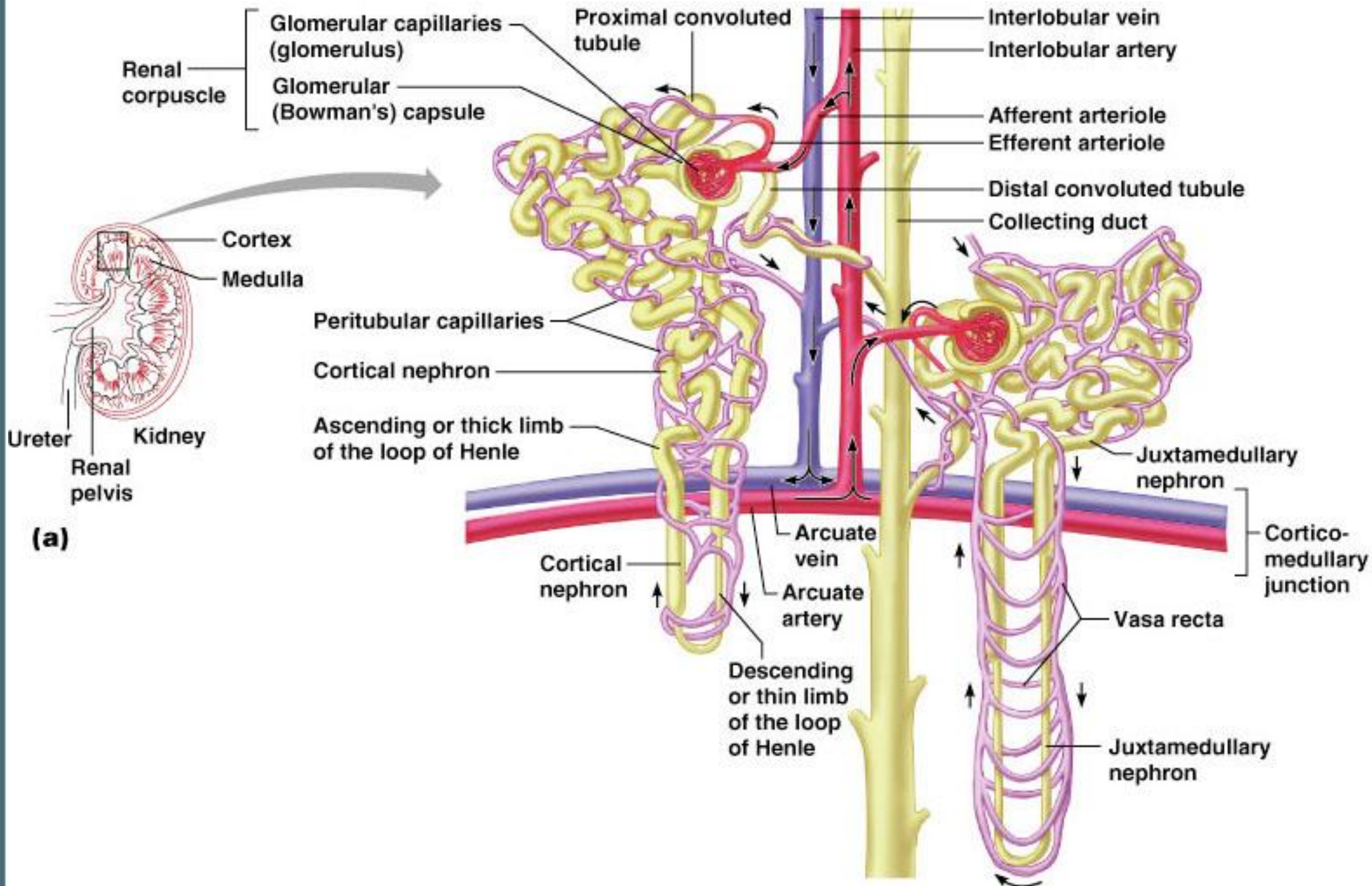
Renal Physiology 2:
Glomerular Filtration Rate

