UGS

UROGENITAL SYSTEM ®

Sheets Physiology

Number 10

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Correction --

This is the last lecture of renal physiology. We will discuss acute renal injury and urine test. At the end of the sheet there are some questions of last year's exam

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Acute renal injury

Acute kidney injury is when there is an abrupt (sudden) decrease in kidney function (in few days). It was previously called acute kidney failure.

Causes:

Causes of acute kidney injury are prerenal, intrarenal or post-renal. 90% of cases are due to prerenal and intrarenal causes, while only 10% are due to post-renal causes.

- **Prerenal**: those that decrease blood flow to the kidneys like heart failure, MI, bleeding, Conn's disease, or dehydration of any cause (e.g. vomiting, diarrhea, overuse of diuretics). Without treatment, these progress into intrarenal acute injury with worse prognosis.
- **Intrarenal**: those that cause a direct damage to the renal tissue (e.g. nephritis, nephrotoxic drugs, such as NSAIDs and some antibiotics). Kidney diseases can be cortical (glomerular), in which the filtration process is impaired, or medullary (tubular), in which the impairment involves reabsorption or secretion.
- **Post-renal**: those that obstruct urine flow like stones in the kidney or bladder and prostate hypertrophy.

**In pre-renal kidney injury, GFR decreases, and urea reabsorption increases; that is, urea to creatinine ratio raises. In contrast, in case of an intrarenal injury, this ratio decreases since the kidneys ability to reabsorb filtered substances, especially urea, is decreased.

Stages:

We classify acute renal injury based on clinical history, laboratory results and volume of urine. We use the ***RIFLE*** criteria which classifies acute renal injury into 5 stages with each stage starting with a letter from the word RIFLE:

	number of damaged nephrons = decrease in GFR	**Serum creatinine level**	**urine output**
Stage1 **Risk**	>25%	1.5 times normal	<0.5ml/kg/hr for 6 hours
Stage2 **Injury**	>50%	2X normal	<0.5ml/kg/hr for 12 hours
Stage3 **Failure**	>75%	3X normal	<0.3ml/kg/hr for 24 hours
Stage4 **Loss**	When the previous criteria last for 4 weeks		
Stage5 **End stage renal failure**	When it lasts for 3 months Here, hemodialysis or kidney transplantation are necessary; patient can't survive without them		

Urine analysis

Urine analysis includes microscopic and biochemical tests. In microscopy, we see RBCs, WBCs and casts.

A. **RBCs**

Urine should not have more than 1-2 RBCs. If there is more than that it is called ***microscopic hematuria***; urine's color appears normal. If it increases even more it becomes ***macroscopic***; i.e. you can see it with your naked eyes (urine appears red).

**Important: Painless hematuria is cancer unless proven otherwise.

Not every patient with painless hematuria has cancer (<5% actually have cancer) but you as a doctor should make full investigations to rule out cancer.

Painful hematuria is most probably due to stones or UTI and because the patient is in pain he will seek medical attention and the doctor makes an ultrasound or IVP

(intravenous pyelogram). On the other hand, painless hematuria is of more concern because it is silent.
If someone told you that he had hematuria before 2 weeks (for example) and then it disappeared you have to advise him to make a full investigation. An ultrasound can usually show the presence of a tumor in the kidney or bladder. If you catch cancer in early stages (no metastasis or invasion) it can be cured.
How does a tumor produce hematuria?
When it enlarges, it might cause rupture of veins or arteries and produce hematuria. The ruptured artery then closes so hematuria disappears but after 3 months or so it happens again but now the tumor progressed even more!

B. WBCs

Presence of WBCs in urine indicates the presence of an infection.

C. Protein

We can sometimes find protein in urine because some proteins have low molecular weight and they are filtered and not reabsorbed.

03:00-11:20

- Protein in urine should be negative
- if it is between **15-30 mg/dl** we consider it normal (traces)
- +1 → **30-100mg/dl**. It is normal in children; we don't have to do any further investigations.
- +2 → **100-300mg/dl**. It is benign in most cases in young people (adolescence) as in orthostatic proteinuria, after exercise or fever. This result does not mean kidney injury. Orthostatic (postural) proteinuria is when someone doesn't have proteinuria when he wakes up, but after walking around during the day proteinuria appears at the end of the day.
- +3 → **300-1000mg/dl**
- +4 → **>1000mg/dl.** This is the case in nephrotic syndromes. The most common nephrotic syndrome in children is minimal change disease. In this disease, you see minimal changes under electron microscopy; you see some damage in podocytes. It is believed that the negative charge of the filtration membrane has been lost. This allows for negatively charged proteins with around 70K Daltons (like albumin) to be filtered.

