BIOCHEMISTRY PART 1

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COMPOSITION OF URINE

بالمحاضرة دي رح نتكلم عن مكونات البول بشكل طبيعي بتكون من 50 غرام من المواد صلبة ذائبة بلتر ونص من الماء

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

• The chief organic solids are:

(I) NPN compounds(non-protein nitrogenous compounds)

(2) Organic acids

(3) Sugars.

• The chief inorganic solids are :

(I) Sodium, (2) Potassium, and (3) Chlorides

رح نبلش فيهم مكون مكون :

(I) NPN compounds(non-protein nitrogenous compounds)

بتشمل المواد اللي بتطلع بمنتصف ال pathways of protein metabolism أو ك end product from protein metabolism

• The non-protein nitrogenous (NPN) compounds include:

1- intermediary (aminoacids, ammonia, and creatine)

2-end products products (urea, uric acid, and creatinine creatinine) of protein metabolism.

• The total urinary NPN normally varies between 11 and 15, average 13 g day.

**ملاحظة حطوها ببالكم : لما بقيس blood urea بختلف تماما عن لما أقيس ال blood urea nitrogen دي قيمة ودي قيمة تانية خالص

A. Urea

إني أقيس ال urea بالبول isn't accurate indication of kidney function لانه ال urea level بتأثر بالأكل الي بوكله مثلا لو أكلت لحوم وكثرت هذا بأدي لزيادة نسبة ال urea +لو عندي أشياء تزود protein catabolism برضو حتزيد نسبة الurea لكن لو أكلت أكل طبيعي ممكن اعتبرها ك indication of kidney function

• Urea is the chief end product of protein metabolism in man. It is formed in the **liver** from the ammonia resulting from the deamination of the amino acids, and is excreted by the kidneys in the urine.

• Its excretion in the urine is more directly affected by protein intake and protein catabolism than any of the other nitrogenous compounds, which tend to remain relatively constant.

**Urinary urea is normally 20 - 30, average 24 g/day.

مرة ثانية لا تخربطوا بين Urinary urea و urea nitrogen فهاي ال 20 -30 هي من total solid (50 gm) مش من total NPN

- It increases on :
  1- high protein diet
  2- increased protein catabolism (fevers, diabetes mellitus, cushing syndrome and hyperthyroidism(

- It decreases decreases on:
  1- a low protein protein diet , زي الناس النباتية
  2- increased protein anabolism (pregnancy and lactation),
  3- in liver failure (decreased formation)
  مش عارفين اصلا يعملوا urea
  4- in acute renal failure (due to retention).

كونه ال kidney failed فمش قادرة تعمل excretion لحاجات كثيرة جدا من ضمنها urea فبتعلى نسبته بالدم وبتقل بالبول

B. Ammonia

بس تزيد Ammonia بالجسم بده يتخلص منها عن طريق اني بستخدمها بتحويل ال Glutamic acid اللي بطلع من الدماغ وبمساعدة انزيم Glutamine synthetas وبوجود الATP الى glutamine بعدها بروح عالكلية وبنزل بالبول

• Urinary ammonia is synthesized in **the distal convoluted tubules.**

• About 60% are produced by the action of the enzyme glutaminase on the glutamine received by the kidneys from other tissues.

(The ammonia resulting from the deamination of AA in extrarenal tissues, particularly the brain, is converted to glutamine then glutamine goes, via the blood, to the kidneys where it becomes hydrolyzed by glutaminase into glutamic acid and ammonia.

• About 40% are produced by the deamination of other amino acids in the kidneys.

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

ال kidney tubules بتساعد بال PH regulation كيف طيب ؟ وايش دخل ال ammonia بالقصة عشان نفهم شو دخل لازم نعرف انه الكلية بتعمل PH regulation لانها بتعمل 3 شغلات :

1- H+ excretion

2-reabsorbtion NaHCO3

3-NH3 formation

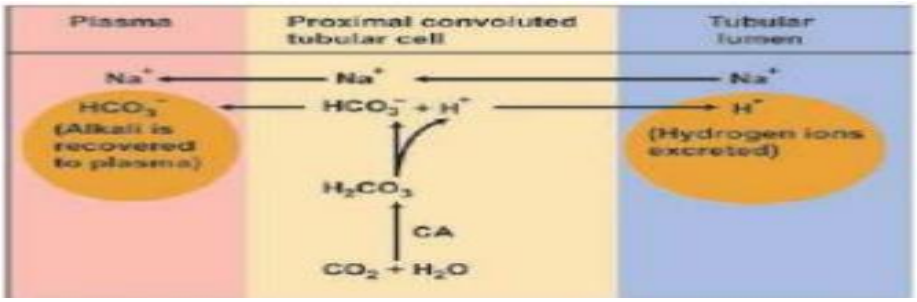
رح ننفهمهم وحدة وحدة بس فيه قانون لازم نخليه براسنا انه ممنوع فقدان ال HCO3 and Na+ in urine

1-- H+ excretion+formation NaHCO3

1- يتحد ال H2O مع ال CO2 بخلايا PCT بوجود (CA (carbonic anhydrase الى H2CO3

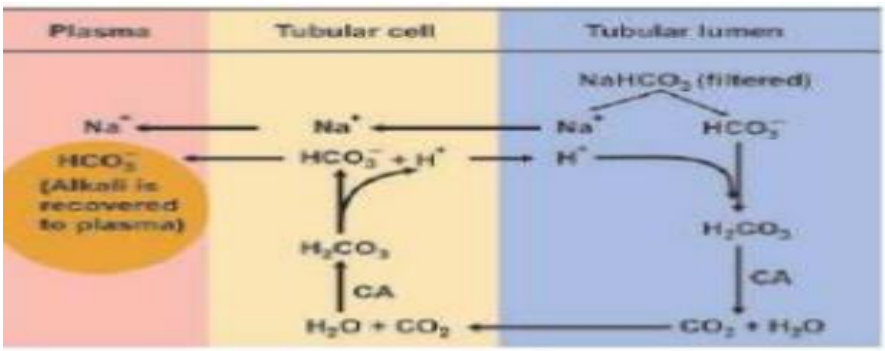
2- بصير تأين سريع ل H2CO3 اللى HCO3 و H+

3-ال H+ بنزل بال Tubular lumen بالتبادل مع ال Na + اللي بدوره بتحد مع ال HCO3 وبدخلوا جوا البلازما وبكونوا NaHCO3 فهيك انا بحافظ على alkali in the plasma عشان ال H+ بنزل بال urine فهيك بتساعد ال PH يضل مزبوط وما ادخل ب Acidosis



2-reabsorbtion NaHCO3

الحتة اللي بصيرلها filtration من NaHCO3 بتتأين داخل ال Tubular lumen وبتعطيني Na+ و HCO3 بتتذكروا بس قلنا انه ال ممنوع فقدان ال HCO3 and Na+ in urine فوق حكيناها ارجوا شوفوها ☺ طيب شو نعمل عشان ما نفقد ال HCO3 ؟ بتحد مع ال H+ اللي طلعلي من الخطوة الثانية من خطوات H+ excretion+formation NaHCO3 وبكونلي H2CO3 اللي بتفكك بوجود CA (carbonic anhydrase الى H2O مع ال CO2 وبدخلوا ال cell Tubular وال Na+ برجع بتبادل مع ال H+ وبتضل تتكرر العملية



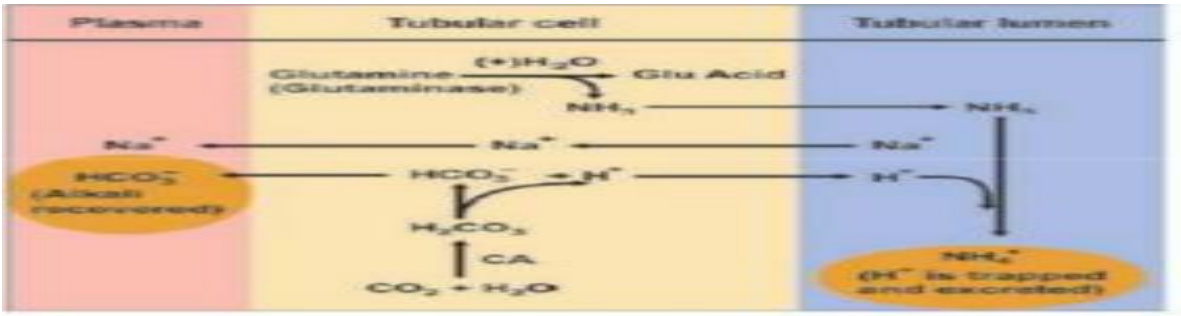
3-NH3 formation+H+ SECRETION

بتصير بال DCT Cells

1- ال Glutaminase بشتغل على glutamine وبحولها اللى (AMMONIA) +NH3 glutamic acid

2-NH3 بتنزل لل Tubular lumen وبتتحد مع H+ بتصير NH4 وبتنزل مع البول

- بحالات ال Acidosis بزيد عندي ال Glutaminase عشان تخلصني من H+



**** In conditions of acidosis the reabsorption of Na+ by Na+ : H+ exchange occurs to a limited extent being stopped when the pH of the glomerular filtrate becomes 4.8. Ammonia is secreted by the distal convolutcd tubules to neutralize this high acidity allowing Na+ : H+ exchange to continue and the alkali reserve to be regained.

Urinary ammonia is normally 0.3 - 1.2, average 0.7 g/day. It markedly increases in acidosis (up to 10 g/day), and is almost absent in alkalosis. It decreases in severe nephritis due to decreased capacity of the kidneys to deaminate amino acids.

• The quantity of ammonia in the urine may increase due to hydrolysis of urea by bacteria either in the bladder (cystitis) or if the urine sample is stored without preservative

**بس نعمل اختبار Urinary ammonia بنلاقي ال ammonia كثير مرتفع بس السبب مش مشكلة بالكلية بكون السبب وجود بكتيريا داخل العينة مثلا اخذتها بطريقة غلط او خزنتها غلط فهاي البكتيريا بتكسر ال urea وبتحولها ل ammonia فلهيك بلاقيها مرتفعة كثير

**برضو بحالة بكون عند المريض infection in urinary bladder like cystitis) بلاقي الامونيا عالية بالبول

C. AMINO ACIDS

• Most of the amino acids (about 80%) excreted in the urine are conjugated amino acids (glycine with benzoic acid and glutamine with phenylacetic acid) only a small part (about 20%) is free amino acids.

بس تدخل حاجة غريبة عالجسم مثل benzoic acid اللي بنستخدمه بحفظ الاطعمة وموجود ببعض الفواكه الجسم بعمله detoxification فبعمله conjugation مع ال AA وبتحول لمركب more soluble and less toxic وبنزل بالبول

• The total urinary amino acid nitrogen normally varies between 0.5 and 1.0, average 0.7 g/day. Increased urinary amino acids (aminoaciduria) may be due to:

1. Decreased Deamination of Amino Acids:

• In liver failure the deamination of amino acids and urea formation are decreased, leading to generalized aminoaciduria. Specific aminoacidurias are caused by defective metabolism of specific amino acids, eg., phenylketonuria causes increased excretion of phenylalanine in the urine.

2. Inability Inability of the Kidneys Kidneys to reabsorb reabsorb Amino Acids:

• In sever nephritis and in fanconi syndrome the kidneys fail to reabsorb all amino acids, leading to generalized aminoaciduria. In cystinuria kidneys fail to reabsorb cystine, ornithine, arginine and lysine, leading to their excretion in the urine.

3. Ingestion of certain toxic substances:

• These include benzoic acid, phenylacetic acid, and bromobenzene. which are respectively, conjugated conjugated with glycine glycine, glutamine, glutamine, and cysteine, leading to the excretion of large amounts of these amino acids in the urine.

D. Creatine and Creatinine

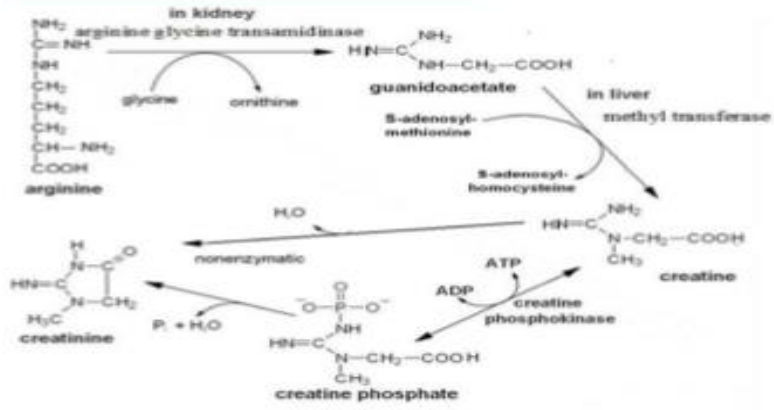
*كيف ال Creatinine؟

1- arginine +glycine بشتغل عليهم انزيم arginine glycine trnsamidinase رح ينقل ال amidine group من ال arginine ويحطها على ال glycine بصير guaniodoacetate هاي الخطوة بتصير بالكلية

2- بالكبد بتم اضافة methyle group من S- adenosyl- methionine فبطلع عندي Creatine

3- Creatine اما بطلع منه H2Oبدون الحاجة لاي انزيم وبتتحول مباشرة لCreatinine أو بدخله فوسفات عن طريق انزيم crestinine phosphokinase بتحول الى بتحول الى Creatinine phosphate بعدين بتطلع المي والفوسفات وتحول الى creatinine

D. Creatine and Creatinine



Creatine is methyl guanido acetic acid. It is a NPN compound.

• It is widely distributed in our tissues: mainly (98%) in muscles as phosphocreatine phosphocreatine (= phosphagen).

• Creatinine is creatine anhydride, it is the excretory product of creatine. The transamidinase reaction occurs in the kidney. The methyl transferase reaction occurs in the liver

*ال creatine بضل بال muscles والجزء اللي منه بتحول ل creatinine بنزل بالبول

•The creatine goes via blood to different tissues mainly to the muscles (98% of the body creatine).

• Androgen (male sex hormones e.g. testosterone) increase the uptake and retention of creatine by muscles, that is why androgen deficiency leads to creatinuria and decreased muscle creatine.

هون ننتبه إنَه ال Creatine هو اللي مرتفع في ال urine وليس ال Creatinine

• Adults excrete very little creatine in the urine (< 50 mg/day in males and < 100 mg/day in females.

ليه نسبة ال creatine في ال urine في ال male أقل ؟؟
لأنه عندهم muscle mass أكثر وعندهم androgen فبيحصل uptake of creatine يعني أغلب ال creatine تبعهم موجود داخل العضلات.
إنما في ال Female ال muscle mass أقل وما في عندها androgen فما رح يحصل uptake of creatine بالتالي نسبة ال creatine in the urine is higher in female