النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Biochemistry

LEC NO. : 2

DONE BY : Batool ALzubaidi

وَقُل رَّبِّ زِدْنِي عِلْمًا

Biochem lecture 2 – GU

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Slides By

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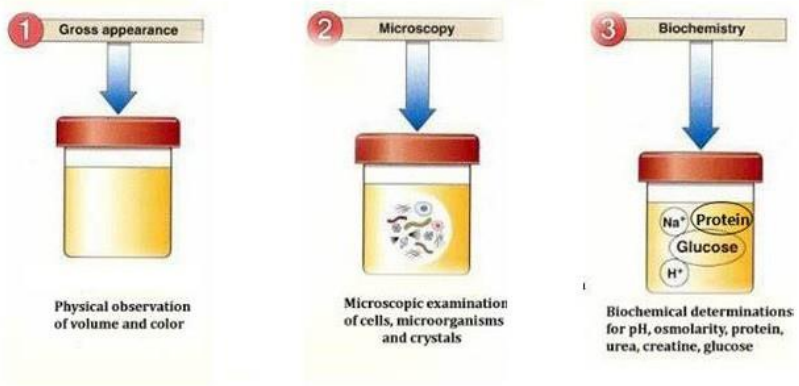
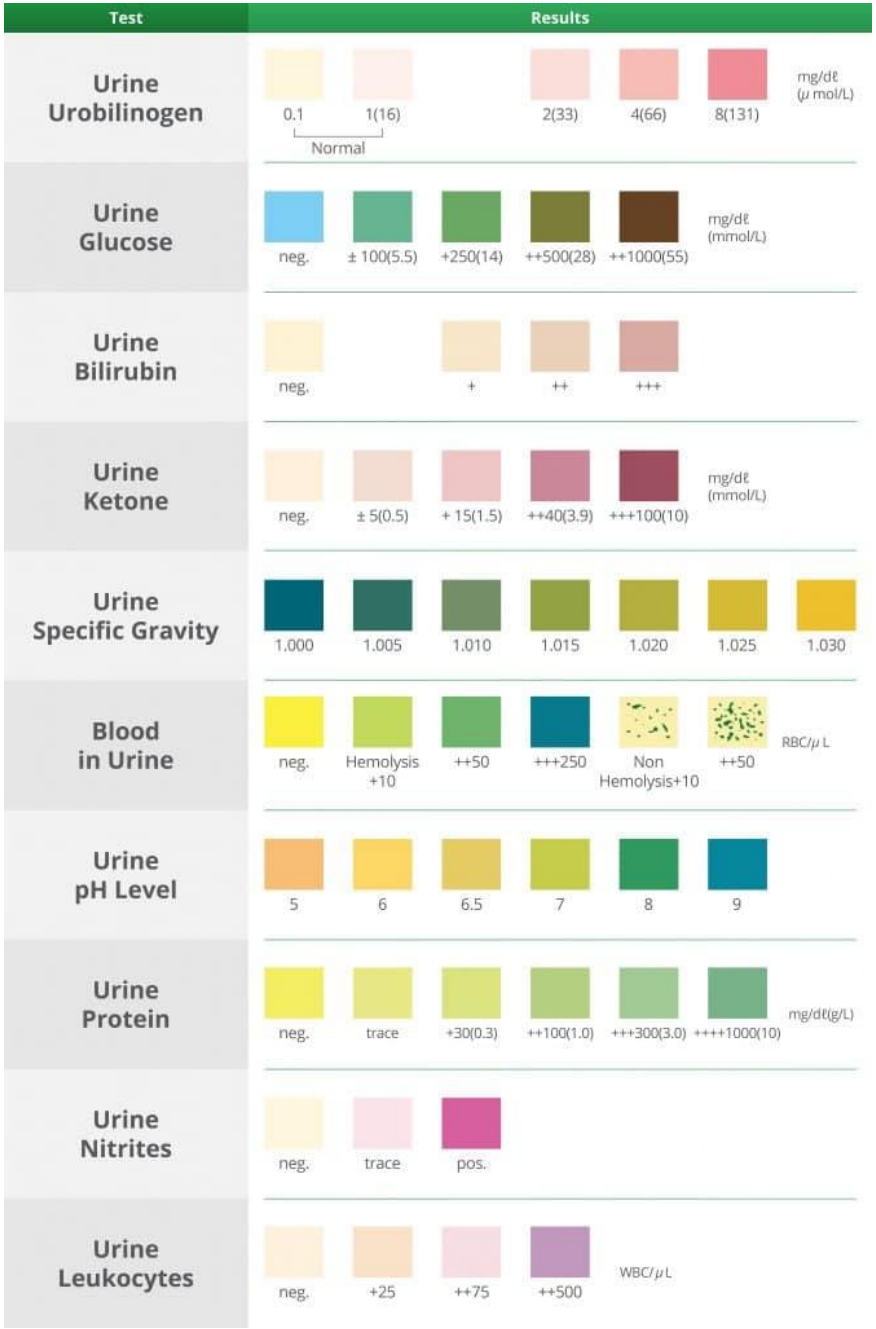
Full Urine Analysis (FUA)



* اول اشي بتطلع عليه grossly بعيني المجردة هل ال urine clear او turbid بعيدن بطلع microscopically بعدين بنحلل ال biochemical composition



The Factors Affecting The composition of Urine

- Diet and nutritional status
- Condition of body metabolism
- Kidney function
- Level of contamination with pathogenic microorganisms (bacteria) or even non-pathogenic microflora

sterile cup لازم نعطيه urine analysis اي حدا بده يعمل

1.3 The Composition of Urine

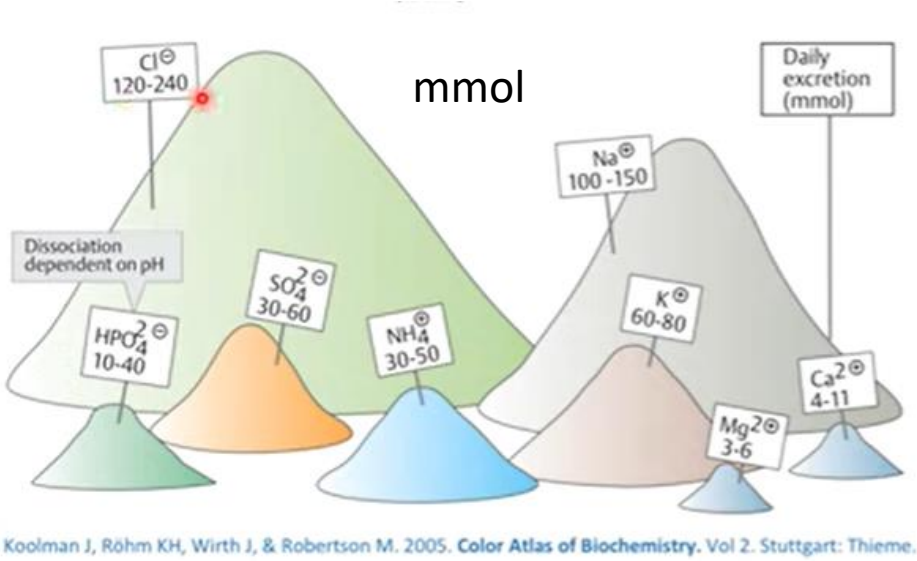
Normal Urine Constituents	Abnormal Urine Constituents
- Water (about 95% of urine)	- Glucose
- Urea	- Protein
- Creatinine	- Bile pigments
- Uric acid	- Blood cells

✽اي اشي بنسبة قليلة بكون طبيعي و لما يزيد بشكل كبير بصفي abnormal مثلا النسبة الطبيعية لل glucose بالدم ٢٠٠ لو زادت عن هيك راح يصير يطلع ال glucose بال urine