Remember: The negative charge of the filtration membrane prevents the filtration of negatively charged proteins.
Cations like dextran are easily filtered. However, a negatively charged protein with the same molecular weight as dextran is not filtered.
Albumin for example has a molecular weight of less than 70 but it is still not found in urine because it is negatively charged.

D. Glucose

Glucose should not be found in urine. We previously discussed what we do if there was glucose in urine.

Recall
Glycosuria can be nephrogenic or diabetogenic. Usually, measuring blood glucose level is differential. High level confirms diabetogenic glycosuria; normal level confirms nephrogenic glycosuria (e.g., low number or affinity of the glucose transporters). Nephrogenic glycosuria is benign (i.e., good prognosis), as it does not progress.

E. pH

pH of urine is usually acidic (5.5)

F. Osmolarity

Urine is hyperosmolar; its osmolarity is usually 600-650mOsm.

Blood test

Indicators include urea, creatinine and electrolytes (mostly Na^+ and K^+). This is the routine kidney function test.
Sometimes imaging is also needed (IVP, CT, etc.).

13:00-17:20

Indicators used to diagnose acute renal failure:

- Elevated plasma urea (normal range is 14-40 mg/dl). Since plasma urea level is affected by protein intake, creatinine level is more a sensitive test.
- Elevated plasma creatinine (normal range is 0.7-1.3 mg/dl).

▪ Oliguria (urine output below 300 ml/day.m2) or anuria (urine output below 100 ml/day.m2). However, urine output may be normal, or even elevated, if the cause of the failure is intrarenal but the urine would be isosthenuric in this case, indicating inability of the kidneys neither to concentrate nor to dilute the urine.

Recovery:

▪ the last kidney function to be regained after acute renal failure is concentrating urine. This is because normal urine osmolarity requires intact hypothalamic function, posterior pituitary function, ascending limb function, collecting ducts response to ADH and renal medullary interstitium.

▪ To test urine concentrating ability, the patient is asked not to drink water at night. Then, urine samples are taken in the next morning at 8:00 AM, 8:30 AM and 9:00 AM. If the osmolarity of any of the samples is higher than 1000 mOsm/L, then the patient's kidneys function are regained.

Questions

Q1: Loop diuretics which inhibit NaCl reabsorption in the thick ascending limb will:

a. decrease osmolarity of the tubular fluid leaving the thick ascending limb
b. increase maximum urine osmolarity
c. increase glucose clearance
d. increase NaCl clearance
e. decrease K^+ excretion

Right answer → d

Discussion: If you inhibit NaCl reabsorption, NaCl will remain in the tubule so the osmolarity will increase (so a is wrong). You give diuretics to get rid of NaCl though urine; i.e. increase its clearance.

$clearance = \frac{Na\ in\ urine}{Na\ in\ plasma} X\ urine\ output$ → when using diuretics urine output will increase so clearance of NaCl increases.

Q2: Regarding glomerular markers:

a. Substances used for measuring GFR and are not suitable for the measurement of renal blood flow
b. Under certain circumstances, we can use Na+ to measure GFR
c. Filtered load of any glomerular marker must equal GFR
d. Any substance that is freely filtered and not reabsorbed can be used to measure GFR
e. PAH (at very low concentration) can be used to measure GFR

Right answer → a

Discussion: Glomerular markers (like creatinine, mannitol, and inulin) are substances used for measuring GFR not renal blood flow. You can find out renal blood flow from GFR if you know the filtration rate but the question doesn't say so. d is wrong because a glomerular marker should be freely filtered, not reabsorbed *AND* not secreted.

Q3: the Pka of NH_3-NH_4^+ is 9.2. When tubular fluid pH is 6.2:

a. NH_3 and NH_4^+ are present in equal concentrations
b. NH_4^+ concentration is 10 times NH_3 concentration
c. NH_4^+ concentration is 100 times NH_3 concentration
d. NH_4^+ concentration is 1000 times NH_3 concentration
e. NH_3 concentration is 1000 times higher than NH_4^+ concentration

Right answer → d

Discussion: Since the difference between Pka and pH of tubular fluid is 3, then $NH_3/NH_4^+ = 1/1000$
Remember: $pH=Pka + \log([base]/[acid])= pka + \log([NH_3]/[NH4^+])$

Q4: Which of the following would cause an increase in both GFR and renal plasma flow (RPF)?

a. Constriction of the afferent arteriole
b. Infusion of amino acids
c. dilation of the afferent arteriole
d. dilation of the efferent arteriole

e. Constriction of the efferent arteriole

Right answer → c

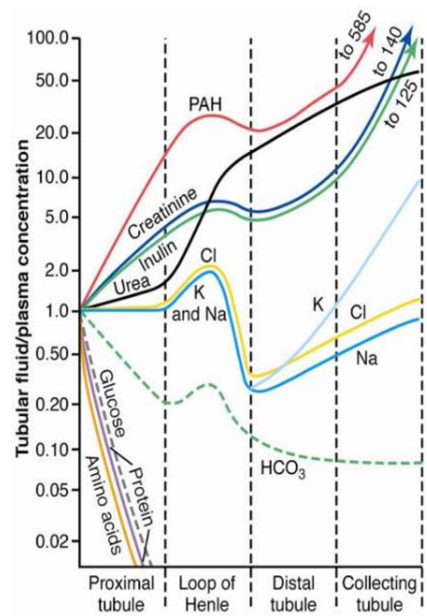
Discussion: when you dilate the afferent arteriole you increase blood flow and GFR at the same time.

Q5: Which of the following substance will be more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

a. Urea
b. PAH
c. Inulin
d. Creatinine
e. Mannitol

Right answer → b

Discussion: Because PAH is secreted. Not urea because it is reabsorbed in the proximal tubule. Inulin is increased (3 times) but not as much as PAH. Creatinine is a little bit more concentrated than inulin because some of it is secreted. But PAH is mainly secreted and the proximal tubule is where it gets secreted. Mannitol and inulin are handled in the same way; so neither of them is the answer.



17:20-27:15

Q6: What is the GFR if concentration of PAH in urine = 30mg/ml, in arterial blood= 0.5 mg/ml, and urine flow= 3 ml/min?

a. 580
b. 110
c. 180
d. 100
e. cannot be calculated from the above data

Right answer → e

Discussion: PAH cannot be used to measure GFR

Q7: Renal clearance of:

a. inulin increases as its plasma concentration increases (linear relationship)
b. creatinine is less than for inulin
c. K^+ is decreased by the administration of loop diuretic (furosemide)

d. Of glucose can sometimes exceed GFR (only at higher non-physiological glucose concentration)
e. substance X May rise, fall or stay the same as plasma concentration of X rises

Right answer → e

Discussion: Clearance of glucose for example rises as glucose concentration in plasma increases. On the other hand, clearance of PAH decreases as its plasma concentration rises. For inulin it stays the same. It depends on X.

Q8: All of the following statements are true of the H^+ secreted into the lumen of the distal nephron except:

a. Can combine with HCO_3^-
b. Can combine with HPO_4^{-2}
c. Can combine with NH_4^+
d. Remains as free H^+
e. Is secreted by an H^+-ATPase pump

Right answer → c

Discussion: H^+ can combine with HCO_3^- and HPO_4^{-2} forming H_2CO_3 and $H_2PO_4^-$ respectively but it cannot combine with NH_4^+.

Q9: increasing plasma concentration of PAH above Tmax can lead to an increase in PAH:

a. Clearance
b. Excretion rate
c. Filtration fraction
d. Reabsorption rate
e. Secretion rate

Right answer → b

Discussion: excretion rate increases because filtered load will increase. Its clearance will decrease. Filtration fraction is not affected. PAH is never reabsorbed. Secretion rate will not increase because we reached Tmax.

Q10: In a normal individual under normal diet and normal physical activity, compared to plasma, urine has: (↑higher, ↓lower, →equal)

	[K+]	pH	[urea]	SG
a.	↑	↑	↑	↑
b.	↓	↓	↓	↓
c.	→	↑	↑	↑
d.	↑	↓	↑	↑
e.	↓	→	↑	↑

Right answer → d

Discussion: We said that we excrete 95mEq of K^+ per day. So its concentration in urine =95mEq/1.5L ≈ 65mEq/L. plasma concentration of K^+ is 4mEq/L. So its concentration in urine is definitely higher. Urine is more acidic than plasma (pH↓). Specific gravity of urine is higher because its osmolarity is higher (650mOsm).

Q11: A climber attempts to reach a high mountain in The Andes (an altitude of 5000m above sea level), what will happen to this person's blood and urine?

a. Both arterial $PaCO_2$ and pH will be higher than normal due to the physical exertion
b. His urine is full of NH_4Cl
c. Plasma and urine [HCO_3^-] will increases
d. Both arterial $PaCO_2$ and pH will be lower than normal
e. Arterial $PaCO_2$ will fall and arterial pH will rise

Right answer → e

Discussion: this climber will have respiratory alkalosis because oxygen deficit will lead to hyperventilation washing out CO_2. The kidney will compensate by increasing HCO_3^- secreted in urine.

