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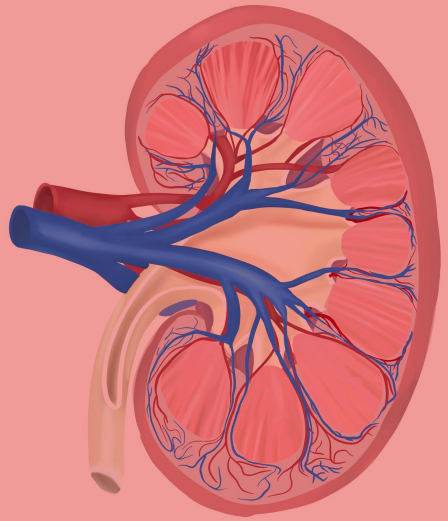
Chemical Examination of Urine



Color index :

Main text

IMPORTANT

Extra Info

Drs Notes

Renal Block - Biochemistry Team

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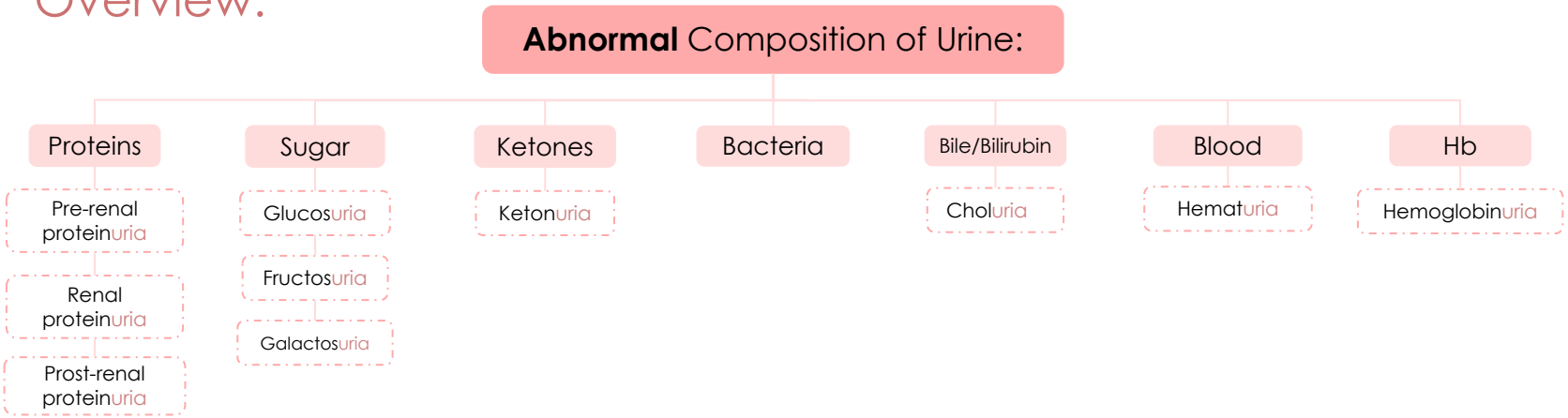
MED439

Objectives:

- To understand the normal and abnormal chemical composition of urine in relation to renal diseases and conditions
- Differentiate between normal and abnormal constituents of urine including: Proteins, sugars, ketone bodies, nitrite, bile pigments, blood etc.
- To differentiate between pre-renal, renal and postrenal proteinuria with clinical examples of each
- To acquire knowledge on the types of Glycosuria, hematuria and hemoglobinuria
- Know the clinical conditions in different types of proteinuria, blood urea and glycosuria etc.

Overview:



Urine

- Urine is a fluid excreted by most animals including humans.
- It is formed in the kidneys (renal glomeruli).
- The fluid undergoes chemical changes before it is excreted as urine.
- Normal urine excretion by a healthy person is about 1.5 L per day might differ depending on physiological or pathological reasons.

★ **Normal** Composition of Urine

Urine contain 95% water, and 5% solutes (organic and inorganic)

Major **organic** constituents:

It contains carbon & hydrogen

- Non-protein nitrogen (NPN) compounds e.g. urea, ammonia, creatinine.
- Organic acids : Compounds found as an intermediate in many pathways e.g. uric acid.
- Sugars "very small amounts" .
- Traces "means very small need unique machine to be indicated "of proteins, vitamins, hormones, pigments.

Major **inorganic** constituents:

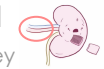
It doesn't contain carbon & hydrogen

- Sodium.
- Potassium.
- Chloride.
- Small amounts of Ca, Mg, sulfur and phosphates.
- Traces of Fe, Cu, Zn, I_2.