Dr Ahmad Ahmeda

aahmeda@ksu.edu.sa

Capillary Beds of the Nephron

- Every nephron has two capillary beds
  - Glomerulus
  - Peritubular capillaries
- Each glomerulus is:
  - Fed by an afferent arteriole
  - Drained by an efferent arteriole
- Blood pressure in the glomerulus is high because:
  - Arterioles are high-resistance vessels
  - Afferent arterioles have larger diameters than efferent arterioles
- Fluids and solutes are forced out of the blood throughout the entire length of the glomerulus


Renal corpuscle
Glomerular capillaries (glomerulus)
Glomerular (Bowman's) capsule
Proximal convoluted tubule
Interlobular vein
Interlobular artery
Afferent arteriole
Efferent arteriole
Distal convoluted tubule
Collecting duct
Cortex
Medulla
Peritubular capillaries
Cortical nephron
Ascending or thick limb of the loop of Henle
Ureter
Renal pelvis
Kidney
(a)
Juxtamedullary nephron
Cortico-medullary junction
Arcuate vein
Arcuate artery
Cortical nephron
Vasa recta
Descending or thin limb of the loop of Henle
Juxtamedullary nephron

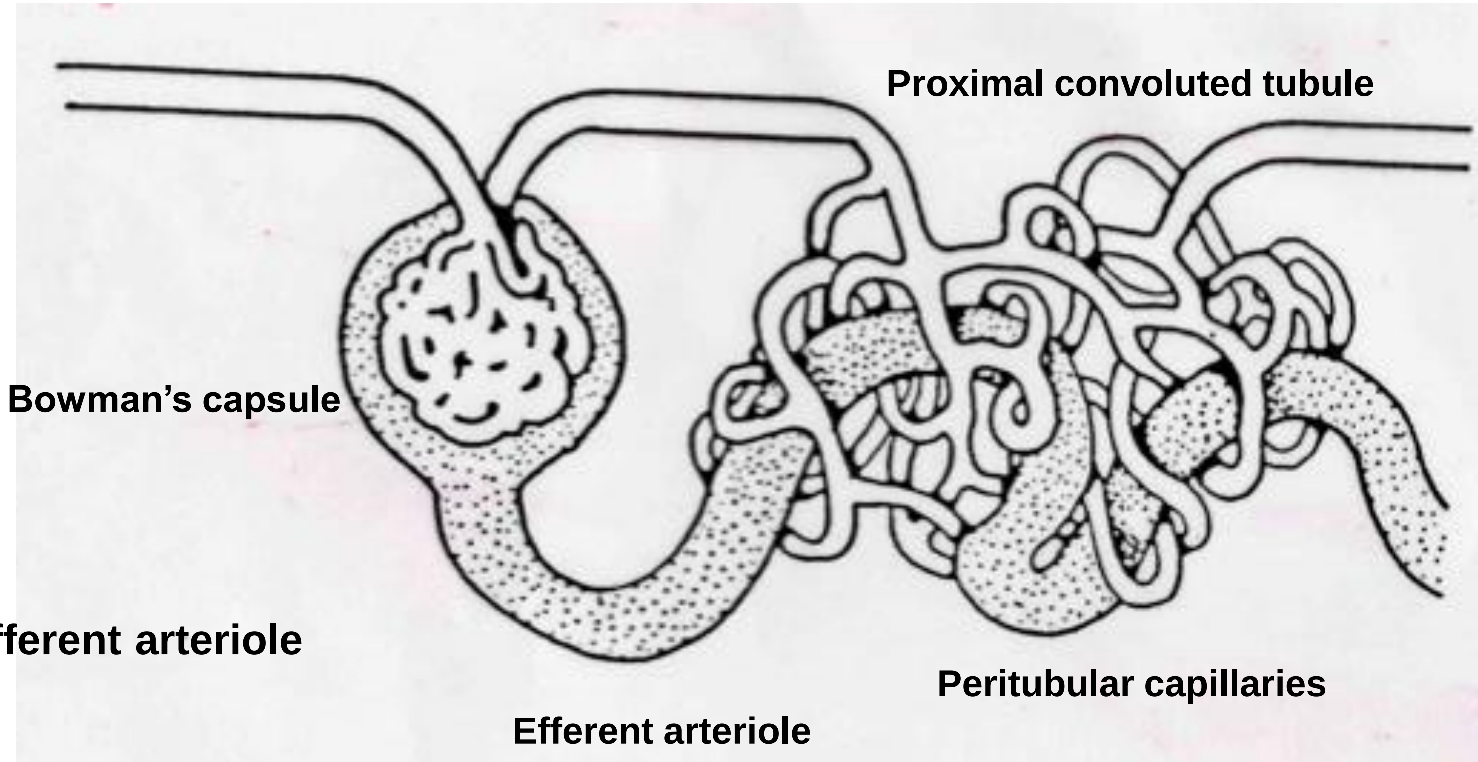
Capillary Beds

- **Peritubular beds** are low-pressure, porous capillaries adapted for absorption that:
  - Arise from efferent arterioles
  - adhere to adjacent renal tubules
  - Empty into the renal venous system

