Use of Clearance Methods to Quantify Kidney Function

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قُلْ يَـٰعِبَادِ ٱلَّذِينَ ءَامَنُوا۟ ٱتَّقُوا۟ رَبَّكُمْ ۚ
لِلَّذِينَ أَحْسَنُوا۟ فِى هَـٰذِهِ ٱلدُّنْيَا حَسَنَةٌ ۗ
وَأَرْضُ ٱللَّهِ وَٰسِعَةٌ ۗ إِنَّمَا يُوَفَّى ٱلصَّـٰبِرُونَ
أَجْرَهُم بِغَيْرِ حِسَابٍ

Quran [39:10]

Translation

Say, "O My servants who have believed, fear your Lord. For those who do good in this world is good, and the earth of Allah is spacious. Indeed, the patient will be given their reward without account [i.e., limit]."

Learning objectives

1. Define the terms clearance and metabolic clearance rate, and differentiates between general clearance and renal clearance.
2. List the information required for clearance calculation
3. State the criteria that must be met for a substance so that its clearance can be used as a measure of glomerular filtration rate
4. states which substances are used to measure glomerular filtration rate and effective renal plasma flow.
5. Predict whether a substance undergoes net reabsorption or net secretion by comparing its clearance with that of inulin or by comparing its rate of filtration with its rate of excretion.
6. Calculate net rate of reabsorption or secretion for any substance
7. Calculate fractional excretion of any substance
8. Describe how to estimate glomerular filtration rate from CCr and describes the limitations.
9. Describe how to use plasma concentrations of urea and creatinine as indicators of changes in glomerular filtration rate.

Clearance

- a general concept that describes the rate at which substances are removed (or cleared) from plasma. Thus whole-body clearance means the total rate of removal of a substance by all organs,
- **Hepatic clearance** means the rate of removal by the liver
- **Renal clearance** means the rate of removal by the kidneys.

Plasma clearance in kidneys

- *The plasma clearance of a substance is equal to the volume of plasma which is completely cleared of that substance by the kidneys per minute.*
- Unit ml/min.

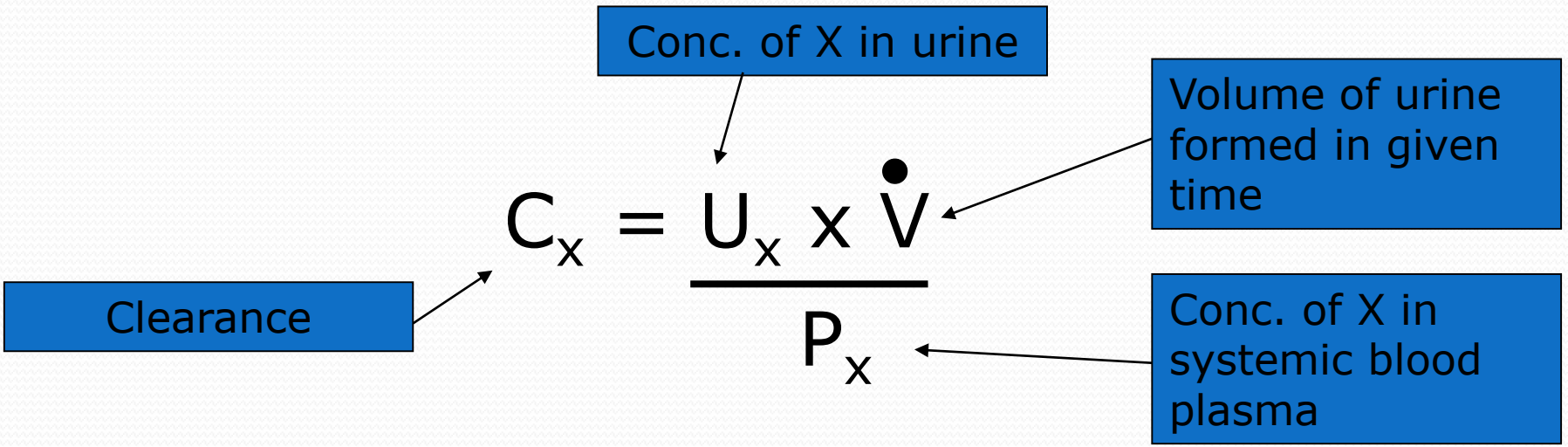
- Substances with the **highest renal clearances** may be completely removed on a single pass of blood through the kidneys;
- substances with the **lowest renal clearances** are not removed at all.

Renal clearance provides a useful way of quantifying the

1. Glomerular filtration rate
2. excretory function of the kidneys .
3. Renal blood flow rate,
4. Tubular reabsorption and tubular secretion.

