جامعة الملك سعود
King Saud University

"اللَّهُمَّ لا سَهْلَ إلاَّ ما جَعَلْتَهُ سَهْلاً، وأنْتَ تَجْعَلُ الحَزْنَ إذَا شِئْتَ سَهْلاً "

Biochemistry437

Kidney Function Test

Biochemistry Team 437

Color index:
Doctors slides
Doctor's notes
Extra information
Highlights

Renal block

EDITING FILE

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Objectives:

- Know the physiological functions of the kidney.
- 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.

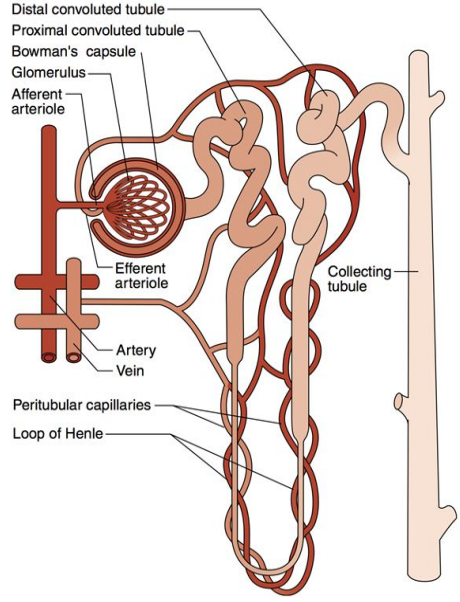
Contents:

- Functional units
- Kidney functions
- Routine kidney function tests (KFTs):
- Serum creatinine
- Creatinine clearance
- Cockcroft-Gault formula for GFR estimation
- Serum Urea

Functional Units

Nephron

- is the functional unit of the kidney
- Each kidney contains about 1,000,000 to 1,300,000 nephrons
- is composed of glomerulus and renal tubules
- performs its homeostatic function by ultra filtration at glomerulus and secretion and reabsorption at renal tubules



Representation of a nephron and its blood supply

Only in males slides

Nephron Parts

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Glomerulus

• Functions to filter incoming blood.(no energy needed)

• Factors facilitate filtration:

- high pressure in the glomerular capillaries, which is a result of their position between two arterioles.
- the semipermeable glomerular basement membrane, which has a molecular size cutoff value of approximately 66,000 Da (if above 66000 it will not be filtered) .

The volume of blood filtered per minute is the glomerular filtration rate (GFR), and its determination is essential in evaluating renal function.

Proximal convoluted tubule

• Returns the bulk of each valuable substance back to the blood circulation.
• 75% of the water, sodium, and chloride.
• 100% of the glucose (up to the renal threshold) (if more than 180 mg/dl of glucose in blood we will have glucose in urine and this glucose in urine is the excess amount beyond renal threshold)
• Almost all of the amino acids, vitamins, and proteins
• Varying amounts of urea, uric acid, and ions, such as magnesium, calcium and potassium.

With the exception of water and chloride ions, the process is active; that is, the tubular epithelial cells use energy to bind and transport the substances across the plasma membrane to the blood.

• Secretes products of kidney tubular cell metabolism, such as hydrogen ions, and drugs, such as penicillin.and 10% of creatinine

Loop of Henle

• Facilitates the reabsorption of water, sodium, and chloride.

The osmolality in the medulla in this portion of the nephron increases steadily from the corticomedullary junction inward

Distal convoluted tubule

• The filtrate entering this section of the nephron is close to its final composition.

• Effects small adjustments to achieve electrolyte and acid-base homeostasis (under the hormonal control of both antidiuretic hormone (ADH) and aldosterone).

The distal convoluted tubule is much shorter than the proximal tubule (reabsorption will be less), with two or three coils that connect to a collecting duct.

Collecting duct

• The collecting ducts are the final site for either concentrating or diluting urine.

• The hormones ADH and aldosterone act on this segment of the nephron to control reabsorption of water and sodium.

• Chloride and urea are also reabsorbed here.

Da : Dalton (it is a unit of measurement)

Kidney Functions

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Regulation of

- Water and electrolyte balance.
- Acid base balance. [1]
- Arterial blood pressure.[2]

[1] controlled by aldosterone

[2] controlled by RAAS and aldosterone

Excretion of

Metabolic waste products and foreign chemicals.

These metabolic wastes will be converted to intoxic (inactive) metabolites in the liver (catabolism reaction), then excreted in the urine by the kidney

Hormonal Function

- Secretion of erythropoietin
- activation of vitamin D and activation of angiotensinogen (in liver) by renin (in kidney)

Metabolic Function

Site for gluconeogenesis [3].

