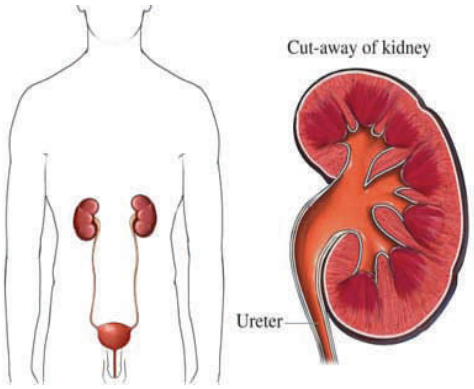
Clinical Interpretation of SCr and CrCl

Serum Creatinine (SCr)



Creatinine is derived from the breakdown products of muscle. Its rate of formation is determined primarily by an individual's muscle mass or lean body weight. Therefore, the serum creatinine (SCr) concentration is often higher in muscular subjects and slightly lower in patients with decreased muscle mass, such as malnourished or elderly patients. Serum creatinine also has a strong correlation with renal function. Once creatinine is released from muscle into plasma, it is excreted renally almost exclusively by glomerular filtration. A decrease in glomerular filtration rate (GFR) will result in an increased serum creatinine concentration (SCr).

Creatinine Clearance (CrCl)

Using an individual patient's serum creatinine (SCr), age, and body weight, creatinine clearance (CrCl) can be calculated. Creatinine clearance (CrCl) is the best estimate of a patient's renal glomerular filtration rate, and is used clinically to monitor renal function, monitor how well a drug is being eliminated from the body, and to adjust medication dosages. Creatinine clearance (CrCl) is also used to determine which drugs should or should not be used in individual patients, due to renal insufficiency and the potential for drug accumulation, drug toxicity and side effects.

Calculating Creatinine Clearance (CrCl):

Cockcroft and Gault formula:

Males: $$\text{CrCl (mL/min)} = \frac{(140-\text{age})(\text{Body Weight in kg})}{\text{SCr (umol/L)} \times 0.81}$$

Females: $$\text{CrCl (mL/min)} = \frac{(140-\text{age})(\text{Body Weight in kg})}{\text{SCr (umol/L)} \times 0.81} \times 0.85$$

**Please note that the calculation of CrCl using Cockcroft and Gault may overestimate actual creatinine clearance in patients who are obese or have liver dysfunction, and thus different calculations must be used.

Ranges of Normal and Decreased Creatinine Clearance

Normal renal function	
Men	95–145 mL/min (1.58–2.42 mL/s)
Women	75–115 mL/min (1.25–1.92 mL/s)
Mild renal insufficiency*	50–70 mL/min (0.83–1.17 mL/s)
Moderate renal insufficiency*	25–50 mL/min (0.42–0.83 mL/s)
Severe renal insufficiency*	< 25 mL/min (< 0.42 mL/s)

*Please note that there is considerable controversy regarding what constitutes mild, moderate and severe renal insufficiency. It is also important to note that creatinine clearance declines by 1 mL/min per year (0.02 mL/s per year) after the age of 40 years. Therefore, these guidelines are for women and men aged < 65 years.

Dose Modification Based on Creatinine Clearance

Drugs requiring dose modification		Drugs not requiring dose modification
All antibiotics	**EXCEPT**	Cloxacillin, clindamycin, metronidazole, macrolides
Antihypertensives Atenolol, nadolol, ACE inhibitors		**Antihypertensives** Calcium channel blockers, minoxidil, ARBs, clonidine, α-blockers such as prazosin
Other cardiac medications Digoxin, sotalol		**Other cardiac medications** Amiodarone, nitrates
Narcotics Codeine, Meperidine		**Narcotics** Fentanyl, hydromorphone, morphine
Psychotropics Lithium, chloral hydrate, gabapentin, Trazadone, paroxetine, primidone, Topiramate, vigabatrin		**Psychotropics** Tricyclic antidepressants, nafazadone, other selective SSRIs
Antidiabetic agents Acarbose, chlorpropamine, glyburide, Glicazide, metformin, insulin		**Antidiabetic agents** Repaglinide, rosiglitazone
Lipid-lowering agents Statins, benafibrate, clofibrate, fenofibrate		**Miscellaneous** Proton pump inhibitors
Diuretics AVOID potassium-sparing diuretics if CrCl <30 mL/min		
Miscellaneous Allopurinol, colchicine, H2 receptor antagonists, diclofenac, ketorolac, terbutaline		**Please note that there may be other medications requiring dose modification that are not included in this list.

Special Considerations for Drug Use By Patients with Renal Insufficiency

Meperidine	Metabolite normeperidine is neurotoxic and may cause seizures
Chlorpropamide	Has increased half-life when taken by patients with renal insufficiency and prolongs hypoglycemia
Metformin	Should not be used if CrCl <50 mL/min because it can cause life-threatening lactic acidosis
Insulin	There is decreased renal clearance of exogenously administered insulin and, therefore, potential for increased hypoglycemic reactions as CrCl declines.
Aminoglycosides Vancomycin	Dosage adjustment is required, because these drugs will rapidly accumulate in renal insufficiency and are potentially nephrotoxic. Therapeutic drug monitoring is recommended.
Cimetidine Triamterene Trimethoprim	Inhibit tubular secretion of creatinine and therefore cause a rise in serum creatinine (SCr), which is reversible when these drugs are discontinued

Key Points:

- Identify those patients at risk for renal insufficiency
- Measure serum creatinine and calculate creatinine clearance
- Consider whether dose modification is required and/or if alternative options should be considered
- Adjust drug doses if required
- Use the least nephrotoxic drug possible
- Monitor drug levels (where applicable) and renal function throughout therapy
- Keep up-to-date medication lists and be aware of over-the-counter and complementary medicines patients may be taking

References:

1. Applied Therapeutics 6th Edition. L. Young, M.A. Koda-Kimble. 1995. Ch.4 Interpretation of Clinical Laboratory Tests. PP 4-9.
2. Nephrology: 3. Safe drug prescribing for patientswith renal insufficiency. J. Kappel, P. Calissi. CMAJ • FEB. 19, 2002; 166 (4). http://www.cmaj.ca/cgi/reprint/166/4/473.pdf

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