Renal Function Tests

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Goals and objectives

• At the end of this discussion you will be able to state:
  • What test you should use to screen a patient for renal disease
  • What can raise the BUN and Creatinine other than kidney disease
  • How to determine prerenal azotemia from acute tubular necrosis (ATN).
MEETINGS
None of Us is as Dumb as All of Us.
When should you assess renal function?

- **Risk factors for kidney disease:**
  - Older age
  - Family history of Chronic Kidney disease (CKD)
  - Decreased renal mass
  - Low birth weight
  - US racial or ethnic minority
  - Low income
  - Lower education level
  - Diabetes Mellitus (DM)
  - Hypertension (HTN)
  - Autoimmune disease
  - Systemic infections
  - Urinary tract infections (UTI)
  - Nephrolithiasis
  - Obstruction to the lower urinary tract
  - Drug toxicity
Primary focus

- Blood Urea Nitrogen (BUN)
- Creatinine
  - Glomerular filtration Rate (GFR)
    - Crockoff-Gault equation
    - MDRD (modification of diet in renal disease) equation
- Fractional Excretion of sodium (FENa)
- Fractional Excretion of Urea (FEUrea)
- Urine concentrating ability
- Uric acid
BUN

- Urea is a relatively nontoxic substance made by the liver to dispose of ammonia resulting from protein metabolism.
- The real urea concentration is BUN x 2.14
- Normal BUN range is 8-25 mg/dL
- BUN is a sensitive indicator of renal disease
• Increased BUN = Azotemia
  – Causes: increased protein catabolism or impaired kidney function
  – Increased protein catabolism:
    • Increased dietary protein
    • Severe stress: MI, fever, etc
    • Rhabdomyolysis
    • Upper GI bleeding
  – Impaired renal function
    • Pre renal azotemia: renal hypoperfusion
    • Renal azotemia: acute tubular necrosis
    • Post renal azotemia: obstruction of urinary flow
Creatinine

- The breakdown product of creatine phosphate released from skeletal muscle at a steady rate.
- **It is filtered by the glomerulus.**
- It is generally a more sensitive and specific test for renal function than the BUN.
- **Normal range is 0.6-1.3 mg/dL**
  - *non pregnant state*
Creatinine

- Increased serum creatinine:
  - Impaired renal function
  - Very high protein diet
  - Anabolic steroid users
  - Vary large muscle mass: body builders, giants, acromegaly patients
  - Rhabdomyolysis/crush injury
  - Athletes taking oral creatine
  - **Drugs:**
    - Probenecid
    - Cimetidine
    - Triamterene
    - Trimethoprim
    - Amiloride
PERSISTENCE

IT'S OVER, MAN. LET HER GO.
Creatinine clearance

• A timed urine sample and serum sample used to approximate the glomerular filtration rate.

• It is *not an exact measure* of the GFR because some is not filtered and some is secreted into the proximal tubule.
  - In health these cancel each other out.
  - When the GFR drops below 30mL/min the tubular secretion exceeds the amount filtered and can give a false elevation.
Glomerular filtration rate: GFR

- GFR: sum of the filtration rates in all of the functioning nephrons

\[
\text{GFR} = \frac{[\text{UCr} \times V]}{\text{PCr}}
\]

**Timed collection over 24 hours

\[
\text{CCr} = \frac{[\text{UCr} \text{ md/dL} \times V \text{ L/day}]}{\text{PCr} \text{ mg/dL}} = \text{liter/day}
\]

*This value can be multiplied by 1000 to convert to mL and divided by 1400 (the number of minutes in a day) to convert into units of mL/min
GFR

- Erroneous values:
- Increasing creatinine secretion
  - As the GFR falls, the rise in the PCr is partially ameliorated by increased creatinine secretion.
GFR

• Erroneous values in GFR:
  – Incomplete urine collection
    • Assess adequacy of collection from steady state creatinine:
      – Adult < 50 years of age (lean body weight)
        » Male 20-35 mgs/kg daily creatinine excretion
        » Females 15-20 mgs/kg daily creatinine excretion
      – Adult ages 50-90 (lean body weight)
        » There is a progressive 50% decline in creatinine excretion
Estimation formulas

• May be less accurate in certain populations:
  – Normal or near normal renal function
  – Children
  – >70 years of age
  – Ethnic groups
  – Pregnant women
  – Unusual muscle mass
  – Morbid obesity

• It is recommended to obtain a creatinine clearance in stable renal function and prior to dosing toxic drugs that are renally excreted.
Cockcroft-Gault Equation (Adults)

\[(140 - \text{Age}) \times \text{lean body wt. kg} \times 72 \times \text{serum creat.} \times 100\]

* females multiply by 0.85
MDRD Equation

GFR (ml/min/1.73m^2) =

186 x (Pcr)^{1.154} x Age^{0.203} x (0.742 if female) x (1.210 if African American)

The equation requires 4 variables:

- Serum creatinine
- Age
- Sex
- African American or not

MDRD = Modification of Diet in Renal Disease Study
Download GFR calculator at www.nkdep.nih.gov
# Staging of chronic kidney disease

**CKD**

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<th><strong>Stage</strong></th>
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<th><strong>Recommendation</strong></th>
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Determining Acute renal failure

Acute Pre renal Azotemia

V.