TABLE 23.2	Properties and Composition of Urine	
Physical Properties		
Specific gravity	1.001–1.028	
Osmolarity	50–1,200 mOsm/L	
pH	6.0 (range 4.5–8.2)	
Solute	**Concentration***	**Output****
Inorganic Ions		
Chloride	533 mg/dL	6.4 g/day
Sodium	333 mg/dL	4.0 g/day
Potassium	166 mg/dL	2.0 g/day
Phosphate	83 mg/dL	1 g/day
Ammonia	60 mg/dL	0.68 g/day
Calcium	17 mg/dL	0.2 g/day
Magnesium	13 mg/dL	0.16 g/day
Nitrogenous Wastes → Organic substances		
Urea	1.8 g/dL	21 g/day
Creatinine	150 mg/dL	1.8 g/day
Uric acid	40 mg/dL	0.5 g/day
Urobilin	125 µg/dL	1.52 mg/day
Bilirubin	20 µg/dL	0.24 mg/day

✱الي عليهم هايلايت حكى عنهم اهم اشي

✱ال ph بشكل عام بكون acidic بس بختلف بشكل عام حسب وضعية الجسم هل هو acidosis or alkalosis لانه ال kidneys احد الاعضاء المسؤولة عن ال acid base balance بالجسم



Koolman J, Röhm KH, Wirth J, & Robertson M. 2005. **Color Atlas of Biochemistry.** Vol 2. Stuttgart: Thieme.

COMPOSITION OF URINE

- Normal urine contains about 50 g of solids dissolved in about 1.5 L of water per day.

The chief organic solids are:

(1) NPN compounds → Non protein nitrogenous compounds » area & amino acids

(2) Organic acids

(3) Sugars

The chief inorganic solids are :

(1) Chloride, (2) Sodium, (3) Potassium, (4) Phosphate, (5) Ammonia

I. NPN COMPOUNDS

- The non-protein nitrogenous (NPN) compounds include:
  - Intermediary (amino acids and creatine)
  - End products (urea, uric acid, and creatinine)

  of protein metabolism

Energy storage in muscles

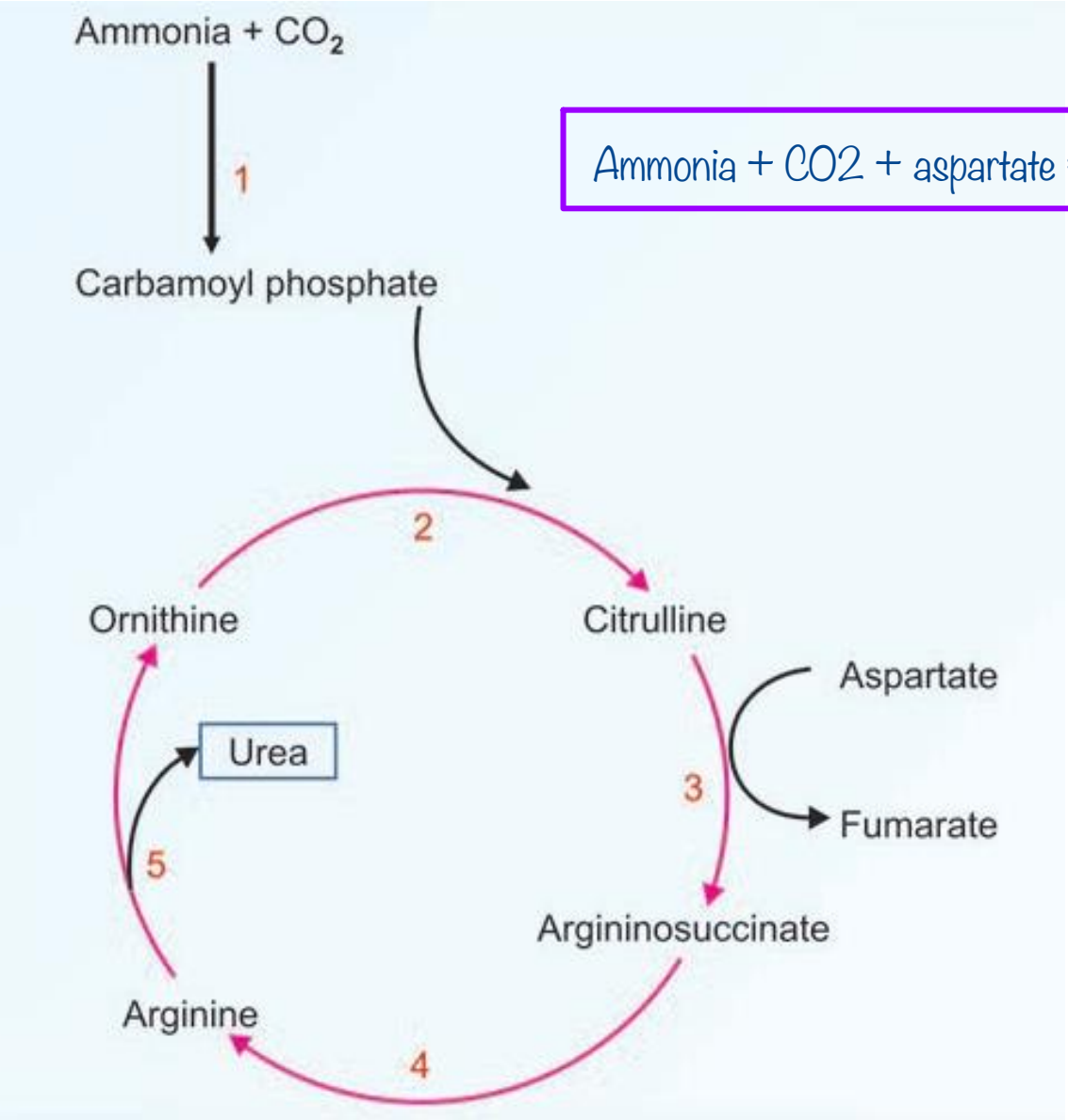
From purine metabolism

From creatine metabolism

- The total urinary NPN is on average **25g**/ day

A. Urea

- Urea is the chief end product of protein metabolism in human
- It is formed in the liver from the ammonia resulting from the deamination of the amino acids
- It is excreted by the kidneys in the urine
- Its excretion in the urine is more directly affected by protein intake & catabolism than other nitrogenous compounds, which tend to remain relatively constant



Ammonia + CO2 + aspartate = urea + fumarate

- Urinary urea is normally 12-25, **average 21 g/day**

- ↑ urinary urea:
  - high protein diet
  - increased protein catabolism (fevers, DM, Cushing syndrome and hyperthyroidism)
    - + Uncontrolled cancer

Because urea is the end product of protein metabolism so if input increased output will increase too

Uncontrolled

- ↓ urinary urea:
  - low protein diet
  - increased protein anabolism (pregnancy and lactation)
  - liver failure (decreased formation)
  - acute renal failure (due to retention)

Of area from ammonia

B. AMINO ACIDS

- 80% of excreted AA in urine are conjugated amino acids:
  - glycine with benzoic acid (found in berries, other fruits)
  - glutamine with phenylacetic acid (found in drugs, BB)

- 20% are free amino acids (escape reabsorption)

- The total urinary amino acid nitrogen normally varies between 0.5-1.0, average 0.7g/day.

Increased urinary amino acids (aminoaciduria)

1. Decreased Deamination of Amino Acids:

- Liver failure:
  - deamination of amino acids and urea formation ↓
  - → generalized aminoaciduria

    ↳ All amino acids will be execreated in urine
- Specific aminoacidurias:
  - Caused by defective metabolism of specific amino acids
  - eg., phenylketonuria causes increased excretion of phenylalanine in the urine

2. Inability of the Kidneys to reabsorb Amino Acids:

+ inability to reabsorb glucose and phosphate

- In severe nephritis & Fanconi syndrome (PCT problem) the kidneys fail to reabsorb **all** amino acids → generalized aminoaciduria

- Cystinuria: kidneys fail to reabsorb cystine, ornithine, arginine and lysine (**COLA**) leading to their excretion in the urine.

