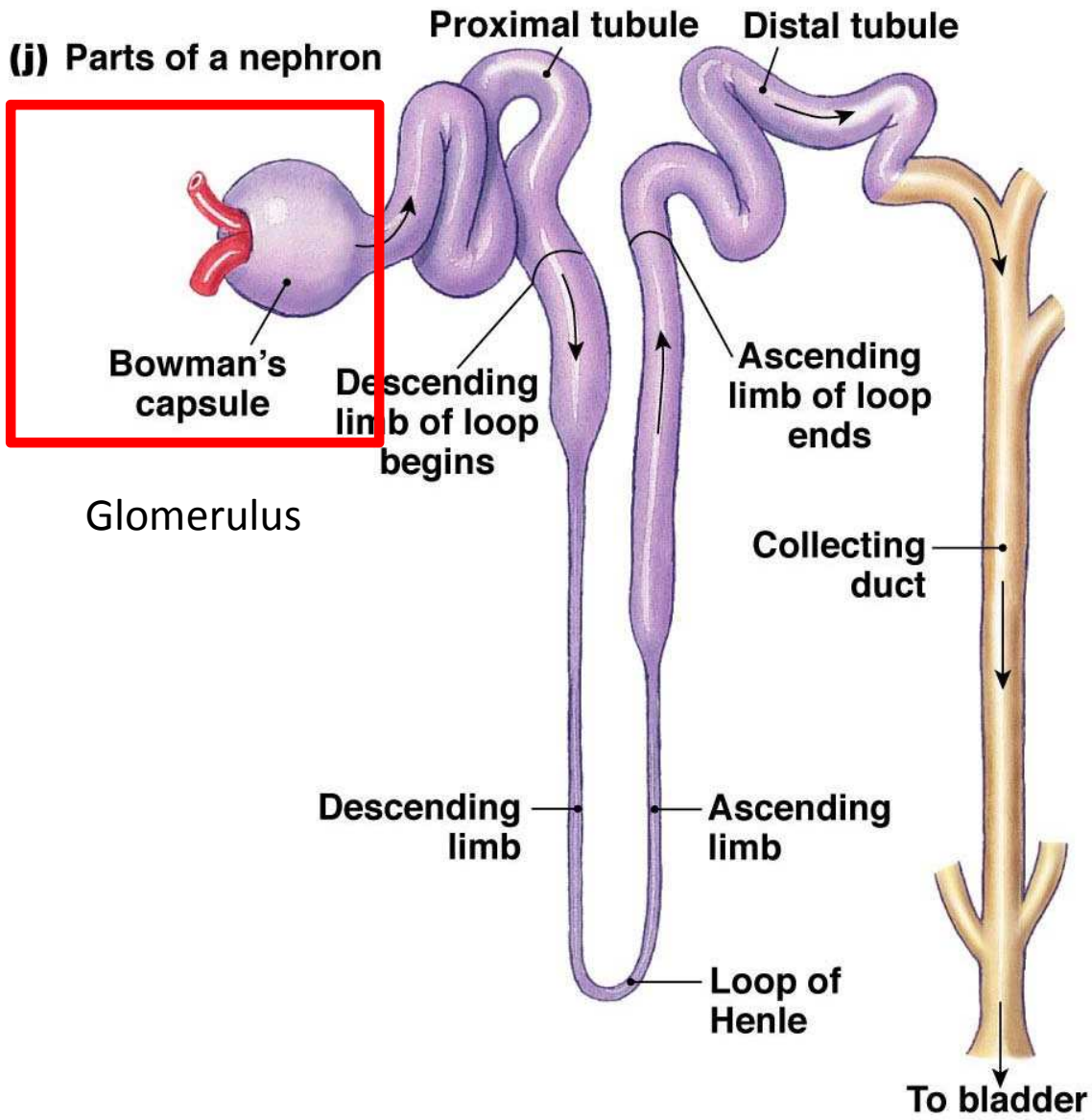
Residual Renal Function

SKC In-service June 2016

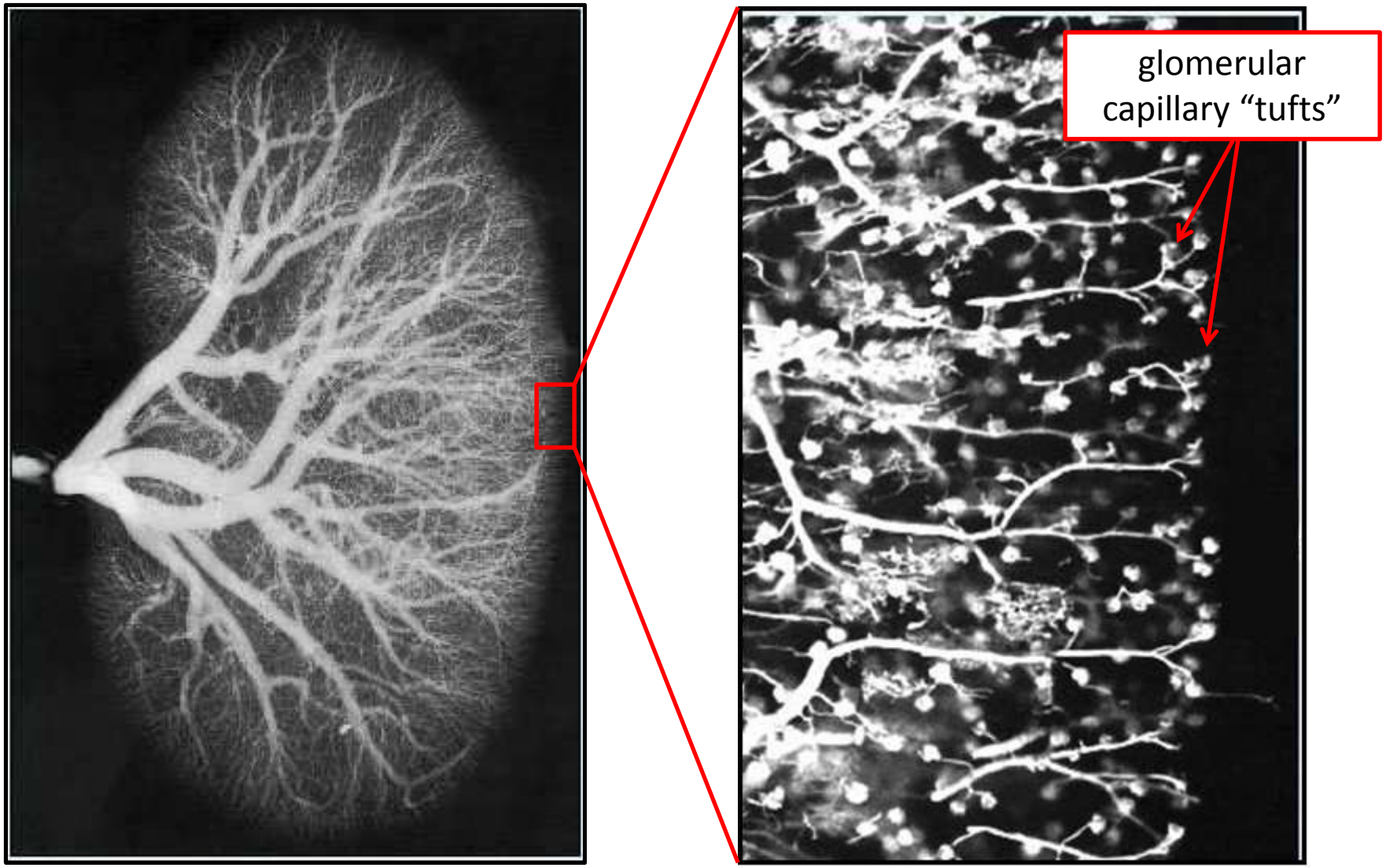