[3] Formation of glucose

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Why to test the renal functions?

- Many diseases affect renal function.
- In some, several functions are affected.
- In others, there is selective impairment of glomerular function (e.g : Glomerulonephritis) or one or more of tubular functions (e.g : Tubular acidosis).
- Most types of renal diseases cause destruction of complete nephron.

Routine KFTs
(Kidney Function Tests)

- Serum creatinine (Cr).
- Creatinine clearance.
- Serum urea.

IMPORTANCE

Also we measure the electrolytes (e.g: Na , K , Cl)

Note ! :-

- Creatinine (end product) is different than creatine
- Renin (which activates angiotensinogen) is different than rennin

Serum Cr 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.
- Follow up the treatment (toxicity of some drugs)
- To check for the response of the treatment before and after dialysis

Serum Creatinine

- **Normal level(55-120 µmol/L in adult) [1]**
- Creatinine is the end product of creatine catabolism.
- 98% of the body creatine is present in the muscles where it functions as store of high energy in the form of creatine phosphate.

- About 1-2 % of total muscle creatine or creatine phosphate pool is converted daily to creatinine through the spontaneous[2], non enzymatic loss of water or phosphate.[3]

[1] Notice that creatinine is measured in micromoles. it is lesser than urea which is measured with millimoles

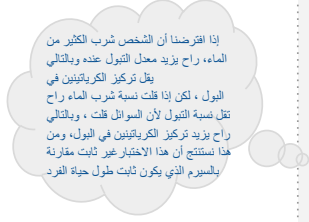
[2] Not being affected by enzymes makes it a good biomarker for kidney function. Since we can't blame the increase of creatinine on a muscle problem

[3] **Creatine is in the form of:**
- Creatine: Converted to Creatinine by water loss
- Creatine Phosphate: Converted to Creatinine by P loss and water loss

Serum Creatinine

1. Creatinine in the plasma is filtered freely (No need for energy) at the glomerulus and secreted by renal tubules (10% of urinary creatinine). [1]
2. Creatinine is not reabsorbed by the renal tubules.

3. Plasma creatinine is an endogenous substance not affected by diet [2]
4. Plasma creatinine remains fairly constant throughout adult life. [3]



[1]Urinary Creatinine:
- 90% by Glomerular filtration
- 10 % by Secretion

Therefore, if we want to calculate Glomerular filtration, we should subtract urinary creatinine by 10%

[2]Making it a good index for kidney function, whereas urea is affected by meat consumption so creatinine is a better biomarker

[3]That means the serum creatinine test is better than creatinine clearance.

people with sedentary lifestyle & vegetarians have lower creatinine levels, Usually each person (Male or Female) or (Athlete or non athlete) have their own different Creatinine levels.

To recap, serum creatinine is a good biomarker of kidney function because:
- Filtered freely at the glomeruli
- Not reabsorbed
- Constant through adult life
- Endogenous substance not affected by diet

Creatinine Clearance (GFR)

نشوف كمية السيرم او البلازما الي صار له فيلتريشن ونظف من الويست الي موجودة فيه

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- The glomerular filtration rate (GFR) provides a useful index of the number of functioning glomeruli.
- It gives an estimation of the degree of renal impairment by disease. "How many nephrons are functioning"

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

The test is done on both a blood sample and on a sample of urine collected over 24 hours

مو كل المواد ينفع نستخدمها لقياس ال GFR
لأن بعضها يعاد امتصاصه أو تفرز زيادة أو تتأثر بعوامل كثيرة ما تخليها مقياس دقيق للاستخدام وبكذا كل ما تطابقت مواصفات المادة مع النقاط هذي بتصير أدق ..مثلاً اليوريا ما تنطبق عليها هذه الخصائص

- Freely filtered at glomerulus. < 66,000 Da
- Neither reabsorbed nor secreted by tubules.
- Its concentration in plasma needs to remains constant throughout the period of urine collection.
- Better if the substance is present endogenously
- Easily measured.

This is not the case for creatinine but Creatinine meets most of the criteria., and usually only 10% is secreted by the tubules which is often negligible.

Creatinine meets most of these criteria.

Except: Secreted by tubules

Cont.

For the numbers just know that the normal range is around 110 ml/min

- Creatinine clearance is usually about **110 ml/min** in the 20-40 year old adults.
- It **falls slowly but progressively to about 70 ml/min** in individuals over 8o years of age.* because it's related with the muscles.
- In children, the GFR should be related to surface area, when this is done, results are similar to those found in young adults.*110ml/min
- **Clearance** is the volume of plasma cleared from the substance excreted in urine per minute.