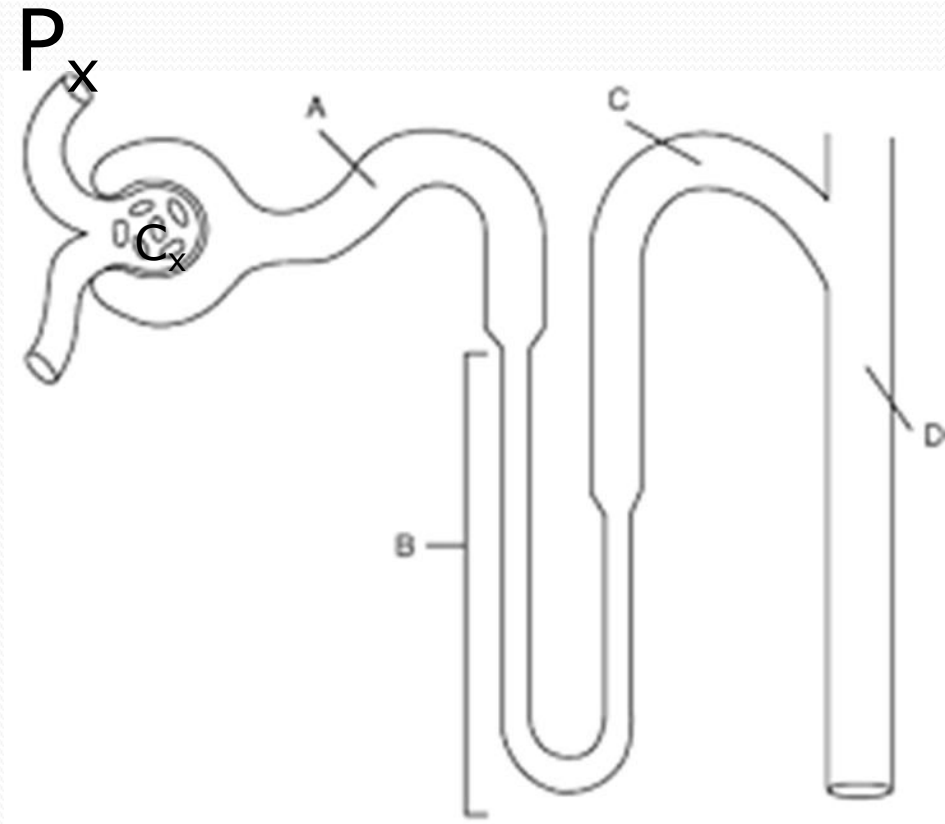
2. List the information required for clearance calculate

- For solute X:



C_x can be labelled GFR if a specific substance is used

$P_x x C_x$ (GFR)= U_x x V



A Schematic Drawing of a Nephron


IT'S
QUIZ
TIME!

3. Criteria of a substance used for GFR measurement

1.freely filtered
2.not secreted by the tubular cells
3.not reabsorbed by the tubular cells.
4.should not be toxic
5.should not be metabolized
6.easily measurable.

which substances are used to measure glomerular filtration rate

1. **Creatinine** (endogenous): by-product of skeletal muscle metabolism
2. **Inulin** (exogenous): It is a polysaccharide with a molecular weight of about 5200 and it fits all the requirements.

Inulin

- *Inulin, a polysaccharide* molecule with a molecular weight of 5200.

- Inulin, which is not produced in the body, is found in the roots of certain plants and must be **administered intravenously to a patient to measure GFR.**

