هاد الشابتر سبن داخل معنا
لحتد slide 16 بالعيترست

Acid-base balance

bicarbonate
oxygen
saturation

1

Type 1 diabetes
Ketoacidosis
↓
ICU

Acid-base balance

➢ The data are used to assess patients in life-threatening situations

➢ Blood hydrogen ion concentration [H+] is maintained within tight limits in health. Normal levels lie between 36 and 44 nmol/L (pH 7.35-7.45)

0.05

← تركيز ال H+ المسموح

➢ Any H+ values outside this range will cause alteration in the rates of chemical reactions within the cell and affect many metabolic processes of the body

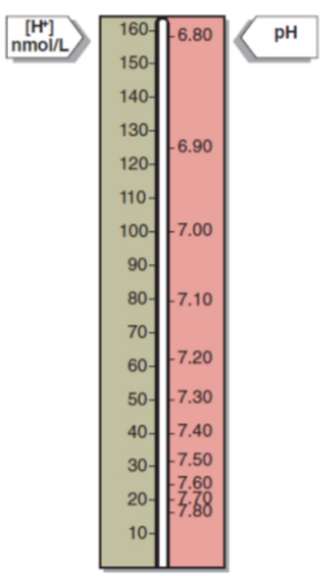


Fig 20.1 **The negative logarithmic relationship between [H+] and pH.**

2

Acid base balance يعني قدريش معي مجال انه تطلع وتنزل ال Acidity تبع الدم

مسموحلي تغيير ال PH بمقدار 0.05 فقط فا مي رينج واسع للتغيرات

اي تغير بسيط و بعمل acidosis بده عناية مركزة يعني مثلا الاطفال اللي عندهم Type 1 diabetes و بلش عندهم ketoacidosis بضلوا اسبوع لأسبوعين بالعناية المركزة لحد ما يروح الketoacidosis

اذا كان [H+] اعلى من 120 او اقل من 20 و ال PH اقل من 6.9 و اعلى من 7.7 المريض بكون dead فالتغيرات بال PH ← very dangerous لأنه الانزيمات كل وحدة الها optimal PH و هي اللي بتحكم بكل عمليات ال metabolism فأي تغيير بال PH ممكن يقلل ال activity تبعت الانزيم و اول خلايا بتتضرر هي ال brain

H+ Production

- Hydrogen ions are produced in the body as a result of **metabolism** (from the oxidation of the sulphur-containing amino acids of protein ingested as food)

cysteine , methionine
extra H+ in urine

- The total amount of H+ produced each day in this way is of the order of 60 mmol but all the H+ produced are efficiently excreted in urine. Everyone who eats a diet rich in animal protein passes an acidic urine
- Large amounts of **CO2** are produced by cellular activity each day with the potential to upset acid-base balance
- Under normal circumstances all of this CO2 is excreted via the **lungs**. Having been transported in the blood, Only when **respiratory function** is impaired do problems occur

ممكن ناكل اشياء Acidic بس ما بأثر كتير وعمليات ال metabolism تطلع كميات كبيرة من ال Co2 وهو Acidic بس بطلع بال breathing وفي ال sulphur containing aa اللي هي ال cysteine و ال Methionine هدول ال metabolism تبعهم بتطلع H+ معناته اذا ماكل اشي فيه لحوم يعني بروتين حيواني فنسبة ال cysteine فيه تكون عالية بالتالي بطلع H+ زيادة وبتروح باليورين

اي كميات زيادة من ال Co2 تطلع من خلال عملية التنفس حتى تحافظ على ال Acid - base balance

بالوضع العادي ال respiration ما فيه اي مشاكل بس اذا صار مشكلة فيه Asthma , COPD - suffocation او مشاكل بالقلب انه مش عم يوصل الدم للرئة ففي هاي الحالة كمية ال Co2 اللي بتطلع صارت اقل وصارت تنحبس جوا

3

Buffering and buffers

- Buffer is a solution of the salt of a weak acid that is able to bind H+. Buffering does not remove H+ from the body but mop up any excess H+ produced (as a sponge)
- **Buffering** is only a short term solution to the problem of excess H. Ultimately, body must get rid of H by renal excretion
- The body contains a number of buffers to correct sudden changes in H production
- **Proteins** can act as buffers and the haemoglobin in the erythrocytes has a high capacity to bind H

كمية ال bicarbonate هي الي بتحدد اذا عندي acidosis او alkalosis

4

Buffers

- In the ECF, **bicarbonate buffer** is the most important. In this buffer system, bicarbonate (HCO3-) combines with H+ to form carbonic acid (H2CO3)
- The association of H with bicarbonate occurs rapidly, but the breakdown of carbonic acid to CO2 and water happens relatively slowly.
- The reaction is accelerated by an enzyme, **carbonic anhydrase**, which is present particularly in the erythrocytes and in the kidneys.

5

ال bicarbonate buffer هو احسن بيشتغل بالجسم و عملية التخلص من ال H+ الزيادة عن طريق ال Co2 عملية سريعة جدًا

في buffers تانية زي الهيموغلوبين و البروتينات ممكن تسحب جزء من ال H+ خصوصًا اذا كانت الكميات قليلة

الكمية الاكبر بروح لل bicarbonate و بتحوله لـ Co2 و بطلعه من خلال الrespiration و في عندها buffer capacity معين

Buffers

- In the ECF, **bicarbonate buffer** is the most important. In this buffer system, bicarbonate (HCO3-) combines with H+ to form carbonic acid (H2CO3)
- The association of H with bicarbonate occurs rapidly, but the breakdown of carbonic acid to CO2 and water happens relatively slowly.
- The reaction is accelerated by an enzyme, **carbonic anhydrase**, which is present particularly in the erythrocytes and in the kidneys.
- Only when all the bicarbonate is used up does the system have no further buffering capacity
- The acid base status of patients is assessed by consideration of the bicarbonate system in plasma

6

اذا صار excess من ال H+ ح يرتبط . bicarbondate و يتحول لـ Co2 و يطلع من خلال عملية ال respiration

اذا نقصت ال H+ يعني alkalosis . سيلتش الجسم يحبس ال Co2 و يحولها لـ $HCO_3^- + H^+$ حتى ترتفع ال H+ و ال bicarbonate الزيادة تتروح عال kidney

Buffers

- The **bicarbonate buffer** system is unique in that:
  - The (H2CO3) can dissociate to water and CO2 allowing CO2 to be eliminated by lung
  - Changes in CO2 modify the ventilation rate
  - HCO3- concentration can be altered by the kidney

- **Phosphate buffer** system (HPO4= - H2PO4-) plays a role in plasma and RBC's and is involved in the exchange of Na/H+ ion in the urine filtrate

- **Plasma proteins**, especially the imidazole groups of histidine, forms important buffer system in plasma. Most circulating proteins has net negative charge capable of H+ binding

عملية التخلص من الـ Co2 بتتم عن طريق الـ lung في أي تغيرات فيه الـ ventilation rate هو اللي بتتحكم بالعملية يعني اذا الـ Co2 ارتفع الـ ventilation رح يطلعه بال exhalation و اذا الـ PH تغيرت عكتر ينخفض الـ ventilation و يصير بتنفس شوي شوي حتى نعادل الـ PH

اذا الـ respiration متل ملحق عالـ kidney برجع عالـ Co2

كميته كتير قليلة بس مكن بيشتغل بالبلازما و اهميته الاكبر بالبورين

Regulation of the acid-base balance

- In plasms at 37oC, the value for the combination of the solubility constant for PCO2 and the factor to convert mm Hg to mmol/L is 0.0307 mmol L-1. mm Hg-1

$$pH = pK' + \log \frac{cHCO_3^-}{0.031 \times PCO_2}$$

concentration of bicarbonate

partial pressure of Co2

الـ PH بالدم 7.4 و الـ pka الـ bicarbonate ← 6

بضرب بـ 0.031 عشان أحول وحدة الـ PCo2 لـ mmol/L

لو صار Acidosis الـ bicarbonate بتقل فالجسم بحاول تقلل الـ Co2 عن طريق الـ hyperventilation انه ازيد الـ ventilation

يعني لما يكون الـ Bicarbonate ناقص بدي انقص الـ PCO2

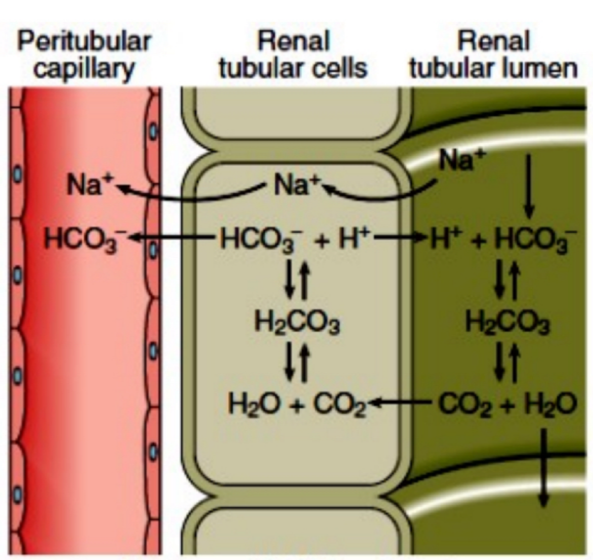
H+ excretion in the kidney

- All the H+ that is buffered must eventually be excreted from the body via the kidneys, regenerating the bicarbonate used up in the buffering process and maintaining the plasma bicarbonate concentration within normal limits.
- Secretion of H+ by the tubular cells serve initially to reclaim bicarbonate from the glomerular filtrate so that it is not lost from the body
- When all bicarbonate has been recovered, any deficit due to the buffering process is regenerated.
- The mechanisms for bicarbonate recovery and for bicarbonate regeneration are very similar and sometimes confused.
- The excreted H+ must be buffered in urine or the [H+] would rise to very high levels, phosphate acts as one such buffer, while ammonia is another

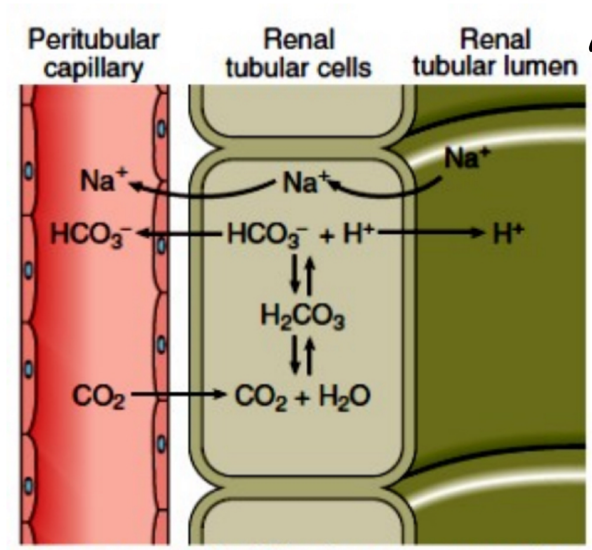
9

بالوضع العادي لما يكون التنفس شغال و ما فيه اي مشاكل و اكلت اشي acidic و ال lung طلعلي اياه و كل اشي stabilized و اي كمية من ال bicarbonate راحت لليورين برجعها فعادةً الكمية اللي بتطلع من اليورين بتكون ضئيلة جداً و ما في اشي بطلع لأنه ال regulation جيد بال respiratory

H+ excretion in the kidney



'Recovery' of bicarbonate



'Regeneration' of bicarbonate — excretion of hydrogen ion

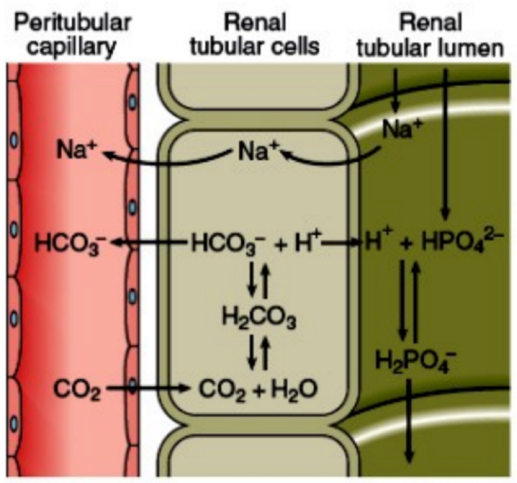
10

بالوضع العادي ، بال lumen بربط ال bicarbonate بال H+ و بحولها ل CO2 وهاي الجهة من ال membrane ما بتمرق ions لأنه ما في pump لل HCO_3^- عشان هيك بحولها ل CO2 لأنه ما عليها charge فبقدر يمر من خلال ال lumen بعدين بحوله مرة ثانية ل HCO_3^- بعدين ال H+ بطلع و بيرتبط مع HCO_3^- جديد وفيه sodium proton pump بتطلع H+ و بتدخل صوديوم

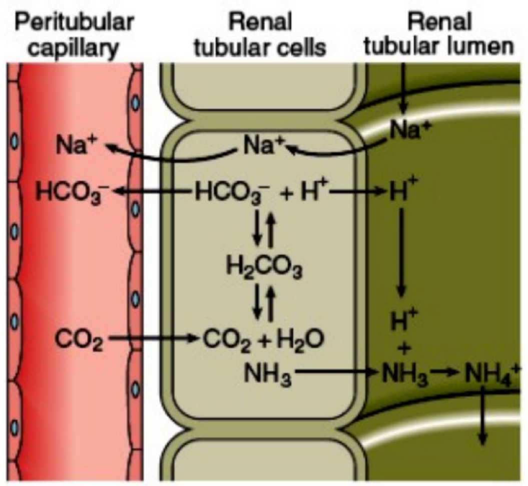
لو كان ال respiratory فيه مشكلة و ال CO2 لبلش يتراكم جوا الدم و ال H+ بلشت ترتفع و صار Acidosis وهاد ال membrane بمرق كلشي و بطلع CO2 و بتحول ل HCO_3^- و بترجع و ال H+ بتطلع و بدخل مقابلها Na+ فهيك طلعت ال acid و رجعت ال base

ال acid لما يكون عال
damage بجللها urinary tract
فلازم تطلع مع buffer اما
Ammonia buffer او phosphate buffer
فعشان يكون ال PH ضمن ال urine PH

H+ excretion in the kidney



Phosphate buffer



Ammonia buffer

11

Assessing status

- ➢The carbonic acid (H2CO3) component is proportional to carbon dioxide, which is in turn proportional to the partial pressure of the CO2
- ➢Because the body's cellular and metabolic activities are pH dependent, the body tries to restore acid-base homeostasis whenever an imbalance occurs (**Compensation**)
- ➢The body accomplishes this by altering the factor not primarily affected by the pathologic process. For example, if the imbalance is of **non-respiratory** origin, the body compensates by altering **ventilation** (fast response).
- ➢For disturbances of the **respiratory** components. The **kidneys compensate** by selectively excreting or reabsorbing anions and cations. The kidneys are slower to respond (2-4 days)

12

عادةً ال cellular metabolic acidity
او اي تغير تجاول تعمل compensation
يعني اذا كانت المشكلة metabolic
بكون ال compensation ← respiratory
واذا كانت المشكلة respiratory بكون ال
compensation من خلال ال kidney

اذا كان respiratory compensation
بكون تغيير بال ventilation اما
hyperventilation او hypoventilation

ال kidney بكون ال response الها بطيء
من يومين ل ٤ ايام

Assessing status

- The H concentration in blood varies as the bicarbonate concentration and pCO2 change. If everything else remains constant.
- Adding H, removing bicarbonate or increasing the pCO2 will all increase [H+] Acidosis
- Removing H, adding bicarbonate or lowering pCO2 will all cause the [H+] to fall. Alkalosis
- An indication of the acid base status of the patient can be obtained by measuring the components of the bicarbonate buffer system

١٣

Normal ranges

حكمة

TABLE 16-1 ARTERIAL BLOOD GAS REFERENCE RANGE AT 37°C

pH	7.35–7.45
pCO_2 (mm Hg)	35–45
HCO_3^- (mmol/L)	22–26
Total CO_2 content (mmol/L)	23–27
pO_2 (mmol/L)	80–110
SO_2 (%)	>95
O_2Hb (%)	>95

١٤

Causes of metabolic acidosis

- Metabolic acidosis with an **elevated anion gap** occurs in:
- **Renal disease.** Hydrogen ions are retained along with anions such as sulphate and phosphate.
- **Diabetic ketoacidosis.** Altered metabolism of fatty acids, as a consequence of lack of insulin causes endogenous production of acetoacetic and β–hydroxybutyric acids
- **Lactic acidosis.** Particularly tissue anoxia. In acute hypoxic states such as respiratory failure or cardiac arrest. It can be caused by liver disease. The presence of lactic acidosis can be confirmed by the measurement of plasma lactate concentration.
- Certain disease of overdosage or **poisoning**. As in **salicylate** overdose where build-up of lactate occurs, or **methanol** poisoning when formate accumulates, or **ethylene glycol** poisoning where oxalate is formed.

15

Anion gap + acidosis

الـ lactate مرتفع و عامل acidosis و عامل anion gap

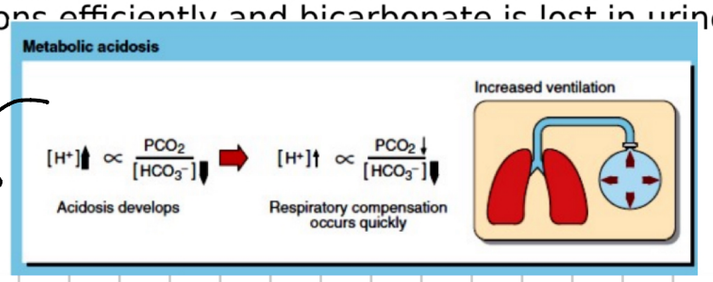
في نوعين من الـ metabolic acidosis يعني في اشي مع elevated anion gap و عامل و في اشي anion gap بدون ارتفاع بال

يكون في retention of H+ في acidosis و بالمقابل في فوسفات و sulphate مرتفعين في anion gap

الـ ketone bodies مرتفعة و عاملة acidosis

Causes of metabolic acidosis

- Metabolic acidosis with a normal anion gap is sometimes referred to as **hyperchloraemic acidosis** because a reduced HCO3 is balanced by increased Cl concentration. It is seen in chronic diarrhea or intestinal fistula. Fluids containing bicarbonate are lost from the body
- **Renal tubular acidosis**: Renal tubular cells are unable to excrete hydrogen ions efficiently and bicarbonate is lost in urine



16

هاد مثل مرتبط بال anion gap انه يكون مقابل الـ ↓ of HCO3 في ارتفاع بال Cl⁻

يعني الـ HCO3 عم يصير loss من الـ Cl

انه ما بيكون قادر يفل الـ HCO3 بينما الـ excretion للـ H+ فبيكون الـ Cl⁻ عم يصير loss in urine مرتفع

بعكس بيكون Alkalosis

Clinical effect of acidosis

- The compensatory response to metabolic acidosis is hyperventilation, since the **increased [H+]** acts as a powerful stimulant of the respiratory centre.

- The deep rapid and gasping respiratory pattern is known as Kussmaul breathing. Hyperventilation is the appropriate physiological response to acidosis and it occurs rapidly.

يعني نفس عميق وسريع حتى الجسم يخفف من الـ Acidosis

- The raised [H+] leads to increased neuromuscular irritability. There is a hazard of arrhythmia progressing to cardiac arrest and this is more likely by the presence of hyperkalemia, which will accompany the acidosis.

لأنه يجل خلل بالبوتاسيوم

- Depression of consciousness can progress to coma and death