سال سؤال ليش هدول ال amino acids بالذات و حكى دوروا عليها راح تيجي بالامتحان

بحثت و حطيتلكم الجواب تحت

* The common chemical property shared by cystine, ornithine, arginine, and lysine is that they all contain amino groups, which are basic in nature. This makes them polar and hydrophilic molecules, meaning they have an affinity for water. Additionally, they all have relatively large side chains compared to other amino acids, which contributes to their poor solubility in urine when present in high concentrations. These properties make them prone to precipitation and crystal formation, particularly in conditions like cystinuria where their reabsorption by the kidneys is impaired.

3. Ingestion of certain toxic substances:

- These include:
  - benzoic acid (conjugated with glycine) — In fruits
  - phenylacetic acid (conjugated with glutamine)
  - Bromobenzene (industrial solvent; conjugated with cysteine)

* What is the difference between cysteine and cystine?
Cystine is a dimer of cysteine (2 cysteine)

→ excretion of large amounts of these amino acids in the urine

Ammonia (inorganic):

* ال ammonia ككمية بتخزنلك النيتروجين مقابل ال urea هي ولا اشي

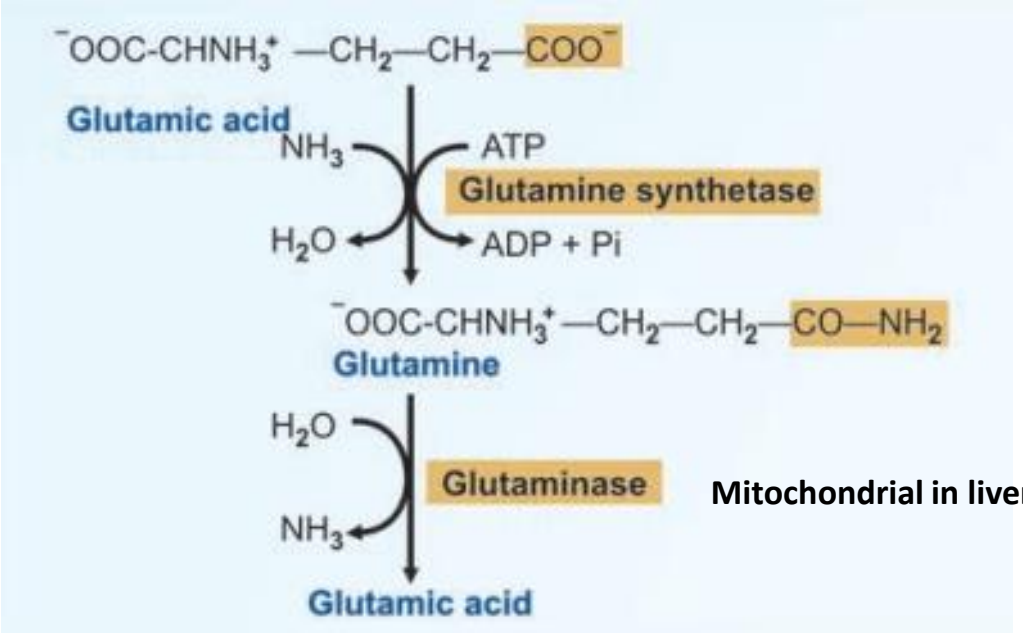
- **Urinary** ammonia is synthesized in the distal convoluted tubules

* كمية النيتروجين الي بتنزل بال urine بالوضع الطبيعي بدون acidosis هي قليلة

  - 60% are produced by the action of the enzyme **glutaminase** on the glutamine received by the kidneys from other tissues

  - 40% are produced by the deamination of other amino acids in the kidneys

Ammonia trapping as glutamine



Glutamate is critical to intracellular AA metabolism

Glutamate synthetase: mitochondrial enzyme, high concentration in brain, liver & kidney

Mitochondrial in liver, kidney

✽ بتعمل trapping لل hydrogen ions و بتسمحلك تعمل acidification لل urine اكتر

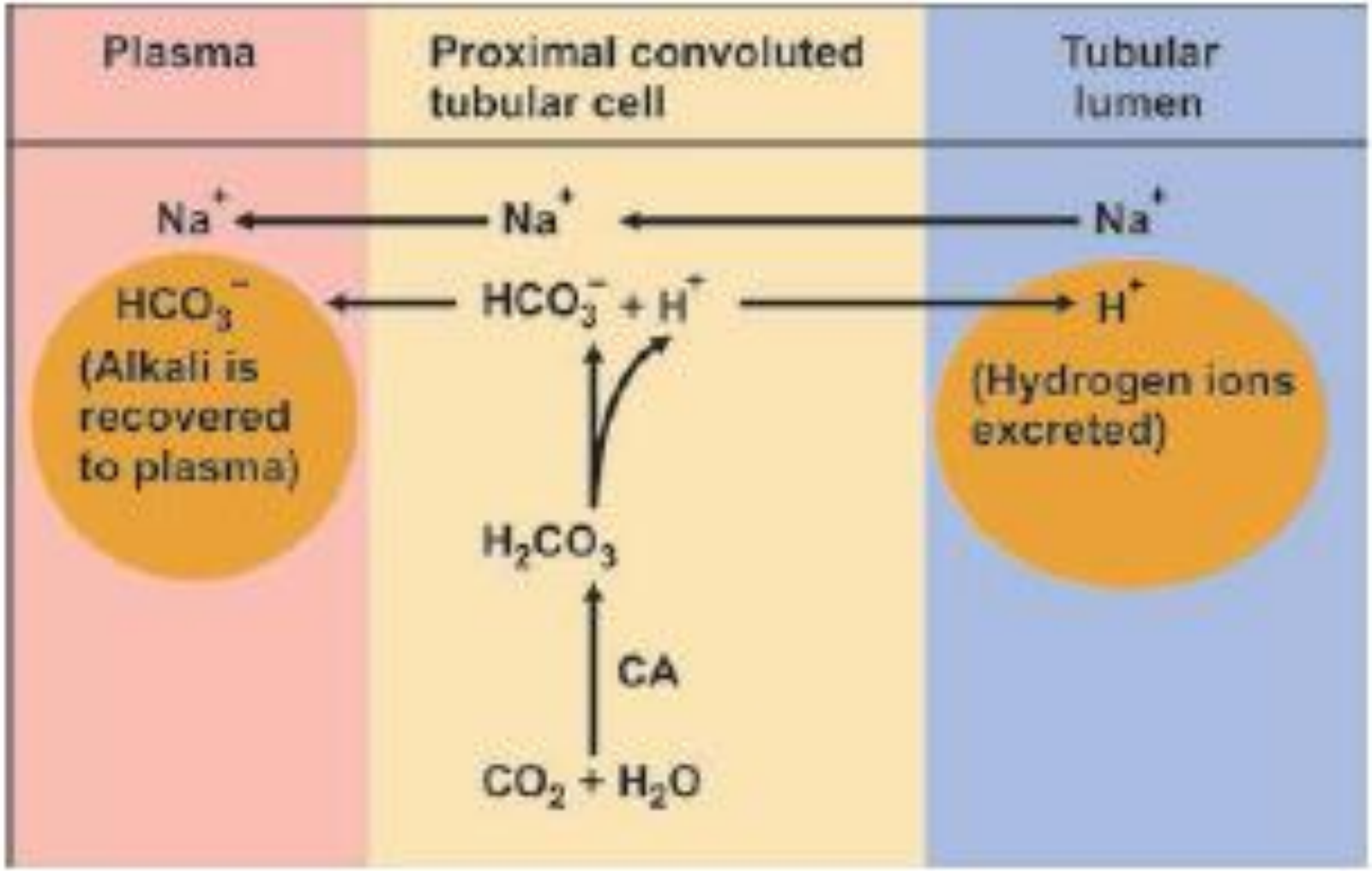
- Urinary ammonia appears to be entirely concerned with the acid-base balance

  - In conditions of acidosis → reabsorption of Na^+ by $Na^+ : H^+$ exchange occurs to a limited extent being stopped when the pH of the glomerular filtrate becomes 4.8

    حكى بتوصل ل 4.4

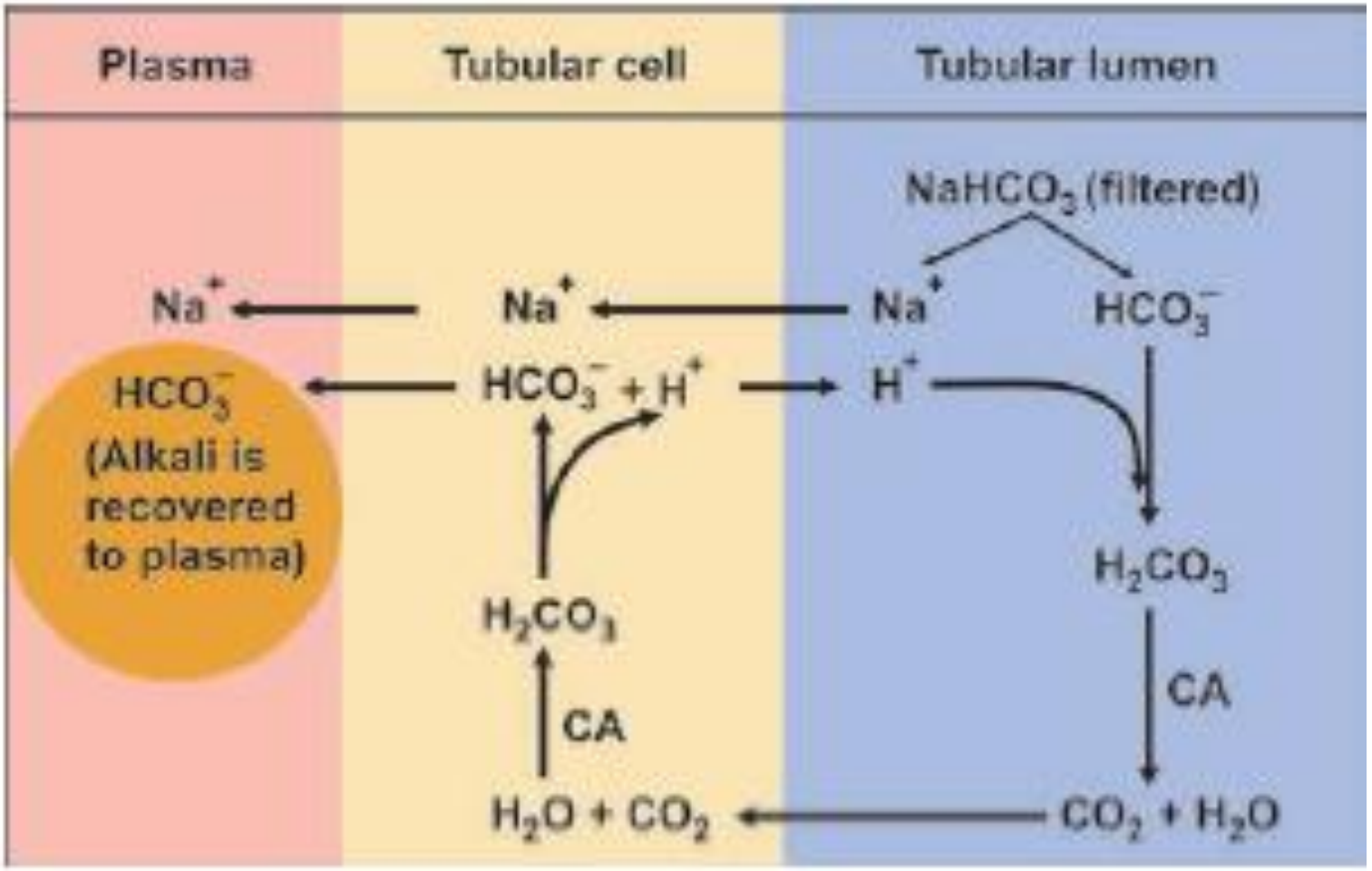
  - Ammonia is secreted by the distal convoluted tubules to neutralize this high acidity allowing $Na^+ : H^+$ exchange to continue and the alkali reserve to be regained

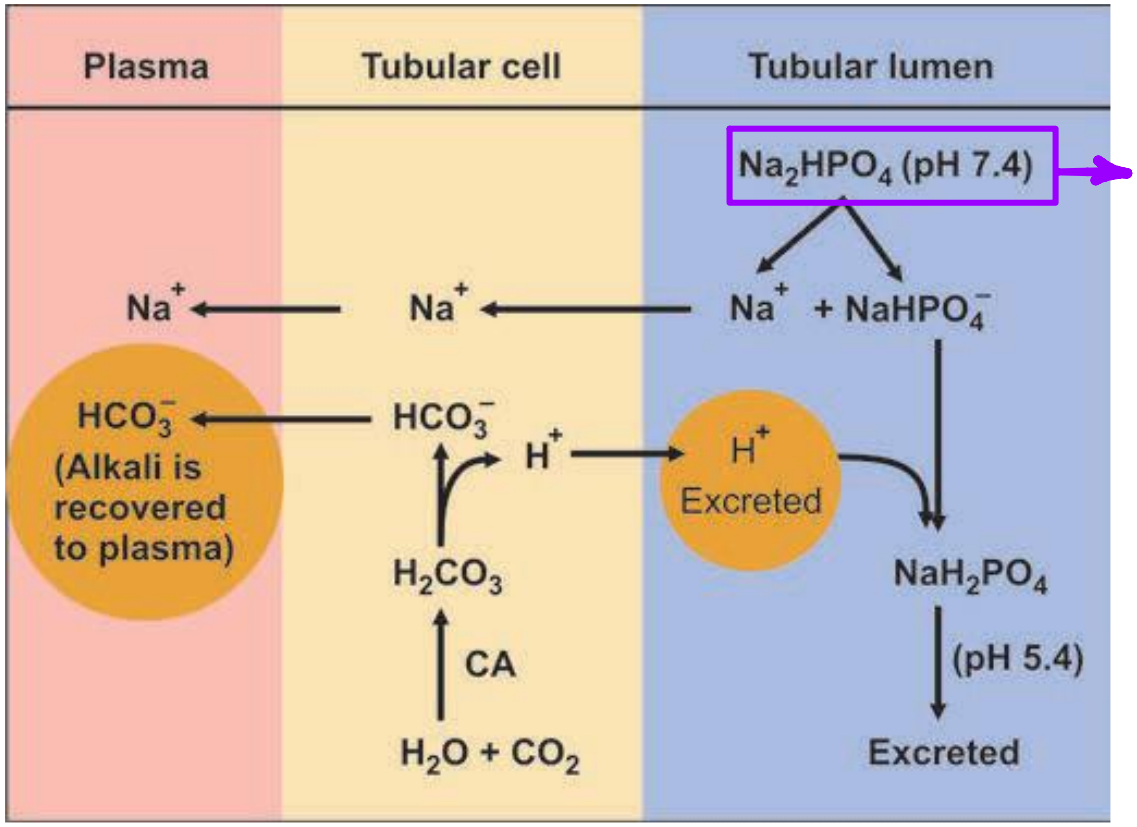
✽احنا عنا 2 buffers ال phosphate and ammonia، ال phosphate buffer بعمل trapping للهدروجين و بالتالي تعمللها excretion و لكن هاد ما بشتغل الا باتجاه ph معينة ما بقدر ينزل تحتها فبعدها بستلم ال ammonia ك trapping mechanism



✱بال proximal convoluted tubules بصير عنا excretion لل hydrogen ions و reabsorption لل HCO3-

*كل ما مشينا باتجاه ال distal convoluted tubules بتختلف الامور شوي بس الي بنهتمله هون انه عندي 2 buffers





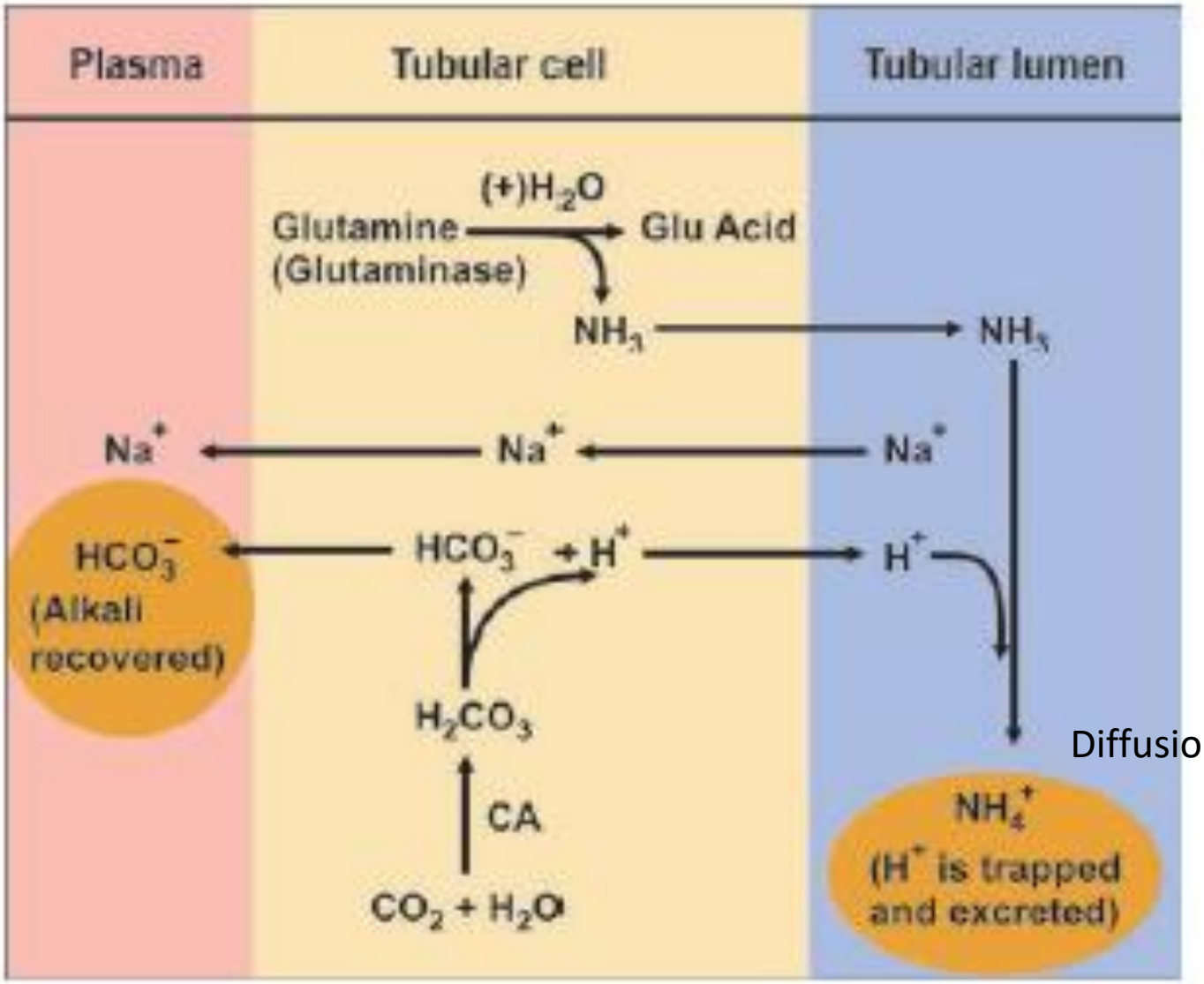
* هاد لما يمسك معه hydrogen ion بتحول ل acidic phosphate و هيك بكون phosphate buffer

لانه سمحلنا نعمل trapping للهيدروجين + سمحلنا نعمللهم excretion بال urine و تنزل ال ph

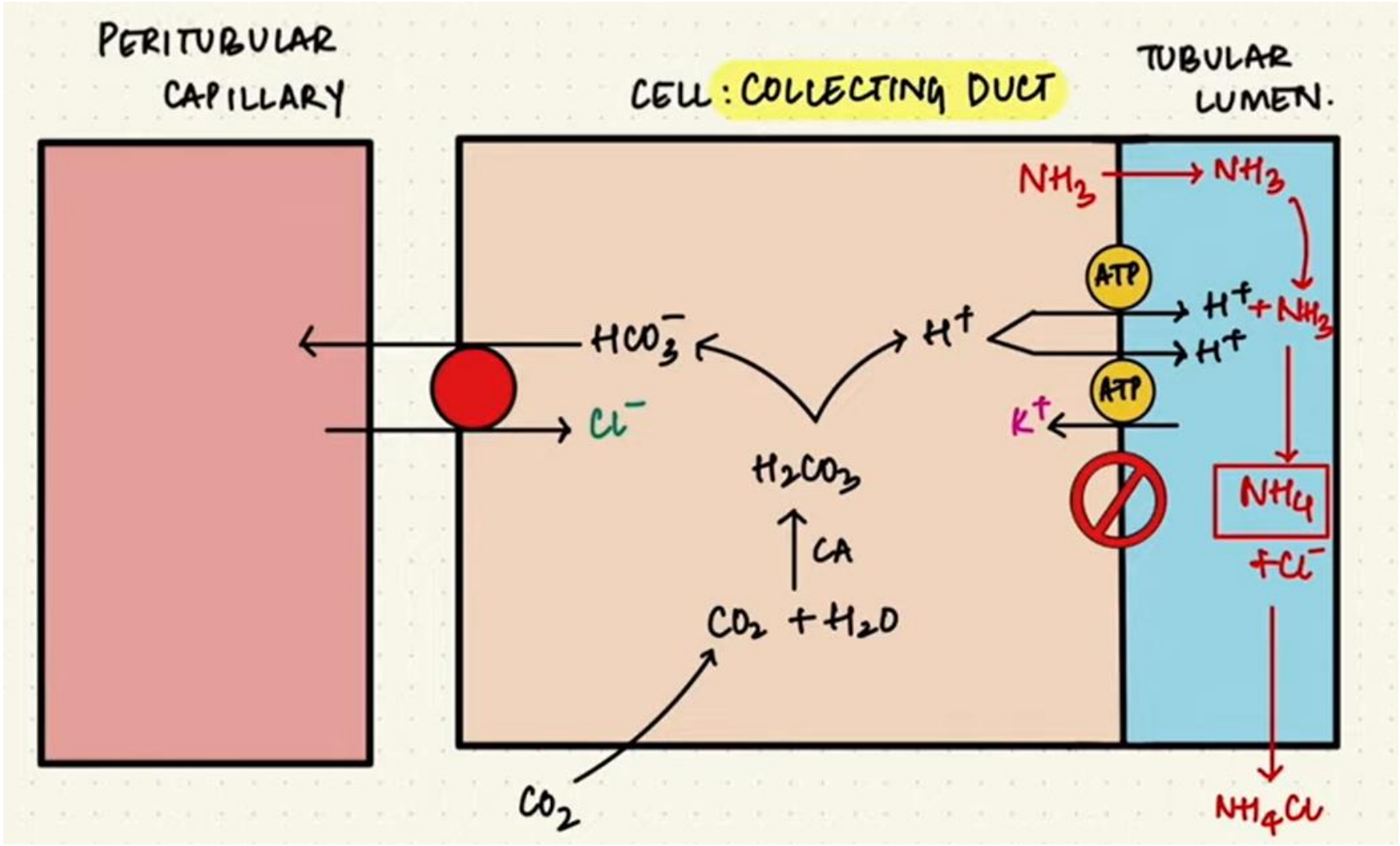
تاعت ال urine لرقم معين يعني اله حد معين للشغل و بعد هيك ما بقدر يشتغل

