Biochemistry Team 435

جامعة الملك سعود
King Saud University 1957

RENAL FUNCTION TESTES

"LIFE IS 10% WHAT HAPPENS TO YOU AND 90% HOW YOU REACT TO IT"-CHARLES R. SWINDOLL

Color index:

- Important.
- Doctors notes.
- Extra explanation.

*** Please check out this link to know if there are any changes or additions.**

****We advise you to study physiology "renal clearance" and "GFR" lectures, before studying this lecture .**

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Creatine phosphate

Recall

- What is "creatine phosphate" ?

Creatine phosphate is a high energy compound that acts as a **storage form** of energy in the muscles.

- What does it provide?

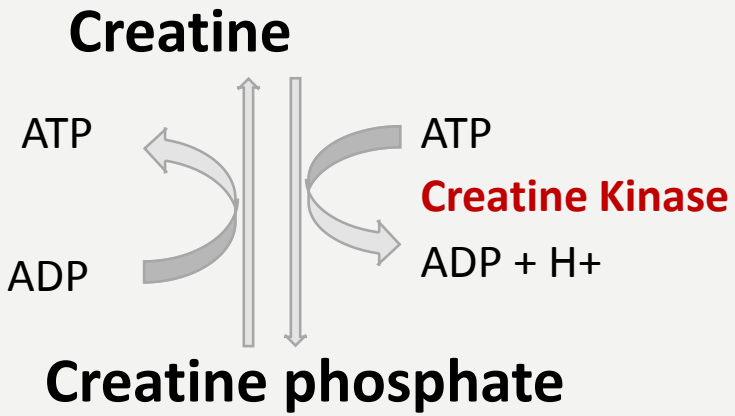
It Provides a small but, ready source of energy during first few minutes of intense muscular contraction.

Notes:

-The amount of creatine phosphate in the body is **proportional** to the muscle mass

↑ large muscle mass : ↑ amount of creatine

- The amount of creatinine and creatine phosphate are also proportional to muscle mass



Notes:

* reversible reaction
* ATP is used for the synthesis of creatine phosphate. (it gives one of its phosphates)

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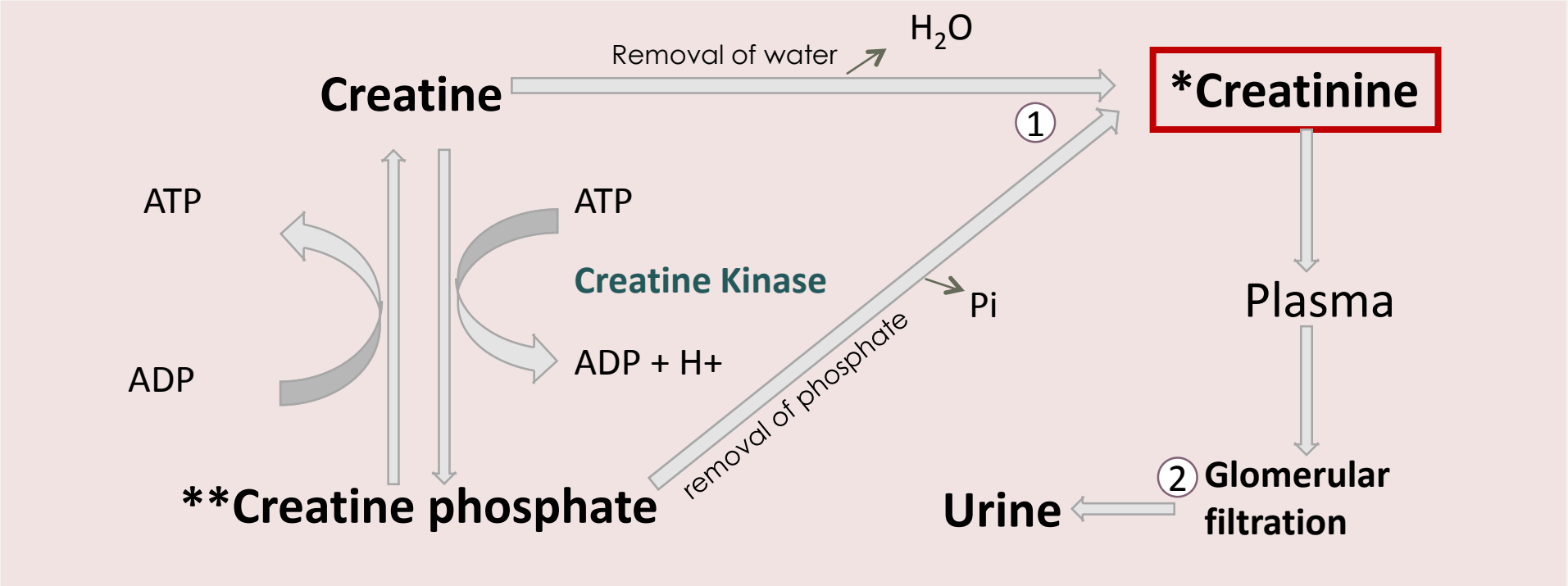
Creatine degradation

