Approach to Acid Base

Nephrology

Introduction

- pH in the body is tightly regulated for normal physiology and cell function (proteins denature if they are in abnormal pH)

- Normal Arterial pH 7.36 – 7.44

pH equation

- pH= 6.1 + log [HCO3/(0.03xpCO2)]
- HCO3 measured in meq/L
- pCO2 measured in mmHg

H2O equation

- $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3 + H$

Regulation and Buffer systems

Definitions

Metabolic acidosis	Process that primarily reduces bicarbonate: Excessive H^+ formation e.g. lactic acidosis, ketoacidosis Reduced H^+ excretion e.g. renal failure Excessive HCO_3^- loss e.g. diarrhoea
Metabolic alkalosis	Process that primarily raises bicarbonate: Extracellular fluid volume loss e.g. due to vomiting or diuretics Excessive potassium loss with subsequent hyperaldosteronism
Respiratory acidosis	Process that primarily causes elevation in $PaCO_2$: Reduced effective ventilation e.g. many chronic respiratory diseases or drugs depressing the respiratory centre
Respiratory alkalosis	Process that primarily causes reduction in $PaCO_2$: Increased ventilation e.g. in response to hypoxia or secondary to a metabolic acidosis

Approach

Step 1.

- Take a thorough history and physical examination, look for clues that may lead to the abnormalities in pH
  - Vomiting
  - Diarrhea
  - Hypoventilation
  - Respiratory disease
  - Medications (laxatives, diuretics, etc)
  - Diabetes
  - etc

Vomiting for example, causes loss of acid and gastric contents, which suggests development of alkalosis

Step 2

- Look at the pH:
- Determine if this is
  - Normal 7.35 – 7.45 (No abnormality or mixed acidosis and alkalosis)
  - Low <7.35 (acidemic)
  - High >7.45 (alkalemic)

Step 3 - a

- Determine the primary abnormality that is causing the abnormal pH

- If the pH is acidemic (<7.35), then look for
  - Low HCO_3 (Metabolic) or High PCO_2 (Respiratory)

- If the pH is alkalemic (>7.45), then look for
  - High HCO_3 (Metabolic) or Low PCO_2 (Respiratory)

Step 3 - b

- If pH is normal, rule out mixed acidosis and alkalosis
  - Look for high or low PCO_2
  - Look for high or low HCO_3

Determine what is being mixed

- **Low** PCO2 suggests **respiratory alkalosis**
- **High** PCO2 suggests **respiratory acidosis**
- **Low** HCO_3 suggests **metabolic acidosis**
- **High** HCO_3 suggests **metabolic alkalosis**

Step 4

- After determining the primary abnormality, check for compensation
- Compensation is the mechanism by which the body adapts to either acidosis or alkalosis, it will fully correct the abnormality
- For example
  - A patient has diabetic ketoacidosis, pH is 7.29, HCO_3 is 15
  - Expected PCO_2 by using Winter's formula
  - $PCO_2 = 1.5 \times HCO_3 + 8 \ (\pm 2)$

    $= 1.5 \times 15 + 8 = 30.5$

  So you expect the PCO_2 in this patient to be in the range of 28.5– 32.5
  - If the PCO_2 in this patient is higher than 32.5 → consider additional respiratory acidosis
  - If the PCO_2 in the patient is lower than 28.5 → consider additional respiratory alkalosis

Step 4

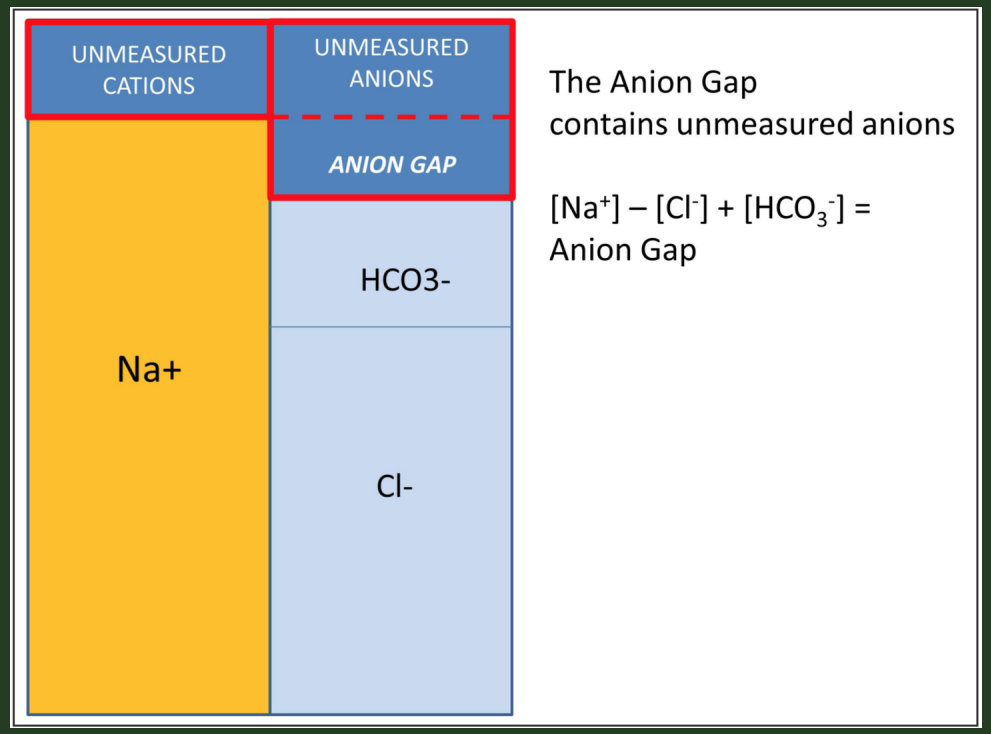
Compensation calculations

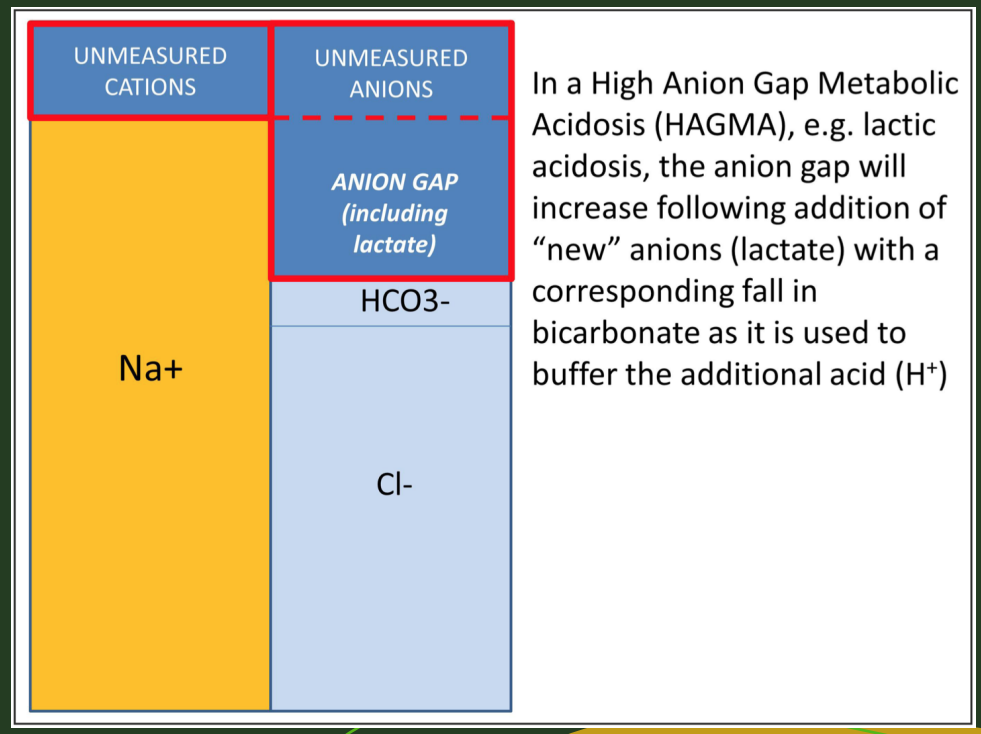
Primary Disorder	*Expected Compensation*
Metabolic Acidosis	$\downarrow PaCO_2 = 1.2 \times \Delta HCO_3$ or $PaCO_2 = 1.5 \times HCO_3 + 8 \pm 2$ or $PaCO_2$ ~ last two digits of pH.
Metabolic Alkalosis	$\uparrow PaCO_2 = 0.7 \times \Delta HCO_3$
Acute Respiratory Acidosis	$\uparrow HCO_3 = 0.1 \times \Delta PaCO_2$
Chronic Respiratory Acidosis	$\uparrow HCO_3 = 0.35 \times \Delta PaCO_2$ also $\downarrow pH = 0.003 \times \Delta PaCO_2$
Acute Respiratory Alkalosis	$\downarrow HCO_3 = 0.2 \times \Delta PaCO_2$
Chronic Repsiratory Alkalosis	$\downarrow HCO_3 = 0.4 \times \Delta PaCO_2$

Step 5

- Calculate the anion gap (AG)

Albumin is the main unmeasured anion
To overcome the effects of the hypoalbuminemia on the AG, the corrected AG can be used which is AG + (0.25 X (40-albumin) expressed in g/L





Delta ratio

- **Delta ratio = (change in anion gap) / (change in bicarbonate)**
- (The normal anion gap is assumed to be 12, and the normal HCO_3 is assumed to be 24.)
- **Interpretation of the generated ratio:**
- 0.4 = normal anion gap metabolic acidosis
- 0.4-0.8 = mixed high and normal anion gap acidosis exists.
- 0.8-1.0 = purely due to a high anion gap metabolic acidosis
- 1.0-2.0 = still purely a high anion gap metabolic acidosis
- Over 2.0 = high anion gap acidosis with pre-existing metabolic alkalosis

Case 1

- 40 yo gentleman presenting to ER with coma labs : pH 7.14/ pCO_2 15; Na 138/ K 6.4/ Cl 100/ HCO_3 5; BS 6/ Urea 7/ S- OSM 340/ ETOH 0/ALB 40
- Funduscopic showed optic neuritis
- How do you approach the differential of this acid base disorder?

Answer

- 1. Acidosis or alkalosis - ACIDOSIS
- 2. Metabolic or respiratory- METABOLIC
- 3. Compensation appropriate- YES
- 4. Anion gap – HIGH (138 – 105 =23)
- 5. Δ gap = Δ HCO3 - YES
- **6. Osmolar gap – YES (340 – 289 = 51)**

- Corrected anion gap = 2.5 X (4-albumin)

Case 2

- An elderly man present with tachypnea, diarrhea and weakness labs - pH 7.24/ pCO_2 24; Na 140/ K 6.7/ Cl 120 / HCO_3 10; urine pH 5.0/ U Na 40/ U K 20/ U Cl 50
- How do you approach the differential of this acid base disorder?

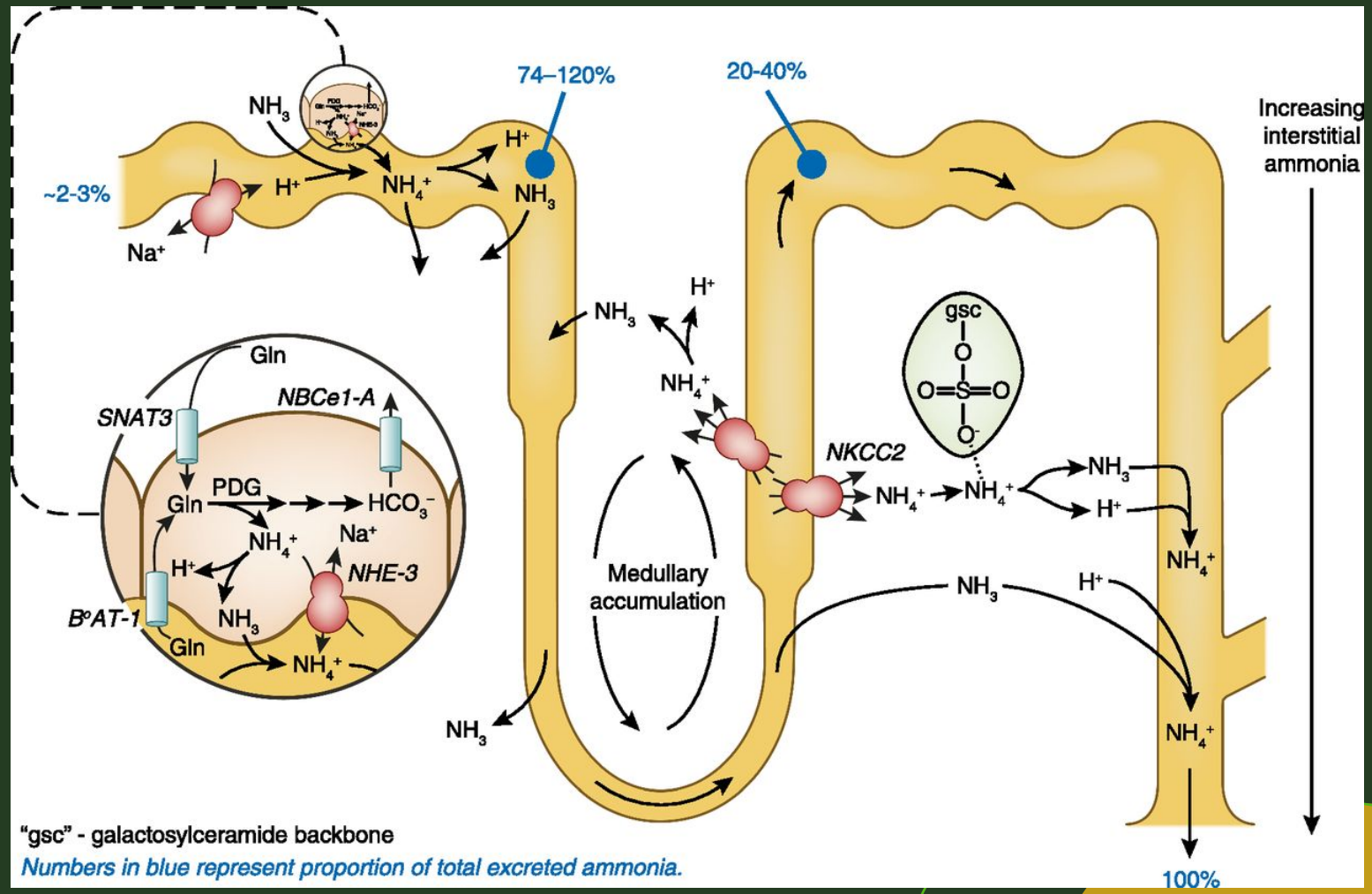
Answer

- 1. Acidosis or alkalosis - ACIDOSIS
- 2. Metabolic or respiratory- METABOLIC
- 3. Compensation appropriate - YES
- 4. Anion gap – NORMAL (10)
- 5. Δ gap = Δ HCO3 - YES
- 6. Osmolar gap - NONE

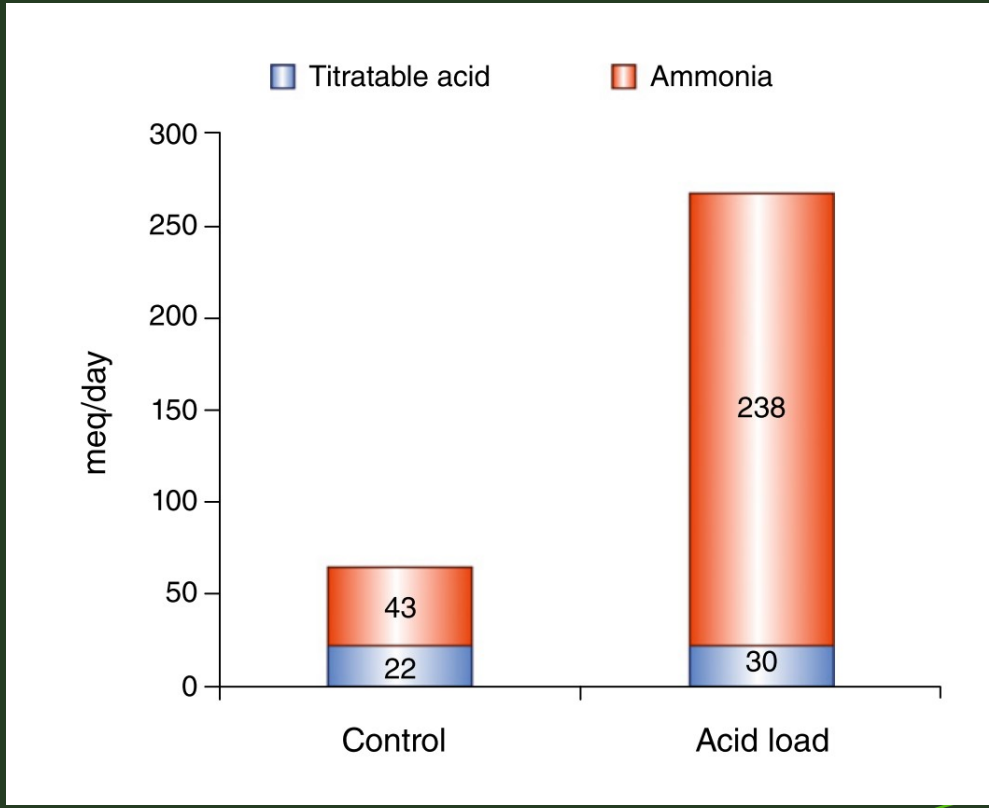
Urine Anion Gap

- HCO_3 is either resorbed (prox) or regenerated (distal)
- To regenerate HCO_3 - NH_4 is formed distally
- In an acidic urine $Na+K+NH_4 = Cl$
- NH_4 can not be measured therefore
  - $Cl > Na+K$ if NH_4 is present → Normal DISTAL FX
  - If $Cl < \text{or} = Na+K$ then distal urinary acidification is impaired (UAG abnormal)

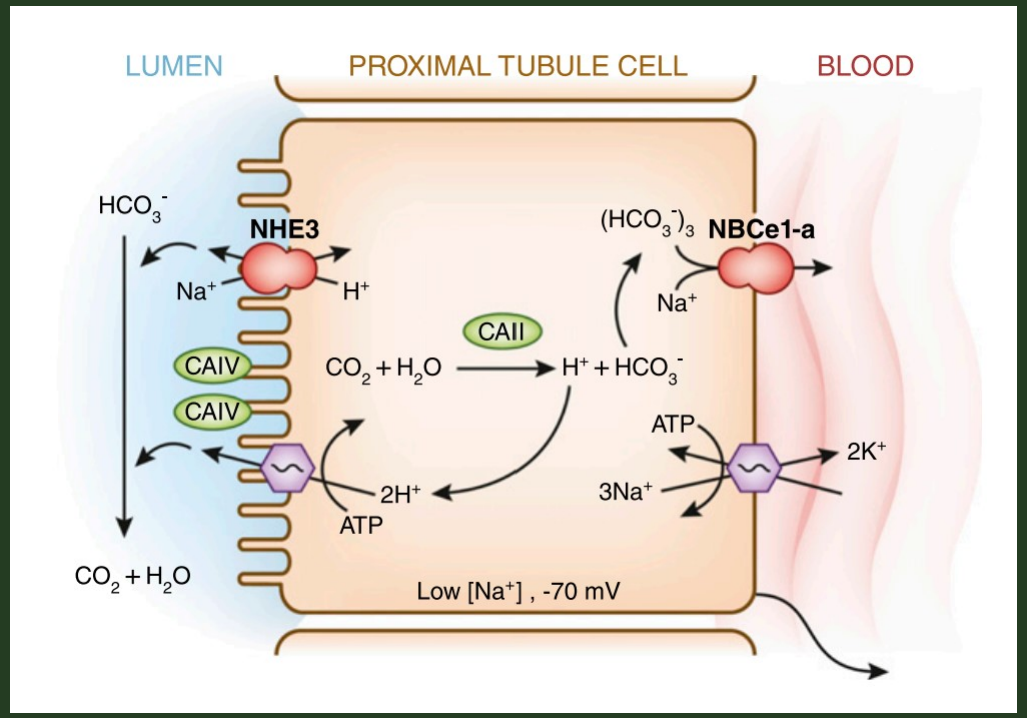
Ammonium Secretion

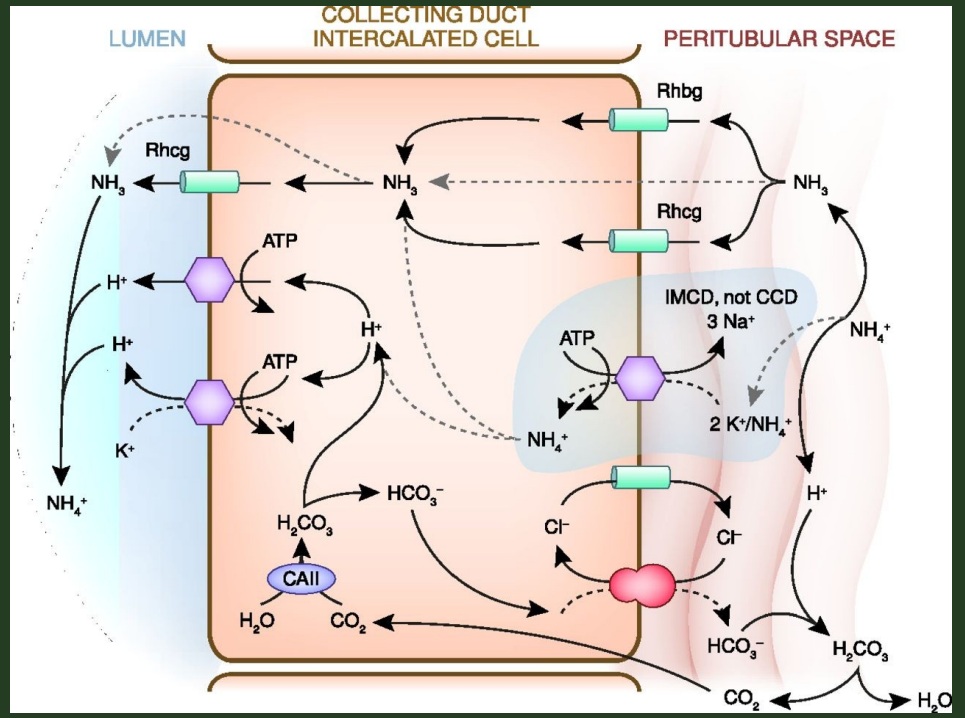


NH4 response to acid load



Kidney regulation





Urine Anion Gap

- Urine Anion Gap the urine anion gap is useful in distinguishing disorders with normal ammonium excretion from those with abnormal excretion
- Normal UAG – Proximal RTA or non renal acidosis (diarrhea etc.) ($Cl > Na + K$)
- Abnormal UAG - CKD (lack of NH_4 production), distal RTA Type I and IV or aldosterone deficiency) ($Cl \leq Na + K$)

Hyperchloremic Metabolic Acidosis Normal Urine NH_4 (Cl > Na + K)

- This is due to HCO_3 loss with normal distal tubular function
- GI - loss of HCO_3 due to diarrhea, urinary diversion or pancreatic fistulae
- Renal - proximal RTA (type 2) leads to renal HCO_3 loss with normal distal regeneration.
- May be associated with other proximal defects (Fanconi's), hypergammaglobulinemia, drugs (toluene, toperimate, zonisamide, tenofovir, azetazolamide) or multiple myeloma

Hyperchloremic Metabolic Acidosis Abnormal Urine NH_4

- Classic Distal - a defect in the proton pump leads to a U pH >5.5 and acidosis (Type 1) (ampho B, HyperPTH, Sjogren’s, medullary sponge kidney Hyperkalemic Distal - a defect in the aldo sensitive collecting duct leads to acidosis and hyperkalemia with preserved renal acidification (Type 4) (obstruction , aldo resistance) NH_3 Defect - CKD leads to abnormal NH_3 production with preserved urinary acidification (GFR < 30)

Non Anion Gap Acidosis

Defect	U pH	UAG	K (serum)	GFR
Proximal RTA (II)	< 5	Nl	Low	nl
Distal RTA (I)	> 5	Low	Low	Nl
Distal RTA (IV)	< 5	Low	High	Nl to low
CKD	< 5	Low	Nl to high	< 30

Case 3

- A normotensive body builder presents with weakness
- Labs : pH 7.54/ pCO_2 45; Na 140/ K 2.8/ Cl 95/ HCO_3 38;
- U Cl 50 U Na 70
- Repeat U Cl < 20
- How do you approach the differential of this acid base disorder?

Answer

- 1. Acidosis or alkalosis - ALKALOSIS
- 2. Metabolic or respiratory - METABOLIC
- 3. Compensation appropriate – YES
- 4. Anion gap – NORMAL (7)
- 5. Δ gap = Δ HCO3 – YES
- 6. Osmolar gap - NONE

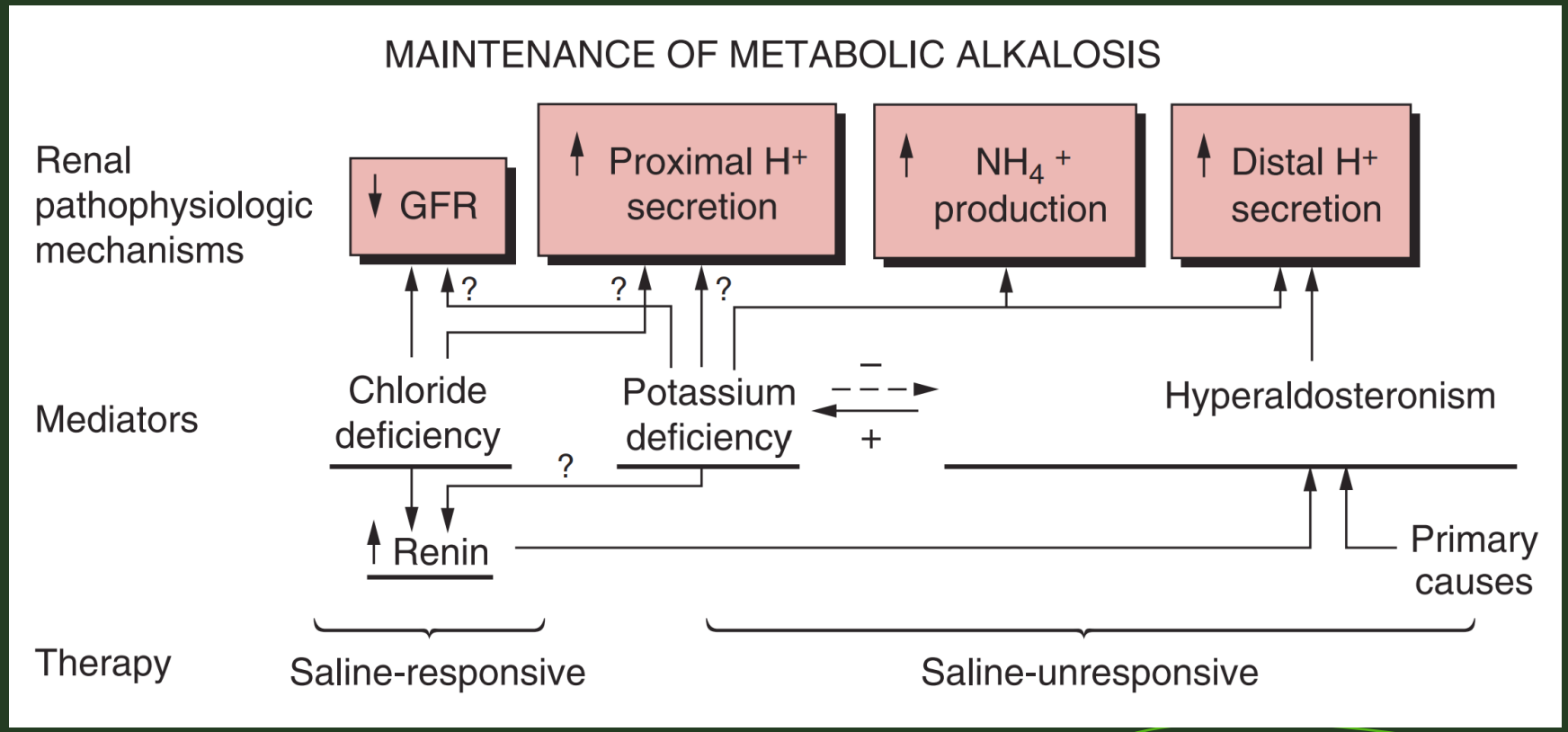
Cl responsiveness

- Generation - loss of HCl from kidneys or GI tract
- Maintenance - because of prerenal state, hyperaldosteronism, and hypokalemia the body is unable to excrete HCO3
- Cl responsive - when Cl is given it will shut off the maintenance phase and allow the kidney to excrete HCO3 by restoring volume and normalizing aldosterone production
- Cl unresponsive - even when Cl is given it will not shut off aldosterone production

Cl responsiveness

- When NaCl and KCl are given they restore volume and replete K and Cl shutting off aldosterone production
- This plus the correction of the prerenal state allow the kidneys to excrete excess HCO_3
- Treatment - administration of NaCl and KCl

Maintenance of Metabolic Alk



Cl responsive

- Diuretic alkalosis - U Cl < 20 after diuretics are stopped
- Chloridarrhea - congenital or villous adenoma
- Posthypercapnic - usually with chronic respiratory acidosis
- Gastric alkalosis - hypokalemia due to renal K wasting
- Milk Alkali – hypercalcemia, AKI, and alkalosis Cystic Fibrosis – skin Cl loss

Cl unresponsive

- This group of disorders is all have elevated aldosterone or defects in kidney
- However, this is not volume (NaCl) responsive but rather volume independent
- Administration of NaCl will not inhibit aldo nor will it correct the prerenal state
- Treatment - diamox, HCl, spironolactone