Acute Tubular Necrosis
PLANNING

Much work remains to be done before we can announce our total failure to make any progress.
CALCULATION OF FRACTIONAL SOLUTE EXCRETION

\[ \text{GFR} \times P_s \]

\[ U_s \times V \]

\[ \text{FE}_s = \frac{\text{excreted solute}}{\text{filtered solute}} \]

\[ \text{FE}_s = \frac{U_s \times V}{\text{GFR} \times P_s} = \frac{U_s / P_s}{U_{cr} / P_{cr}} \times 100 = \% \]
Fractional excretion of sodium

\[ \text{FENa} \text{ } (\%) = \frac{\text{Urine sodium/plasma sodium}}{\text{Urine creat./plasma creat.}} \times 100 \]

*useful only in the presence of oliguria*
Fractional Excretion of Urea

\[
\left( \frac{\text{UUN}}{\text{BUN}} \right) \times \left( \frac{\text{Serum Creat.}}{\text{Urine Creat.}} \right) \times 100\%
\]
Renal Failure Index

RFI = Urine sodium × Plasma creatinine
    Urine creatinine
## Urine and Serum diagnostic indices

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Urine concentrating ability: specific gravity

- Provide important information about tubular function and hydration.
- Pre renal azotemia
  - high urine specific gravity (>1.010) and low or zero urinary sodium
- Renal azotemia
  - Will have low urine specific gravity or isosthenuria
    - ATN, severe bilateral pyelonephritis, interstitial nephritis, diuretic, or CKD 5
Uric Acid

- Metabolite of purine metabolism
- Filtered by the glomeruli and both reabsorbed and secreted by the renal tubules.

Increased in:
- Renal failure
- Gout
- Liver and sweetbread gourmets
- Lead poisoning
- Thiazide diuretics
- High dose aspirin
- Burns,
- Crush injuries
- Severe hemolytic anemia
- Myeloproliferative disorders
- Plasma cell myeloma
- Tumor lysis: post chemotherapy
POTENTIAL

Not everyone gets to be an astronaut when they grow up.
Summary

- What test you should use to screen a patient for renal disease
- What can raise the BUN and Creatinine other than kidney disease
- How to determine prerenal azotemia from acute tubular necrosis (ATN).
Questions

???????????
Overview of Renal Function Tests

Patients presenting with renal disease frequently have a myriad of clinical presentations. These range from actual kidney symptoms such as hematuria or to extrarenal symptoms such as edema, hypertension and signs of uremia. However, most are asymptomatic. Frequently the first sign of renal disease is seen on routine testing noting an elevated serum creatinine or an abnormal urinalysis. This discussion is limited to renal function testing not urinalysis or urinary sediment examination.

By performing renal function testing the physician can better manage the individual patient’s health care. This includes:
- Quantification of renal function
- Medication usage/radiocontrast use
- Identification and quantification of the degree of renal impairment:

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- Noting patients who require referral to Nephrologist:
  - Stage 2 CKD and up

BUN and Creatinine

Both the BUN and serum Creatinine can reflect renal function. The BUN is very sensitive but not as specific as the serum Creatinine. The elevation of the BUN (azotemia) can be affected by either changes in increased protein catabolism (large meat protein meals, severe stress: MI, fever, Upper GI bleeding) or impaired renal function (Pre renal, renal and post renal azotemia). The serum Creatinine is more specific. It is the breakdown product of creatine phosphate released from skeletal muscle at a steady rate. It is filtered by the glomerulus. A general rule of thumb: if the serum creatinine doubles then the glomerular filtration rate (GFR) halves. The serum creatinine and glomerular filtration rate are affected by muscle mass, aging, ethnic background and medications.
Factors that increase the BUN and Creatinine other than reduced renal function:

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</tr>
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<td>o Increased dietary proteins</td>
<td>o Anabolic steroid use</td>
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Creatinine clearance

