Biochemistry Team 435

جامعة الملك سعود
King Saud University 1957

CHEMICAL EXAMINATION OF URINE

"THE FOUNDATION STONES FOR A BALANCED SUCCESS ARE HONESTY, CHARACTER, INTEGRITY, FAITH, LOVE AND LOYALTY" –ZIG ZIGLAR

Color index:

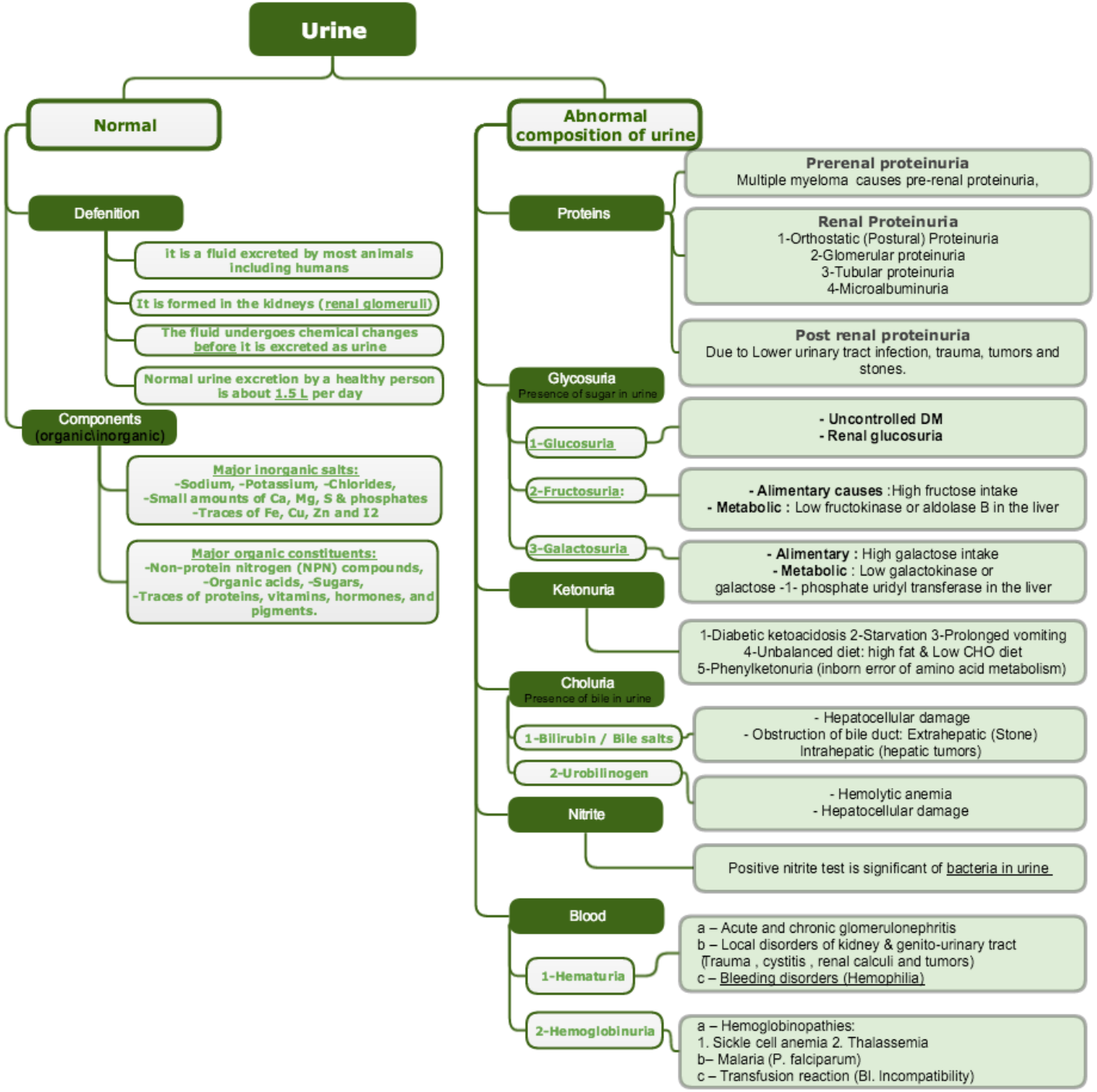
- Important.
- Doctors notes.
- Extra explanation.