Q12: Match the acid-base status of the following arterial blood sample to the correct disorder: pH=7.4, $PaCO_2$=58 mmHg, HCO_3^-= 33 mM/L

a. Fully compensated metabolic alkalosis
b. Fully compensated respiratory acidosis
c. Fully compensated respiratory alkalosis
d. Mixed respiratory and metabolic alkalosis
e. Mixed respiratory and metabolic acidosis

Right answer → b

Discussion: We first look at pH; it is normal. CO_2 is high, so there is respiratory acidosis but HCO_3^- is also high. So it appears that there is full compensation. The kidney can fully compensate for respiratory acidosis keeping pH normal (but not higher). It can be confused with mixed respiratory and metabolic disorder but it is not in the choices. We differentiate depending on the extent of the increase.

27:15-37:00

Q13: The following information was obtained in a human subject:

Urine output= 1ml/min

	plasma	Urine
[Inulin] mg/ml	**1**	**150**
[X] mg/ml	**2**	**100**

Assuming that X is freely filtered, which of the following statements is most correct?

a. There is net secretion of X
b. there is net reabsorption of X
c. there is both reabsorption and secretion
d. X is a glomerular marker
e. The clearance of X is equal to the clearance of inulin

Right answer → b

Discussion: clearance of X is 50 (1*100/2), clearance of inulin=150. Since $C_x<C_{inulin}$, then X is reabsorbed. If $C_x=C_{inulin}$ then it is handled as inulin. If $C_x>C_{inulin}$ then inulin is secreted.

Q14: All of the following values will be above normal in a diabetic ketoacidosis patient with a blood glucose concentration of 600mg/dl except:

a. Urine flow rate
b. Urine [NH_4Cl]
c. plasma [HCO_3^-]
d. plasma [K+]
e. plasma anion gap

Right answer → c

Discussion: a patient with diabetic ketoacidosis has metabolic acidosis. In metabolic acidosis plasma [HCO_3^-] is low.

Q15: Which of the following statements is true regarding a normal person who donated one kidney (unilateral nephrectomy)? Assume the individual has come into equilibrium but has not undergone any compensatory hypertrophy of the remnant nephrons yet.

a. Plasma creatinine concentration remains unchanged
b. The clearance of creatinine remains unchanged
c. The urinary excretion of creatinine falls by 50%
d. The filtered load of creatinine falls by 50%
e. Homeostasis is perfectly maintained

Right answer → e

Discussion: we can maintain homeostasis by one kidney but without any compensation, plasma creatinine will be doubled because GFR decreased by half.

Q16: Acute kidney injury (AKI) was previously known as acute renal failure (ARF). Which of these findings is NOT a feature of prerenal ARF?

a. Decreased GFR
b. Urine specific gravity always equal 0.010
c. Fractional sodium excretion less than 1%
d. Blood urea:creatinine ratio >100:1
e. Blood BUN:creatinine ratio >20:1

Right answer → b

Discussion: prerenal ARF can turn into intrarenal ARF if not treated. If someone has hemorrhage for example and it was not managed, his kidney will be damaged.

How to know whether the patient has prerenal or intrarenal ARF? If the kidney is still intact (prerenal), it can still reabsorb sodium. So sodium in urine will be low. There will be also reabsorption of urea because GFR is low and flow in the proximal tubule is slow. As a result, urea:creatinine ratio in blood is high (>100).

When the kidney in damaged (intrarenal), urea:creatinine ratio in blood is less than that (<40) because it cannot reabsorb urea. The damaged kidney also cannot reabsorb sodium, so Na^+ concentration in urine will be high.

When someone is bleeding (prerenal), he will not tolerate losing sodium or water, so urine output is low and the amount of lost sodium is also low. And because urine is very concentrated, its specific gravity will be high.

When the kidney is damaged (intrarenal), urine output might be low or normal but concentration of sodium in urine might be normal or above normal. When there is an intrarenal problem, specific gravity of urine will always be 0.010 because the kidney cannot dilute or concentrate urine.

Q17: Regarding renal clearance, choose the correct statement:

a. Inulin clearance measures renal blood flow
b. Filtration fraction measured as inulin clearance÷PAH clearance
c. Creatinine clearance underestimate GFR

d. Sodium clearance normally exceeds potassium clearance (under normal diet and physical exercise)
e. Clearance concept has no clinical use, it is only used for academic purposes

Right answer → b

Discussion: $filtration\ fraction = \frac{GFR}{RPF}$, RPF= renal plasma flow
Inulin clearance measures GFR and PAH clearance measures RPL.

Q18: When the plasma concentration of glucose becomes higher than transport maximum (Tm):

a. Clearance of glucose exceeds inulin clearance
b. Excretion rate of glucose equals glucose filtered load
c. Reabsorption rate of glucose equals glucose filtered load
d. Excretion rate of glucose increases with increasing plasma glucose concentration

Right answer → d

Discussion: filtered load increases as plasma glucose concentration increases. And since we reached Tmax excretion rate will also increase.

37:00-44:00

THE END

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