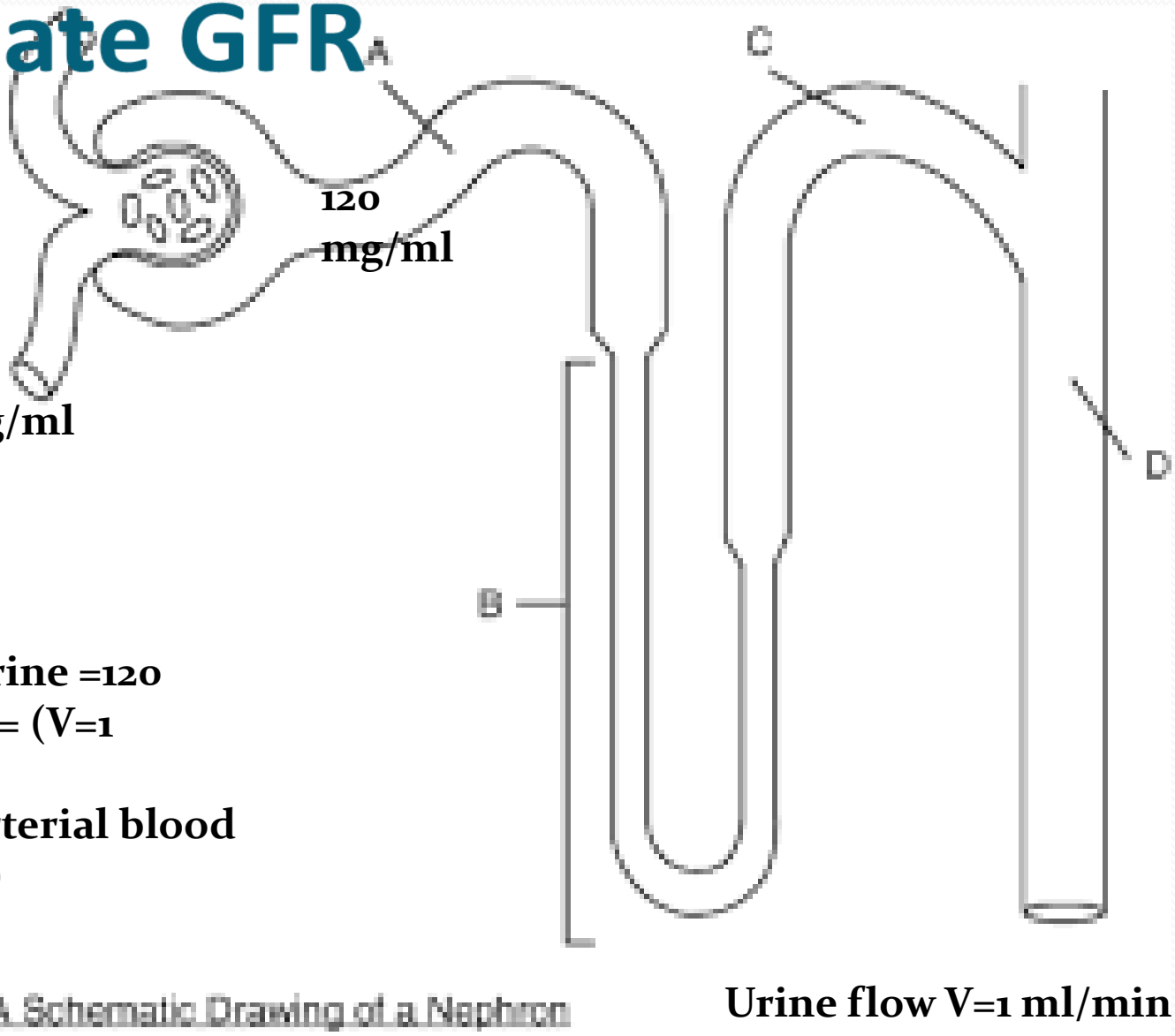
- Non toxic, does not affect renal function, not metabolized in body, not bound to plasma proteins.

- Inulin is freely filtered by glomeruli ,conc in glomerular filterate is same as plasma.

- it is neither reabsorbed, nor secreted by the tubules.
- So amount of inulin filtered/minute and the amount excreted in urine/minute are the same.

- In the actual determination of inulin clearance,
- the concentration of inulin in the plasma is kept constant by a slow intravenous infusion and is measured chemically.
- The urine excreted during a known time is measured for its volume (for which urine formed/minute can be calculated) and
- the urinary concentration of inulin is also measured.

Inulin Clearance Can Be Used to Estimate GFR



120 mg/ml

Plasma =1 mg/ml

Calculate GFR if
Conc. of inulin in urine =120 mg/ml) Urine flow = (V=1 ml/min)
Conc. of inulin in arterial blood = (Pinulin=1 mg/ml)

A Schematic Drawing of a Nephron

Urine flow V=1 ml/min

consciously prep your mind every morning with the assumption that people will annoy you, interrupt you, and steal your time.

Creatinine clearance

- This is the most commonly done laboratory test to assess renal function in patients.
- It is freely filtered by the glomeruli and is neither reabsorbed nor secreted by the tubules. Therefore, its clearance value is same as GFR.
- The great advantage of determining creatinine clearance is that creatinine is present normally in the plasma.

- Creatinine is a by-product of muscle metabolism and is cleared from the body fluids almost entirely by glomerular filtration.

- Measurement of creatinine clearance does not require intravenous infusion into the patient, this method is much more widely used than inulin clearance for estimating GFR clinically