*We advise you to study physiology "renal clearance" lecture, before studying this lecture .
** Please check out this link to know if there are any changes or additions.

OBJECTIVES:

- Differentiate between normal and abnormal constituents of urine including: Proteins, sugars, ketone bodies, nitrite, bile pigments, blood etc.

- Know the clinical conditions in different types of proteinuria, blood urea and glycosuria etc .



An overview mind map

Click here for a clear vision.

Urine

What is the urine ?

it 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 excreted by a healthy person:** 1.5L

COMPOSITION OF URINE :

Normal composition

Organic

1-Non-protein nitrogen (NPN) compound Content
2- Organic acids
3- Sugars
4- Traces of proteins, vitamins, hormones, and pigments

Inorganic

1- Sodium (Na) **(high concentration)**
2- Potassium (K)
3- Chlorides (Cl)
4- Small amounts of Ca, Mg, S & phosphates
5- Traces of Fe, Cu, Zn and I2

concentration

-traces: very small, need unique machine to be indicated
-The difference between organic & inorganic is presence of carbon in organic matters

abnormal composition

- Proteinuria
- Glycosuria
- Nitrite
- Choluria
- Blood

ظهور إحدى هذه الأشياء دليل على حدوث مرض، وهذا ماسنتحدث عنه في محاضرتنا.

1-Proteins:

- **Proteinuria :** the presence of abnormal quantities of protein in the urine, which may indicate damage to the kidneys, **more than** 200 mg/day .
- Normal urine contains **very little protein (< 200 mg/day)**

PROTEINURIA HAS THREE TYPES (ACCORDING TO THE ETIOLOGY) :

A- pre-renal.

before the kidney , there is some condition add proteins that protein filter to the urine.

B- renal .

kidney will produce the proteins.

C- Post-renal .

the urine excreted from the kidney will be clear then the proteins will be added to the urine after it passes the kidney .

Proteinuria

C- Post renal proteinuria

❖ **What is it?**

- It's proteins added to the urine as it passes through the structures of the lower urinary tract (**ureters**, **bladder** ,**urethra**, **prostate** and **vagina**)

❖ **Due to:**

Lower urinary tract infection (most common), **trauma**, **tumors** and **stones** of one of the lower urinary tract structures.

في حالة البوست-رينال : إضافة البروتينات لليورين تكون في التراكيب مابعد الكلية (بوست) ، وذلك بسبب عدوى للـ: Lower urinary tract أو أسباب أخرى.

A- Pre-renal : (kidneys are intact)

Some abnormal conditions increase plasma protein levels before reaching the kidneys --> so that cause increase in filtration of these proteins in the kidneys.

→ This exceeds the normal reabsorptive capacity of renal tubules.

→ Results in **overflow** of proteins in the urine

#Multiple myeloma causes pre-renal proteinuria:

Extra: what is "Multiple myeloma"?
It is a form of blood cancer that develops in the bone marrow. In multiple myeloma, normal plasma cells transform into malignant myeloma cells and produce large quantities of an abnormal immunoglobulin called monoclonal protein or M protein. The monoclonal protein produced by myeloma cells, interferes with normal blood cell production.

- **Multiple myeloma cases are diagnosed by using:**
  - **Serum electrophoresis**
  - **Immunoelectrophoresis**

❖ البلازما سيل راح تتكسر بصورة سريعة مما ينتج عن ذلك immunoglobulin و زي ما إحنا عارفين ال immunoglobulin يتكون من heavy chain and light chain طبعا ال heavy chain ما راح يصير له اخراج في البول لكن light chain راح يصير له اخراج في البول لانه اصغر)غالبا الايميونوجلوبلين لا يظهر ابدا في البول)

Light chains =Bence-jones proteins

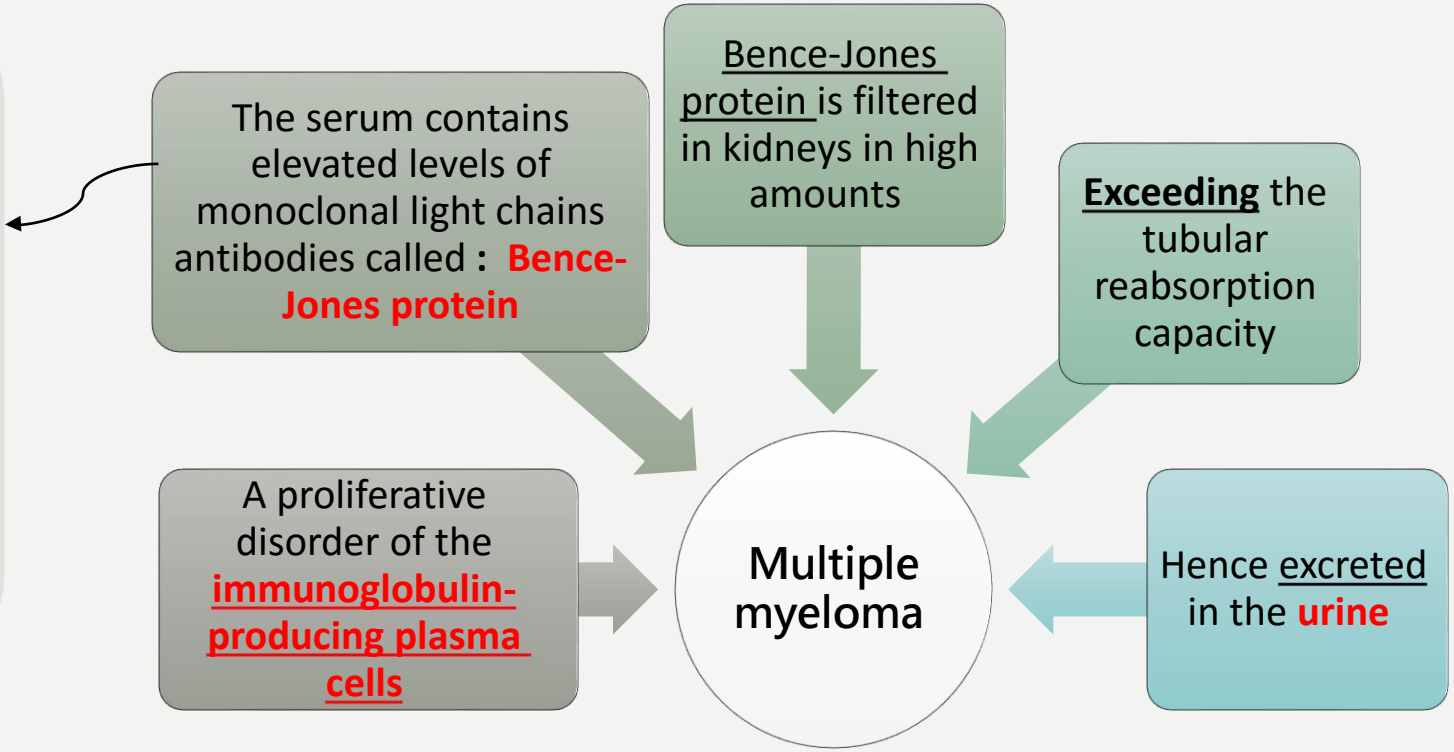
❖ The Bence-Jones protein:

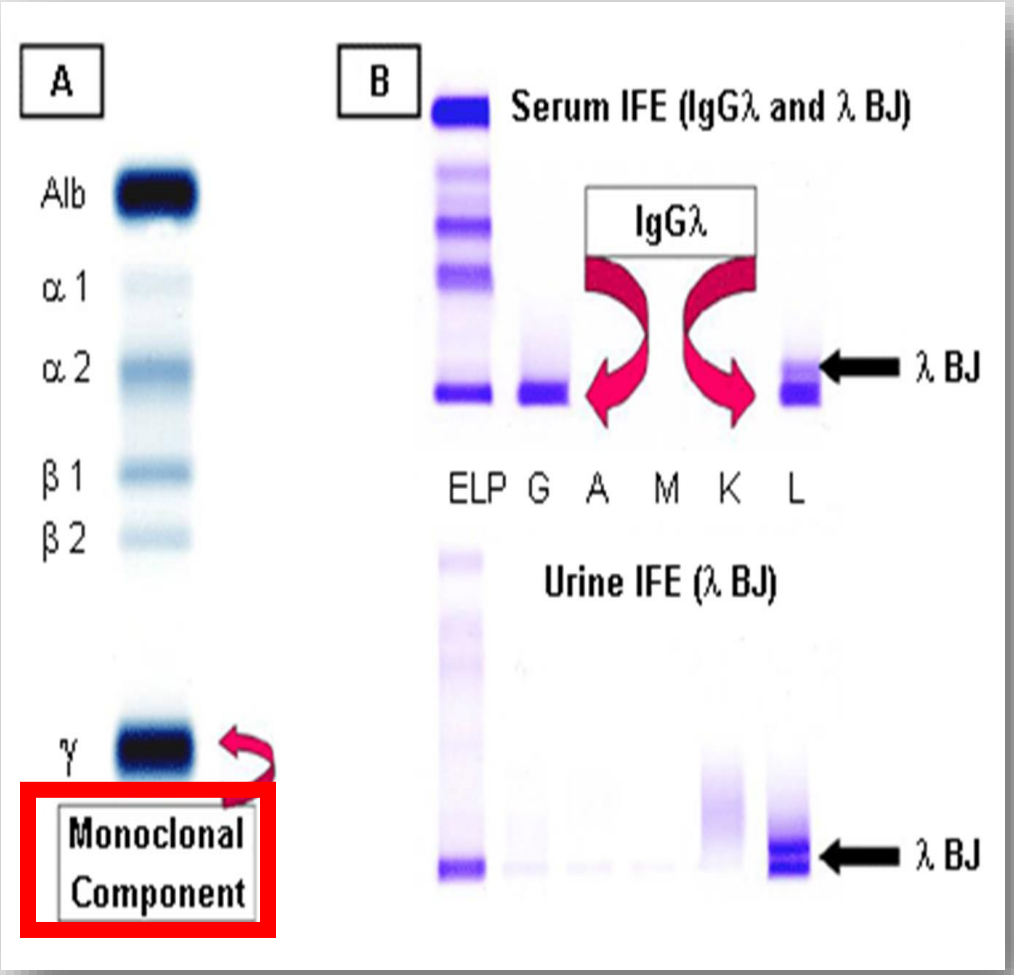
- **coagulate at** 40–60 °C
- **Dissolves at** 100 °C

It's like when you're boiling an egg, at high temperatures it will coagulate, but the difference here is that the egg cannot dissolve while the bence-jones proteins can dissolve at 100 °C.