Nephron: Fundamental Unit of the Kidney

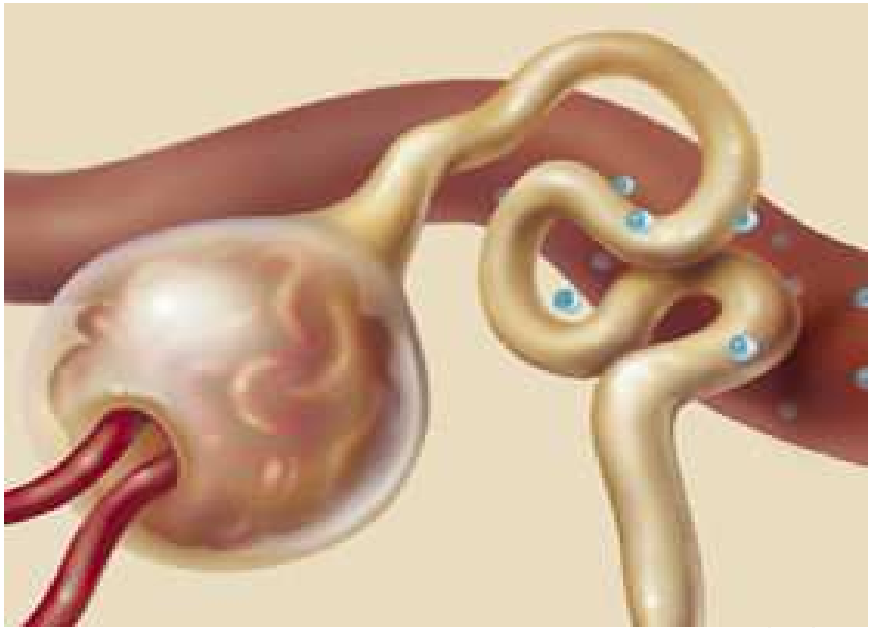


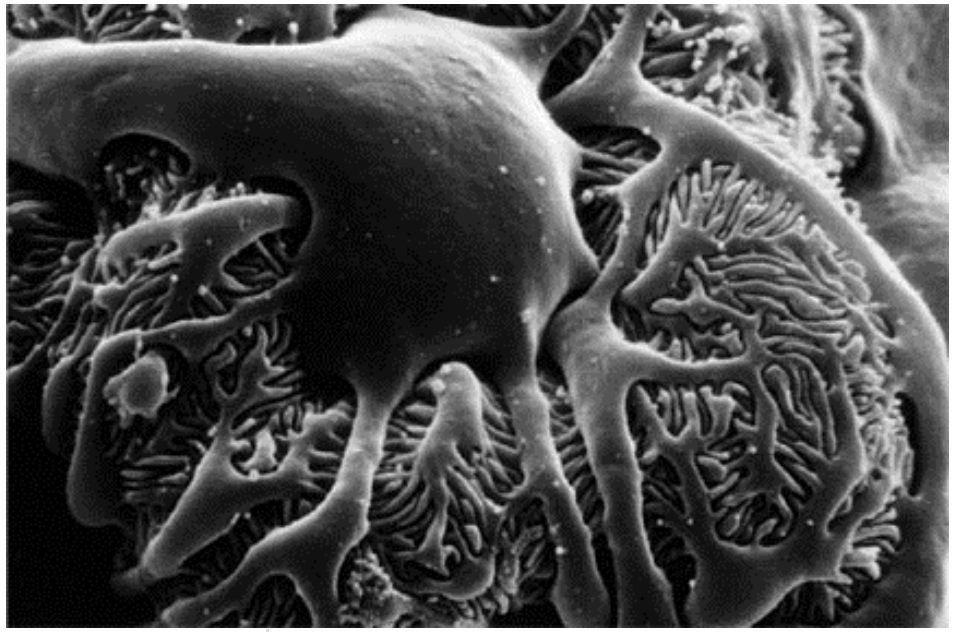