*هون ال buffer التاني الي هو ال ammonia لما يصيرلها secretion لل tubular lumen راح تعمل trapping لل hydrogen ions

و تكون ammonium و بعدها اعمل excretion للهدروجين بال urine و هاي الطريقة بتنزل ال ph تاعت ال urine ل 4.4



Diffusion trapping


PERITUBULAR CAPILLARY
CELL : COLLECTING DUCT
TUBULAR LUMEN.
NH_3
NH_3
ATP
$H^+ + NH_3$
H^+
HCO_3^-
H^+
ATP
Cl^-
K^+
H_2CO_3
NH_4
$+Cl^-$
CA
$CO_2 + H_2O$
CO_2
NH_4Cl

- Urinary ammonia is normally 0.3 - 1.2, average **0.7 g/day**

✱في انواع بكتيريا بتشتغل على ال urea الموجودة بال urine و بنتج عنها ammonia هاد هو سبب ال smell in unclean bathrooms

- ↑ Urinary ammonia:
  - Acidosis (up to 10 g/day)
  - Hydrolysis of urea by bacteria either in the bladder (cystitis) or if the urine sample is stored without preservative → Infections
- ↓ Urinary ammonia:
  - Alkalosis (almost absent)
  - Severe nephritis:
    - ↓ capacity of the kidneys to deaminate amino acids

Response to acidosis

- The enhanced activity of glutaminase and increased excretion of NH_4 takes about 3-4 days to set in under conditions of acidosis

- But once established, it has high capacity to eliminate acid

  ↳ Because kidney can increase amount of excreted ammonia ten times

- Normally, about 70 mEq/L of acid is excreted daily; but in condition of acidosis, this can rise to 400 mEq/day

II. Organic Acids

A. Oxalic acid

- Urinary oxalic acid is mostly exogenous, being derived from foods containing oxalates (spinach, artichokes, tomatoes, strawberries, mangoes, apricots and peaches)

- A small part is endogenous, being derived from the metabolism of glycine or from the metabolism of ascorbic acid

  → Vitamine C » water soluble

- Very small amounts of oxalates are normally excreted in the urine (10 - 30 mg/day), mostly in the form of calcium oxalate

- ↑ urinary oxalates (hyperoxaluria) may be dietary or the intake of large amounts of vitamin C. It also occurs in an error in glycine metabolism called "primary hyperoxaluria"

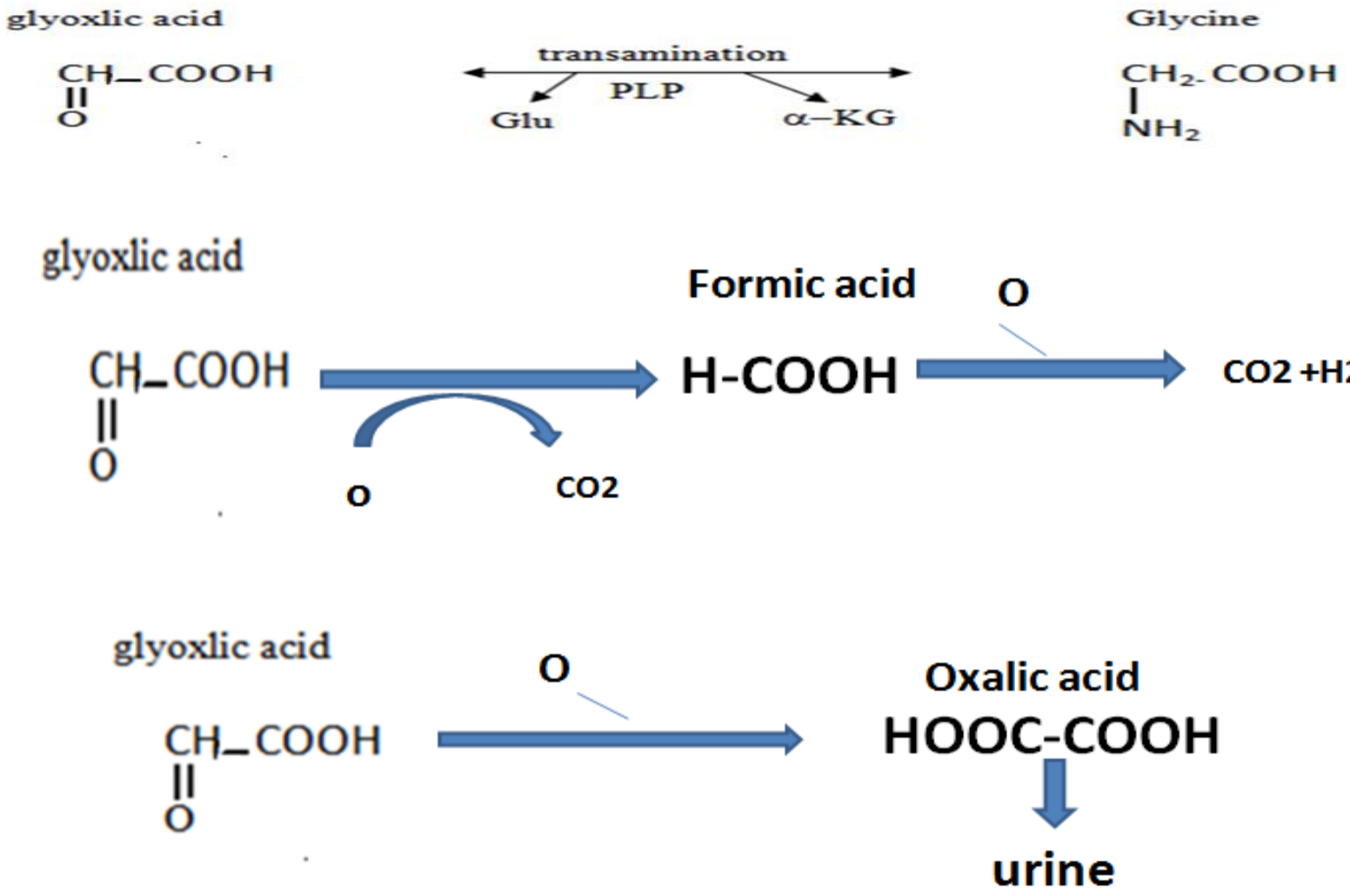
- Hyperoxaluria leads to the formation of calcium oxalate stones in the renal tract.

  → Resulting in renal colic

Primary hyperoxaluria:

- Congenital disease caused by decreased metabolism of glyoxylic acid either by:
  - oxidative decarboxylation to formic acid
  - transamination to glycine → Simplest amino acid
- Accumulated glyoxylic acid is oxidized to oxalic acid
- There is excretion of large amounts of oxalate in urine
- Oxalate reacts with calcium forming the insoluble Ca-Oxalate → leads to the formation of Ca-Oxalate stones

Fate of glyoxylic acid



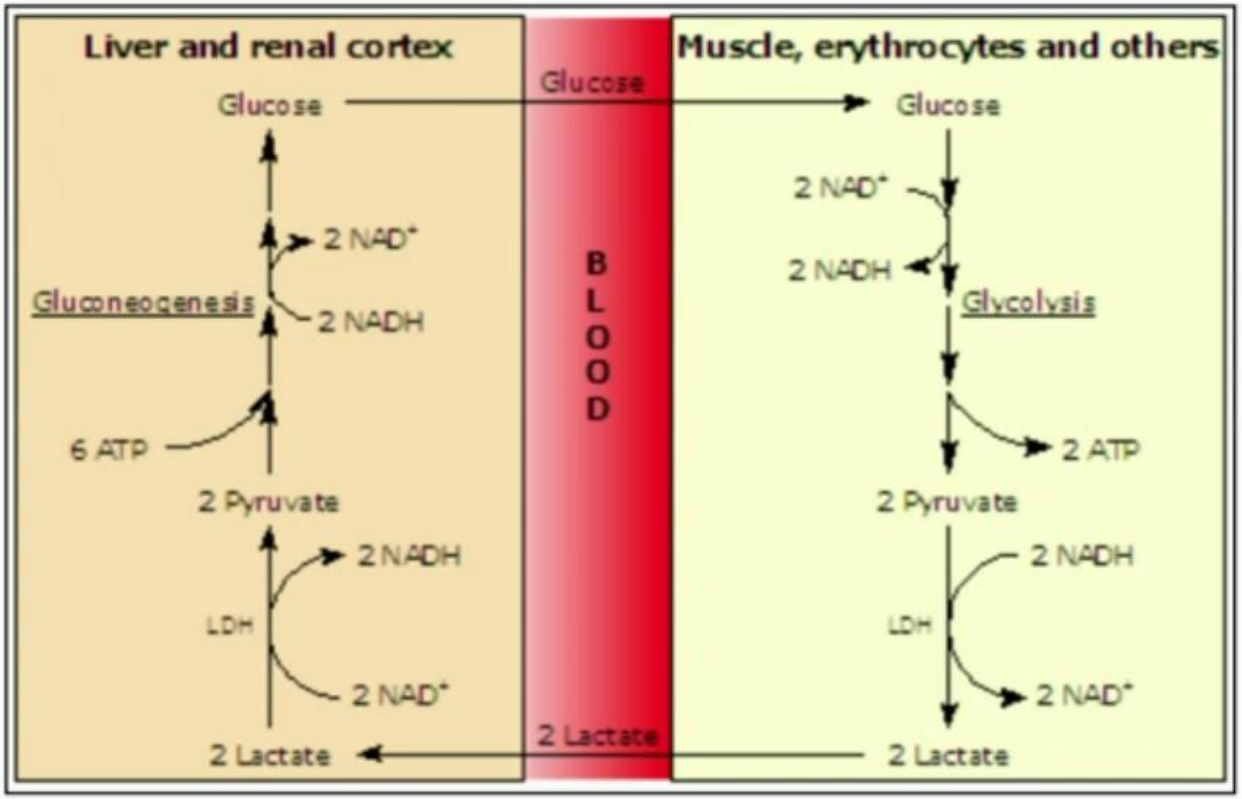
B. Lactic acid

- Lactic acid is the end product of glycolysis in erythrocytes and in muscles during exercise
  - Cori cycle » transforms lactate to pyruvate then to glucose
- It mostly goes to the liver where it becomes converted to glucose
- Little lactic acid is excreted in the urine (50 -200 mg / day)

C. Citric acid

- The citric acid in urine is mostly derived from intermediary metabolism
  - Little amounts in urine is normal
- Some citric acid is excreted in the urine 200-1200 mg/day

Cori Cycle


Liver and renal cortex
Muscle, erythrocytes and others
Glucose
Glucose
Glucose
2 NAD+
2 NADH
Gluconeogenesis
Glycolysis
BLOOD
2 NAD+
2 NADH
6 ATP
2 ATP
2 Pyruvate
2 Pyruvate
2 NADH
2 NADH
LDH
LDH
2 NAD+
2 NAD+
2 Lactate
2 Lactate
2 Lactate

D. Ketone bodies:

*They increase in uncontrolled diabetes (diabetic ketoacidosis)

- The ketone bodies include: acetone, acetoacetic acid, and β-hydroxybutyric acid

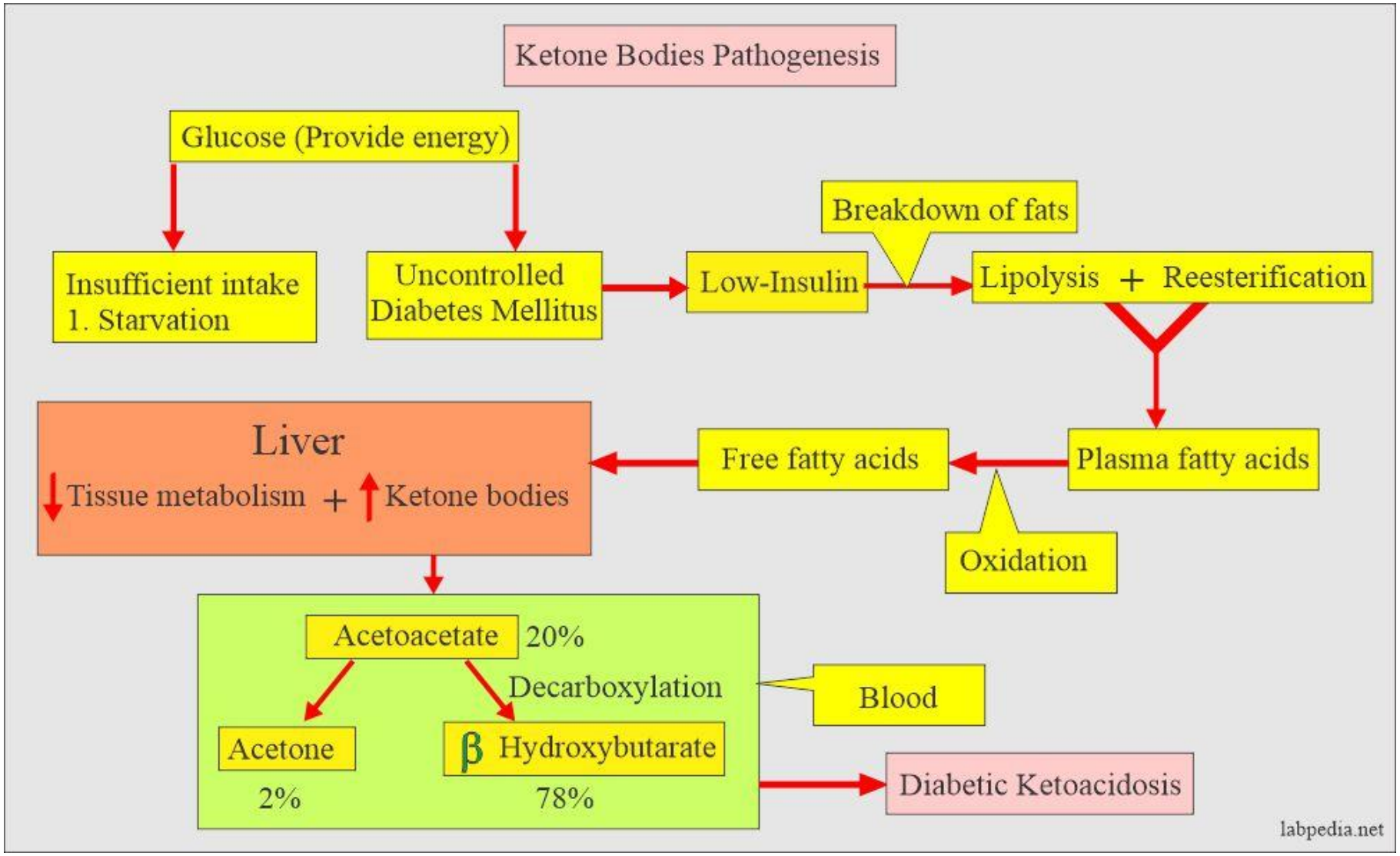
*اذا كان ال ketone bodies عالي افحص glucose اذا كمان عالي معناها السبب diabetic ketoacidosis اما لو ال glucose صفر بكون السبب starvation

- They are formed in the liver as intermediates in the metabolism of fatty acids

*Presence of ketone bodies in urine » starvation (no carbohydrate intake) or someone with diabetic ketoacidosis

- Small amounts of ketone bodies (less than 15 mg/day on an average diet, and up to 100 mg/day on a high fat diet), mostly β -hydroxybutyric acid, are excreted in the urine

- Their excretion markedly increases in ketosis


Ketone Bodies Pathogenesis
Glucose (Provide energy)
Insufficient intake
1. Starvation
Uncontrolled
Diabetes Mellitus
Low-Insulin
Breakdown of fats
Lipolysis + Reesterification
Liver
Tissue metabolism + Ketone bodies
Free fatty acids
Plasma fatty acids
Oxidation
Acetoacetate 20%
Decarboxylation
Acetone
2%
β Hydroxybutarate
78%
Blood
Diabetic Ketoacidosis
labpedia.net

E. Hippuric Acid

- Hippuric acid is the product of detoxication of **benzoic acid**, by conjugation with **glycine**
- Benzoic acid is present in many fruits and vegetables, especially in plums and prunes
- It is used as preservative in some food products, such as jams and ketchup
- It also results from the action of intestinal bacteria on phenylalanine
- The amount of hippunc acid excreted in the urine is related to the dietary intake of benzoic acid as well as to intestinal putrefaction
- It normally ranges between 0.1 and 1.0 g/day

III. Sugars

- Normally not more than 1 g of sugars is excreted in the urine per day

Sugar acid

- The chief sugar is glucuronic acid (about 0.5 g/day). which is present in urine conjugated with xenobiotics

بس ما ببينوا بالفحص

- In addition, smaller quantities of glucose , lactose, and L-arabinose may be present in urine.

Pentose sugar present is some fruits like burries and grapes, one of the few sugars in L form naturally

Xenobiotics are foreign organic substances, which are substances not normally metabolized in the body. Xenobiotics of medical importance include drugs, toxins, food additives.

IV. Proteins

- Urine of normal subjects contains small amounts of glycoproteins, which are derived from the mucous glands of the renal tract. Tracts of albumin (< 30 mg /day) are excreted in urine. They cannot be detected by the heat coagulation test.

ABNORMAL CONSTITUENTS

I. Proteinuria :

- This is the presence of detectable amounts of proteins in the urine. It may be:

A- Prerenal Proteinuria

1. **Albuminuria:** This occurs in heart failure due to increased renal venous pressure

2. **Bence Jones Proteinuria:** this is an abnormal globulin, composed of light chains only (22–24 kDa), formed by malignant plasma cells (multiple myeloma)

3. **Myoglobinuria:** Myoglobinuria occurs in crush syndrome and in myocardial infarction due to release of myoglobin from crushed skeletal muscles and heart, respectively

4. **Hemoglobinuria:** Hemoglobin appears in the blood plasma and in the urine if intravascular hemolysis occurs, e.g,, in hemolytic anemia and in malaria

Collapsed building from 1985 Mexico earthquake.
Earthquakes are a main cause of crush syndrome

B-Renal Proteinuria

- This is due to kidney affection

- Albumin, having a **higher plasma concentration** and a **lower molecular weight**, appears in the urine in higher concentrations than globulins, and hence the name albuminuria.

1. False Albuminuria (Functional Albuminuria):

- This is not pathological; no organic lesion is detectable in the kidneys. It is intermittent, occurring only when the renal venous pressure increases, e.g., during muscular exercise and on assumption of the erect posture (orthostatic), and disappears on lying down. Thus, it is absent in the morning sample, and only present in the day samples.

2. Microalbuminuria:

- Albumin is detected by ordinary tests only if urinary albumin exceeds 200 mg/d
- Levels between 20 and 200 mg/L, called microalbuminuria, can only be detected by special tests
- It is an early sign of glomerular affection in uncontrolled diabetes mellitus

3. True Albuminuria :

- This is pathological
- It is more commonly due to lesions of the renal glomeruli (e.g. glomerulonephritis)

B-Postrenal Proteinuria

- This is caused by inflammation, tumors, or stones of the renal tract, leading to the secretion of mucus and the passage of blood (albumin, globulins, and hemoglobin) in the urine.

II. Glycosuria:

- This term has long been used to indicate the presence of detectable amounts of glucose in the urine

- More properly, it should be used to indicate the presence of any sugar in the urine, these include glucose, fructose, galactose, pentoses, or lactose.

اخر تلاتة بس ذكر اساءهم ذكر

III. Chyluria

- Chyluria is the presence of absorbed fat (chylomicrons) in the urine
- It rarely follows the ingestion of large amounts of fats, particularly in severe diabetic patients (decreased clearance of chylomicrons and VLDL due to decreased activity of lipoprotein lipase)
- It may also be caused by an abnormal connection between the intestinal lymphatics and the urinary tract
- This may be congenital and may be caused by filariasis
- The urine acquires a milky appearance that disappears upon shaking with ether

IV. Choluria

- Choluria is the appearance of bile in the urine. It includes:

1. Bilirubin and Bile Salts: Bilirubin and bile salts appear in the urine in obstructive Jaundice
    - due to obstruction of the biliary passages and regurgitation of bile into the blood

2. Urobilinogen: Urobilinogen is normally present in the urine in very small amounts (less than 4 mg/day)
    - It markedly increases hemolytic jaundice

V. Ketonuria

- Ketonuria is the presence of delectable amounts of ketone bodies in the urine.

✱ هون عنا اسئلة و cases من الدكتور ✱

هون عنا probably urine
infection ال WBC عنا عاليين
كتير و بهاي الحالة بتسال عن ال
symptoms الي عنده، كمان ال
appearance مكتوب hazy و هاد
sign of infection، ال ph
طبيعية .. شو بنعمله ؟ لو كان
لاول مرة ما في داعي نعمل
culture بعطيه simple antibiotic
اذا كان عنده recurrent UTI
بعمل culture

Urine Analysis :

colour	: Pale yellow.	Protein	: Negative
Appearance	: Hazy	Glucose	: Normal
Specific Gravity	: 1.020	Bilirubin	: Negative
Reactin,PH	: 5	Urobilinogen	: Normal
Nitrite	: Negative	W.B.C./Epithelial	: +3
Ketone	: Negative	R.B.C./HB	: Negative

MICROSCOPY

W.B.C	: 350	Normal Range :Up to 10x10^6/L Normal Range :Up to 5x10^6/L
R.B.C.	: 5	
Epithelial cell	: Not Seen	
Mucus	: Not Seen	
Cast	: Not seen	
Crystals	: Not seen	

Comments :
Bacterial cells seen

هاد نفس المريض اعطيناه
antibiotic و عملناله كمان
تحليل، اول اشي بنلاحظ اللون
اختلف من pale yellow ل
yellow يعني قل شرب المي، ph
طبيعية، ال WBC نزلوا شوي
فوضع المريض عم يتحسن، في
شوية crystals بنصحه يزود
شرب المي لانه مش شرط يكونوا
واصلين مرحلة ال stones

Urine Analysis :

colour	: Yellow	Protein	: Negative
Appearance	: Hazy	Glucose	: Normal
Specific Gravity	: 1.020	Bilirubin	: Negative
Reactin,PH	: 6	Urobilinogen	: Normal
Nitrite	: Negative	W.B.C./Epithelial	: +2
Ketone	: Negative	R.B.C./HB	: Negative

MICROSCOPY

W.B.C	: 38	Normal Range :Up to 10x10^6/L Normal Range :Up to 5x10^6/L
R.B.C.	: 3	
Epithelial cell	: Not Seen	
Mucus	: Not Seen	
Cast	: Not seen	
Crystals	: Calcium oxalates	

Comments :

- Which of the following substances is NOT normally found in urine?
- A) Urea
- B) Creatinine
- C) Glucose
- D) Red blood cells
- E) Sodium

- What is the most common cause of false-positive proteinuria on dipstick testing?

- A) Vigorous exercise
- B) Glomerulonephritis
- C) Diabetic nephropathy
- D) Multiple myeloma
- E) Urinary tract infection

- A 30-year-old female presents with a history of joint pain and swelling. Urine analysis shows the presence of needle-shaped crystals. What is the likely diagnosis?

- A) Rheumatoid arthritis
- B) Osteoarthritis
- C) Gout
- D) Systemic lupus erythematosus (SLE)
- E) Psoriatic arthritis

Answers : c , a , c