Proteinuria

- Normal urine contains small amount of protein "only traces" less than 200 mg/day.
- Excretion of more than this level causes proteinuria .
- Proteinuria : Excretion of abnormal amounts of protein in urine more than 200 mg/day .

Classification of proteinuria according to the etiology

- A) Pre-renal — Before the kidney 
- B) Renal — Within the kidney 
- C) Post -renal — After the kidney 

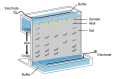
Proteinuria A) pre-renal 

- Some diseases or conditions increase plasma protein levels not involving the kidneys.
- Causes increased filtration of these proteins in the kidneys.
- This exceeds the normal reabsorptive capacity of renal tubules.
- Results in overflow of proteins in the urine. they haven't been reabsorbed due to their high concentration so they will be excreted with urine .

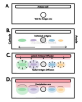
★ The most important example of it is Multiple myeloma .

Proteinuria A) pre-renal
"Multiple myeloma"

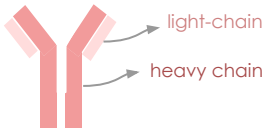
- Cancer (a proliferative disorder) of the antibody/immunoglobulin-producing plasma cells.
- Causes pre-renal proteinuria (keep in mind that antibodies are proteins).
- The serum contains elevated levels of light-chain monoclonal antibodies called Bence-Jones protein.
- This protein is filtered in the kidneys in high amounts and exceeding the tubular reabsorption capacity, hence excreted in the urine.
- Bence-Jones protein coagulates at (40–60)°C and dissolves at 100°C.
- Can be diagnosed by :



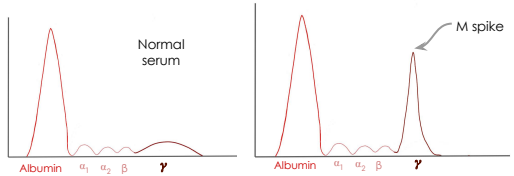
Serum electrophoresis



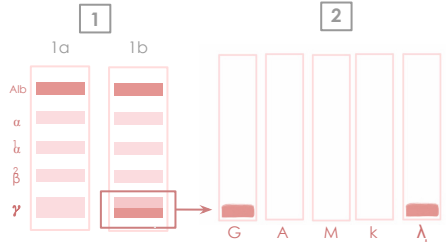
Immunoelectrophoresis
(immunofixation)



as we know the immunoglobulins specifically γ (gamma)- globulins are proteins & composed of 2 heavy and 2 light polypeptide chains.
We have heavy chains subtypes which are as we studied MAGED and 2 light chains subtypes which are K (kappa) and λ (lambda). Normally in our bodies light chains (K and λ) are excreted in the urine less than 10 mg/day , If it exceeds 10 mg/day we call it Bence-Jones protein.



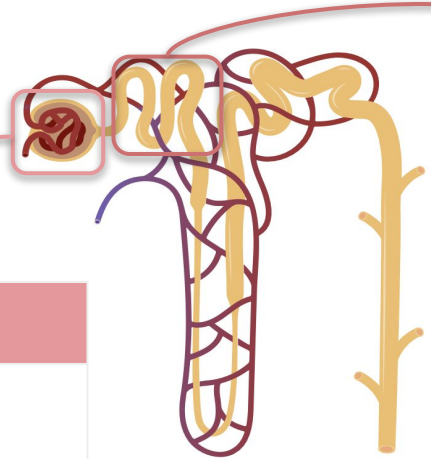
electrophoresis is a test that separates the plasma proteins components . So we can see the amount of each protein in the curve , normally the much abundant protein is albumin , and if we see a spike shape for γ - globulins in the curve we call it M spike " M stands for monoclonal which is cancer ", Keep in mind in this test we can't know which type of immunoglobulins and specifically which type of light chains in the serum that's why we need a specific test to know the type.



immunofixation test permits the detection of immunoglobulins in serum or urine by adding an antigen to the antibody and then precipitation occurs
So this test allow us to know which type of the immunoglobulin is present
1a : represents normal serum
1b : represents multiple myeloma showing Monoclonal component in the γ region.
2 : represents serum and urine immunofixation electrophoresis - in this patient the type Bence-Jones protein is **IgGλ**

Proteinuria B) Renal

Associated with renal disease



A) Glomerular proteinuria	
★ Definition	**High** glomerular permeability.
Pathogenesis	Causes filtration of high molecular weight proteins low and high molecular weight proteins are filtered because the pores of glomeruli are wide.
★ Example	Glomerulonephritis.