Glomerulus

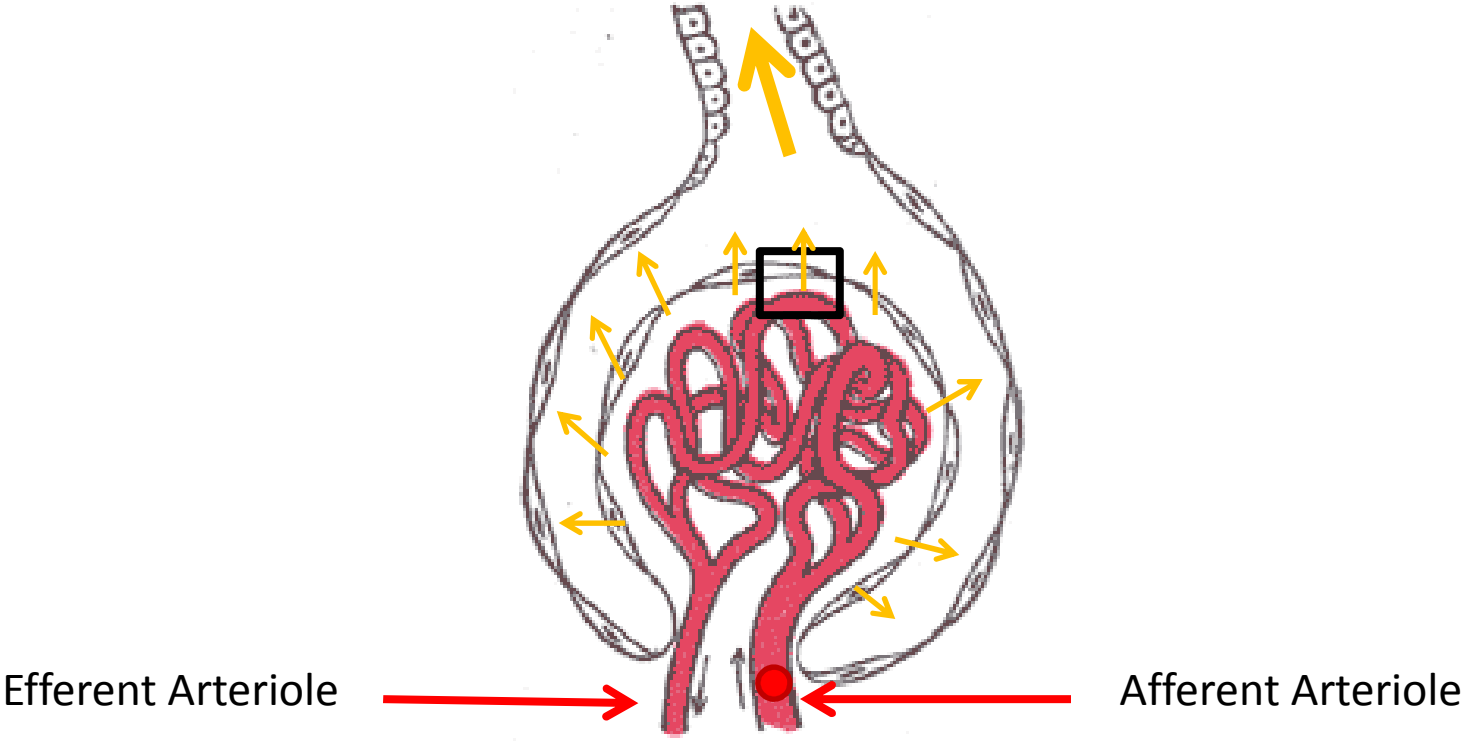
Glomerular Anatomy

- Each kidney contains about 1 million nephrons








Efferent Arteriole
Afferent Arteriole

Renal blood flow (RBF), Renal Plasma Flow(RPF), Glomerular Filtration Rate (GFR)

