UGS

Physiology
Doctor 2021

Sheet (7)

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Clearance

Clearance is the most important function of the kidney.

• "Clearance" describes the rate at which substances are removed (cleared) from the plasma.

All substances have the same glomerular filtration rate (for a healthy person); however, clearance is different from a substance to another.

Clearance depends on GFR.

• Renal clearance of a substance is the volume of plasma completely cleared of a substance per min by the kidneys.

Clearance Technique

Renal clearance (Cs) of a substance is the volume of plasma completely cleared of a substance per min. (Volume/time)

Cs x Ps = Us x V = The total excretion of the substance (urine excretion rate)

$$C_s = \frac{U_s \times V}{P_s} = \frac{\text{Urine excretion rate}}{P_s}$$

Where:

Cs = clearance of substance s

Ps = plasma conc. of substance s

Us = urine conc. of substance s

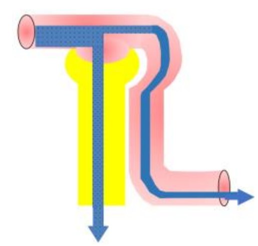
V = urine flow rate

s = substance

Clearances of Different Substances:

Substance	Clearance (ml/min)	
Glucose	0	Because its excretion rate = 0
Albumin	0	Because its excretion rate = 0
Sodium	.9	
Urea	70	High, because it's a waste product
Inulin	125	The same as GFR, used to measure it
Creatinine	140	Endogenous, used to estimate GFR
PAH (Paraminohippuric acid)	600	Used to estimate renal plasma flow because it is too close to it

Use of Clearance to Measure GFR



For a substance that is freely filtered, but not reabsorbed or secreted (inulin, ^{125}I-iothalamate, creatinine), renal clearance is equal to GFR.

Amount filtered = amount excreted (GFR = C), only for the previous substances.

Inulin is the most accurate to estimate GFR, however it's not used clinically only experimental because in order to use it the patient have to be hospitalised and inulin to give infuse it to the patient and measure the urinary flow rate, the concentration of inulin in the urine and the plasma concentration of inulin when it is in a steady state, which is not practical and will expose the patient to many risks one of them is renal failure.

When we used those substances, we can replace C (from the previous equation) with GFR.

GFR x P_{inulin} = U_{inulin} x V = urinary excretion

$$GFR = \frac{U_{in} \times V}{P_{in}}$$

Calculate the GFR from the following data:

P_{inulin} = 1.0 mg / 100ml

U_{inulin} = 125 mg/100 ml

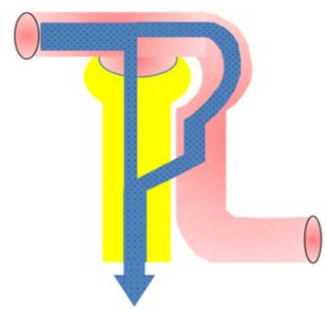
Urine flow rate = 1.0 ml/min

$$GFR = C_{inulin} = \frac{U_{in} \times V}{P_{in}}$$

$$GFR = \frac{125 \times 1.0}{1.0} = 125 \text{ ml/min}$$

We can calculate GFR from the clearance of inulin, in normal kidneys = 125 ml/min.

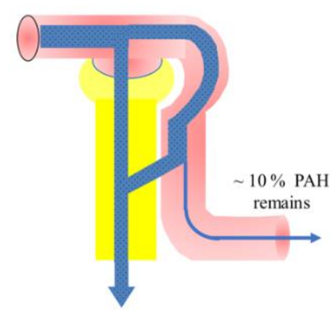
Use of Clearance to Estimate Renal Plasma Flow



Theoretically, if a substance is <u>completely cleared</u> from the plasma <u>(freely filtered then completely secreted,</u> see the image)**, its clearance rate would <u>equal renal plasma flow.</u>**

Cx = renal plasma flow

If x was completely cleared and secreted, one example that can mostly fulfil these conditions is PAH.



Paraminohippuric acid (PAH) is freely filtered and almost completely **secreted, so it is almost completely cleared from the renal plasma.**

amount enter kidney = RPF x P_{PAH} (here we replaced clearance with renal plasma flow) because **amount entered ≈ amount excreted.**

What we get is ERPF: effective renal plasma flow not the actual renal plasma flow because the secretion of PAH isn't complete, 10% of PAH will remain in the plasma in the renal vein. So, this gives us an estimation for RPF and it need to be corrected.

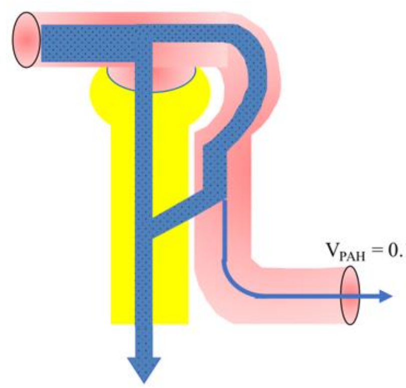
ERPF x P_{PAH} = U_{PAH} x V

$$ERPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

ERPF = Clearance PAH

ERPF = estimated renal plasma flow

To calculate <u>actual</u> RPF, one must correct for incomplete extraction of PAH.



A_{PAH} = 1.0 or 10%

$$E_{PAH} = \frac{A_{PAH} - V_{PAH}}{A_{PAH}}$$

Extracted PAH = $\frac{\text{arterial PAH} - \text{veinous PAH}}{\text{arterial PAH}}$

Arterial PAH= 100% because we said that it is freely filtered.

Veinous PAH= 10% (remained in the renal vein).

$$= \frac{1.0 - 0.1}{1.0} = 0.9$$

normally, E_{PAH} = 0.9 or 90%

i.e PAH is 90 % extracted.

Now we correct.

$$RPF = \frac{ERPF}{E_{PAH}}$$

Actual RBF = $\frac{\text{effective RPF}}{\text{extracted PAH (90\%)}}$

Calculation of Tubular Reabsorption

Reabsorption = Filtration - Excretion

Filt s = GFR x Ps

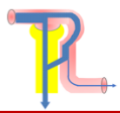
Excret s = Us x V

Calculation of Tubular Secretion

Secretion = Excretion - Filtration

Filt s = GFR x Ps

Excret s = Us x V



- The doctor didn't read these slides.

Question: **The maximum possible clearance rate of a substance that is completely cleared from the plasma by the kidneys would be equal to:**

A. glomerular filtration rate
B. the filtered load of the substance
C. urine excretion rate of the substance
D. renal plasma flow
E. none of the above

Answer: D

Clearances of Different Substances

Substance	Clearance (ml/min)
Inulin (=GRH)	125
PAH (=ERPF)	600
Creatinine (estimate GFR)	140
Glucose	0
Urea	70

Clearance of inulin (C_{in}) = GFR

- ✓ **if $Cx < C_{in}$: indicates that reabsorption of x has happened.**
- ✓ **if $Cx > C_{in}$: indicates that secretion of x has happened.**

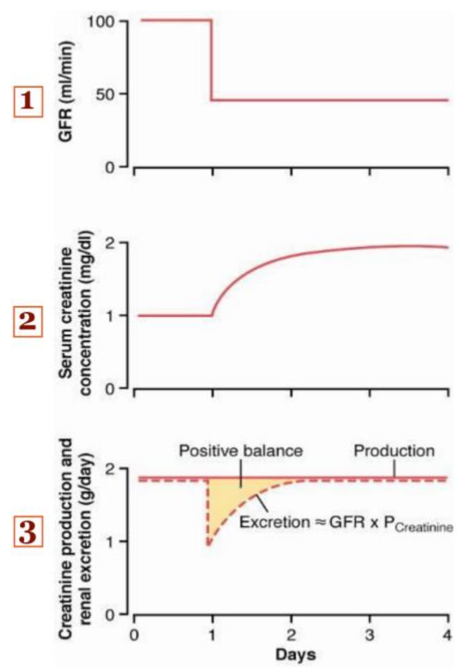
Clearance creatinine (C_{creat}) ~ 140 (used to estimate GFR)

Clearance of PAH (C_{PAH}) ~ effective renal plasma flow

Effect of reducing GFR by 50 % on serum creatinine concentration and creatinine excretion rate.

In patients with reduced GFR because of renal diseases or loss of nephrons.

- At first, when GFR is reduced to half normal GFR (see the 1st pic), the serum creatinine will increase gradually, and then will be in plateau (see the 2nd pic).
- When we look at the creatinine production and renal excretion as gm/day we see that at first when there is a reduction in GFR, the creatinine production is the same, however the renal excretion will be reduced transiently and then will increase (see the 3rd pic).
  This happened because the secretion of creatinine = GFRx plasma creatinine concentration, so because at first GFR has been reduced, then the plasma creatinine concentration will increase, this increase will result in an increase in the excretion of creatinine.



Excretion =GFR x $P_{creatinine}$

At first, GFR is decreased by half → decreased creatinine excretion.