It could be calculated from the following equation:

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

U: Concentration of creatinine in urine µmol/l
V: Volume of urine per min
P: Concentration of creatinine in serum µmol/l
So we need to collect two samples, a blood sample and a 24 h urine sample

The problem with this equation is that it has *subjective values (U & V).*
We're not sure that patient collected his urine for 24h exactly. Meaning patient compliance can limit the accuracy of the test

Cockcroft-Gault Formula for Estimation of GFR

- As indicated above, 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.
- 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.

An example is **the** Cockcroft-Gault Formula

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

This formula is good because we **excluded urine** and replaced it by easier parameters. (because we need to measure the urine volume, and once we give the patient the urine container we take a blood sample from him at the same time to measure the creatinine in the blood)
فمن هالمنطلق اخترعوا معادلة بسيطة تغنيهم إلى حد ما عن تجميع اليورين .

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.

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

Obesity will give a normal GFR even if creatinine serum is high. Because the increase in weight will balance the increase in serum creatinine in the equation

So Serum creatinine is inversely proportional to GFR

It should not be used if

- Serum creatinine is changing rapidly
- The diet is unusual, e.g., strict vegetarian
- Low muscle mass, e.g., muscle wasting
- Obesity

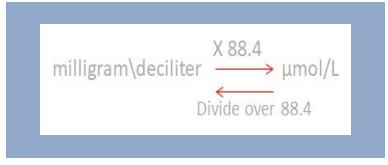
Chemotherapy and malnutrition might result in very low serum creatinine, giving us a normal gfr but the patient has renal disease.

Extra explanation for the limitation of GFR test

For example when some patients hang out without their container and they go to bathroom, so they didn't urinate in the container so there will be error in the final urine volume. Also some patients may add water to the container which damages the sample.

HOW TO CONVERT CREATININE CONCENTRATION FROM MG/DL TO MICROMOL/L?

THE CONVERSION FACTOR IS (88.4)
e.g: 1mg/dl = 88.4 micromol/l
That is : (mg/dl)



Serum Cr is a better KFT than creatinine clearance because:

- Serum creatinine Is More accurate.*
- Serum creatinine Level is constant throughout adult life.

- *Accurate because it measures one variable only which will decrease the chances of errors. Whereas Creatinine clearance because has potential for errors.
- In early stages of renal disease, creatinine in serum remains normal or moderately elevated, so we can't use it to detect an early disease

IMPORTANT!!

Creatinine clearance is only recommended in the following conditions:

- Patients with early (minor) renal disease.
- Assessment of possible kidney donors.
- Detection of renal toxicity of some nephrotoxic drugs. E.g roaccutane, chemotherapy

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 mmol/L

A raised serum creatinine is a good indicator of impaired renal function
But 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%

Creatinine clearance:

90 – 140 ml/min (Males)

80 – 125 ml/min (Females)

Serum Urea (2.5-6.6 mmol/L) in Adult

Urea is formed in the liver from ammonia released from deamination of amino acids.

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

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

Urea is not endogenous it is affected by diet

High protein diet and dehydration increases urea formation.

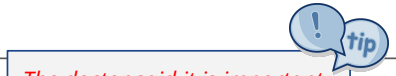
*Any condition of - proteins catabolism *(Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis)* increase - urea formation.

*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

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

Normal values of Internal Chemical Environment controlled by the Kidneys

SODIUM	135 to 145 mEq/L
POTASSIUM	3.5 to 5.5 mEq/L
CHLORIDES	100 to 110 mEq/L
BICARBONATE	24 to 26 mEq/L
CALCIUM	8.6 to 10 mg/dl
MAGNESIUM	1.6 to 2.4 mg/dl
PHOSPHORUS	3.0 to 5.0 mg/dl
URIC ACID	2.5 to 6.0 mg/dl
pH	7.4
CREATININE	0.8 to 1.4 mg/dl
BUN (Blood Urea Nitrogen)	15 to 20 mg/dl



The doctor said it is important to know the anion and cation (The numbers are not important, only the red ones)

Summary

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Kidney Function Tests

Serum creatinine (55-120 umol/L in adult):
- Creatinine is the end product of creatine catabolism.
- 98% of the body creatine is present in the muscles
- About 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.
- Creatinine in the plasma is filtered freely at the glomerulus and secreted by renal tubules (10 % of urinary creatinine).
- Creatinine is not reabsorbed by the renal tubules.
- Plasma creatinine is an endogenous substance not affected by diet.
- Plasma creatinine remains fairly constant throughout adult life

Creatinine clearance:
- The glomerular filtration rate (GFR) provides a useful index of the number of functioning glomeruli.
- It gives an estimation of the degree of renal impairment by disease.