Cardiac output = 6 L / min

Renal blood flow = 20% of cardiac output = 1,200 ml / min

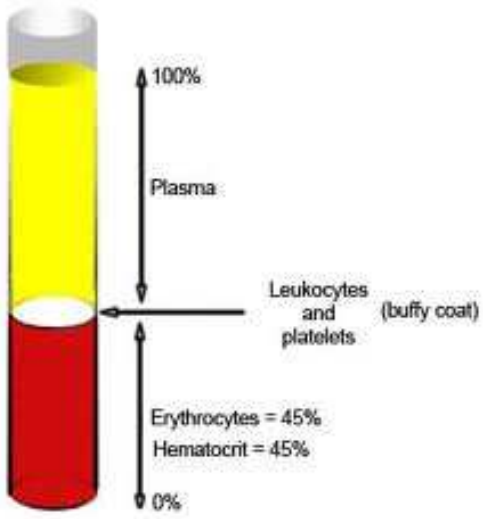
Given a hematocrit = 45%, plasma volume = 55%

Renal plasma flow = 55% of renal blood flow = 660 ml/min

20% of renal plasma flow is filtered (called the filtration fraction)

Therefore, a normal GFR = ~20% of renal plasma flow

= ~125 ml / min



Key Point!

GFR ≠ Urine Output

125 ml/min * 1440 min/day = 180 Liters / day

The kidney will take the filtrate and refine it further in the tubular portion of the nephron to maintain fluid and electrolyte homeostasis.

Typical urine output is closer to 2L per day –> tubules have a lot of work to do!

Measurement of Kidney Function: GFR

(non-dialysis patient)

- Serum creatinine
  - "Eyeball" method
  - Estimating Equations (MDRD, Cockcroft-Gault)
- 24 hour urine collection
- Iothalamate or Inulin study (research only)