B) Tubular proteinuria	
Definition	**Low** tubular reabsorption with **normal** glomerular permeability.
Pathogenesis	excretion of low molecular weight proteins.
Example	chronic nephritis and can lead to renal failure.

Proteinuria B) Renal 

Not associated with renal disease

A) Orthostatic (postural) proteinuria

- **Definition:** A form of persistent benign or physiological proteinuria and occurs frequently in young adults.
- **Due to:** periods spent in a vertical posture (body position) or during muscular exercise and disappears in horizontal posture.
- **Pathogenesis:** increased pressure on the renal vein in the vertical position .
- **Diagnosed** : By taking urine sample after overnight sleeping .

B) Microalbuminuria

- **Definition:** Presence of small amounts of **albumin** in the urine 20–200 mg/L Normal range of albumin in urine (5-10 mg/day) .
- **Diagnosed by:** special tests for detection such as nephrometry or tergotometer because it can't be detected by ordinary urine testing like Electrophoresis .
- Early indicator of glomerular dysfunction. Due to:
  - Uncontrolled diabetes mellitus.
  - Hypertension.

If you have Microalbuminuria it doesn't mean that you have proteinuria

Proteinuria C) Post-renal 

- Proteins are added to the urine after kidney filtration While passing through the lower urinary tract (ureters, bladder, urethra, prostate, vagina).
- **Due to:**
  - Lower urinary tract infection most common .
  - Trauma.
  - Tumors.
  - Stones.

★ 2) Glycosuria

Presence of **sugar** in urine.

★ A) Glucosuria	B) Fructosuria	C) Galactosuria
Presence of: detectable amount of **glucose** in urine. normally the amount of glucose in the urine is **not detectable**	Presence of: **fructose** in urine.	Presence of: **galactose** in urine.
Causes:		
1) Diabetes mellitus: - Plasma glucose level exceeds the renal threshold. Renal threshold for glucose is: 180 mg/dL. Whenever plasma glucose exceeds 180 mg/dL, proximal tubule becomes overwhelmed and begins to excrete glucose in the urine. 2) Renal disease (renal glucosuria): - Normal plasma glucose level with proximal tubular malfunction. - Decreased renal threshold (so even someone with normal plasma glucose level can develop glucosuria) as observed in : 1) **Gestational diabetes** [1]. "سكر الحمل" 2) **Fanconi's syndrome** [2].	1) Nutritional/Alimentary: - High **fructose** intake. 2) Metabolic: Low amount of one of these enzymes in the liver : - Fructokinase [3]. - Aldolase B [3].	1) Nutritional/Alimentary: - High **galactose** intake like drinking too much milk. 2) Metabolic: Low amount of one of these enzymes in the liver : - Galactokinase [3]. - Galactose-1-PO_4 uridyl transferase [3].

So in case of Glucosuria we have 3 conditions :
- Plasma glucose level **exceeds** the renal threshold (I.e : Plasma glucose level higher than 180 mg/dL)
- **Decreased** renal threshold (E.g: when the renal threshold become 150 mg/dL)
- **Normal** plasma glucose level with proximal tubular **malfunction**. (I.e PCT can not reabsorb glucose back to the blood)

(1) condition in which a woman without diabetes develops high blood sugar levels during pregnancy.
(2) It can be inherited syndrome or due to lead poisoning. when the proximal convoluted tubule can not reabsorb amino acids and glucose anymore .
(3) These enzymes are involved in the metabolic (degradation) pathway of fructose or galactose .

3) Ketonuria

A helpful video

- Under normal conditions our body use glycogen as an energy source. but once the glycogen reserve is over, fatty acids from adipose tissue will undergo β-oxidation to produce acetyl CoA. After that acetyl CoA will undergo chemical reactions to produce ketone bodies which can be used to make energy for many tissues in our body.
- Types of ketone bodies : 1) acetone 2) acetoacetic acid 3) β-hydroxybutyric acid .
- Presence of: ketones, acetone, acetoacetic acid and β-hydroxybutyric acid in urine.
- Due to:

1. **Diabetic ketoacidosis**
   serious complication of type1 diabetes.
2. **Starvation**
   because you have consumed all the glucose and did breakdown all the glycogen in your body. Then you start to breakdown fatty acids to produce energy.
3. **Unbalanced diet:**
   high fat & Low CHO diet.
   In this case your body also will shift to breakdown fatty acid to produce energy.
4. **Phenylketonuria**
   inborn error of amino acid metabolism
   More details in Inborn errors of amino acid metabolism lecture.
5. **Prolonged vomiting**

