



Renal Clearance and Dosing Adjustments

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What are the two general approaches to estimating renal function?

(1) Modification of Diet in Renal Disease (MDRD) equation

- Provides an estimation of glomerular filtration rate (GFR)
- Best overall index of renal function in health and disease
- Can be directly measured, but collection is often unreliable
- Estimated based on substances that are freely filtered in the glomerulus
- Must have minimal secretion/reabsorption in the renal tubules (creatinine)
- Thought to be the most accurate method of estimating renal function
- Pros - more accurate in severe renal impairment, accounts for ethnicity
- Cons - does not address height or weight, underestimates GFR in healthy people, and use is not recommended for dosing adjustments

(2) Cockcroft-Gault equation

- Estimates creatinine clearance (CrCl)
- Most commonly used
- Basis for most renal dosing recommendations provided in the package insert
- Pros - easy to calculate, produces consistent results in adult patients of average size and build with stable renal function and a SCr <3 mg/dL
- Cons - not a true marker of renal impairment, may overestimate renal function (especially in the elderly), and validity in obese patients is questionable

In general, how are renal dosing adjustments made?

Three approaches are commonly utilized: (1) decrease the drug dose and retain the usual dosage interval, (2) retain the usual dose and prolong the dosage interval, or (3) simultaneously decrease the dosage and prolong the dosage interval. The approach used depends on the route of administration, the dosage forms available, and the pharmacodynamic response to the drug.

What steps should I use to dose medication in the setting of renal insufficiency?

- (1) Calculate CrCl using Cockcroft-Gault equation
- (2) Use a reference to identify renal dosing parameters
- (3) Identify suggested dosage adjustment
- (4) Determine if the dosage adjustment is logical and appropriate for your patient
- (5) Factors to consider when making renal dosing recommendations
 - CrCl is a starting point (as it is only an estimation)
 - Toxicities of agents (ie- aminoglycosides vs. cephalosporins)
 - Clinical condition of the patient
 - SCr trends, stability of patient, severity of disease

Wargo et al. Comparison of the Modification of Diet in Renal Disease and Cockcroft-Gault Equations for Antimicrobial Dosage Adjustments. *The Annals of Pharmacotherapy*. 2006;40:1248-1253.

Moranville M et al. Implications of using Modification of Diet in Renal Disease versus Cockcroft-Gault Equation for Renal Dosing Adjustments. *Am J Health-Syst Pharm*. 2009;66:154-161.

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