- **Vasa recta** – long, straight efferent arterioles of juxtamedullary nephrons

Vascular Resistance in Microcirculation

- Afferent and efferent arterioles offer high resistance to blood flow
- Blood pressure declines from 95mm Hg in renal arteries to 8 mm Hg in renal veins
- Resistance in afferent arterioles:
  - Protects glomeruli from fluctuations in systemic blood pressure
- Resistance in efferent arterioles:
  - Reinforces high glomerular pressure
  - Reduces hydrostatic pressure in peritubular capillaries



Glomerular capillary bed
High pressure vascular bed,
increasing oncotic pressure

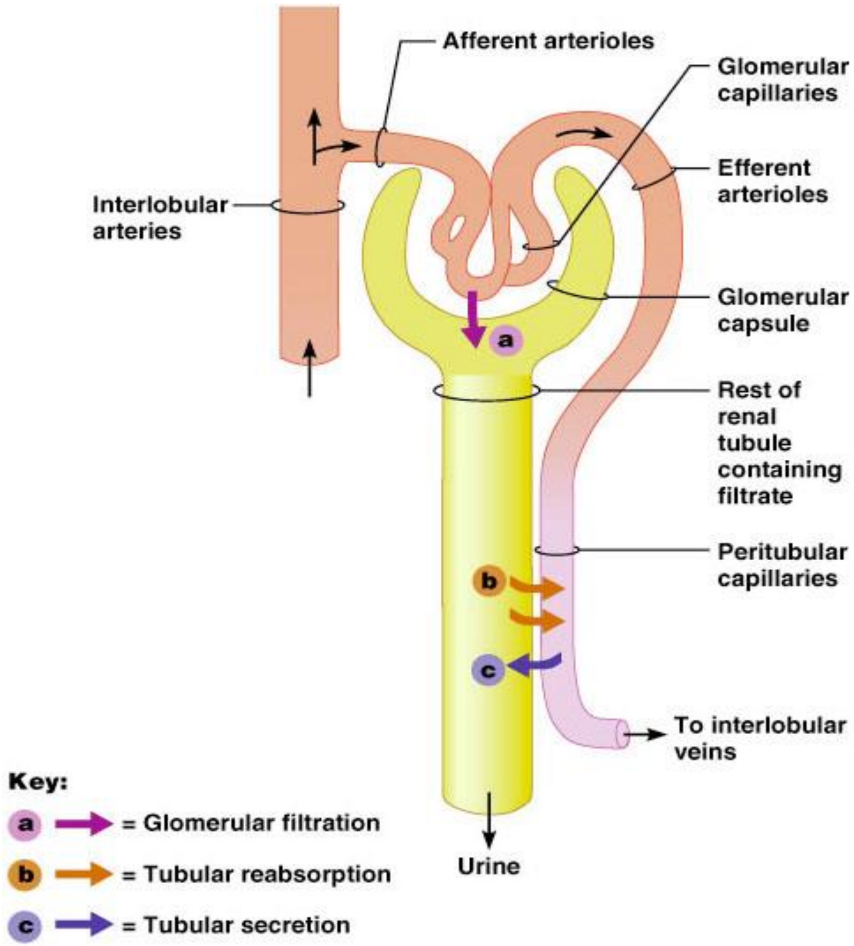
Good for filtration

Peritubular capillary bed,
Low pressure vascular bed,
high oncotic pressure.