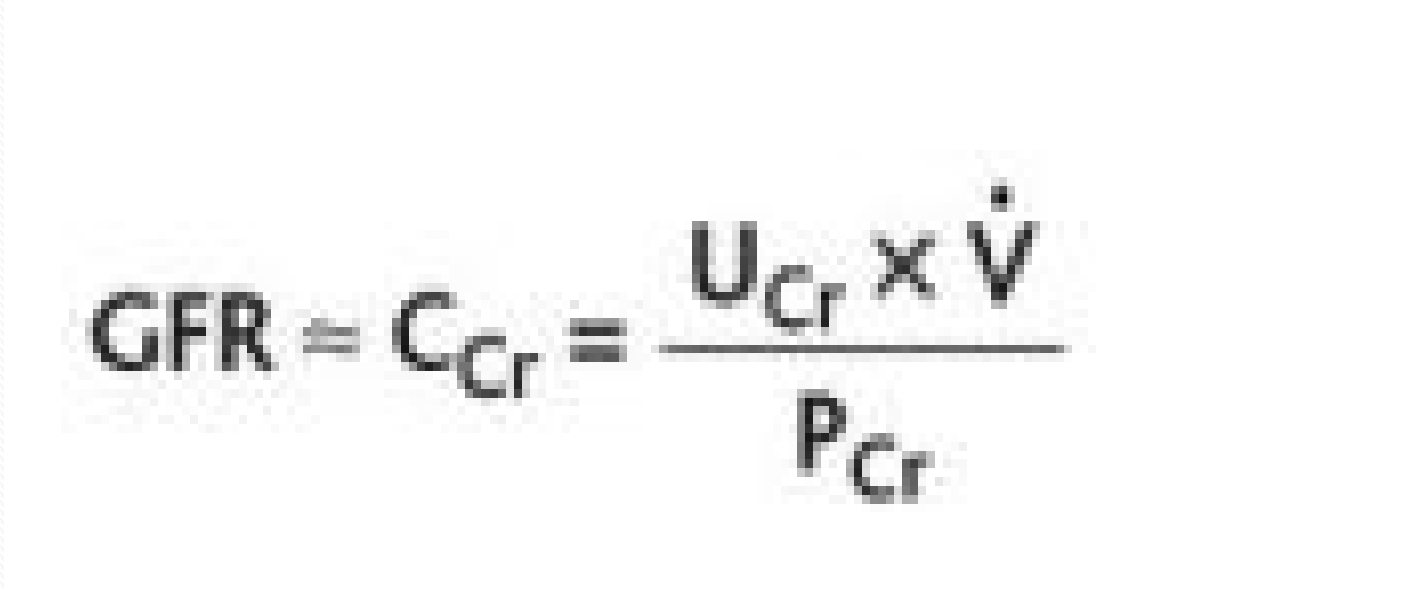
1. The urine of the patient is collected over 24-hours period. Creatinine level urine (U) is measured, One-minute urinary volume is calculate
2. A blood sample is also obtained once during this period. Creatinine levels of the serum (P)
3. clearance of creatinine found out by the formula:

$$\text{Creatinine clearance} = (U \times V)/P$$

its normal value in males is 97 to 140 mL/minute

- A small amount of it is secreted by the tubules, so the amount of creatinine excreted slightly exceeds the amount filtered.

- Normally a slight error in measuring plasma creatinine leads to an overestimate of the plasma creatinine concentration.
- these two errors tend to cancel each other


GFR ≈ C_Cr = (U_Cr × V̇) / P_Cr

TRYOUT THIS ONE

Calculate the Renal clearance of creatinine, if

Concentration of creatinine in urine = 10mg/ml ,
in the plasma = 6mg/ml and
urine flow rate = 18ml/min ?

Changes in GFR

- Can be obtained by simply measuring plasma creatinine concentration (P_{Cr}), which is inversely proportional to GFR
- (without urine collection)
- More is the level of creatinin in plasma less will be GFR

$$(P_{Cr} \times GFR) = (U_{Cr} \times V)$$

- If GFR suddenly decreases by 50%(1/2), the kidneys will transiently filter and excrete only half as much creatinine, causing accumulation of creatinine in the body fluids and raising plasma concentration.

$$(P_{Cr} \times GFR) = (U_{Cr} \times V)$$

Plasma concentration of creatinine will continue to rise until the filtered load of creatinine ($P_{Cr} \times GFR$) and creatinine excretion ($U_{Cr} \times V$) return to normal and a balance between creatinine production and creatinine excretion is re-established.

- This will occur when plasma creatinine increases to approximately twice normal

- filtered load of creatinine = creatinine excretion

- $(P_{Cr} \times GFR) = (U_{Cr} \times V)$

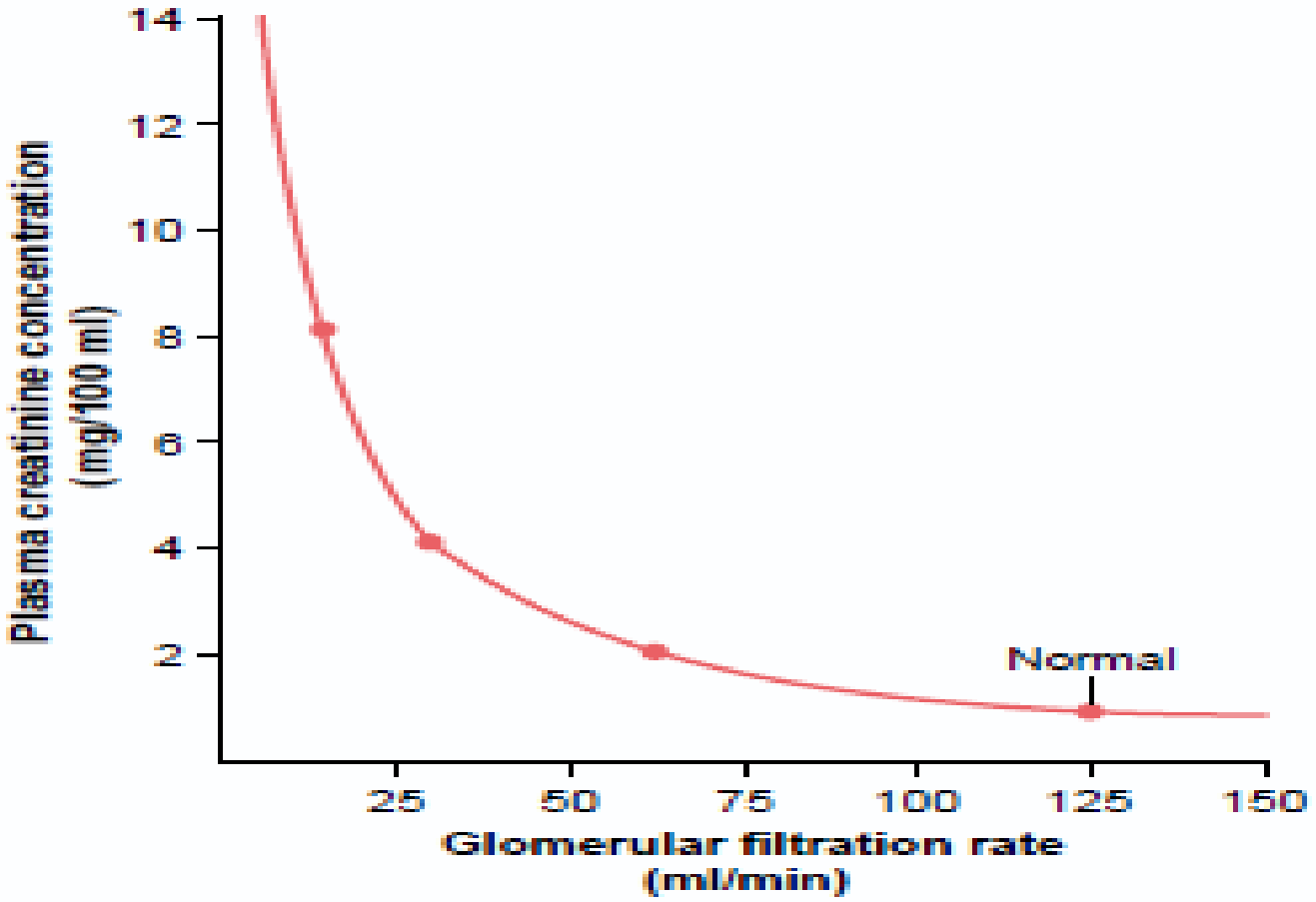


Figure 27–19

Approximate relationship between glomerular filtration rate (GFR) and plasma creatinine concentration under steady-state conditions. Decreasing GFR by 50 per cent will increase plasma creatinine to twice normal if creatinine production by the body remains constant.

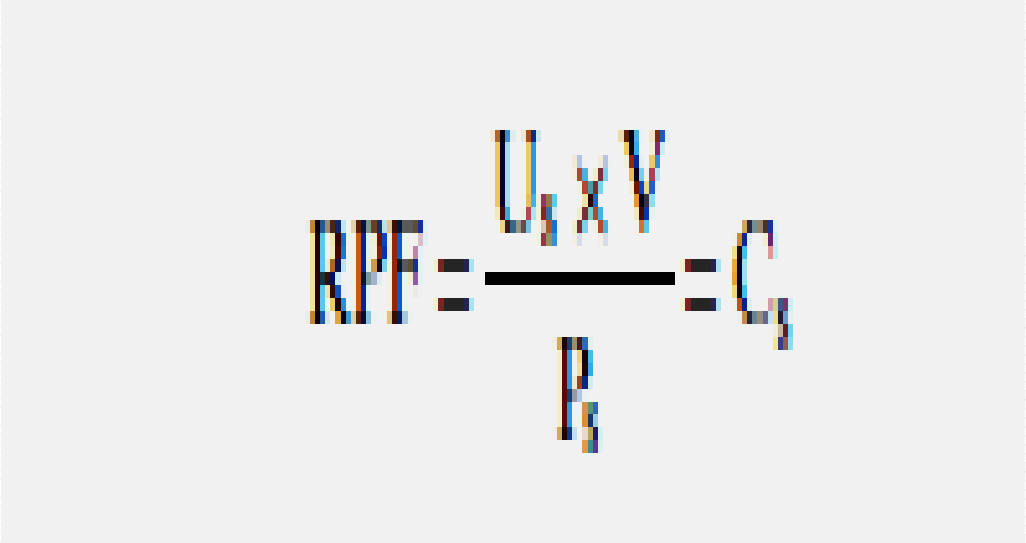
Zee
@prestigepls

Having sabr doesn't mean you're not allowed to have emotions. Sabr means that even with all the anger, even with all the sadness, even with the nights you cried your eyes out, you still were grateful to Allah swt. You still turned to Him and trusted His plan.

To Estimate Renal Plasma Flow

- if a substance is *completely cleared from* the plasma, the clearance rate of that substance is equal to the total renal plasma flow.

- GFR is only about 20 per cent of the total plasma flow, a substance that is completely cleared from the plasma must be excreted by tubular secretion as well as glomerular filtration


RPF = U_s x V / P_s = C_s

Para amino Hippuric acid

PAH Clearance Can Be Used to Estimate Renal Plasma Flow

- There is no known substance that is *completely cleared by the* kidneys.
- PAH, is 90 percent cleared from the plasma. The clearance of PAH can be used as an approximation of renal plasma flow.
- The percentage of PAH removed from the blood is known as the *extraction ratio of PAH* and averages 90 per cent in normal kidneys.

- Total renal plasma flow = PAH clearance/ 0.9
- Total renal blood flow = renal plasma flow / 1- heamatocrit

Calculate renal plasma flow

- the plasma concentration of PAH is 0.01 mg/ml,
  urine concentration is 5.85 mg/ml, and
  urine flow rate is 1 ml/min.

PAH clearance

- If the hematocrit is 0.45 and the total renal plasma flow is650 ml/min,
- the **total blood flow** through both kidneys is 650/(1 - 0.45), or 1182 ml/min.

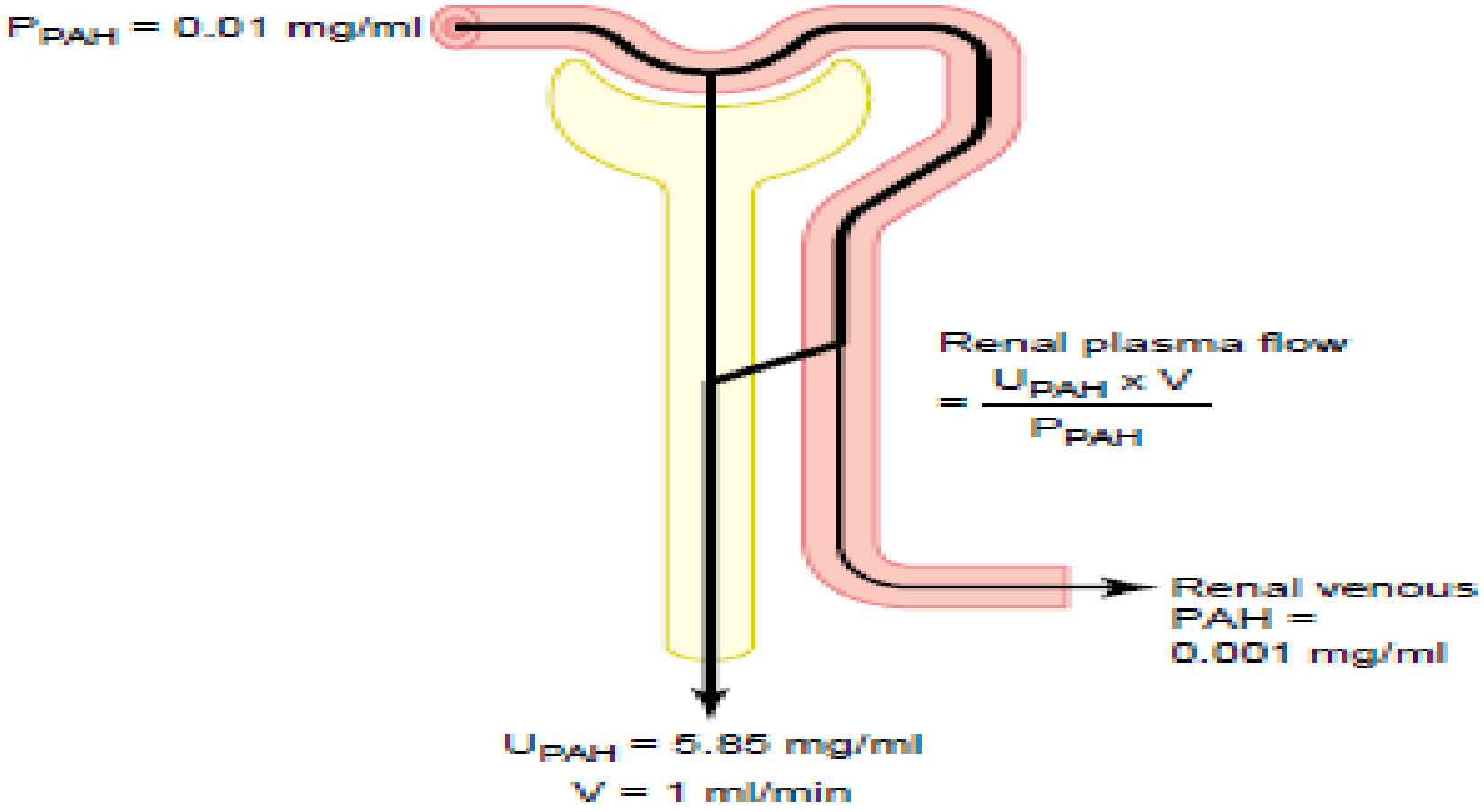


Figure 27–20

Measurement of renal plasma flow from the renal clearance of para-aminohippuric acid (PAH). PAH is freely filtered by the glomerular capillaries and is also secreted from the peritubular capillary blood into the tubular lumen. The amount of PAH in the plasma of the renal artery is about equal to the amount of PAH excreted in the urine. Therefore, the renal plasma flow can be calculated from the clearance of PAH (C_{PAH}). To be more accurate, one can correct for the percentage of PAH that is still in the blood when it leaves the kidneys. P_{PAH}, arterial plasma PAH concentration; U_{PAH}, urine PAH concentration; V, urine flow rate.

Filtration Fraction

- Is the fraction of plasma that filters through the glomerular membrane
- Is Calculated from GFR Divided by Renal Plasma Flow.

- The renal plasma flow (PAHclearance) and
- the GFR (inulin clearance).
- If renal plasma flow is 650 ml/min and GFR is 125 ml/min, the filtration fraction (FF) is calculated as
- FF = GFR/RPF = 125/650 = 0.19

Calculation of Tubular Reabsorption or Secretion from Renal Clearances

If the rates of glomerular filtration and renal excretion of a substance are known, one can calculate whether there is a net reabsorption or a net secretion of that substance by the renal tubules.

For example, if the rate of excretion of the substance (Us X V) is less than the filtered load of the substance (GFR X Ps), then some of the substance must have been reabsorbed from the renal tubules.

- if the excretion rate of the substance is greater than its filtered load, then the rate at which it appears in the urine represents the sum of the rate of glomerular filtration plus tubular secretion.

Example

- Urine flow rate = 1 ml/min
- Urine concentration of sodium (UNa) = 70 mEq/L
  = 70 mEq/ml
- Plasma sodium concentration = 140 mEq/L
  = 140 mEq/ml
- GFR (inulin clearance) = 100 ml/min

- **Filtered sodium load** is GFR X PNa,
- or 100 ml/min X 140 mEq/ml = 14,000 mEq/min.

- **Urinary sodium excretion** (U Na X urine flow rate) is 70 mEq/min.
- Tubular reabsorption of sodium is the difference between the filtered load and urinary excretion,

- 14,000 mEq/min - 70 mEq/min = 13,930 mEq/min.

Comparisons of Inulin Clearance with Clearances of Different Solutes.

(1) if the clearance rate of the substance equals that of inulin, the substance is only filtered and not reabsorbed or secreted;

(2) if clearance rate of a substance is less than inulin clearance,the substance must have been reabsorbed by the nephron tubules;

(3) if the clearance rate of a substance is greater than that of inulin, the substance must be secreted by the nephron tubules.

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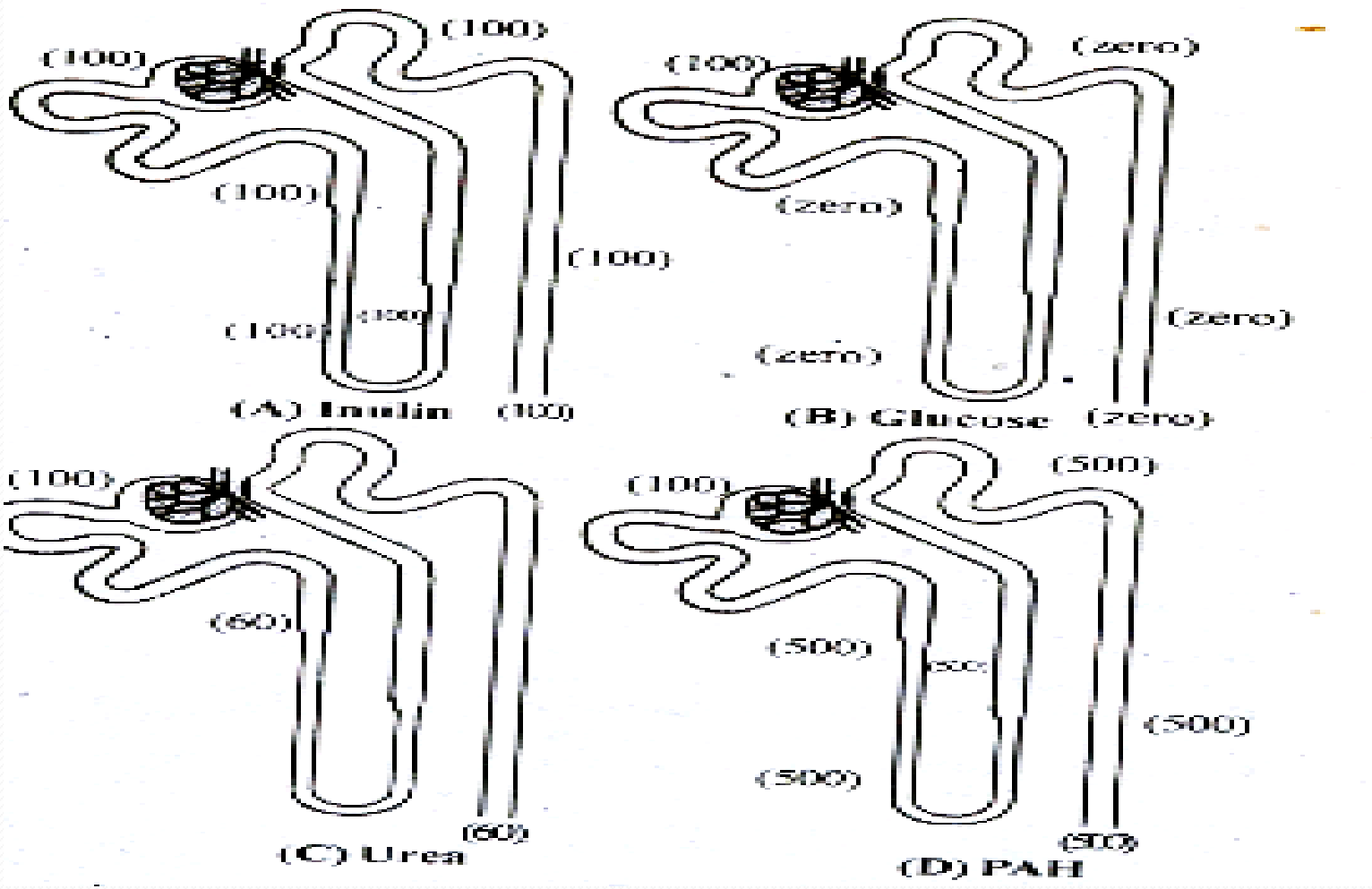
Say, "O My servants who have believed, fear your Lord. For those who do good in this world is good, and the earth of Allah is spacious. Indeed, the patient will be given their reward without account [i.e., limit]."