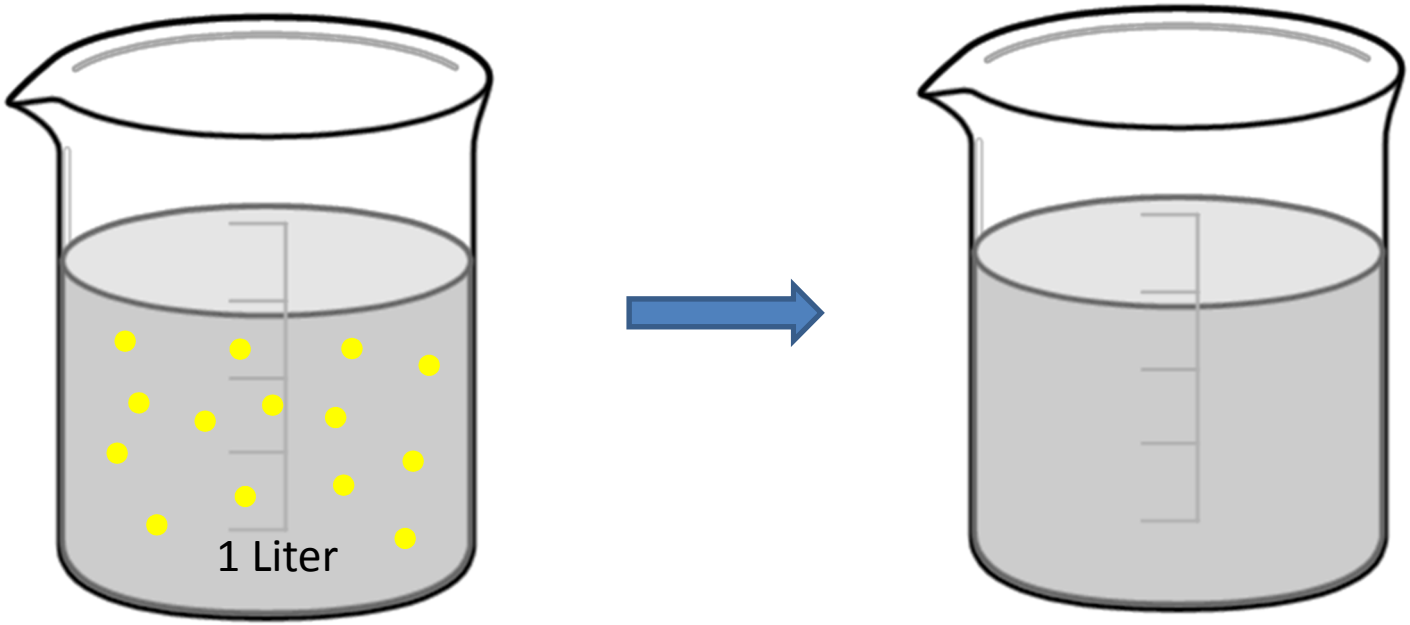
Measurement of Kidney Function

- The kidney is responsible for more than just GFR!

- With advancing CKD:
  - Anemia worsens
  - Phosphorus and PTH tend to increase
  - Sodium and fluid retention worsen, HTN worsens
  - Urine volume drops
  - Hyperkalemia develops (as anuria sets in)
  - In diabetics blood sugars can improve or drop too low (due to declining excretion of insulin and loss of gluconeogenesis by the kidneys)

Clearance

- Clearance is the volume from which a substance has been completely removed, usually expressed per unit time.



Clearance by Estimating Equations

- MDRD or Cockcroft-Gault Equations:

Table 1: Methods for estimating creatinine clearance (GFR) in ml/min/1.73 m^2.

Cockcroft-Gault formula:[w4]

$$\text{Creatinine clearance} = \frac{(140\text{-age})(\text{weight in kilograms})}{\text{Serum creatinine } (\mu\text{mol/L}) \times 0.81} \times (0.85 \text{ if female})$$

MDRD equation:[w5]

$$GFR = 186.3 \times (\text{serum creatinine level (mg/dl)})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black})$$

- Available with most lab reports
- NOT accurate in advanced CKD / ESRD

24-hour urine collection

- We can measure clearance by comparing blood and urine concentrations of creatinine over time.
- How to do it:
  - Patient wakes in AM and flushes first void
  - After that clock starts
  - All urine collected in jug until next AM when the first void in the AM is included
  - Specimen sent to lab, concentration of creatinine in the urine measured, volume of urine recorded and a blood sample drawn for blood creatinine concentration

Calculating Clearance from 24 hour urine collection

$$\text{Creatinine Clearance} = \frac{\text{Creatinine}_{urine} \times \text{Volume}_{urine}}{1{,}440 \times \text{Creatinine}_{serum}}$$

Result in ml/min of clearance, roughly equivalent to GFR
(using creatinine overestimates GFR slightly)