Recall



1 Creatine and creatine phosphate **spontaneously** (without enzyme) form **creatinine** as an end product.

2 Creatinine will leave muscle cell and get excreted in the urine.

*Serum creatinine is a sensitive indicator of **kidney disease** (Kidney function test) and **increases** with the impairment of kidney function And it means that the excretion of creatinine by the kidney is decreased

OBJECTIVES:

- Know the physiological functions of the kidneys.
- Describe the structure and function of the nephron.
- Identify the biochemical kidney function tests with special emphasis on when to ask for the test, the indications and limitations of each kidney function test.
- Interpret the kidney function tests properly.

kidney function test

Routine kidney function test include the measurement of :

Serum creatinine.

It shows how well your kidneys are working. A high level may mean your kidneys are not working as they should. The amount of creatinine in the blood depends partly on the amount of muscle tissue you have. Men generally have higher creatinine levels than women.

Creatinine clearance.

It measures how well creatinine is removed from your blood by your kidneys. The test is done on both a blood sample and on a sample of urine collected over 24 hours.

Serum urea.

It measures the amount of urea in your blood. Urea is a waste product made when protein is broken down in your body. Urea is made in the liver and passed out of your body in the urine.

Both serum creatinine and creatinine clearance are used as kidney function tests to:

- Confirm the diagnosis of renal disease.
- Give an idea about the severity of the disease.

(بمعنى هل يؤثر على الكلية كلها؟ أو على بعض النيفرونز؟ وهكذا)

- Follow up the treatment.

For example, to check them before and after the dialysis to know if the treatment has worked well or not.

Serum creatinine

❖ **What is it?**

It is the end product of creatine catabolism.

Normal value = 55-120 micro-mol/L in adult

100% of serum creatine

98% of the body creatine

it functions as store of high energy in the form of creatine phosphate.