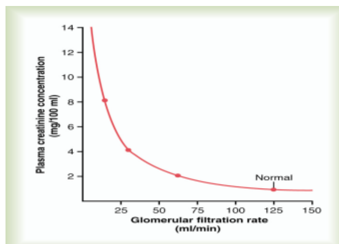
Then, $P_{creatinine}$ is doubled (neutralize the excretion) → creatinine excretion returns back to normal (decreasing GFR results in no net effect on the excretion rate of creatinine).

In patients with reduced GFR, the excretion rate of different substances isn't going to change (e.g. creatine or urea) because of the increased level of that substance in the plasma. (IMPORTANT as an implication of measurement of GFR)

True or False? Reduction of GFR by 50 % will increase serum creatinine to double while, creatinine excretion rate will remain the same as normal in steady state conditions.

Answer: true

Plasma creatinine can be used to estimate changes in GFR.



Clinical Perspective

Clinical GFR estimation equations using GFR.

In clinical use, GFR is estimated using creatinine estimation of GFR, using different formulas.

This is not required for the exam.

Model	Equation
Creatinine model	$36.76 + 1.91 \times Wt - 0.47 \times SCr$
Weight model	$16.25 + 1.67 \times Wt$
Cockcroft function[a]	$\frac{(130 + 0.09 \times Age) \times Wt \times (1 + 0.11 \times Sex)}{SCr}$
Jelliffe function[a]	$\frac{(2530 + 126 \times Age) \times BSA \times (1 + 0.13 \times Sex)}{SCr}$
Léger model	$\frac{(56.7 \times Wt + 0.142 \times Hght^2)}{SCr}$
Schwartz regression	$\frac{0.55 \times Hght}{SCr \times 0.01131} \times (BSA/1.73)$ if female $\left(1.5 \times Age + \frac{0.5 \times Hght}{SCr \times 0.01131}\right) \times (BSA/1.73)$ if male

Coefficients derived from modelling data set, except for Schwarz and Léger equations where the original coefficients are used. Wt: weight (kg); Age: age (years); Sex: 1 if male, 0 if female; SCr: serum creatinine ($\mu mol\,l^{-1}$); BSA: body surface area (m^2); Hght: height (cm). [a]Coefficients re-estimated from current data set using nonlinear mixed effects modelling.

Online calculator:
[eGFR Calculator | National Kidney Foundation]

Chronic kidney disease evaluation by GFR

Estimation of GFR can be used clinically to assess the progression of chronic kidney disease and divid them into stages according to their GFR.

This table isn't for memorization.

Stage	Description	GFR (mL/min)
1	Kidney damage (protein in the urine) with normal or elevated GFR	90 or more
2	Kidney damage with mildly decreased GFR	60–89
3	Kidney damage with moderately decreased GFR	30–59
4	Kidney damage with severely decreased GFR	15–29
5	Kidney failure: end-stage renal disease (ESRD). Patients who have Stage 5 disease require dialysis or transplantation to survive.	Less than 15

E-learning & Past paper questions:

1- Calculate GFR knowing: Urine flow rate = 1 ml/min, Urine inulin concentration = 100 mg/ml, Plasma inulin concentration = 2 mg/ml:

A. 50 ml/min
B. 100 ml/min
C. 125 ml/min
D. 25 ml/min

2- Fill in the blanks with (The best, no change, the worst, decreased, increased):
If the glomerular filtration rate (GFR) of a patient is reduced to 50% of normal and sustained at that level, you would expect to find A_____ renal creatinine excretion rate, B_____ renal creatinine clearance, and C_____ serum creatinine concentration 6 weeks after the decrease in GFR compared with normal. Assume steady-state conditions and that the patient has maintained the same diet.

3- The highest renal clearance rate of any substance would not exceed:

a. Glomerular filtration rate.
b. Renal plasma flow.
c. Renal blood flow.
d. Tubular reabsorption rate.
e. None of the above.

4- Given that Urine flow= 10ml/min and the concentration of creatinine in urine= 5mg/ml and the plasma concentration of creatinine equals= .5mg/ml. What is the value of GFR?

A. 25
B. 10
C. 100

D. .1

5- The maximum possible clearance rate of a substance that is completely cleared from the plasma by the kidneys would be equal to renal plasma flow, so we use _______ clearance to estimate RPF.

A. Paraminohippuric acid (PAH)
B. Creatinine
C. Inulin
D. Sodium
E. Urea

ANSWERS:

1. A

2. A. No change
B. Decreased
C. Increased

3. B

4. C (Creatinine clearance =GFR, C = urine conc. x urine flow / plasma conc.)

5. Aة

"صامدون، ثابتون، مرابطون... لن نغادر...إلا إلى السماء... أو إلى بيوتنا كراما"

د.عدنان البرش، الطبيب المرابط الشهيد.