharmacokinetics changes**:

- ***Absorption:***
  - **GI absorption is variable** e.g.: it is normal for diazepam and digoxin, for ampicillin, flucloxacillin and amoxicillin is greater in neonates due to decreased gastric acidity, and reduced for paracetamol.
  - **Percutaneous absorption increases** due to skin hydratation and thin keratine layer (e.g.: for steroid creams)
  - **Parenteral injections**: absorption is **slower** after IM injection due to small muscle mass and decreased fat

Summary

- Prolonged gastric emptying time and irregular gut motility.

- Reduced trans time in upper intestine.
- Presence of food decreases absorption of ampicillin and penicillin.
- Absorption of lipid soluble drugs is reduced in infants as they have low concentrations of lipase and acid.

- ***Distribution:***
  - Total **body water** is more than in adults and is mostly extracellular, so **increased Vd** of water soluble drugs
  - **Fat content** is lower in children, so **decreased Vd** for lipid soluble drugs (e.g. diazepam)
  - **GI function**: **gastric emptying** time is **more** while **gastric acid** output is **less** in neonate than in adults
  - **Plasma protein** binding is **reduced** in neonate due to lower albumin concentration and altered binding capacity, so concentration of free active fraction is increased (.highly bound drugs e.g.: phenytoin)

- ***Distribution:***
  - **BBB** is more **permeable** in neonate and children leading to increased risk of drug penetration to the CNS.
  - Example:
    - Lipid soluble drugs
    - morphine

- ***Excretion:***
  - **Renal clearance** is **less** efficient, so t½ of drugs eliminated mainly by kidney is prolonged (e.g. ampicillin and digoxin). Adult glomerular filtration rate is attained after 3-5 months; adult secretory and reabsorptive capacity is attained after 7 months (e.g.: aminoglycosides, and diuretics are cleared from the body very slowly in the first weeks of life)
  - In **older children** drug elimination by metabolism or renal excretion is more **faster** than in adult, so t½ of drugs is shortened

- ***Metabolism:***
  - **Hepatic enzyme** activity is **low** in neonate for some drugs, this would increase t½ of drugs eliminated by liver.
  - Hepatic microsomal enzyme system is relatively immature in infants in the first 4 weeks after birth.
  - Hepatic drug metabolism increases in older infants and children (e.g. phenobarbitone metabolism is faster in children than adults).

3. **Changes in pharmacodynamic:**

- **Increased sensitivity** to CNS depressants (e.g. morphine)
- heart is more tolerant to digoxin toxicity.
- **Hyperkinesia with phenobarbitone.**
- **Sedation of hyperactive children with amphetamine.**

Dose calculation

- **Clark's rule:**

  Child dose= adult dose x child BW (kg)/ 70kg

BW: body weight in Kg

- **Young's rule:**

  Child dose= adult dose x child age (years)/ (age+12)

Calculation based in BW or age tend to underdose the child

- **Determination of drug dosage from surface area (SA):**

  Child dose= adult dose x SA child (M^2)/ 1.8

SA: surface area (in square meters)

BW (Kg)	Age	SA(M^2)	% adult dose
3	Newborn	0.2	12
6	3months	0.3	18
10	1 year	0.45	28
20	5.5 years	0.8	48
30	9 years	1	60
40	12 years	1.3	78
50	14 years	1.5	90
60	Adult	1.72	100
70	Adult	1.76	103

Children's prescription writing:

- Age is a legal requirement in the case of drug prescription for children under 12 years of age (preferable to stage the age for all prescriptions)
- To stage the strengths of capsule and tablets is very important. Liquid preparations sugar-free are better for children (reduce dental decay)
- Parents should be advised not to add any medicine to the infant's feed (may interact)

Children's prescription writing:

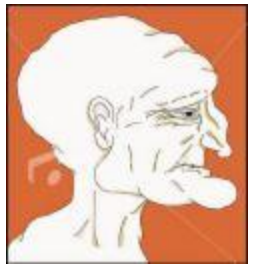
- Parents must be warned to keep all medicine out of reach of children
- Avoid prolonged treatment that have delayed complications (e.g. steroids).
- Use suitable dosage form

Drugs and the elderly:

Drugs response in the elderly differ from adult due to:

1. **Reduced muscle mass** and **body weight**
2. **Changes in pharmacokinetics:**

- ***Absorption:***
  - **Reduce gastric acid** secretion, delayed **gastric emptying** and reduced **gut motility** and **blood flow**, increased incidence of duodenal diverticulae and bacterial over growth resulting in malabsorption, but in general no major effect on absorption from intestine (e.g.: reduced absorption of iron, calcium, thiamine, xylose, and galactose (all need active transport mechanisms)



- ***Distribution:***
  - **Reduce** total **body water**, so decreased Vd of water soluble drugs; so, Lower doses are required for lithium, and digoxin.
  - **Relative increase in fat,** so increased Vd of lipid soluble drugs (e.g.: benzodiazepines, lignocaine, gentamycin, morphine, tolbutamide)
  - **Decreased albumin** (increases the unbound fraction of highly protein binding drugs like lidocaine, and propranolol) and **increased gamma globulins** (for acidic drugs; e.g. warfarin, phenytoin and digoxin).

- ***Metabolism:***
- The use of alcohol and medications and the long term exposure to environmental toxins and malnutrition lead to **Decreased hepatic blood flow** and reduced capacity for **microsomal enzyme induction**, and decreased ability of liver to **recover from injury**. Thus t½ of drugs mainly eliminated by liver is prolonged (e.g.: diazepam, quinidine, theophylline, propranolol, nortriptyline)

- ***Excretion:***
  - **Decreased glomerular filtration** rate and **tubular secretion**, so t½ of drugs mainly eliminated by kidney is prolonged (e.g.: aminoglycosides, digoxin, lithium, methotrexate, procainamide, tetracycline, penicillins, cephazolin)

Note: serum creatinine remains normal due to decrease in its production as a result of decrease in skeletal muscle mass

3. **Changes in pharmacodynamic:**

- Age-related **impairment** of **baroreceptor reflex** (decreased response)
- **Organ sensitivity**: certain systems **more** sensitive to drug action. Brain function is easily disturbed (hypnotic and other centrally acting drugs can easily produce confusion and excessive drowsiness). The control of blood pressure is more easily disturbed, causing fainting. Increased sensitivity to digoxin

Note: All these pharmacodynamic changes might be due to **receptor changes, kinetic changes and impaired homeostatic reflexes especially in CVS**

4. **Compliance** may be **poor** due to complicated drug regimes or polypharmacy may be impossible for elderly to follow so they either give up taking their drugs or take the wrong doses at the wrong times

5. **Adverse reactions:** are very **common** in elderly than in younger due to:
   - Often need several drugs at the same time
   - The elimination of drugs are impaired so that they are exposed to higher concentrations on the body (unless the doses the doses is suitable adjusted)
   - Are often severely ill and this may interfere with elimination
   - Drugs associated with adverse reactions (digoxin, diuretics, NSAIDs, hypotensives, centrally acting agents) are often prescribed for elderly

General principles when using drugs in elderly:

- A full **drug history** is important as the patient may have experienced an adverse effect from a drug in the past. Medication already being taken may raise the possibility of an interaction
- Keep the **regime simple**
- Prescribe the **smallest effective dose**, if possible, use drugs which are **short-acting**
- Do **not** continue to **use a drug for longer** than necessary
- If the **condition** of the patient is **deteriorates**, remember that a drug may be **responsible**
- **Elixirs** may be **easier** than tablets
- Clear a simple **instructions**