1-2 % of total muscle creatine or creatine phosphate pool

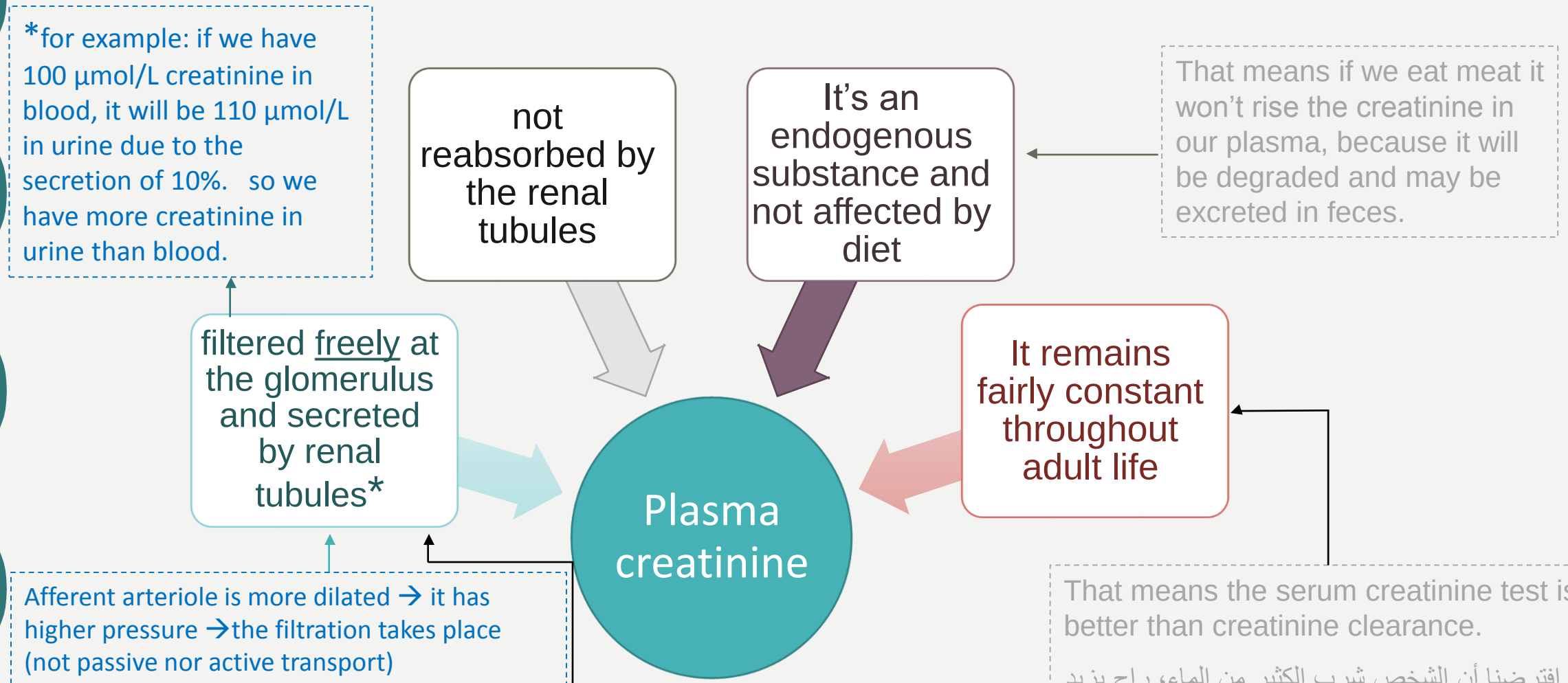
is converted daily to creatinine through the spontaneous, non enzymatic loss of water or phosphate.

Helpful video

Note:

although the creatinine is secreted from muscle, we use it as a kidney marker because it is converted daily from creatine to creatinine **spontaneously** without an enzyme. if there were an enzyme it will be an unspecific marker.

Serum creatinine



(10 % of urinary creatinine is secreted from the capillaries around the proximal tubules).

So if we want to calculate the GFR we subtract 10% of the creatinine clearance, because we want to glomerular rate only.

Creatinine clearance :

❖ What is "Clearance"?

it is the volume of plasma cleared from the substance excreted in urine per minute.

In other words, the volume of plasma from which a substance is completely removed by the **kidney** in a given amount of time (usually a minute).

❖ It could be calculated from the following equation:

$$\text{Clearance (ml/min)} = \frac{U \times V}{P}$$

علشان ما نلخبط : البسط فقط فيه أشياء متعلقة باليورين ، حجمه وتركيز الكيراتنين فيه

U = Concentration of creatinine in urine µmol/l

V = Volume of urine per min

P = Concentration of creatinine in serum µmol/l

clearance كلما قل creatinine serum نستنتج من القانون انه كلما زاد

This equation is not accurate , because the urine volume is not constant.