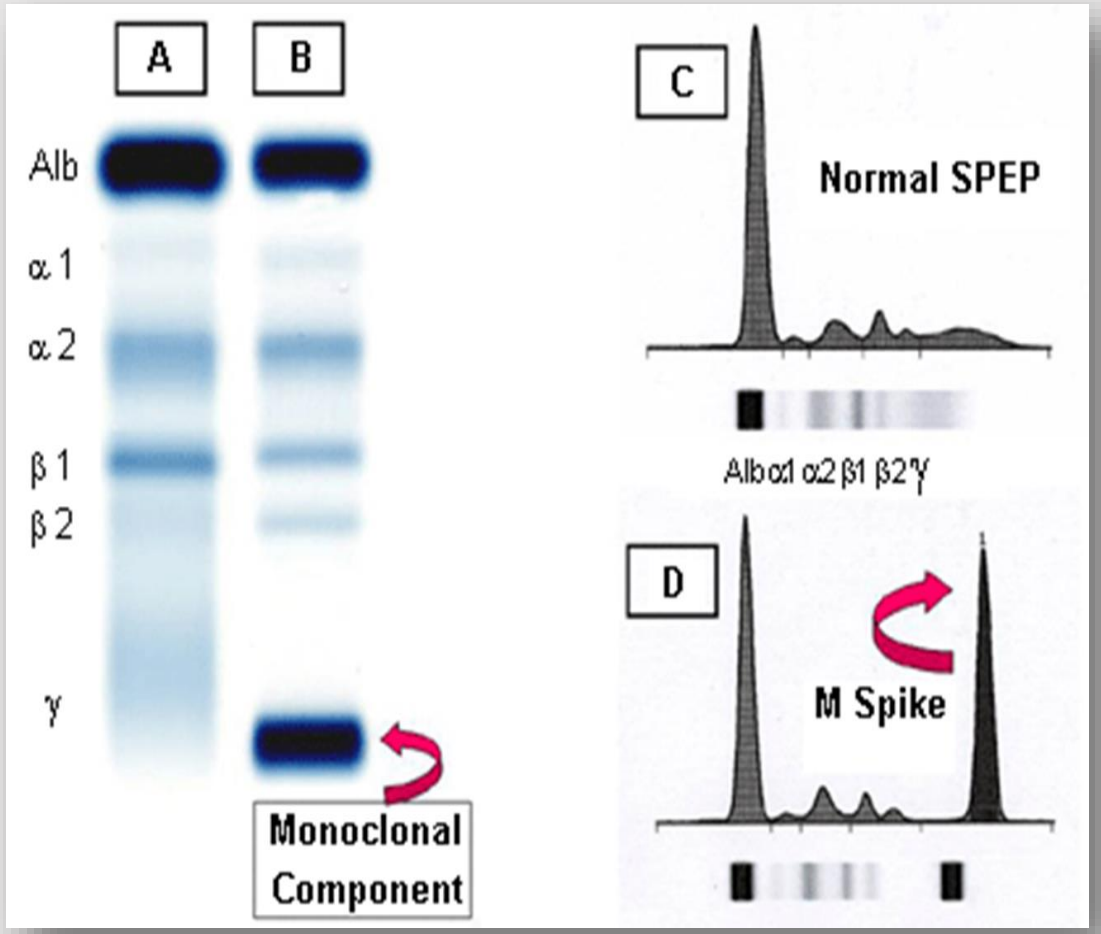
❖ Extra: **What is Bence Jones protein?**

It is a monoclonal globulin protein or immunoglobulin light chain (lamda light chain) found in the urine, with a molecular weight of 22-24 kDa. Detection of Bence Jones protein may be suggestive of multiple myeloma.





A: serum protein electrophoresis demonstrating the M component.
B: serum and urine immunofixation electrophoresis



the second spike in D indicate that there is multiple myeloma

A: normal serum.
B: multiple myeloma showing M component in the gamma region.
C: densitometry tracing of A showing the 5 zones of the high resolution agarose electrophoresis.
D: densitometry of the M component of B, termed the M Spike

B- Renal proteinuria"associated with renal diseases"

1-Glomerular proteinuria

-**glomerular permeability:** High

- Causes filtration of **high molecular weight** proteins

(e.g. glomerulonephritis)

لتسهيل الفهم:
نتخيل أن لدينا مصفاة ، هذه المصفاة كل مازاد حجم ثقوبها (اللي تمثل glomerular permeability) كل ما زاد حجم لأشياء اللي بتمر خلالها .

2-Tubular proteinuria:

- **glomerular permeability:** normal.
- **tubular reabsorption:** Low .

- Causes excretion of **low** molecular weight proteins .

(e.g. chronic nephritis)

3- Orthostatic (Postural) Proteinuria

4- Microalbuminuria

The chronic nephritis eventually leads to renal failure

Note:
It's important to differentiate between them especially :
in glomerular proteinuria we'll find high molecular protein.
in tubular proteinuria we'll find low molecular proteins.

B- Renal proteinuria"associated with renal diseases"

- 1-Glomerular proteinuria
- 2-Tubular proteinuria:
- 3- Orthostatic (Postural) Proteinuria
- 4- Microalbuminuria

What is it?