Estimating the creatinine clearance is useful to stage the degree of renal impairment. This is necessary to properly dose medications and to appropriately manage the stages of chronic kidney disease. The creatinine clearance is a timed specimen. The creatinine in the urine is measured and compared to a serum creatinine measured within 24 hours of the urine specimen. Creatinine is both filtered at the glomerulus and secreted by the proximal tubule in the kidney. Therefore, unlike inulin, excretion overestimates the true glomerular filtration rate to the secreted portion. Errors can occur in the collection of the specimen. Therefore, careful instructions must be given the patient. The patient must be educated to discard the first morning urine specimen, to collect all other urination for the day of collection, through the night and the first specimen of the following day. The amount of creatinine in the 24 hour collection can be compared to the expected amount of creatinine production (in a steady state) based on the size of the patient:

\[
\text{Adult < 50 years of age (lean body weight)}
\]

- Male 20-35 mgs/kg daily creatinine excretion
- Females 15-20 mgs/kg daily creatinine excretion

\[
\text{Adult ages 50-90 (lean body weight)}
\]

- There is a progressive 50% decline in creatinine excretion

For example: A 42 year old 60 Kg (lean body weight) female with a measured serum creatinine of 2.2 mg/dL, urine volume of 2500mL/24 hours, urine creatinine of 100 mg/dL (1000mg/L).

\[
\frac{(2500\text{ml/day})(100\text{mg/dL})}{(1440\text{min/day})(2.2\text{mg/dL})} = 81.16 \text{ ml/min}
\]

To assess adequacy of collection you would multiply by the expected milligrams of creatinine in a 24 hour timed collection. Here it is either 20 x 60 =1200mg/day  15 x 60 = 900mg/day; therefore, her collection at 1000mgs is adequate.

Estimating GFR from serum values can be done using several formulas the **Cockcroft-Gault** equation (using the serum creatinine, age, weight and gender) **Modification of Diet in Renal Disease (MDRD)** equation (using age, serum creatinine, sex and African American or not). The estimation equations may be less accurate in some patient populations. Those individuals with normal or near-normal renal function, children, patients older than 70 years of age, other ethnic
groups, pregnant women, and those with unusual muscle mass, body habitus, and weight (morbid obesity or malnourished).

**Determining between pre renal azotemia and acute tubular necrosis (renal azotemia)**

Pre renal azotemia results from a reduction in renal blood flow and is the most common form of acute renal failure. The more common causes of pre renal azotemia are true volume depletion, advanced liver disease, and congestive heart failure. The kidneys try to increase the renal blood flow by saving sodium; hence, a low urinary sodium excretion with a high specific gravity/increased urine osmolality. This yields a fractional excretion of sodium <1% and a fraction excretion of urea of <35%.

Renal azotemia (ATN) is characterized by renal tubular injury. There are many causes ranging from renal ischemia and exposure to exogenous and endogenous nephrotoxins. The net effect is a rapid decline in renal function that may require a period of dialysis before spontaneous resolution occurs. The major causes of ATN are severe prerenal disease causing renal ischemia, exposure to nephrotoxins such as aminoglycosides, NSAIDS, radio contrast agents, cisplatin, acyclovir, pentamidine, Heme Pigments, etc. The kidneys are damaged and therefore cannot concentrate urine and waste sodium. The fractional excretion of sodium is >2% and the fractional excretion of urea is >35%. *(The fractional excretion of sodium may be affected by diuretics, radiocontrast agents and urine volume. It is valid in oliguric acute renal failure. The FEUrea is more reliable in these conditions.)*

**Table Correlating indices with Acute Renal Failure Classification**

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Uric Acid

The Serum Uric Acid can correlate with decreasing renal function. It can also serve as a cause of decreased renal function. Increase values may cause precipitation within the tubules and cause intra tubular slugging and stone formation with blockage of urine flow. This blockage of urine flow can cause renal damage and subsequent failure.

Summary:

Renal function tests should be ordered on patients who are at risk of kidney disease. They are used to monitor renal function, stage chronic kidney disease, classify acute renal failure, and dose medications. Knowing the various tests available and the idiocracies of each test will provide patients with a better health care plan and monitoring.

Equations:

Cockcroft-Gault:

\[
\text{GFR (ml/min/1.73m2)} = \frac{(140 - \text{Age}) \times \text{Wt. Kg. (lean body wt.)}}{(\text{serum Creatinine}) \times 72}
\]

- multiply by 0.85 for women

MDRD:

\[
\text{GFR (ml/min/1.73m2)} = 186 \times (\text{Pcr})^{1.154} \times \text{Age}^{0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})
\]

FENa:

\[
\text{FENa} = \frac{\text{Urine sodium/plasma sodium}}{\text{Urine creat./plasma creat.}} \times 100
\]

FEUrea:

\[
\text{FEUrea} = \frac{(\text{UUN ÷ BUN})}{\text{(Serum Creat. ÷ Urine Creat.)}} \times 100\%
\]

Renal Failure Index:

\[
\text{RFI} = \frac{\text{Urine sodium} \times \text{Plasma creatinine}}{\text{Urine creatinine}}
\]
References:


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