Creatinine clearance :

❖ **Values:**

In children:

the GFR should be related to surface area, when this is done, results are similar to those found in young adults.

Kidney function is proportional to kidney size, which is proportional to body surface area. In young adults, there's a normal mean value of the body surface which is 1.73 m2, while it is variable in children "that's why we should relate the GFR to surface are in children".

in the 20-40 year old adults:

Creatinine clearance is usually about 110 ml/min

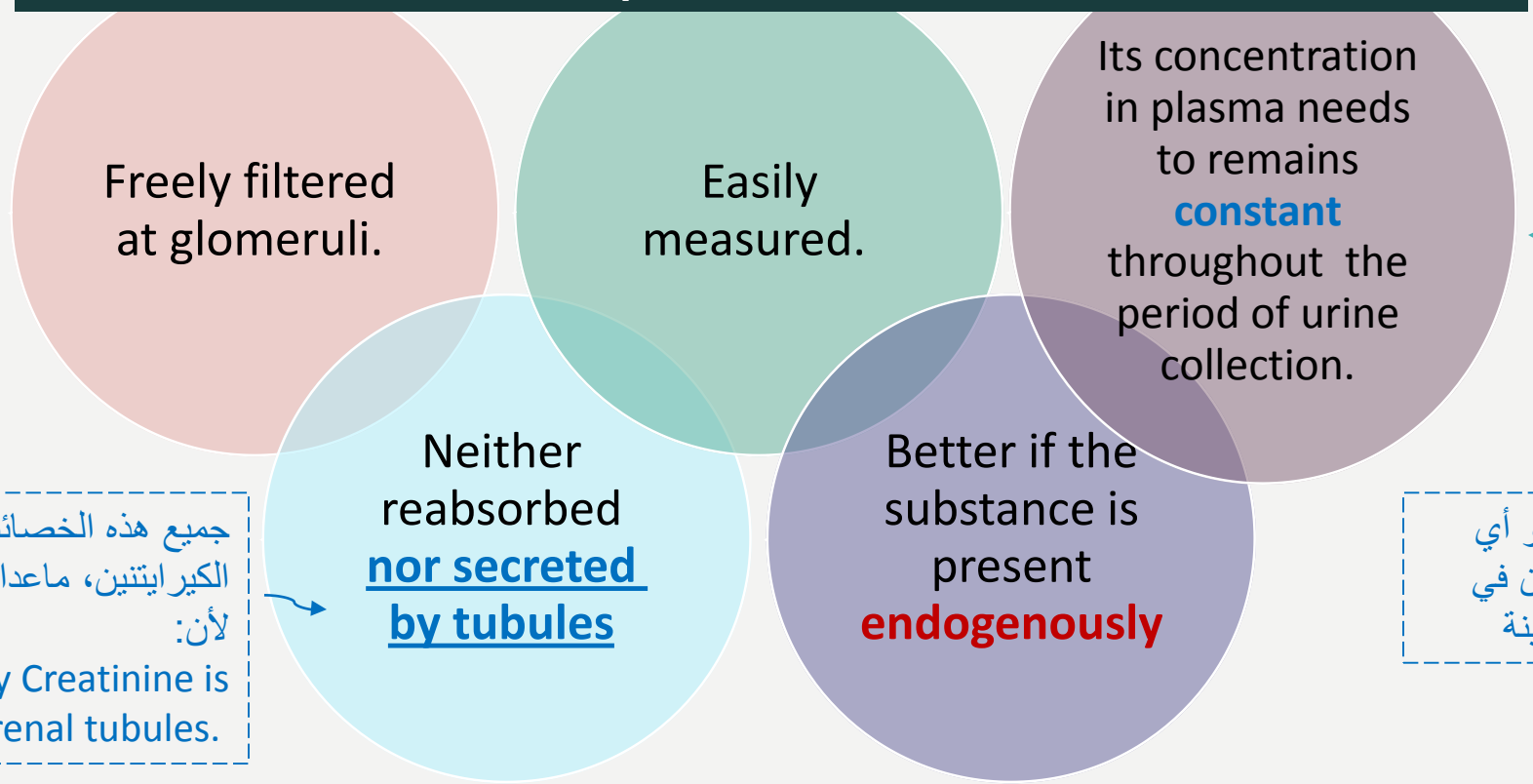
in individuals over 8o years of age:

It falls slowly but progressively to about 70 ml/min

Creatinine clearance :

- The **creatinine clearance** test is used to estimate glomerular filtration rate (GFR).
- **GFR:**
  - **gives an estimation of the degree of renal impairment by disease.**
  - **provides a useful index of the number of functioning glomeruli.**

Accurate measurement of GRF by clearance tests requires determination of the concentration in plasma and urine of a substance that is:



جميع هذه الخصائص متوفره في الكيرايتنين، ماعدا هذه الخاصية .. لأن:
10% of urinary Creatinine is secreted by renal tubules.

بمعنى أننا نمنعه من التمرن أو أي شيء يمكن أن يزيد الكرياتينين في الدم إلى أن ننتهي من أخذ العينة

Cockcroft-Gault Formula for Estimation of GFR

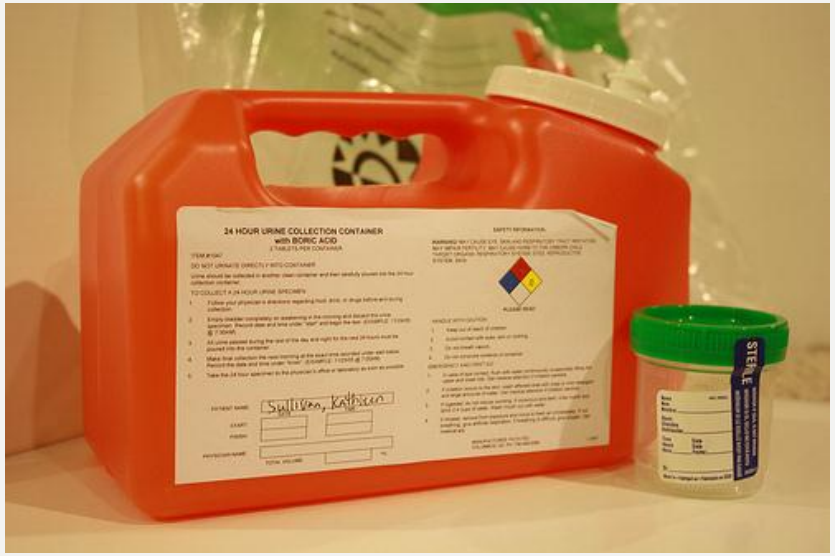
- the creatinine clearance is measured by using **a 24-hour urine collection**, but this does introduce the potential for **errors** in terms of **completion of the collection**

- تجميع اليورين خلال ٢٤ ساعة في بعض الحالات صعب مثل لمن الشخص يبغى يطلع برا بيته، هل بيأخذ معه الكونتاينر؟ أو مثلا عنده إجتماع هل بيجيب الكونتاينر معه بالإجتماع؟ طبعا لا ، فبهذي الحالات أحيانا المريض يغش ويضيف ماء للكونتاينر «شوفوني مكمل التست» وهالشي طبعا بيأثر على نتيجة الإختبار فمن هالمنطلق أخترعو معادلة بسيطة تغنيهم إلى حد ما عن تجميع اليورين

- An alternative and convenient method is to employ various formulae devised to calculate creatinine clearance using parameters **such as** **serum creatinine level**, **sex**, **age**, and **weight of the subject**.

the creatinine clearance's measurement can be inaccurate due to some mistakes during collecting the urine. that's why we use the cockcroft-gault formula because there's no need for collecting urine.