A comparison of renal handling of Inulin, Glucose, Urea, PAH



Substance	Clearance Rate (ml/min)
Glucose	0
Sodium	0.9
Chloride	1.3
Potassium	12.0
Phosphate	25.0
Inulin	125.0
Creatinine	140.0

Use of Clearance to Quantify Kidney Function

Term	Equation	Units
Clearance rate (C_s)	$C_s = \frac{U_s \times V}{P_s}$	ml/min
Glomerular filtration rate (GFR)	$GFR = \frac{U_{inulin} \times V}{P_{inulin}}$	
Clearance ratio	$\text{Clearance ratio} = \frac{C_s}{C_{inulin}}$	None
Effective renal plasma flow (ERPF)	$ERPF = C_{PAH} = \frac{U_{PAH} \times V}{P_{PAH}}$	ml/min
Renal plasma flow (RPF)	$RPF = \frac{C_{PAH}}{E_{PAH}} = \frac{(U_{PAH} \times V/P_{PAH})}{(P_{PAH} - V_{PAH})/P_{PAH}} = \frac{U_{PAH} \times V_{PAH}}{P_{PAH} - V_{PAH}}$	ml/min
Renal blood flow (RBF)	$RBF = \frac{RPF}{1 - \text{Hematocrit}}$	ml/min
Excretion rate	$\text{Excretion rate} = U_s \times V$	mg/min, mmol/min, or mEq/min
Reabsorption rate	$\text{Reabsorption rate} = \text{Filtered load} - \text{Excretion rate} = (GFR \times P_s) - (U_s \times V)$	mg/min, mmol/min, or mEq/min
Secretion rate	Secretion rate = Excretion rate – Filtered load	mg/min, mmol/min, or mEq/min

S, a substance; U, urine concentration; V, urine flow rate; P, plasma concentration; PAH, para-aminohippuric acid; P_{PAH}, renal arterial PAH concentration; E_{PAH}, PAH extraction ratio; V_{PAH}, renal venous PAH concentration.

Table 38-5. Renal handling of various plasma constituents in a normal adult human on an average diet.

Substance	Per 24 Hours				Percentage Reabsorbed	Location[1]
	Filtered	Reabsorbed	Secreted	Excreted		
Na^+ (meq)	26,000	25,850		150	99.4	P, L, D, C
K^+ (meq)	600	560[2]	50[2]	90	93.3	P, L, D, C
Cl^- (meq)	18,000	17,850		150	99.2	P, L, D, C
HCO_3^- (meq)	4,900	4,900		0	100	P, D
Urea (mmol)	870	460[3]		410	53	P, L, D, C
Creatinine (mmol)	12	1[4]	1[4]	12		
Uric acid (mmol)	50	49	4	5	98	P
Glucose (mmol)	800	800		0	100	P
Total solute (mosm)	54,000	53,400	100	700	98.9	P, L, D, C
Water (mL)	180,000	179,000		1000	99.4	P, L, D, C

[1] P, proximal tubules; L, loops of Henle; D, distal tubules; C, collecting ducts.

[2] K^+ is both reabsorbed and secreted.

[3] Urea moves into as well as out of some portions of the nephron.

[4] Variable secretion and probable reabsorption of creatinine in humans.


THANK
YOU