- A persistent benign protenuria. (type of renal proteinurea).

- it affects:

young adults (teanagers between age 14 and 19).

- **It happens due:**

periods spent in a vertical posture (it is found in young teenage boys after playing. they complain of having frothy or white dish in their urine).

- it's believed that the reason for this conditon is **the increase in orthostatic pressure on the renal vein** while the person is in the vertical position, and thus that will cause orthostatic proteinuria (by forcing the proteins to filtrate by the pressure).

- **It disappears in: horizontal posture**.

How can we diagnose it?

-they diagonse it by exclusion. (because they didn't find an exact hypothesis for it)

بمعنى إننا نستبعد كل الحالات المحتملة لهذه الاعراض وإذا مالقينا سبب فالسبب المرجح هو هذه الحالة

B- Renal proteinuria"associated with renal diseases"

- 1-Glomerular proteinuria
- 2-Tubular proteinuria:
- 3- Orthostatic (Postural) Proteinuria
- 4- Microalbuminuria

What is it?

- Presence of small amounts of albumin in the urine. (between 20– 200 mg/day)

*micro refers to the small amount, not to the size of albumin.

Note:
normal result: <20 mg/L
microalbuminuria: 20-200 mg/L
proteinuria: >200 mg/L

- How it's detected?

it needs **special tests** for detection, because It cannot be detected by ordinary urine testing.

Ordinary urine test = deep stick test

-What does it detect?

it is an Early indicator of glomerular dysfunction (renal impairment), due to uncontrolled **diabetes mellitus** or **hypertension**.

Note:
people with hypertension or diabetes should have this test each year. The test checks for signs of early kidney problems. Abnormal results may mean kidneys are starting to get damaged

- What is the benefit of it?

it is an early indicator of glomerular dysfunction which is reversible in early stages, thus if detected early, the dysfunction can be reversed.

2-Glycosuria "Presence of sugar in urine"

Glucosuria

Presence of detectable amount of glucose in urine

1-Uncontrolled Diabetes mellitus

The conc. of glucose in the plasma **exceeds** the renal threshold

2- Renal glucosuria

Normal plasma glucose conc. with a malfunction in **proximal tubule** leads to **decrease in renal threshold** e.g. gestational diabetes and Fanconi's syndrome (which affects the proximal tubules).

- Ordinarily, urine contains no glucose because the kidneys are able to reclaim all of the filtered glucose back to the blood stream.
- **The proximal tubule** can only reabsorb a limited amount of glucose. When glucose level exceeds that limit, the proximal tubule becomes overwhelmed and begins to excrete glucose in the urine (this is what happens in uncontrolled diabetes mellitus: the glucose levels are high while the threshold is normal).

- In renal glucosuria, there's a reduction in the blood glucose limit at which glucose begins to be excreted in urine (reduced threshold for glucose) and, in some instances, a reduction in the maximum rate at which glucose may be reabsorbed into the blood stream (TmG).

Fructosuria

Presence of fructose in urine
in fruit and honey

1- Alimentary

High fructose intake

2- Metabolic (congenital):

Low fructokinase or aldolase B in the liver

Galactosuria

Presence of galactose in urine
in milk

1- Alimentary

High galactose intake

2- Metabolic

Low galactokinase or galactose -1-phosphate uridyl transferase in the liver

3- Ketonuria

❖ **What is it?**

- Presence of ketones, acetone, acetoacetic acid & beta-hydroxybutyric acid in urine.

Causes:

- **Diabetic ketoacidosis** — the pancreas releases insufficient amounts of insulin or no insulin at all. Consequently, glucose goes largely undelivered. In a desperate attempt to provide fuel, the body begins feeding on itself -- that is, it breaks down muscle and fat to burn as fuel. Ketone bodies are a byproduct of this process.
- **Starvation**
- **Prolonged vomiting**

who can low CHO diet cause ketonuria?
limited consumption of carbohydrates switches the body's metabolism from metabolizing glucose as energy over to converting stored body fat to energy. This process, called *ketosis,* begins when insulin levels are low; in normal humans,insulin is lowest when blood glucose levels are low (mostly before eating). Reduced insulin levels inducelypolysis, which consumes fat to produce ketone bodies

- **Unbalanced diet** — high fat & Low CHO diet
- **Phenylketonuria** — inborn error of amino acid metabolism **(will be discussed in the last lectures)**

Ketonuria and glycosuria

Diabetic ketoacidosis : in type 1 diabetes : there's a defect in imsulin production → glucose can't be transported to the cell → aacumulation of glucose → no energy → burning fat as alternative pathway → "ketone bodies" as a result from fat metabolism.

Catabolism of heme –Extra- :

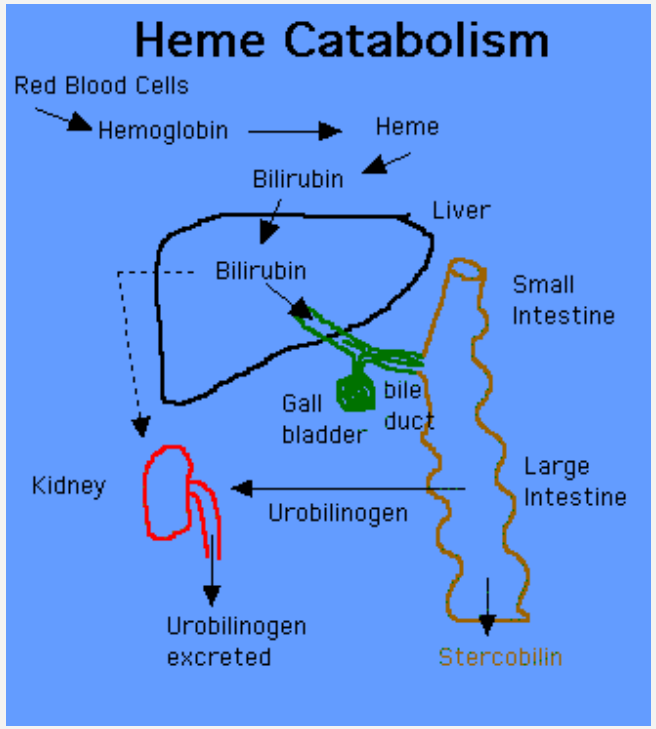
❖ The catabolism of hemoglobin is outlined in the graphic on the right:

- **Red blood cells** are continuously undergoing a hemolysis (breaking apart) process. the average life-time of a red blood cell is 120 days.

- As the red blood cells disintegrate, **the hemoglobin** is degraded or broken into globin, the protein part, iron (conserved for latter use), and heme.

- The heme initially breaks apart into **biliverdin**, a green pigment which is rapidly reduced to **bilirubin**, an orange-yellow pigment

- **The bilirubin** is then transported to the liver where it reacts with a solubilizing sugar called **glucuronic acid**. This more soluble form of bilirubin (conjugated) is excreted into the bile.



- **The bile** goes through the gall bladder into the intestines where the bilirubin is changed into a variety of pigments:

→ The most important ones are stercobilin, which is excreted in the feces,

→ + **urobilinogen**, which is reabsorbed back into the blood. The blood transports the urobilinogen back to the liver where it is either re-excreted into the bile or into the blood for transport to the kidneys. **Urobilinogen is finally excreted as a normal component of the urine (so normally it presents in the urine but in trace amounts!!! And high amounts can identify some diseases)**

4-Choluria :

❖ **What is a Choluria?**

Presence of bile in urine

	Bilirubin / Bile salts	Urobilinogen
What is it?	Presence of **bilirubin** in the urine, which **normally** (physiologically) not detectable in the urine. Remember: bilirubin resukts from breaking of RBCs	Presence of High amounts of urobilinogen, which is **normally** (physiologically) present in trace amounts in urine.
Detected in:	**1- Hepatocellular damage**	**1-Hemolytic anemia**
	2- Obstruction of bile duct: **- Extrahepatic (Stone)** **- Intrahepatic (hepatic tumors).**	**2- Hepatocellular damage.**

##5-Nitrite (not nitrate) :

Positive nitrite test is significant **of bacteria** in urine

why it is significant for urinary tract infection?