Translation to the patient

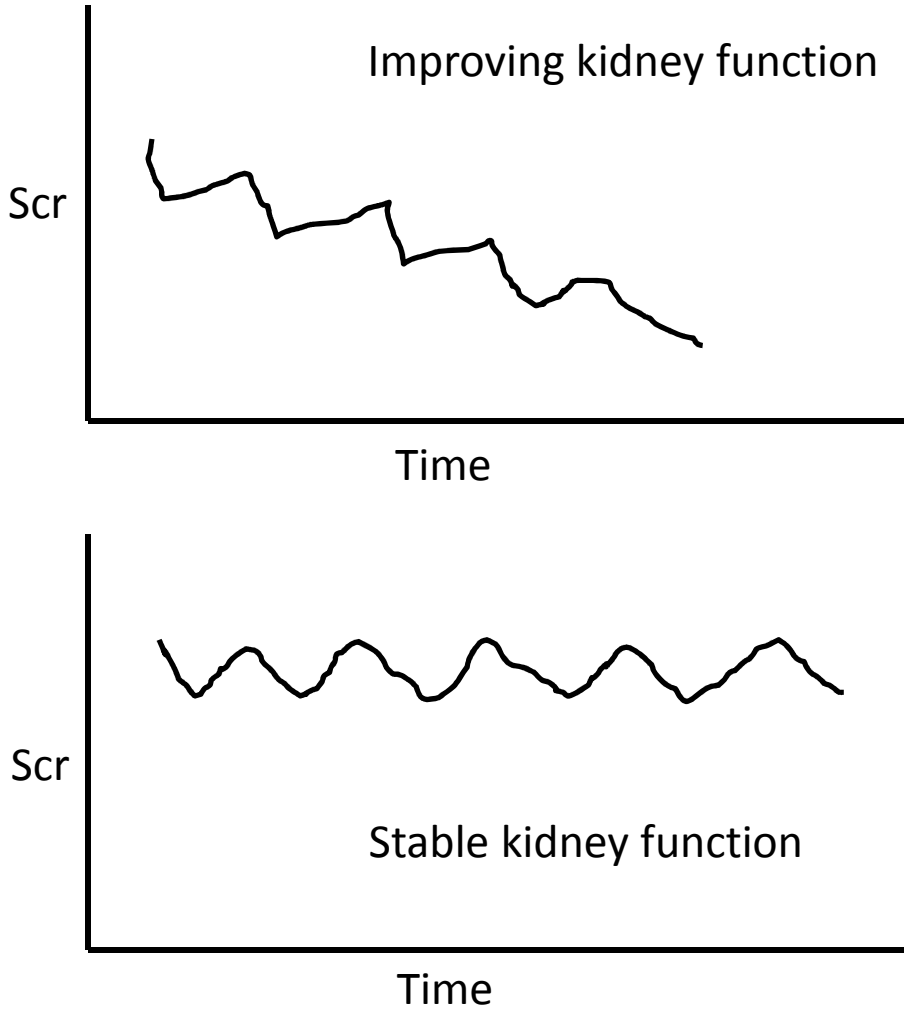
- Normal GFR is around 100-130 ml/min

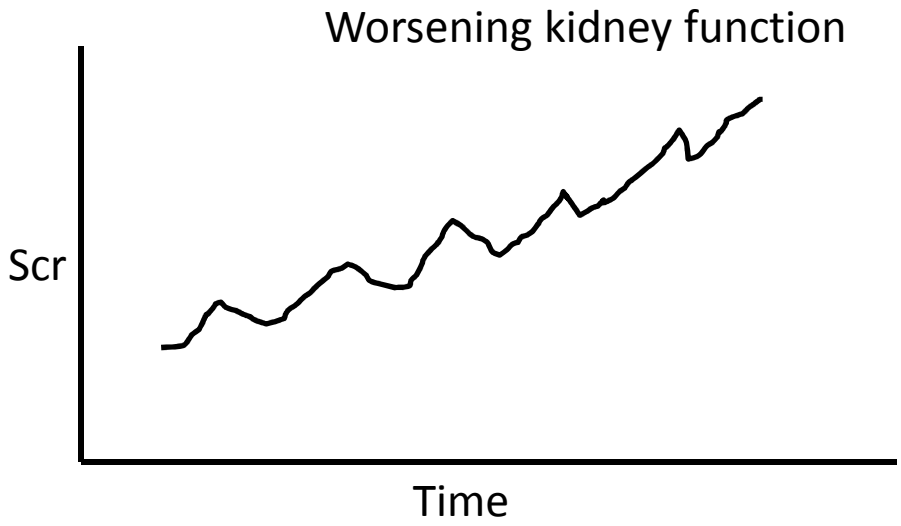
- Therefore it is reasonable to tell patients that their GFR is roughly equivalent to their % kidney function
  - Example, if the GFR is 20 ml/min then you have roughly 20% of your kidney function left
  - Dialysis is usually not required until the GFR drops below 10 ml/min

What about dialysis patients?