Extra information:
A **24-hour urine collection** is a simple lab test that measures what's in your **urine**. The test is used to check kidney function. It is done by collecting your **urine** in a special container(s) over a full **24-hour** period. More information



Cockcroft-Gault Formula for Estimation of GFR

$$GFR = \frac{K \times (140 - age) \times Body\ weight}{Serum\ creatinine\ (\mu mol/L)}$$

From this formula we can conclude that:
- Serum creatinine is inversely proportional to GFR, so high serum creatinine levels mean that the GFR is low.

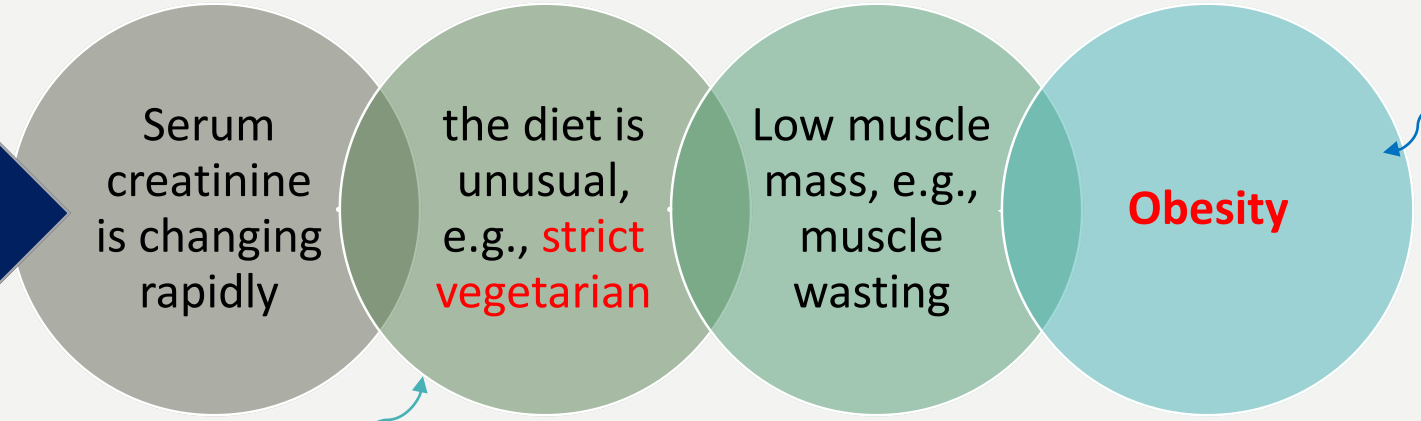
K is a constant that varies with sex:

- 1.23 for male
- 1.04 for females

The constant K is used as females have a relatively lower muscle mass.

muscle mass ⇩
=
creatinine ⇩

It should not be used if:



Obesity will give a normal GFR even if creatinine serum is high.

Because the body will be short of energy so it will take the energy by breaking creatine phosphate

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Serum creatinine is a better kidney function test than creatinine clearance.. Why?

Serum creatinine is more accurate

Serum creatinine level is constant throughout adult life

Creatinine clearance is only recommended in:

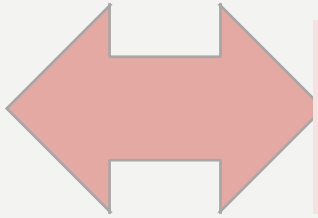
- **Patients with early (minor) renal disease.**
- **Assessment of possible kidney donors.**
- **Detection of renal toxicity of some nephrotoxic drugs.**

we use creatinine clearance for early renal disease due to its tight range. as for creatinine serum its range is wide and therefore it won't indicate impaired renal function unless its highly raised.