Good for re-absorption

Mechanisms of Urine Formation

- Urine formation and adjustment of blood composition involves three major processes
  - Glomerular filtration
  - Tubular reabsorption
  - Secretion



- **Glomerular Filtration:**
  - The first step in urine formation
  - Filtered through the glomerular capillaries into the Bowman's capsule.
  - ~20% of plasma entering the glomerulus is filtered
  - 125 ml/min filtered fluid

- **Tubular Reabsorption:**
  - Movement of substances from tubular lumen back into the blood.
  - Carried by the peri-tubular capillaries to the venous system.
  - Most of the filtered plasma is reabsorbed.

- **Tubular Secretion:**
  - The selective transfer of substances from the peritubular capillary into the tubular lumen.
  - Allows for rapid elimination of substances from the plasma via extraction of the 80% of unfiltered plasma in peritubular capillaries and adding it to the substances already in tubule as result of filtration.

- **Urine Excretion:**
  - The elimination of substances from the body in the urine
  - All plasma constituents filtered or secreted, but not reabsorbed remain in the tubules and pass into the renal pelvis to be excreted as urine and eliminated from the body

Net Filtration Pressure (NFP)

- The pressure responsible for filtrate formation
- NFP equals the glomerular hydrostatic pressure (HP_g) minus the oncotic pressure of glomerular blood (OP_g) combined with the capsular hydrostatic pressure (HP_c)

$$NFP = HP_g - (OP_g + HP_c)$$

Or

$$NFP = P_{GC} - P_{BS} - O_{GC}$$

Glomerular Filtration Rate

- Glomerular filtration rate (GFR) is the rate of production of filtrate at the glomeruli from plasma
  - Typically 80 – 140 ml/min depending on age, sex etc
  - Sum of the filtration rates of all functioning nephrons
  - Index of kidney function

GFR

- Factors governing filtration rate at the capillary bed are:
  - Total surface area available for filtration
  - Filtration membrane permeability
  - Net filtration pressure

- GFR is directly proportional to the NFP
- Changes in GFR normally result from changes in glomerular blood pressure

GFR

- If the GFR is **too high**:
  - Needed substances cannot be reabsorbed quickly enough and are lost in the urine

- If the GFR is **too low**:
  - Everything is reabsorbed, including wastes that are normally disposed of

Filtration: **Hydrostatic Pressure**

glomerular hydrostatic pressure (GHP)
push fluid out of vessels

capsular hydrostatic pressure (CsHP)
push fluid back into vessels

net hydrostatic pressure (NHP)

NHP = GHP - CsHP

35 = 50 - 15 mm Hg

Filtration: Colloid Pressure

blood colloid osmotic pressure (BCOP)

proteins in blood (hyperosmotic)

draw water back into blood

~ 25 mm Hg

Filtration: **Filtration Pressure (FP)**

FP = NHP - BCOP

10 = 35 - 25 mm Hg

importance of blood pressure

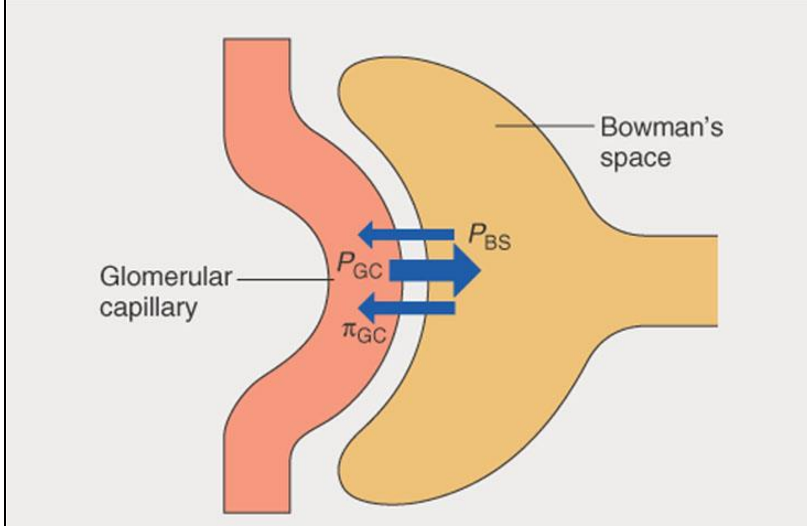
20% drop in blood pressure
50mm Hg to 40mm Hg
filtration would stop

- Driven by **Starling** forces
- Pressure inside capillaries > Pressure outside

$\Rightarrow$ movement of fluid from blood

- Forces in capillaries: hydrostatic pressure P_{GC} = + 60mmHg
- oncotic pressure π_{GC} = - 29 mmHg