Bacteria that cause a **urinary** tract infection (UTI) make an enzyme that changes **urinary nitrates** to **nitrites**, So that's why **Nitrites in urine** show a UTI is present.

6-Blood :

	Hematuria	Hemoglobinuria
What is it?	**presence of detectable amount of blood in urine**	**Presence of hemolysed blood in urine**
Detected in:	**1-Acute and chronic glomerulonephritis**	**1- Hemoglobinopathies:** **- Sickle cell anemia** **- Thalassemia**
	2- Local disorders of kidney & genito-urinary tract (Trauma , cystitis , renal calculi and tumors)	**2- Malaria (P. falciparum),** Plasmodium falciparum is a protozoan parasite, one of the species of Plasmodium that cause malaria in humans.
	3- Bleeding disorders (Hemophilia).	**3- Transfusion reaction (Bl. Incompatibility).**

Hematuria

MCQs

1- The presence of intact RBC in urine is termed as:

A- hematouria
B- hemoglobinuria
C- Choluria

2 - One of the clinical presentations of hepatocellular damage is:

A- Urobilinogen
B- hemoglobinuria
C- glucosuria

3- A child was presented with Increased pressure on the renal vein in the vertical position and proteinuria

A- Multiple myeloma
B- Microalbuminuria
C- Orthostatic (Postural) Proteinuria

4- Which of the following is a normal major urine component :

A- Na
B- protein
C- glucose

5- In which case of proteinuria proteins have low molecular weight:

A. pre-renal
B. Post-renal
C. Tubular
D. Glomerular

6- In chronic nephritis:

A- high glomerular permeability.
B- Filtration of high molecular weight.
C- Low tubular reabsorption.
D- Low glomerular permeability.

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

MCQs

7-Multiple myeloma is a:

A- Pre-Renal proteinuria.
B- Renal proteinuria.
C- Post-renal proteinuria.
D- none of the above.

8- monoclonal band in the gamma region is present in which of the following diseases?

A- glomerulonephritis.
B- chronic nephritis.
C- Multiple Myeloma.
D- lower urinary infection.

9- In case of Lower urinary tract infection, which of the following can be founded in the urine ?

A- Post renal proteinuria.
B- Nitrate.
C- blood.
D- both A and B.

10-A patient with diabetes mellitus will most likely have:

A- kidney stones
B- proteinuria
C- inflamed tubules
D- glucosuria

11. In case of multiple myeloma the urine analysis will reveal traces of:

A- Bence-Jones protein
B- blood
C- color pigments
D- Bilirubin

12- the presence of nitrite in urine indicates:

A- hemolytic anemia
B- bacteria
C- PKU
D- hepatocellular damage

7-A
8-C
9-D
10-D
11-A
12-B

SAQs

❖ **A 40 years old male came to the clinic feeling loss of appetite, nausea, fatigue, chest pain and constipation. A blood test shows m protein and beta2 microglubin protein which are produced by myeloma cells.**

- What do you expect to find in urine?

M protein (Bence Jones) so it's proteinuria.

- What do you need to use to diagnose multiple myeloma?

Serum electrophoresis Immuno electrophoresis

- What do you expect to see in the kidneys?

Nothing. It is normal.

❖ **A woman came to the clinic with a bone pain, weakness and passing large amount of urine. Her blood sugar level is normal. She was diagnosed with Fanconi syndrome after some tests.**

- What do you expect to find in the urine?

Glucose

- What is the pathophysiology of her condition?

Glucose, amino acids, Na and many important molecules are reabsorbed in the proximal tubules before urine excretion. People with Fanconi syndrome have proximal tubule malfunction. So in urine analysis we see glucose.

- What other associated conditions come with Fanconi syndrome?

acidosis=due to poor bicarbonate reabsorption.

Hypokalemia=due to poor Na reabsorption so K shift from ICF to ECF

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Special thanks to our friend
Nouf Alabdulkarim ☺

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