NORMAL ADULT REFERENCE VALUES:

Urinary excretion of creatinine is:	0.5 - 2.0 g per 24 hours in a normal adult, varying according to muscular weight.	
Serum creatinine :	55–120 ml/min	
Creatinine clearance:	Males	90 – 140 ml/min
	Females	80 – 125 ml/min

raised Serum creatinine:
a good indicator of impaired renal function



normal serum creatinine
does not necessarily indicate normal renal function, as serum creatinine may not be elevated until GFR has fallen by as much as 50%

SERUM UREA

- Urea is formed **in the liver** from ammonia released from deamination of amino acids.
- Its normal level = (2.5-6.6 mmol/L) in adult
- **Urea is increased due to dehydration.**

As a kidney function test, serum urea is inferior (secondary) to serum creatinine because:

High protein diet increases urea formation

Any condition of ↑ proteins catabolism *(Cushing syndrome, diabetes mellitus,* starvation*, thyrotoxicosis)* →↑ urea formation.

50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules.

يعني الترتيب من حيث الأهمية :
1- serum creatinine.
2- serum urea.
3- creatinine clearance.

Urea is a waste product made when protein is broken down in your body.
Urea is made in the liver and passed out of your body in the urine.
لهذا السبب أي شي يزيد هدم البروتين بيزيد تكوين اليوريا

MCQs

1.Kidney functions in

A. Cori's cycle
B. Water and salt balance
C. Protein filtration
D. None of the above

2.Creatinine secreted by renal tubules equals what percentage of urinary creatinine

A. 10%
B. 5%
C. 15%
D. 20%

3.To measure glomerular filtration you need a substance that is

A. Exogenous
B. Reabsorbed by renal tubules
C. endogenous
D. Has limited filtration

4.Creatinine clearance is recommended in

A. Minor renal impairment.
B. Renal failure
C. glomerulonephritis
D. Cystitis

5.Urea formation is increased with

A. Protein anabolism
B. Diet without meat
C. High carbohydrate diet
D. Cushing syndrome

6.Which of the following is the most superior kidney function test

A. Serum urea
B. Serum creatinine
C. Creatinine clearance
D. All are the same

1-B
2-A
3-C
4-A
5-D
6-B

MCQs & SAQs

7.Cockgroft-gault formula should not be used with

A. low muscle mass patients
B. Vegetarians
C. while exercising
D. All the above

8.Serum creatinine is better than creatinine clearance because

A. more accurate
B. It keeps changing
C. Normal levels indicate normal function
D. None of the above

9.Most renal diseases affect

A. proximal tubules
B. the glomerulus
C. Complete nephron
D. distal tubules

7-D
8-A
9-C

❖ **A 35 year old male smoker was diagnosed with small cell lung carcinoma. He is undergoing chemotherapy to eradicate the cancer. The drugs used in the treatment plan are known to be nephrotoxic.**

- **What is the recommended test to asses kidney function?**

Creatinine clearance is measured in this case.

❖ **A 20 year old woman came to the emergency room after three days of excessive vomiting and diarrhea with fever and excessive sweating.Predict the level of urea and serum creatinine in this patient.**

This is a case of hypovolemic shock
So creatinine level will be **NORMAL** but urea concentration will be HIGH.
Doctor Rana said that this is an important case.

SAQs

❖ **A 60 year old male brought to the emergency room by son ,known case of diabetes (with no known cardiac disease) .Patient presented with abnormally dark skin, excessive thirst ,he also reported blood in his stool .His physicians are concerned with the possibility of renal impairment.**

A- Evaluate the glomerular filtration rate to determine renal function. Calculate the GFR knowing that the patient weighs 78 kg ,with serum creatinine 198=micromol/L.

(K=1.23)

GFR=(K×(140-AGE) × BODY WEIGHT) ÷ SERUM CREATININE

GFR=(1.23×(140-60) × 78) ÷198 =38.7ml/min

B- Does the patient suffer from renal impairment? Explain your answer.

Yes ,because the GFR is significantly below the normal value which is about 125 ml/min

❖ **Why is cockcroft – gault formula not used for calculating GFR in obese patients?**

Because obese patients obviously have increased body weight which will lead to an increased GFR even if kidney impairment is present.So the use of this formula will lead to false assessment of renal function and hence a false diagnosis

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