  $\therefore$ net outward pressure = 60 – 29 = 31mmHg
- Forces in capsule: hydrostatic pressure P_{BS} = -15mmHg
- oncotic pressure π_{GBS} = 0 mmHg
- Overall: 31 – 15 = 16 mmHg outward
- Male adults GFR: ~ 90 – 140 ml/min
- Female: 80 – 125 ml/min
- 125 ml/min usually good average



Forces	mmHg
Favoring filtration:	
Glomerular capillary blood pressure (P_{GC})	60
Opposing filtration:	
Fluid pressure in Bowman's space (P_{BS})	15
Osmotic force due to protein in plasma (π_{GC})	29
Net glomerular filtration pressure = $P_{GC} - P_{BS} - \pi_{GC}$	16

Glomerular Filtration Rate

$$GFR = \frac{[sub]_{urine} \times \text{urine flow rate}}{[sub]_{plasma}}$$

Substances Used to Measure GFR

- **Inulin**, a polymer of fructose, is used in research to precisely measure GFR
  - Freely filtered into the Bowman's capsule
  - Not reabsorbed, secreted or metabolized by the nephron
  - Non-endogenous, has to be infused intravenously
- **Assume**:
  - $[\text{Inulin}]_{urine}$ = 30 mg/ml
  - $[\text{Inulin}]_{plasma}$ = 0.5 mg/ml
  - urine flow rate = 2 ml/min

- GFR = 120 ml/min or 172.3 L/day

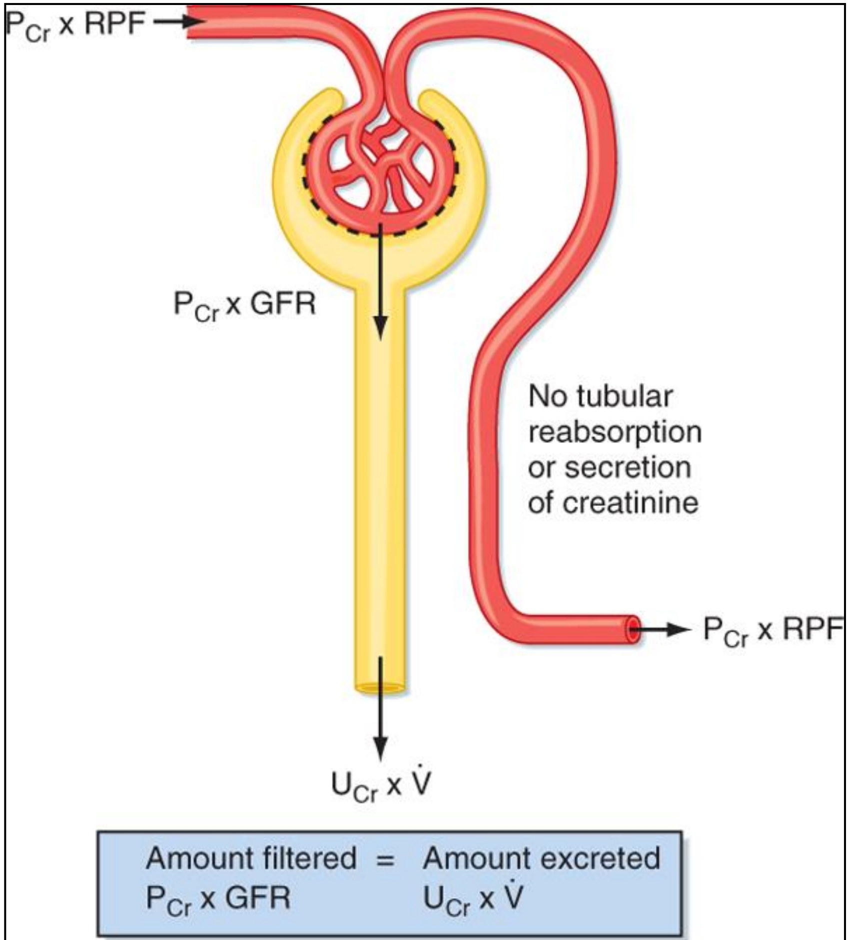
Substances Used to Measure GFR

- Clinically, **creatinine**, endogenously released into plasma by skeletal muscle, is used to measure GFR
  - Not as accurate as inulin as a small quantity is secreted into the proximal tubule
  - amount excreted > amount filtered
  - Reasonably accurate measurement of GFR

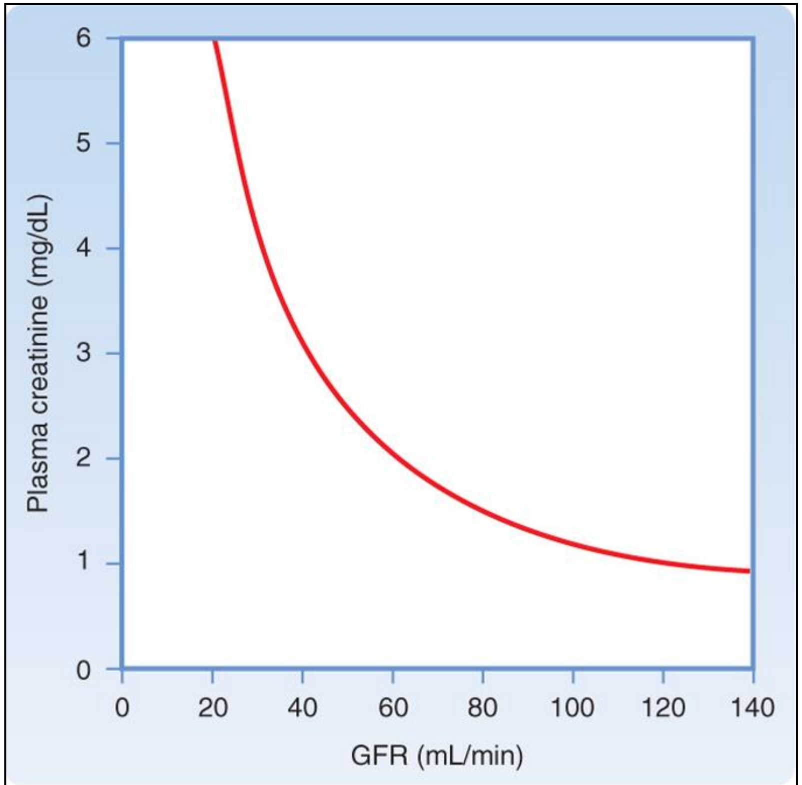
Substances Used to Measure GFR

- The usual analytical method for creatinine measurement (alkaline picrate method) also detects substances in the plasma other than true creatinine, leading to increase in plasma creatinine value.

- Thus, these two errors usually cancel each other and gives a correct estimate of GFR.



P_{Cr} x RPF
P_{Cr} x GFR
No tubular reabsorption or secretion of creatinine
P_{Cr} x RPF
U_{Cr} x $\dot{V}$
Amount filtered = Amount excreted
P_{Cr} x GFR U_{Cr} x $\dot{V}$



Plasma creatinine (mg/dL)
0
1
2
3
4
5
6
0
20
40
60
80
100
120
140
GFR (mL/min)

Glomerular Filtration Rate

$$GFR = \frac{[\text{creatinine}]_{\text{urine}} \times \text{urine flow rate}}{[\text{creatinine}]_{\text{plasma}}}$$

- Measurement of creatinine concentration in a urine sample, urine flow rate and plasma creatinine concentration can be used to determine GFR.

- Only 15 – 20 % of plasma entering glomerulus filtered
- Composition of filtrate:

  Similar to plasma BUT NO large proteins or cells

Regulation of GFR & RBF

- **Intrinsic Autoregulation:**

  - Renal vasculature also exhibits a well developed **intrinsic** ability to adjust its resistance in response to changes in arterial BP and thus to keep BF and GFR essentially constant = **autoregulation.**

  - In man, effective over a range of MBP from 75-160mmHg. Below 75mmHg, filtration falls and ceases altogether when MBP = 50mmHg.

Regulation of GFR & RBF

- If mean arterial P ↑, there is an automatic ↑ in afferent arteriolar constriction, preventing a rise in glomerular pressure . Dilatation occurs if P falls.
- Autoregulation is independent of nerves or hormones, occurs in denervated and in isolated perfused kidneys.
- 2 mechanisms are responsible for the autoregulation: