Drug Dosing in Special Populations

Jami Rozell B.S., CPhT

Special Populations

A special population are persons displaying one or more of the following characteristics:

a. prone to under or over responding to usual dosing regimens
b. least able to tolerate, recognize, or communicate drug effects
c. accidentally frequently mis-dosed

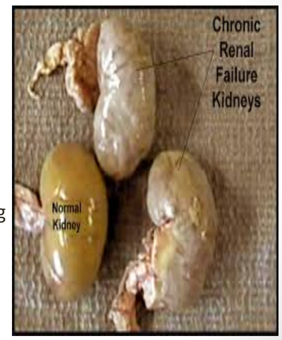
Source: *Clinical Chemistry* Volume 44 no. 2 415-419

Patient conditions that may altered the dosing of most drugs:

- **Renal or hepatic disease**, may decrease the elimination or metabolism of the majority of drugs and change the amount of drug being cleared from the body.
- **Dialysis** procedures, conducted using artificial kidneys in patients with renal failure, removes some medications from the body although the pharmacokinetic of other drugs are not changed
- **Heart failure**, results in low cardiac output, which decreases blood flow to eliminating organs
- **Obesity**, adds excessive adipose tissue to the body, which may change the way that drugs distribute in the body and increase the amount of drug needed for that patient.
- **Age** may affect the amount of medication a person receives. Infant and pediatric patients have different dosing requirements than adult patients.

Renal Disease

- Glomerular filtration is the primary elimination route for many medications
- The most common method of estimating glomerular filtration for the purpose of drug dosing is to measure /estimate Creatinine Clearance (CrCl)



Equations:

$$CrCl(ml/min) = \frac{U_{Cr} x V_{urine}}{S_{Cr} x T}$$

- U_{Cr} = the urine creatinine concentration (mg/dl)
- V_{urine} = the volume of urine collected (ml)
- S_{Cr} = the serum creatinine collected at the midpointof the urine collection (mg/dl)
- T = the time of urine collection (minute)

Problems with routine measurement of patient's CrCl:

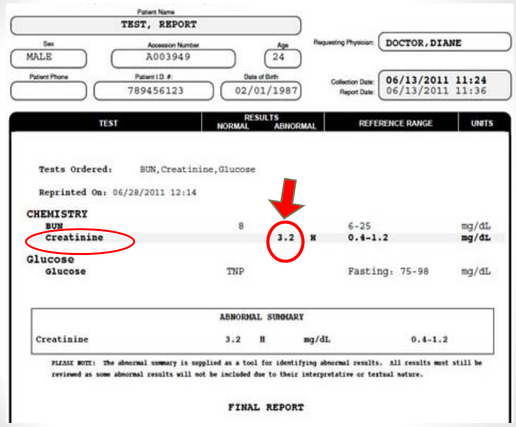
- Incomplete urine collection
- Serum creatinine concentration obtained at incorrect times
- Collection times errors

One example of an Equation to calculate creatinine clearance: Cockroft and Gault

$$CrCl_{est} = \frac{(140 - age)BW}{72 \cdot S_{Cr}} \text{ for males}$$

$$CrCl_{est} = \frac{0.85(140 - age)BW}{72 \cdot S_{Cr}} \text{ for females}$$

- CrCl est = estimated creatinine clearance (ml/min)
- Age in years
- BW = body weight (kg)
- Scr = serum creatinine (mg/dl)



Patient Name: TEST, REPORT
Sex: MALE | Accession Number: A003949 | Age: 24 | Requesting Physician: DOCTOR, DIANE
Patient Phone: | Patient I.D. #: 789456123 | Date of Birth: 02/01/1987 | Collection Date: 06/13/2011 11:24 | Report Date: 06/13/2011 11:36

Tests Ordered: BUN, Creatinine, Glucose

Reprinted On: 06/28/2011 12:14

TEST	RESULTS NORMAL	RESULTS ABNORMAL		REFERENCE RANGE	UNITS
CHEMISTRY					
BUN	8			6-25	mg/dL
Creatinine		3.2	H	0.4-1.2	mg/dL
Glucose					
Glucose	TNP			Fasting: 75-98	mg/dL

ABNORMAL SUMMARY

Creatinine	3.2	H	mg/dL	0.4-1.2

PLEASE NOTE: The abnormal summary is supplied as a tool for identifying abnormal results. All results must still be reviewed as some abnormal results will not be included due to their interpretative or textual nature.

FINAL REPORT

Modifying Doses for patients with renal impairment

- It is possible to decrease the drug dose and retain the usual dosage interval,or
- Retain the usual dose and increase the dosage interval, or
- Both decrease the dosage and prolong the dosage interval
- The choice was made depend on the route of drug administration, the dosage forms available

For drugs with narrow therapeutic index

- Measured or estimated CrCl may be used to estimate pharmacokinetic parameters for a patient based on prior studies conducted in other patients with renal dysfunction
- Estimated pharmacokinetic parameters are then used in pharmacokinetic dosing equation to compute initial dose

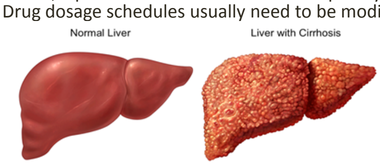
$$\text{Therapeutic index} = \frac{\text{Median toxic dose}}{\text{Median effective dose}}$$

Hepatic Disorders

- Most lipid soluble drugs are metabolized to some degree by the liver

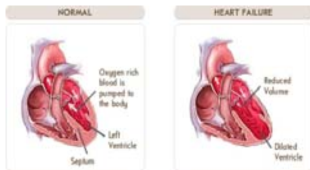
Two major types of liver disease

1. Hepatitis
   - Acute hepatitis: mild, transient decreases in drug metabolism required no or minor changes in drug dosing
   - Chronic hepatitis: irreversible hepatocytes damage required drug dosage changes. Patients with long term hepatocytes damage can progress to hepatic cirrhosis
2. Cirrhosis; a permanent lost of functional hepatocytes. Drug dosage schedules usually need to be modified



Heart Failure

- Is accompanied by a decrease in cardiac output results in lower liver and renal blood flow
- Decreased drug bioavailability has been reported, due to collection of edema fluid in the GI tract difficult absorption and decreased blood flow to GI tract

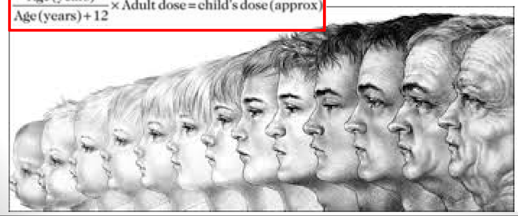


Age

- Children are not small adults but rather distinct individuals who have different absorption, distribution, metabolism, and excretion rates of medications than adults.

(Math Calculations for Pharmacy Technicians. Robert M. Fulcher and Eugenia M. Fulcher. Saunders, 2007.)

$$\boxed{\frac{\text{Age (years)}}{\text{Age (years)} + 12} \times \text{Adult dose} = \text{child's dose (approx)}}$$



Young's Rule example: Dosage based on Age Example

A child is 5 years old and weighs 60lbs. You want to calculate the dose of Acetaminophen for them. The recommended adult dose is 650mg. Use Youngs's rule to calculate a medication dose based on age.

$$Childs\ Estimated\ Dose = Adult\ Dose \text{ x} \frac{Age\ of\ child\ in\ years}{Age\ in\ Years + 12\ years}$$

$$Childs\ Estimated\ Dose = 650mg \text{ x} \frac{5yrs}{5yrs + 12\ years}$$

$$Childs\ Estimated\ Dose = 191mg$$

Weight

- Consideration of height and weight as well as overall physical condition of the patient may be used for prescribing dosages of the drug for those who do not fit the expected definition of "normal."

Math Calculations for Pharmacy Technicians. Robert M. Fulcher and Eugenia M. Fulcher. Saunders, 2007.

$$\boxed{\frac{\text{Weight (lb)}}{150} \times \text{Adult dose} = \text{Child's dose (approx)}}$$

Clark's Rule Example: Dosage based on Weight

A child is 5 years old and weighs 60lbs. You want to calculate the dose of Acetaminophen for them. The recommended adult dose is 650mg. Use Clark's rule to calculate a medication dose based on age.

$$Childs\ Estimated\ Dose = Adult\ Dose \text{ x} \frac{Child's\ weight\ in\ pounds}{150lb}$$

$$Childs\ Estimated\ Dose = 650mg \text{ x} \frac{60lb}{150lb}$$

$$Childs\ Estimated\ Dose = 260mg$$

Weight

- Most drugs in children are dosed according to body weight (mg/kg) or body surface area (BSA) (mg/m^2). Care must be taken to properly convert body weight from pounds to kilograms (1 kg= 2.2 lb) before calculating doses based on body weight. Doses are often expressed as mg/kg/day or mg/kg/dose, therefore orders written "mg/kg/d" which is confusing, *require further clarification from the prescriber*.

(Sourced from: www.drugguide.com)