• ABG (Arterial blood Gas) → to know Acid base status

b Normal values → pH: 7.35 – 7.45 (740) / PCO_2: 35 – 45 (40) / HCO_3^-: 22 – 26 (24 → Average)

*controlled via lungs by excrete CO_2 and kidney by excrete H^+ /reabsorb + generate HCO_3^- (→ Base → kidney)

pH of serum = 6.1 + log [HCO_3^-] / 0.03 * PCO_2 (→ weak → lung acid)

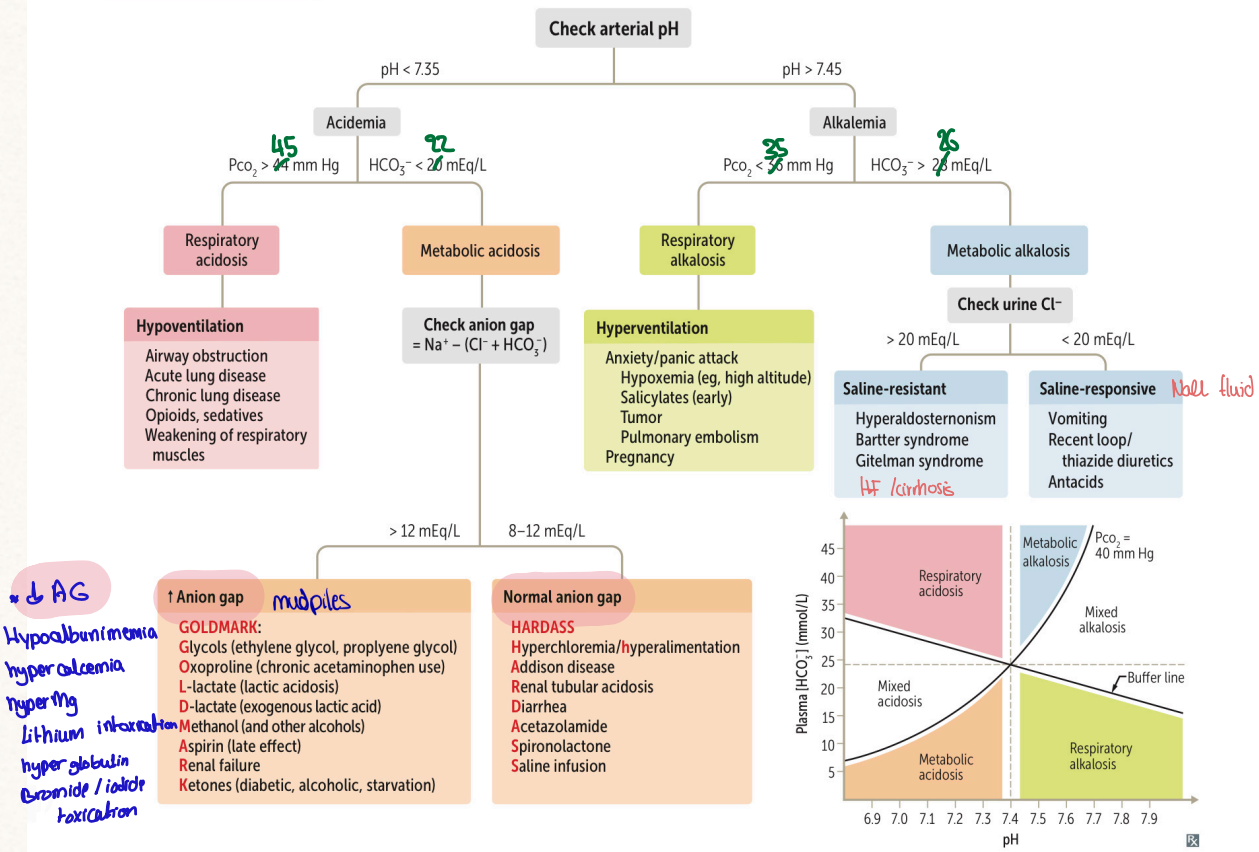
[Henderson – Hasselbalch Equation]

Buffer: intracellular proteins / phosphate; extracellular HCO_3^-

*intracellular pH = 6.8–8

• Acidosis & Alkalosis → 1) pH 2) HCO_3^- / PCO_2 3) Determine Disorder 4) Anion gab ↑ met. Acid 5) check mixed by formula

Acidosis and alkalosis



* ↓ AG
Hypoalbuminemia
hypercalcemia
hyperMg
Lithium intoxication
hyperglobulin
Bromide / iodide toxication

*Acidosis Effects in general →

Hyperventilation / myocardial depression → ↓ contractility → ↓ CO

Cerebral vasodilation (CO_2 main autoregulator of CBF in brain)

PCO_2 → ↓ pH → vasodilation → increase blood flow → ↑ ICP → headaches

Hyperkalemia ← H^+ / K^+

Bone demineralization (chronic)

*Alkalosis Effects in general →

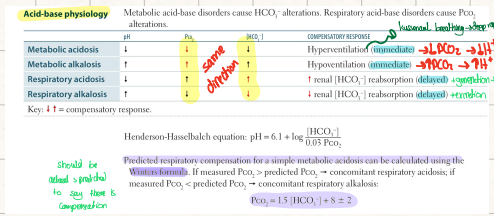
Hypoventilation / Cerebral vasoconstriction ↓ CO_2

Hypokalemia ← H^+ / K^+

*metabolic – HCO_3^- *Respiratory – PCO_2

*Compensations →

HCO_3^- – PCO_2 dependent if one change the other will change to compensate but in same direction ↓↓ / ↑↑



*so both HCO_3^- / PCO_2 abnormal in AB disorders
one call Culprit- causing disorder
one call Compensatory change

*Examples →

① pH = 7.30 HCO_3^- ↓ PCO_2 ↑
R. Acidosis with M. Alkalosis compensation

② pH = 7.10 HCO_3^- = 12 PCO_2 = 40
metabolic Acidosis
witness PCO_2 = 1.5 * 12 + 8 ± 2 = 26 ± 2
40 > 26 → No compensation
mixed with R. Acidosis

1] Metabolic Acidosis

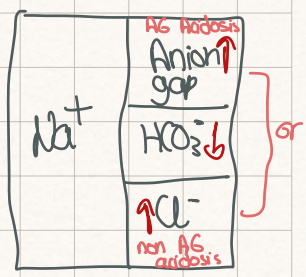
① ↓HCO_3^- ② ↓PH ③ ↓PCO_2 (compensatory) hyperventilation

- Anion Gap = $Na^+ - (Cl^- + HCO_3^-)$ = 8 to 12 → unmeasured Anion (proteins / phosphates / sulfate)

the plasma charges normally balanced -ve = +ve in M.Acidosis the HCO_3^- ↓ so ↓ -ve so either compensated by ↑Cl^- or ↑Anion gap

↓low Albumin <4g/dL → +2.5 on AG on every ↓1 on albumin

hypercalcemia / lithemia



1] Non Anion Gap Metabolic Acidosis / NAGMA

H ↓ Hyperchloremia to correct charge balance

A ↓ Addison disease lose aldo effect so high influx of H^+

R ↓ renal tubular Acidosis I / II / III

D ↓ Diarrhea ↓ Loss of HCO_3^- in stool + hypokalemia
- same mechanism when fluid loss from bowel in fistula

A ↓ Acetazolamide ↓ Block formation + reabsorption of HCO_3^- + hypo mg / K^+

S ↓ Spironolactone (K^+ sparing Diuretics) high influx of H^+ + hyperkalemia

S ↓ normal Saline infusion ↓ high influx of Cl^- ↑Cl^- shift of HCO_3^- to cells ↓HCO_3^- ↓PH
- Lactated Ringers Don't cause that (contains HCO_3^-)

* Diagnosis by History, PE, labs * treat underlying Cause

2] High Anion Gap Metabolic Acidosis / HAGMA

Methanol :- Antifreez / industrial cleaners / windshield wiper fluid → (by alcohol Dehydro) metabolized to Formic Acid (CNS poison) ↓ (when ingested) → Cause confusion / visual loss / Coma + HAGMA
Diagnosis → serum methanol
Treatment :- Fomepizole (Antizol) + Ethanol Inhibit Alcohol Dehydrogenase Dialysis

Uremia :- advanced CKD but the early CKD Cause NAGMA → [caused by less H^+ secretion + phosphate/sulfate] → ↑AG
Treatment : dialysis

Diabetic ketoacidosis :- with type I Diabetic when insulin not adequate → (osmotic diuresis) hyperglycemia → metabolized to Ketone bodies (B-hydroxybutyrate / Acetoacetate)
Cause polyuria / polydipsia / Abd pain / N/V / kussmaul breathing / HAGMA

Propylene glycol :- Antifreeze / solvent for IV benzodiazepines → Metabolized to Pyruvic Acid + Acetic Acid + Lactic acid → CNS depression, seizure, coma, hemolysis + HAGMA
*No visual Symptoms or nephrotoxicity
Treatment → dialysis ± fomepizole

I
- Iron poisining :- ① GI phase 0-6hr → Abd pain → bowel obstruction ② 24 hr CNS toxicity shock coagulopathy hepatic Dys Acute Lung injury
  metabolized to Fe^{+3} ionic + lactate (+3 → 3H^+)
  * Diagnosis → iron Level Treatment :- GI decontamination / Deferoxamine (Chelating → bind to Fe^{+3} → excrete by kidney)
- Isoniazid (INH) → TB Antibiotic → overdose cause seizures which cause LACTic Acidosis
  Treatment :- Anti seizure drugs

Lactic Acidosis :- low tissue O_2 → anaerobic metabolism → pyruvate convert to LACtate >4mmol/L
- Fluids / vasopressin / inotrope ← shock
- surgery ← ischemic bowel
- stop drug ← met-formin therapy
- No treatment ← seizures (post-ictal acidosis)

Ethylene Glycol → Antifreeze / Industrial Cleaners / windshield → metabolized to Glycolate + Oxalate → kidney toxins cause ↓ oliguria + flank pain + anuria
(toxic to renal tubules; calcium oxalate ↑ stones)
AKI + HAGMA Diagnosis → serum ethylene level Treated → Fomepizole / Ethanol / Dialysis

Salicylates → Aspirin overdose → cause 2 AB disorders → shortly After ingestion cause respiratory alkalosis → because activate medulla → hyperventilation
Hours After ingestion cause HAGMA → Pyruvate / Lactate / ketoacids
Diagnosis → serum salicylate Treatment → urinary alkalinization (bicarbonate)

*Osmolar Gap = measured osmolarity − calculated osmolarity
calculated plasma osmolarity = 2* Na^+ + Glucose/18 + urea/2.8
measured plasma osmolarity - Lab
Normally should calculated close to measured → osmolar gap ≤ 10
when osmolar gap > 10 indicate there is another Na / BUN / Glu Raise the osmolarity
① Mannitol ② methanol ③ Ethylene glycol
↳ [↓Acidosis + ↑OG]

Cause	Mechanism	Diagnosis	Treatment
Methanol	Ingestion	Methanol level	Fomepizole/dialysis
Uremia	Renal failure	BUN/Cr	Dialysis
DKA	Insulin deficiency	Serum ketones	Insulin, fluids
Propylene Glycol	Ingestion	Propylene glycol level	Dialysis
Iron	Ingestion	Serum iron level	Deferoxamine
Lactic Acidosis	Hypoperfusion	Serum lactate	Restore perfusion
Ethylene Glycol	Ingestion	Ethylene glycol level	Fomepizole/dialysis
Salicylates	Aspirin overdose	Aspirin level	Urine alkalization

(formic acid; ↓H^+ secretion; Keton (β-hydro, Acetoacetate); pyruvate / lactate / Acetic; Lactate-ferric lactate; Glycolate oxalate; pyruvate / lactate / Acetic)

2] Metabolic Alkalosis

① ↑HCO_3^- ② ↑pH ③ ↑PCO_2 hypoventilation compensation atelectasis
hypokalemia hypocalcemia

① GI Acid Loss

vomiting − gastric suction ... → Loss of stomach content + less HCl synthesis from parietal cells
cause hypochloremia + [hypokalemia + metabolic Alkalosis
↳ loss of fluid → hypovolemia → RAAS → aldosteron → reabsorb Na^+/H_2O
→ secrete K^+/H^+ → hypokalemia / metabolic Alkalosis]

② Contraction Alkalosis → Low volume

vomiting / Diuretics / HF / Cirrhosis / hemorrhage

overloaded but Low Blood Volume

* Loss of Na+ Cl- + fluid → ↓ ECV → ↑ RAAS + ↑ SNS

(Loss Cl- true cause → retention resolves Alkalosis)

→ HCO_3^- reabsorbtion + ↑ ENaC

↑ H^+ secretion

③ Hypokalemia

K^+ out cell H^+ inside cell Alkalosis

④ Milk-alkali Syndrome

Triad → Hypercalcemic - metabolic alkalosis - renal failure

causes → excessive intake of Ca^{++} + alkali (base) → Calcium Carbonate and milk (↳ in dyspepsia)

Ca^{++} cause inhibition of Na/K/Cl + block ADH → polyuria → volume contraction → metabolic Alk

↓GFR ↑BUN ↑Cr

⑤ Hyperaldosteronism / primary Aldosteronism

causes → Adrenal overproduction / Adrenal hyperplasia / Adrenal adenoma (conn syndrome)

so will activate ENaC ↑K^+ / H^+ Loss + Na^+ / H_2O retention

↳ hypokalemia / M. Alk / HTN / hypernatremia / hypervolumic

Diagnosis → ↑ Aldo & renin Treatment → K^+ sparing diuretics / surgery

⑥ Low Renin HTN

because there is many Aldo like effect so kidney lower renin to lower Aldo but not effective

A - Liddle Syndrome → genetic cause increased activity of ENaC (epithelial Sodium Channel) (collecting tubules / principle cell) present in juveniles adult

HTN / Hypo K^+ / M. Alk + Aldo → Low renin → Low

Treatment → amiloride (K^+ sparing)

B - SAME «Syndrome of apparent mineralocorticoid Excess»

cortisol bind to renal aldosterone receptor so when produced convert by renal cell to cortisone by 11-B hydroxysteroid dehydrogenase ← in same the enzyme Deficient so cortisol bind (uses aldo / def)

HTN + Hypokalemia + M. Alk in children/adult

Ald: Low renin: Low

Treatment → K^+ sparing + