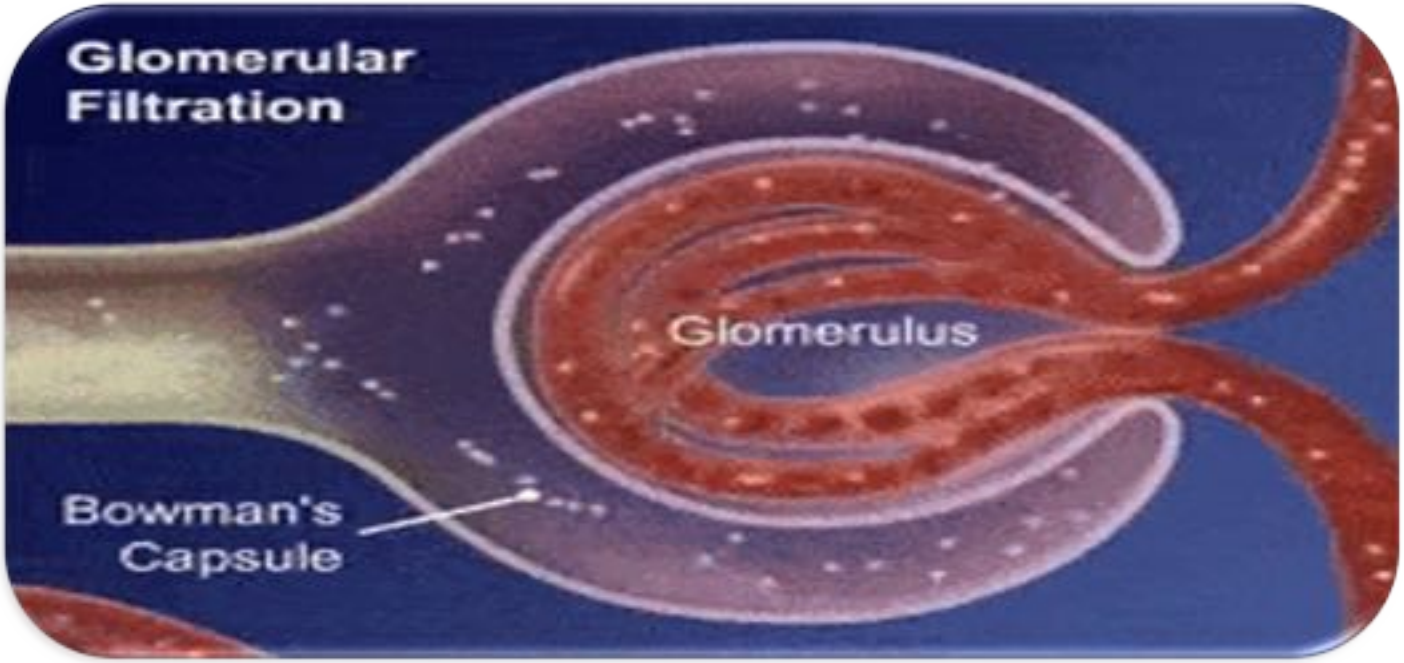
Serious gaps in the measurement of GFR

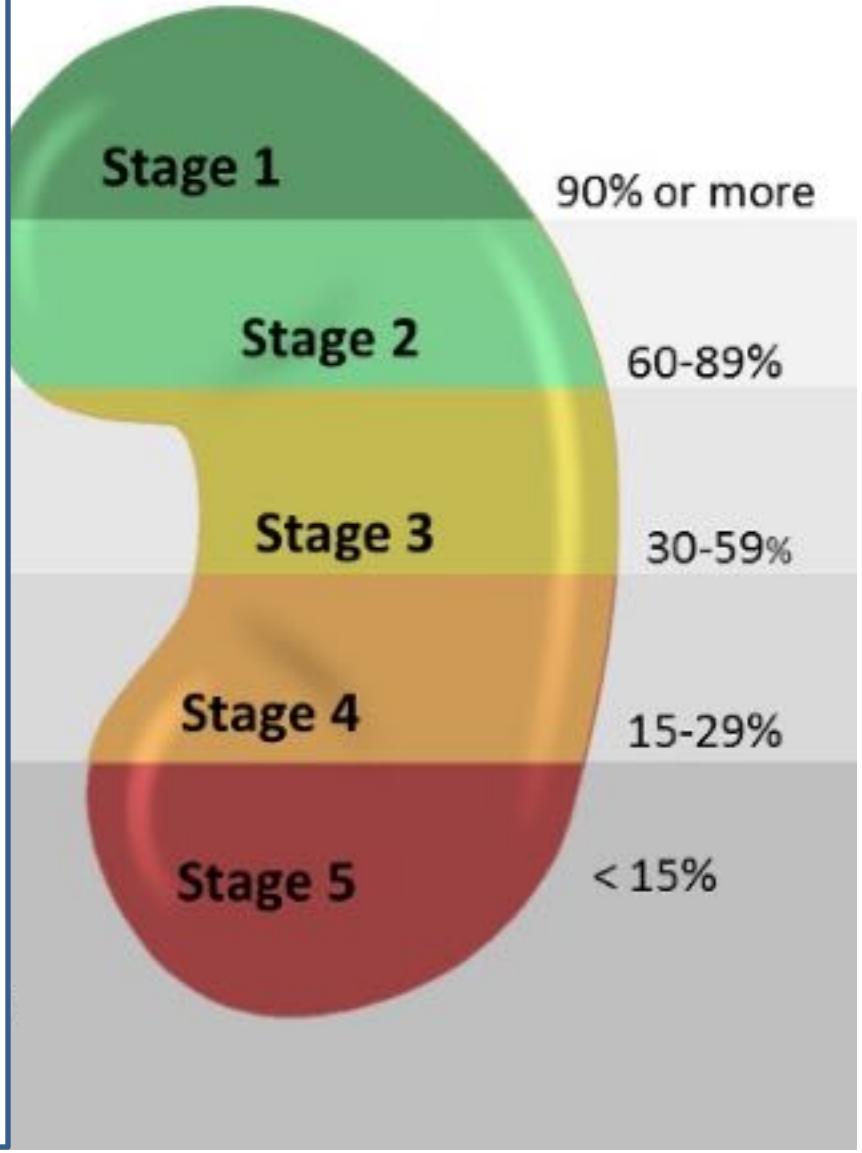
By
Ramzi El-Baroudy
(ESPNT)

We all know that,



the **main** measure of kidney function is the **glomerular filtration rate;**
which describes the flow rate of filtered fluid through the kidney.

GFR will determine what stage of the 5 stages of kidney disease is there.



GFR can be **directly** measured by the clearance of exogenous filtration markers (e.g. inulin) or calculated **indirectly** by the clearance of endogenous filtration markers (e.g. serum creatinine and cystatin C).

U*V/P

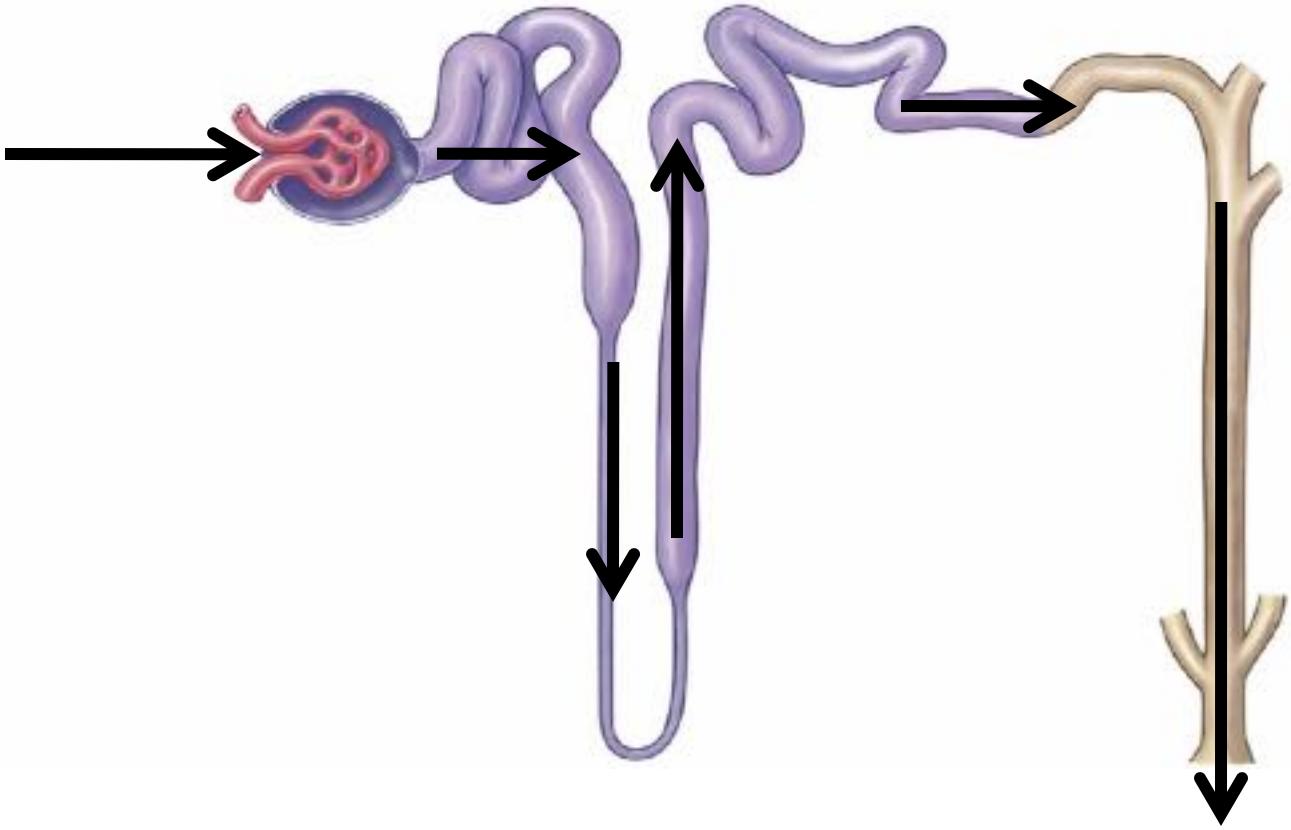
Where the product of urine concentration (U) and urine volume (V) equals the mass of substance filtered.
Dividing this mass by the plasma concentration (P) gives the volume of plasma cleared off this substance.

GFR

is equal to the

renal clearance rate

But on 3 conditions



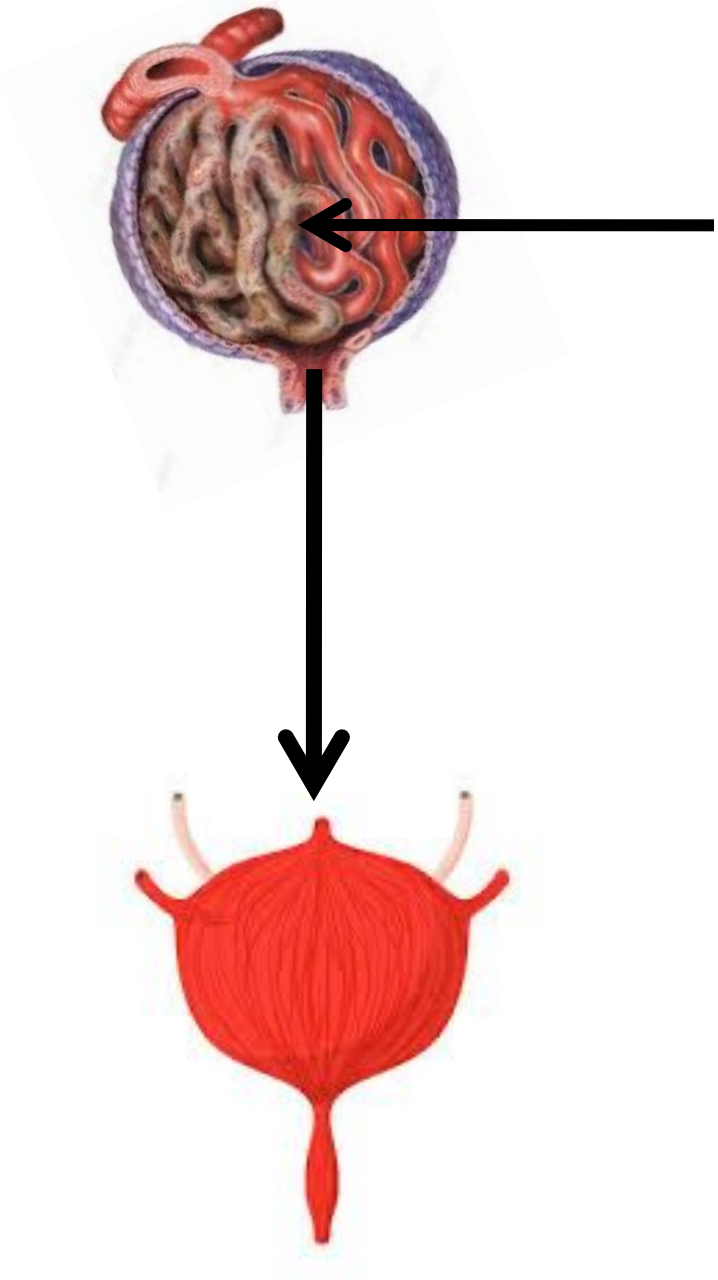
That the substance used should be:

1.freely filtered at the glomerulus,

2.neither reabsorbed

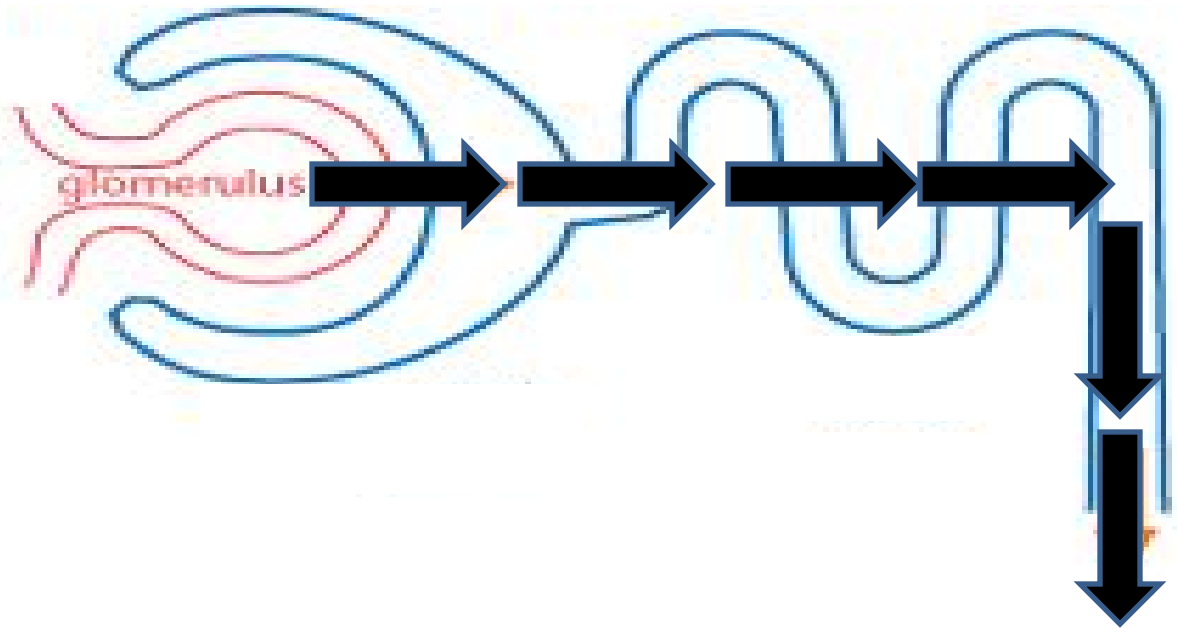
3.nor secreted by the tubules.

i.e. From blood, to bladder, uninterrupted



Then and only then, it is valid

is inulin



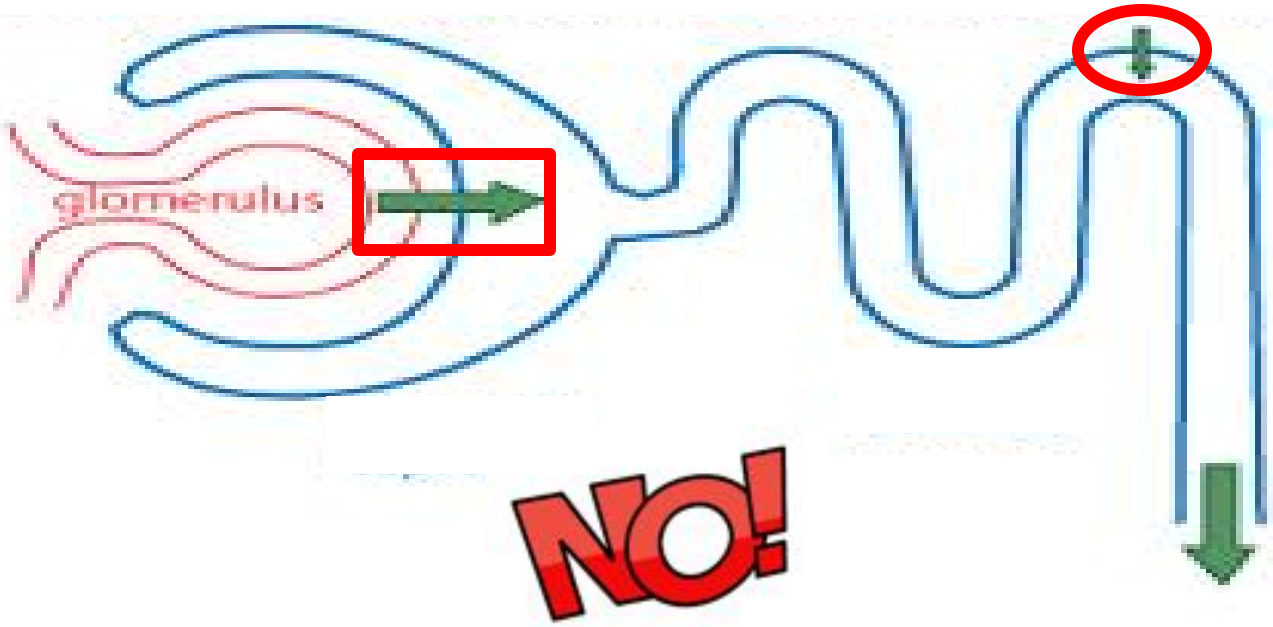
Inulin is the one **most accurate** substance to measure GFR.

Since it readily passes through the glomeruli into the urine *being neither reabsorbed nor secreted by the renal tubules*.

But the most popular is creatinine.

But the most popular is creatinine.

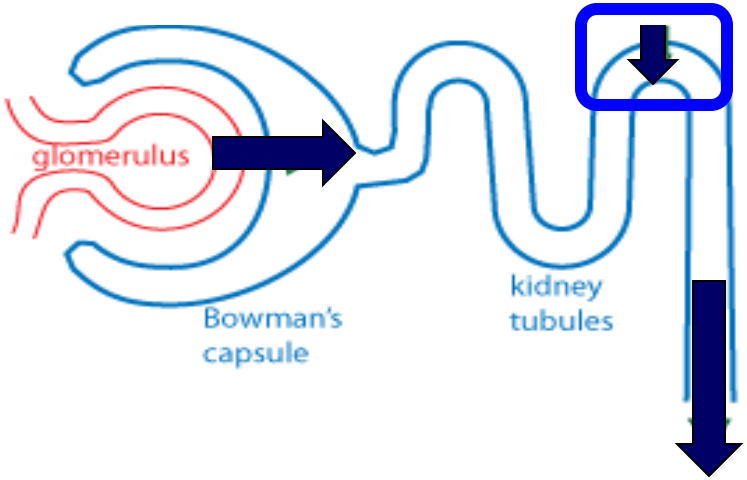
Is it fulfilling?



Creatinine clearance (ClCr) is **not** the ideal method for GFR measurement because Creatinine, although **freely filtered** in the glomerulus,
it is **also secreted in the tubule**.

In fact, 10-20% of the creatinine found in the urine is secreted via the tubules in **normal** individuals, which leads to an **overestimation** of the GFR when measured by ClCr.


However,



This margin of error is acceptable, considering the ease with which creatinine clearance is measured.

Unlike precise GFR measurements involving constant infusions of inulin, which is very annoying to both patient and doctor.

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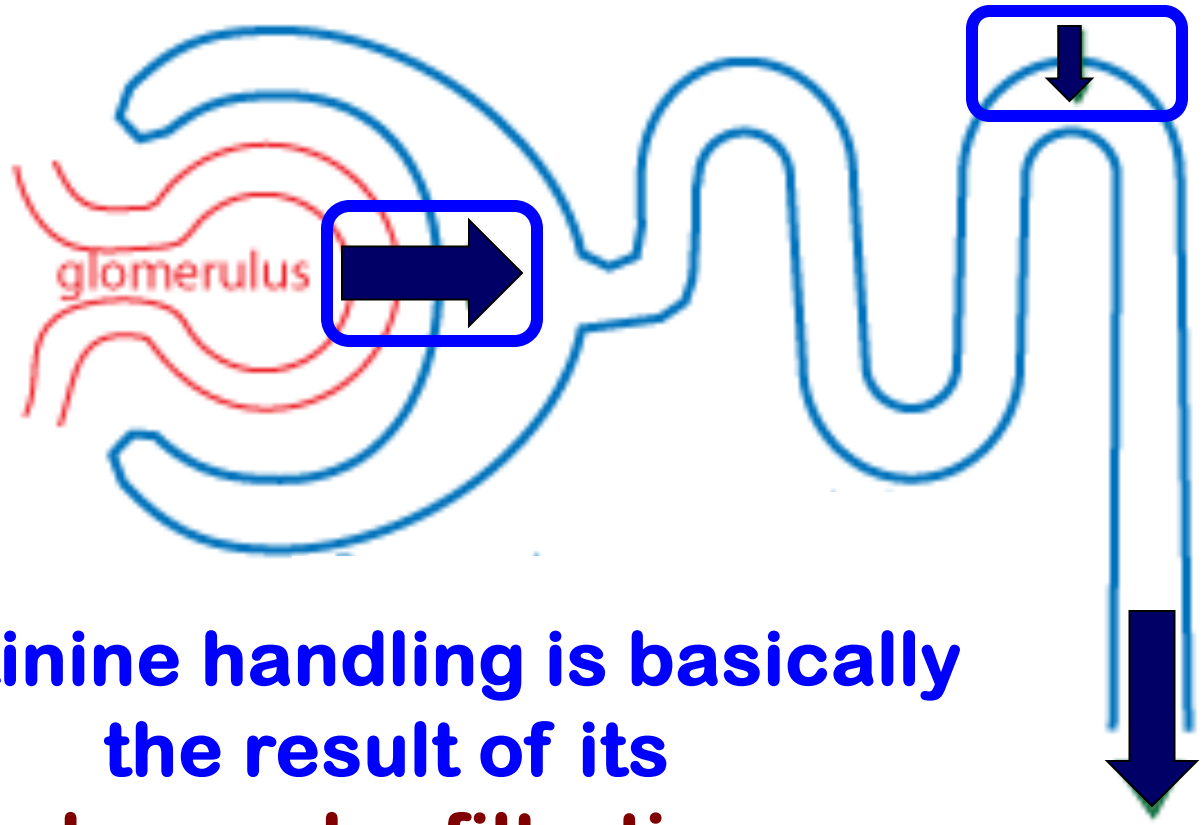
an elevated serum creatinine is usually a sign of glomerular disease

The Schwartz Equation

The equation is eGFR =
(k * height) / Pcr (in mg/dl)

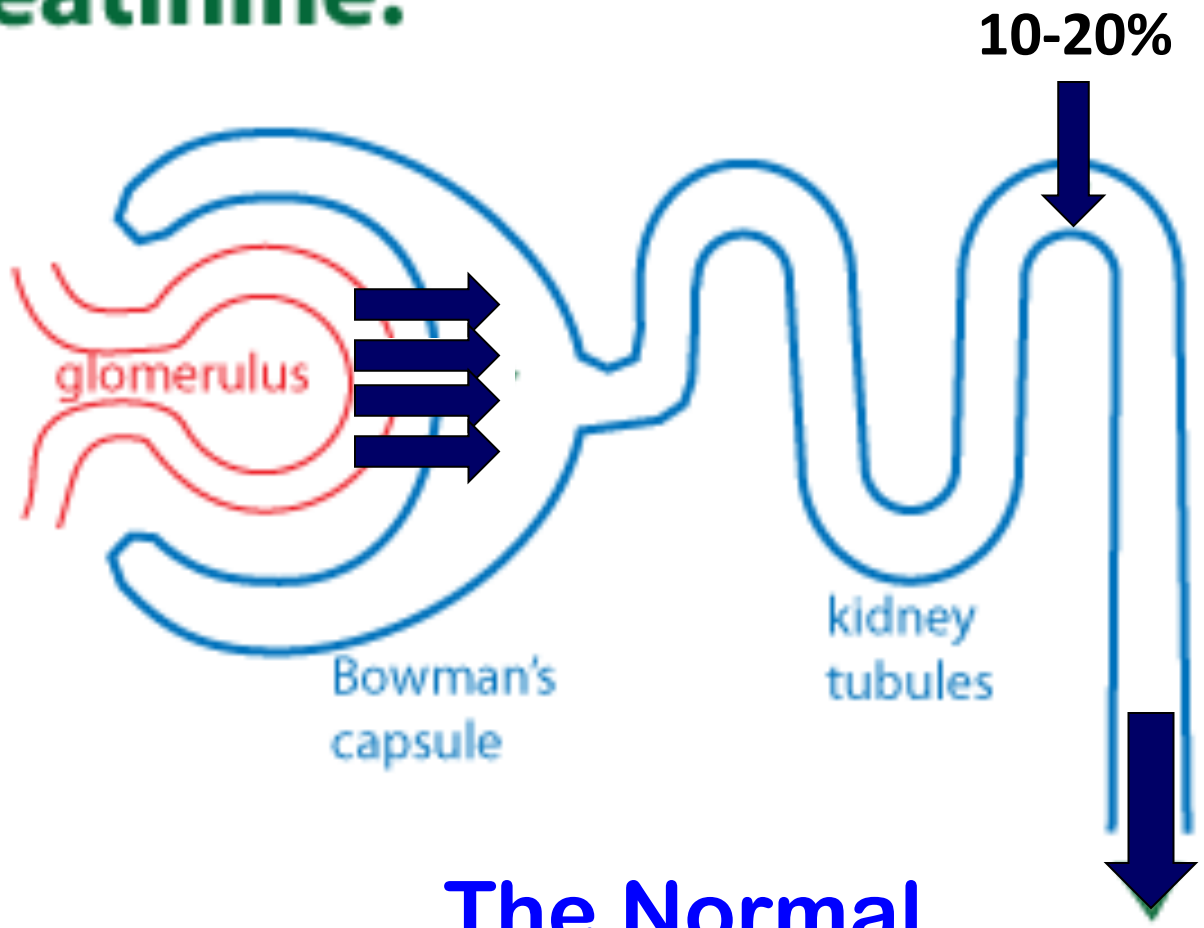
	k
Infant (LBW < 1 year)	0.33
Infant (Term < 1 year)	0.45
Child or Adolescent Girl	0.55
Adolescent Boy	0.70

as stated before



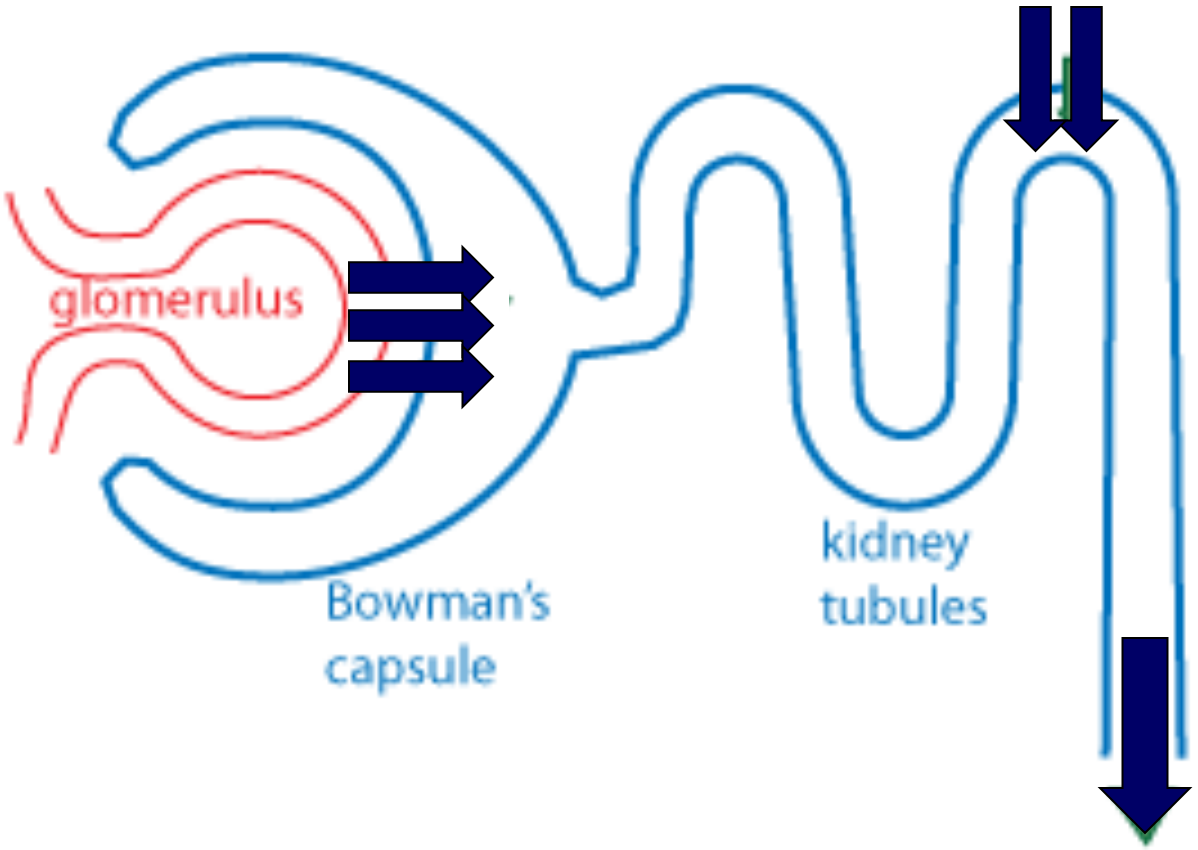
Creatinine handling is basically the result of its glomerular filtration and to a lesser extent to its proximal tubular secretion.

creatinine:



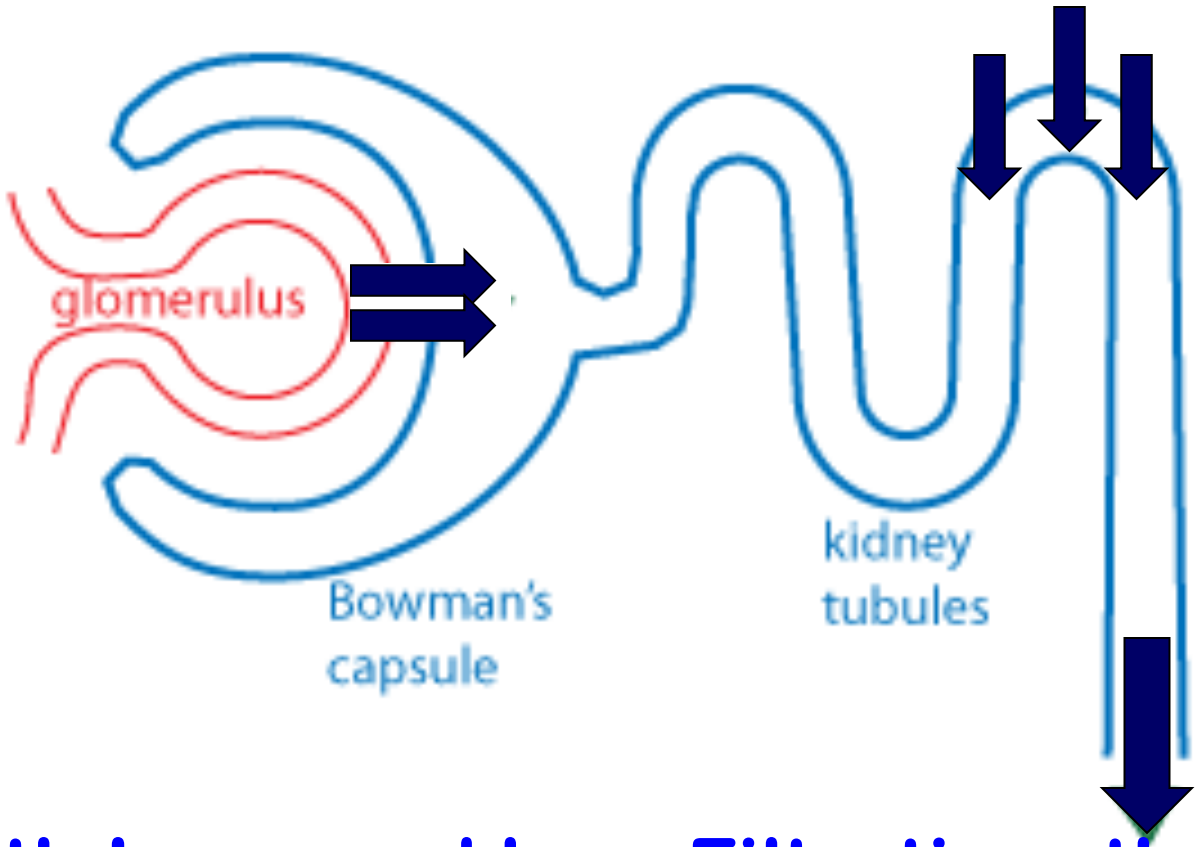
The Normal

creatinine:



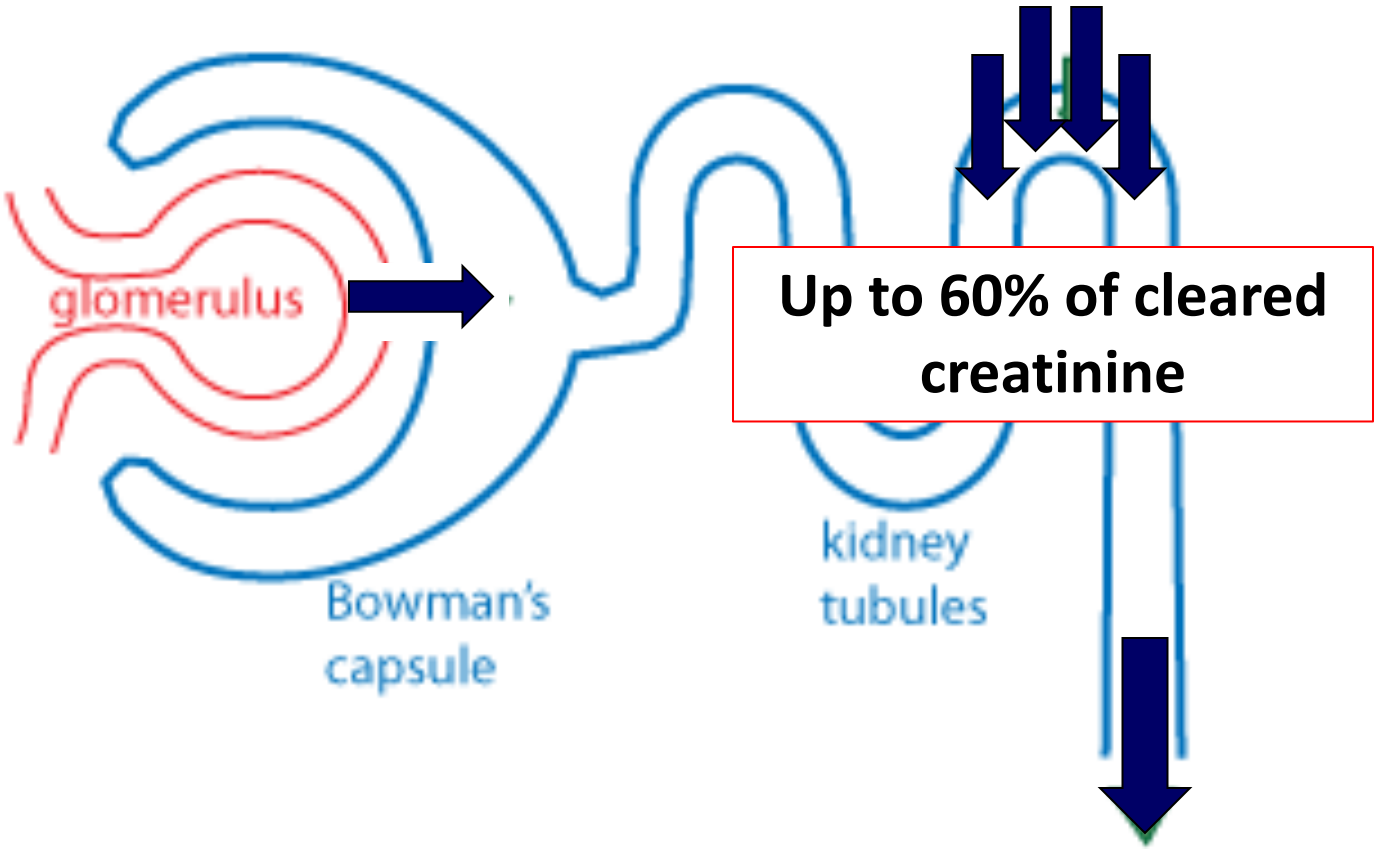
With Less Filtration, more Tubular Secretion occurs

creatinine:



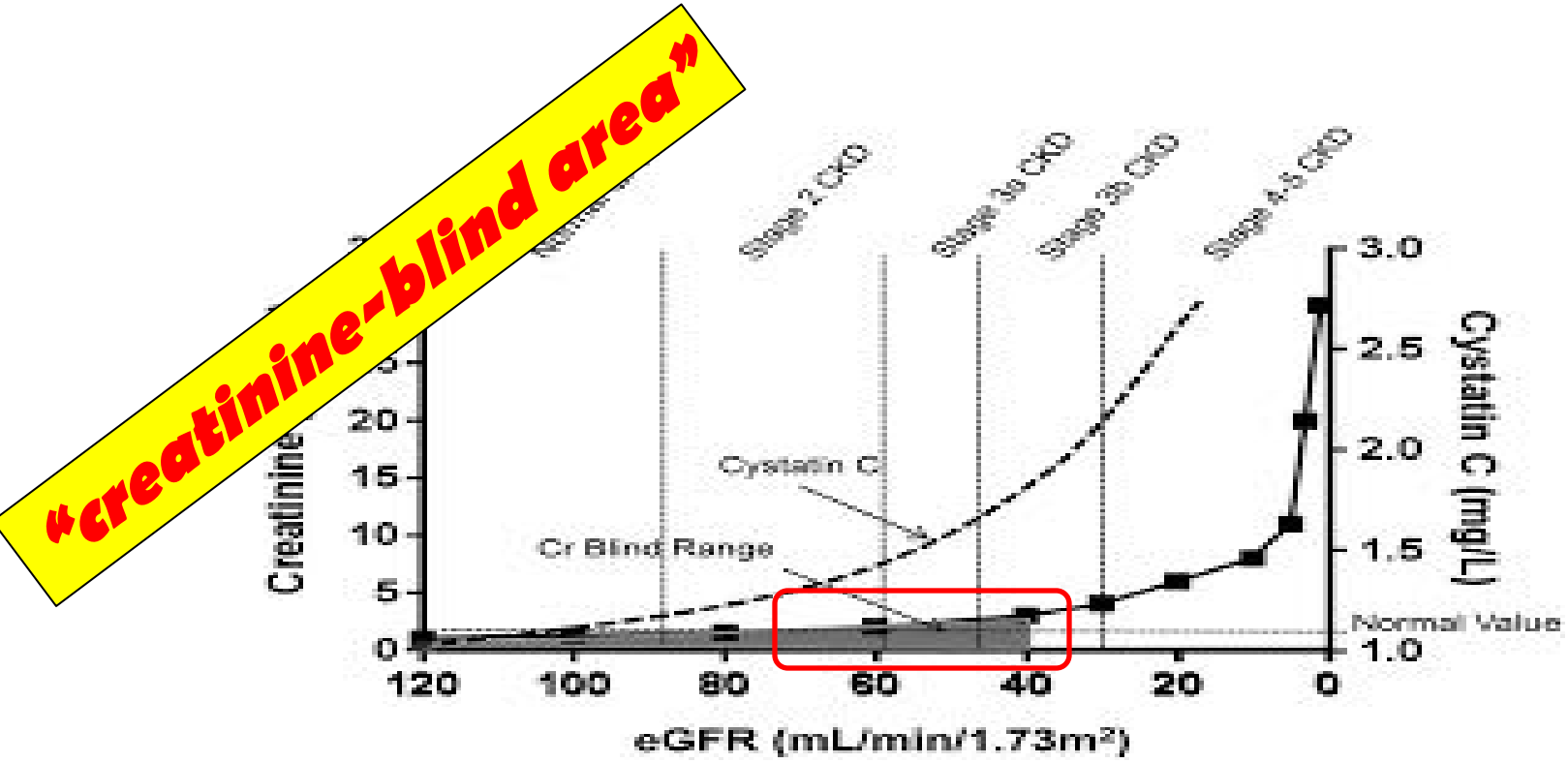
With Less and less Filtration, there is more and more Tubular Secretion occurs

creatinine:

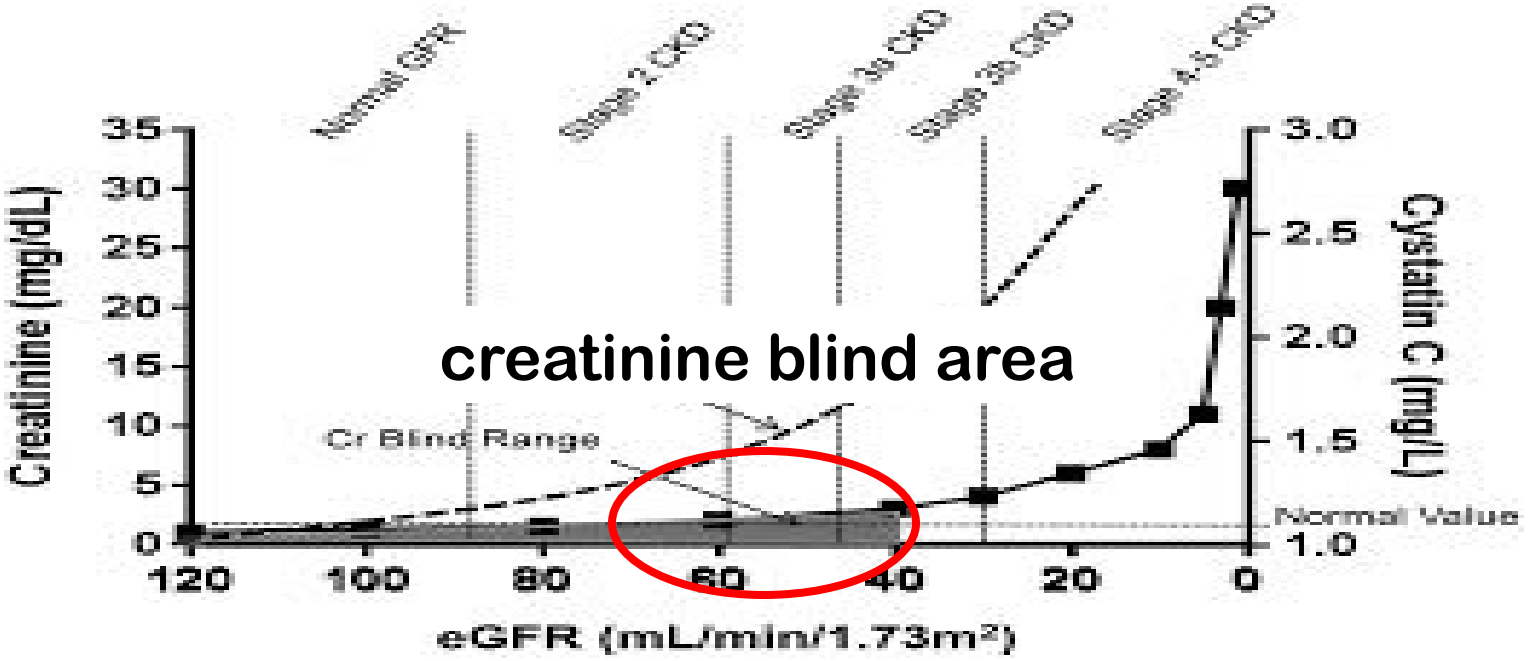


With severe degrees of low Filtration, there is the highest rate of Tubular Secretion


CONSEQUENTLY



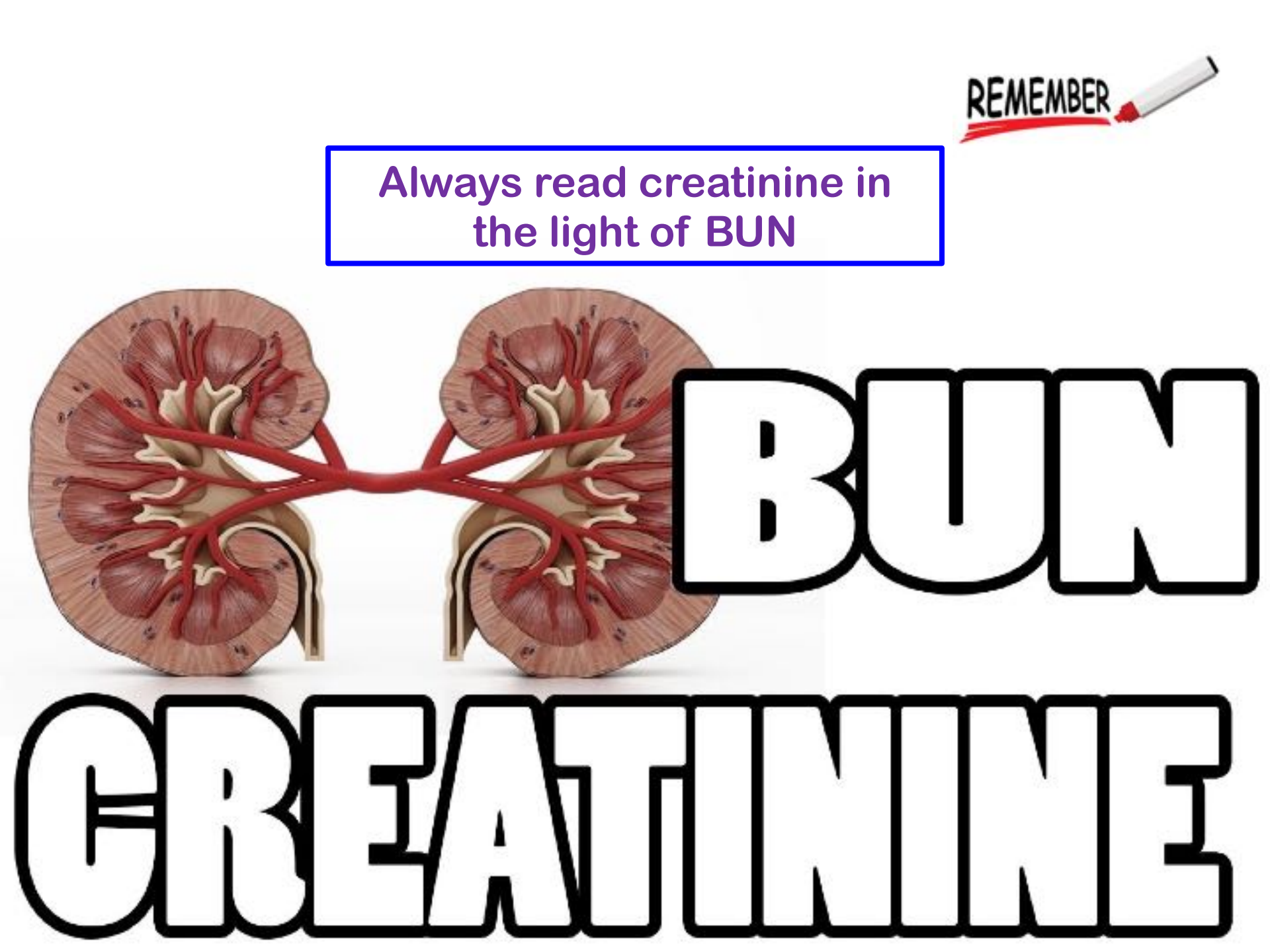
GFR can be much reduced while the serum creatinine value is still within the normal range due to the increased tubular secretion; this is the "creatinine-blind area".



In this creatinine blind area, despite deterioration in GFR, creatinine is normal in blood, due to *increased tubular secretion*,

yet, BUN is elevated (*diminished glomerular filtration*).

Hence, serum creatinine and BUN assay should always be combined.

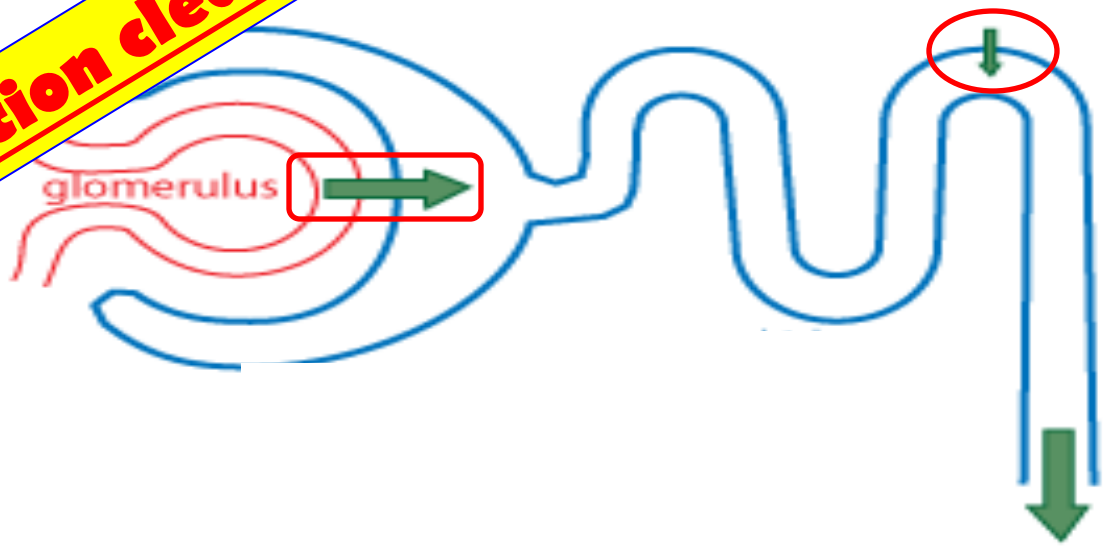

REMEMBER
Always read creatinine in the light of BUN
BUN
CREATININE

Typically, the ratio of BUN to creatinine should be between 10:1 and 20:1.


BUT
BEWARE....

There are surprising gaps in knowledge regarding the relation between CrCl and GFR.

non-filtration clearance



First,

creatinine is freely filtered by the glomerulus, and , as I stated before,

actively secreted by the proximal tubule

i.e. non-filtration clearance

in such that creatinine clearance **overestimates** actual GFR by 10% to over 60% in advanced glomerular disease.

measurement error

Second,

is this overestimation actually due to proportionally greater tubular creatinine secretion , or whether this can be entirely accounted for by measurement error ?

Indeed, Measurement error alone could entirely account for the longstanding observation that CrCl/GFR ratio is larger than expected among patients with CKD

And, keep in mind, Inaccurate collection of urine specimens is the biggest source of measurement error for directly measured GFR and CrCl by urinary clearance.

In a retrospective study, 50.7% of urine collections were inaccurate; either bacteriologically or chemically contaminated specimen, or rather using the Wrong Type and/or amount of preservative.

Drug interaction

Third

Some drugs such as trimethoprim-sulfamethoxazole and the H_2-blocker cimetidine and ranitidine decrease the secretion of creatinine. This can result in a self-limited and reversible increase in the serum creatinine level.

How can you judge if this rise in creatinine is a fallacy or true ?

Check the BUN

In these instances,

the blood urea nitrogen (BUN)

typically

does not change.

Hence, serum creatinine and BUN assay should always be combined.

MUSCLE MASS MATTERS

Fourth

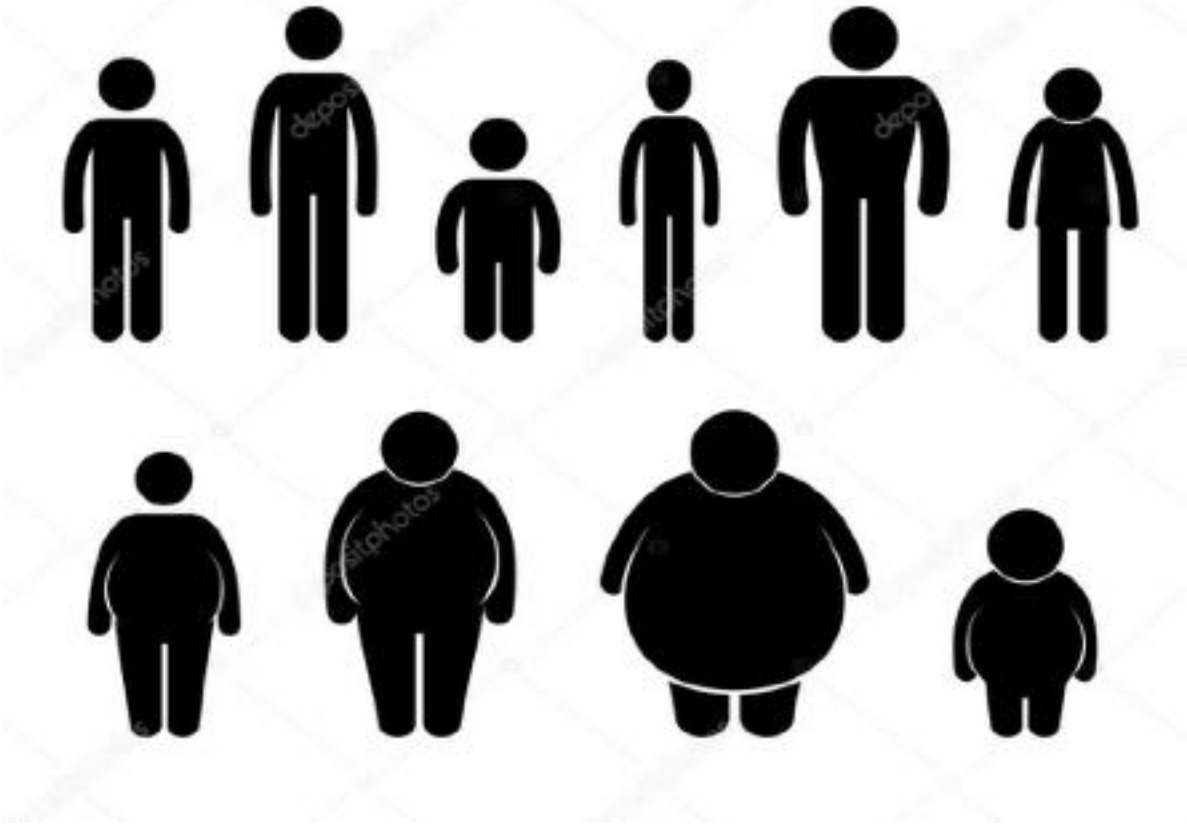
A more serious problem of the GFR assessment based on serum creatinine is that the presumption of its constant flow from the cells into the blood plasma is not fulfilled.

Creatinine formation in the body is a function of muscle mass.

constant flow is **not** fulfilled.

Estimates of GFR can only be based on steady-state serum creatinine values.

As well,



Besides the muscle mass, the interpretation of serum creatinine level should also take into consideration

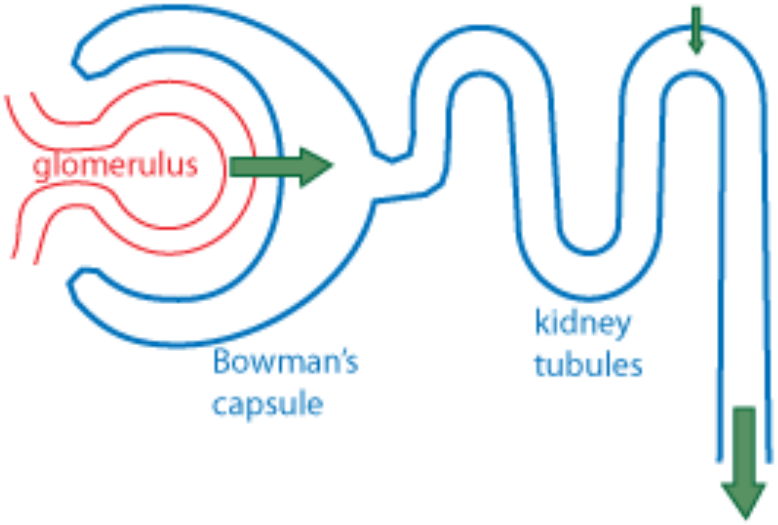
age, sex, and height.

In routine diagnostics the
GFR was in most cases determined by
endogenic creatinine clearance.

Possibilities of errors in
this method are
too many.

creatinine:

creatinine is filtered, and a small amount is secreted



non-filtration clearance

constant flow is not fulfilled.

measurement error

affected by gender, age, race, and muscle mass


STILL

Creatinine remains the gold standard for measuring the glomerular filtration rate and kidney functioning.

My only take home message is, as such,
an increase in creatinine level suggests a true decrease in GFR

only if

accompanied by a corresponding increase in BUN levels.


The
Golden
Rule

Serum creatinine and BUN assay should always be combined.

Ramzi El-Baroudy


MCQs

1. What is creatinine?

a) A hormone produced by the adrenal gland.

b) A protein found in muscle tissue.

c) A waste product produced during muscle metabolism.

d) A neurotransmitter produced by the brain.

2. What is the formula used to calculate creatinine clearance?

a) Urine creatinine concentration x urine volume / plasma creatinine concentration
b) Plasma creatinine concentration x urine volume / urine creatinine concentration
c) Urine volume x plasma creatinine concentration / urine creatinine concentration
d) Urine creatinine concentration x plasma creatinine concentration / urine volume

3. What unit is creatinine clearance expressed in?

a) Grams per liter (g/L)

b) Milliliters per minute (ml/min)

c) Milligrams per deciliter (mg/dL)

d) Liters per hour (L/hr)


Good Luck

4. What does creatinine clearance measure?

a) The amount of creatinine in the blood.

b) The amount of creatinine in the urine.

c) The rate at which creatinine is cleared from the blood by the kidneys.

d) The rate at which creatinine is excreted in the urine.

5. What is the normal range for creatinine clearance?

a) 50-80 ml/min

b) 80-120 ml/min

c) 120-150 ml/min

d) 150-200 ml/min

Answer: b) 80-120 ml/min