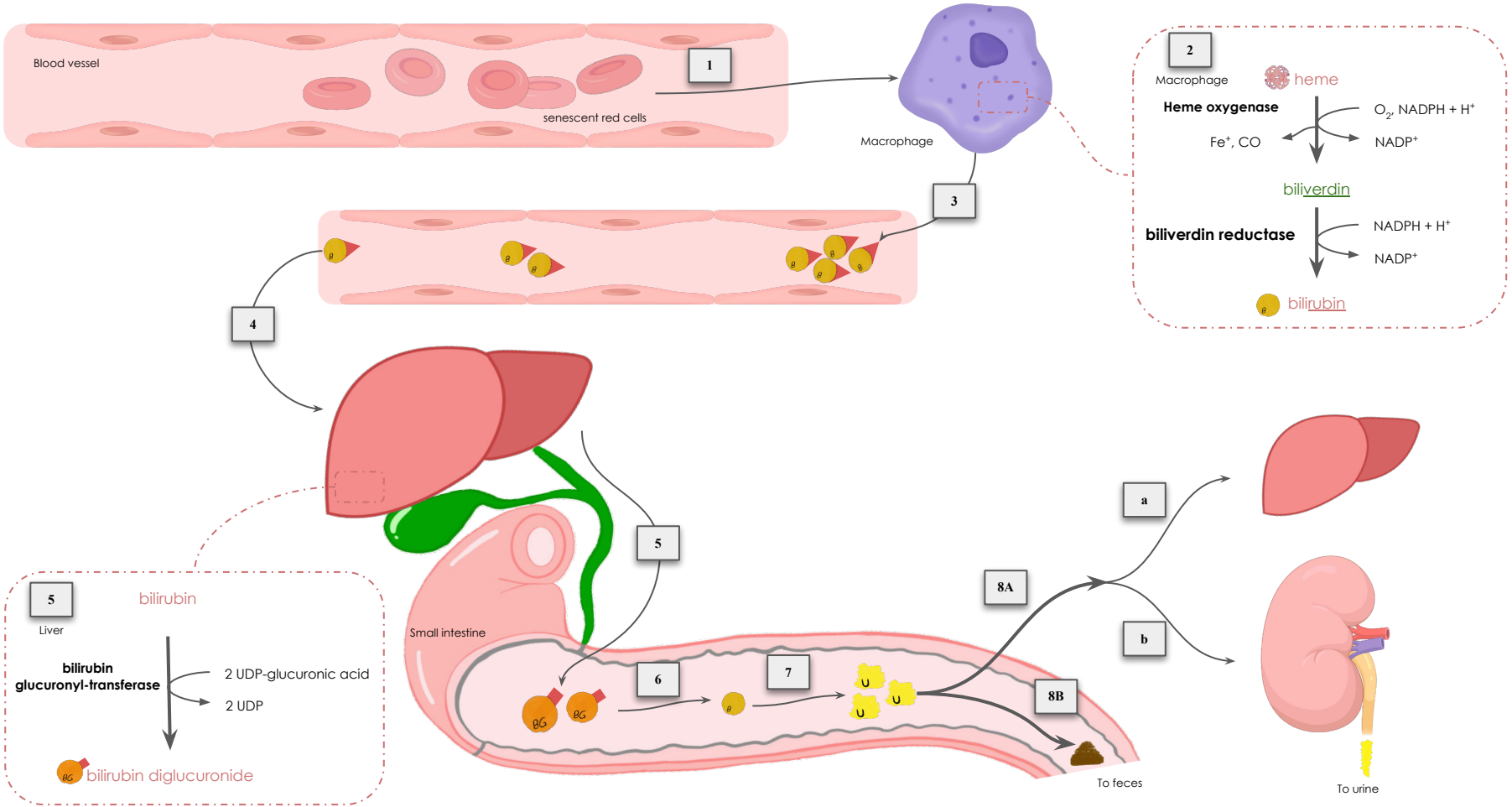
★4) Nitrites

- Positive nitrite test indicates **bacteria** in urine (bacteriuria).
- HOW ? Nitrate reduction to nitrite is catalyzed by nitrate reductases (NAR) in the bacteria.

original pic

Catabolism of heme

A helpful video



Catabolism of heme

In female slide only
But it was mentioned by males' dr
" it's just for you to gain a better understanding " :)

1. senescent (elderly) red cells are a major source of hemeproteins (rupture of RBCs lead to release of heme).

2. Breakdown of heme to **bilirubin** occurs in macrophages of reticuloendothelial system (include : tissue macrophages, spleen, and liver).

3. **Unconjugated** "water insoluble" **bilirubin** is transported through the blood (complexed to albumin) to the liver.

4. Bilirubin is taken up by the liver and conjugated with glucuronic acid.

5. **Conjugated** "water soluble" **bilirubin** (bilirubin diglucuronide) is secreted into bile and then the intestine.
   In other words, In the liver, bilirubin is processed, mixed into bile, and then excreted into the bile ducts. So obstruction of bile ducts will cause accumulation of bilirubin in the liver and blood causing more bilirubin to flow to the kidney.

6. in the intestine (drawn by the amazing Manal ♡) , glucuronic acid is removed by bacteria.

7. The resulting bilirubin in converted to **urobilinogen** .

However there are two fates of urobilinogen now:

8A. Some of the urobilinogen is reabsorbed from the gut and enters the portal blood ."Some enter the portal circulation where:"

   a. A portion of this urobilinogen participates in the enterohepatic urobilinogen cycle.

   b. the remainder of the urobilinogen is transported by the blood to the kidney, where it is converted to yellow **urobilin** and excreted, giving urine its characteristic color.

8B. Urobilinogen is oxidized by intestinal bacteria to the brown **stercobilin** .

Bilirubin converted into urobilinogen in the small intestine then travel to 1) large intestine 2) kidney 3) liver. Therefore damage in liver cell will cause more urobilinogen to remain in the plasma, thus being filtered in higher amount by the kidney.

5) Choluria

- Presence of bile, bilirubin and bile salts in urine.

A) Bilirubin / Bile salts :

- Normally **no** bilirubin is detected in urine.
- It is **detected** in:
  1) Hepatocellular damage
  2) Obstruction of bile duct "explained above" due to:
     - stones (extrahepatic)
     - hepatic tumors (intrahepatic)

B) Urobilinogen :

- Normally present in **trace** amounts.
- **High** urobilinogen is found in:
  1) Hepatocellular damage "explained above"
  2) Hemolytic anemia

	6) Hematuria	7) Hemoglobinuria
Presence of :	Detectable amount of blood in urine (not ruptured)	Hemolyzed blood in urine (ruptured RBCs)
Due to:	1) Acute / chronic glomerulonephritis. 2) Local disorders of kidney and genitourinary tract : - Trauma. - cystitis. - Renal calculi. - Tumors. 3) Bleeding disorders : - Hemophilia.	1) Malaria. 2) Hemoglobinopathies : - Sickle cell anemia. - Thalassemia. 3) Transfusion reaction : - Blood group incompatibility.

Quiz

Q1 : Bence-Jones proteins are _____ antibodies found in the Urine.			
A) Heavy chain	B) Light chain	C) Monoclonal	D) Both B&C
Q2 : All of these are major inorganic constituents in the urine except:			
A) Sodium	B) Potassium	C) NPN	D) Chloride
Q3 : _____ causes excretion of low molecular weight proteins.			
A) Tubular proteinuria	B) Glomerular proteinuria	C) Orthostatic proteinuria	D) Glucosuria
Q4 : Presence of detectable amount of glucose in urine ?			
A) Glycosuria	B) Galactosuria	C) Fructosuria	D) Glucosuria
Q5 : Positive _____ test indicates bacteria in urine ?			
A) Nitrate	B) Nitrite	C) nitrogen	D) IDK :)
Q6 : High urobilinogen can be found in case of ?			
A) stones	B) hepatic tumors	C) Obstruction of bile duct	D) Hemolytic anemia

SAQs :

Q1: List four major organic constituents of urine

Q2: List four causes of Post-renal proteinuria

Q3: List the causes of Glucosuria, and explain each one of them

Q4: list three causes of ketonuria

★ **MCQs Answer key:**

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

★ **SAQs Answer key:**

1) NPN, organic acids, sugars, vitamins

2) Lower Urinary tract infection, trauma, tumors, stones

3) check **slide 7**

4) Diabetic ketoacidosis, Phenylketonuria, starvation

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- Rania Almutiri
- Alia Zawawi
- Noura Alshathri
- Renad Alhomaidi
- Fatimah Alhelal

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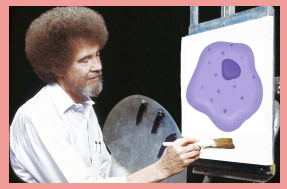
- Abdullaziz Alomar
- Hamad Almousa
- Abdullah Alanzan
- Abdullah Almazro
- Abdullaziz Alrabiah

"No one ever made a difference by being like everyone else"

Special thanks to **Duaa**



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