- “Eyeball” method can be used looking at the pre dialysis creatinine
- Patients who display recovery of renal function will have a down trending pre dialysis serum creatinine
- Patients in a steady state should have a relatively consistent pre dialysis creatinine
- Patients with declining residual renal function will have a increasing pre dialysis serum creatinine

Creatinine trend over time





Inter-dialytic Urine Collection

- Patient empties bladder after dialysis, discarding urine
- All urine between dialysis sessions collected, including a void right before going on next dialysis
- Pre dialysis urea and creatinine is measured, time between dialysis recorded

Inter-dialytic Urine Collection Calculations

- Proximal tubular reabsorption of urea leads to underestimation of GFR by urea clearance
- Tubular secretion of creatinine leads to overestimation of GFR by creatinine clearance
- The average of urea clearance and creatinine clearance is used in estimate the GFR more accurately

Inter-dialytic Urine Collection Calculations

- The UV/P equation is used:
  - Kru = UUN * Volume (ml) / BUN * time (min)
  - UUN = Urine urea nitrogen, BUN blood urea nitrogen
  - Creatinine is calculated similarly
  - GFR is calculated to be the average of the urea (Kru) and the creatinine clearance
  - In a dialysis patient you would expect the GFR to be below 15 ml/min

Does residual renal function matter to dialysis patients?

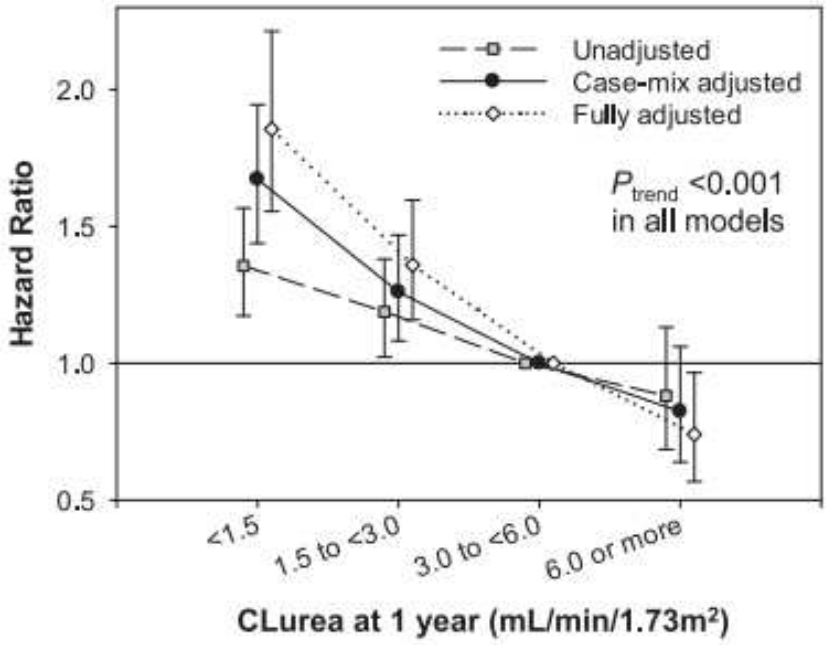


Figure 1. Renal CL_{urea} and all-cause mortality risk in incident hemodialysis patients. The mortality risk associated with renal CL_{urea} at 1 year after initiating dialysis among 6538 incident hemodialysis patients (2007–2010) with three levels of adjustment. There was a significant trend toward lower mortality of higher renal CLurea (*P* for trend <0.001 across all models).

Mortality benefit is fairly consistent across studies (esp. with peritoneal dialysis)

<u>Patient Viewpoint:</u>

More urine output = less UF, improved patient comfort

More urine output = more dietary options, less hyperkalemia / hyperphosphatemia / volume overload

Obi, JASN 2016

How do we preserve residual kidney function?

- Avoid Nephrotoxic medications:
  - NASIDs (ibuprofen, advil, motrin, naproxyen, alleve, etc)
  - Aminoglycosides (gentamicin, tobramycin, amikacin)
  - Proton pump inhibitors (associated with kidney failure)
- Avoid contrast (CT scans, angiograms, this is controversial)
- Avoid hypotension (intradialytic or other)
- Avoid infection / sepsis / inflammatory conditions
- Optimize cardiac function
- ?RAAS Blockade (ACE inhibitors, ARBs, spironolactone)