Clearance: is the volume of plasma cleared from the substance excreted in urine per minute.
Clearance (ml/min) = (UxV)/P

Cockcroft-Gault Formula for Estimation of GFR: GFR = (Kx(140 - age)xBody weight)/Serum creatinine (umol/L)

where K is a constant that varies with sex: 1.23 for male & 1.04 for females

It should not be used if
- Serum creatinine is changing rapidly
- the diet is unusual, e.g., strict vegetarian
- Low muscle mass, e.g., muscle wasting obesity

Serum Cr is a better KFT than creatinine clearance because:

- Serum creatinine is more accurate.
- Serum creatinine level is constant throughout adult life

Serum Urea (2.5-6.6 mmol/L) in adult:
Urea is formed in the liver from ammonia released from deamination of amino acids.

As a kidney function test, serum urea is inferior to serum creatinine because:
- High protein diet increases urea formation.
- Any condition of increase proteins catabolism (Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis) ->increase urea formation.
- 50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules.

Functional units :

- The nephron is the functional unit of the kidney
- Each kidney contains about 1,000,000 to 1,300,000 nephrons.
- The nephron is composed of glomerulus and renal tubules.
- The nephron performs its homeostatic function by ultra filtration at glomerulus and secretion and reabsorption at renal tubules.

Each nephron is a complex apparatus comprised of five basic parts:

1. Glomerulus: functions to filter incoming blood.

2. Proximal convoluted tubule: Returns the bulk of each valuable substance back to the blood circulation

3. Loop of Henle: Facilitates the reabsorption of water, sodium, and chloride

4. Distal convoluted tubule: The filtrate entering this section of the nephron is close to its final composition

5. Collecting duct: The collecting ducts are the final site for either concentrating or diluting urine

Kidney functions :
- Regulation
- Excretion
- Hormonal Function
- Metabolic Function

Why to test the renal functions?

- Many diseases affect renal function.
- In some, several functions are affected.
- In others, there is selective impairment of glomerular function or one or more of tubular functions.
- Most types of renal diseases cause destruction of complete nephron.

Routine KFTs include themeasurement of :
1. Serum creatinine (Cr).
2. Creatinine clearance.
3. Serum urea.

Both serum Cr and Cr clearance are used as kidney function tests to :
- Confirm the diagnosis of renal disease.
- Give an idea about the severity of the disease.
- Follow up the treatment.

MCQs:

1- Which of the following doesn't require ATP to be reabsorbed by the proximal convoluted tubules?

A) Magnesium
B) Chloride
C) Calcium
D) Potassium

2- Which of the following doesn't affect the concentration of serum creatinine?

A) Age
B) Gender
C) Diet
D) Muscle mass

3- Normal adult creatinine clearance is between?

A) 90 – 140 ml/min
B) 80 – 125 ml/min
C) 55 – 120 mmol/L
D) 25-175 ml/min

4- Serum creatinine may not be elevated until GFR has fallen by as much as?

A) 40%
B) 20%
C) 30%
D) 50%

5- Urea is formed in the …?

A) Kidney
B) Ureter
C) Liver
D) Lung

6- Which of the following doesn't increases urea formation?

A) Thyrotoxicosis
B) Starvations
C) Hypertension
D) Proteins catabolism

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

SAQ

Name three criteria for a substance that can accurately measure the GFR

- Freely filtered at glomeruli.
- Neither reabsorbed nor secreted by tubules.
- Its concentration in plasma needs to remains constant throughout the period of urine collection.
- Better if the substance is present endogenously.
- Easily measured.

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Team leaders

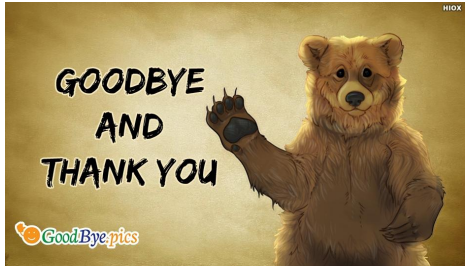
- رهام الحلبي
- معاذ الحمود

Boys team

- طارق العميم
- فيصل الطحان
- محمد الصويغ
- أنس القحطاني
- صالح الوكيل
- عبد الملك الشرهان
- سعيد القحطاني
- محمد الاصقه
- نواف اللويمي
- معن شكر
- عبدالرحمن التركي

Girls team

- رهف الشنيبر
- شهد الجبرين
- لينا الرحمة
- منيرة المسعد
- ليلى الصّباغ
- العنود المنصور
- أرجوانة العقيل
- ريناد الغريبي
- رزان الزهراني
- ليان المانع
- مشاعل القحطاني
- شيرين الحمادي



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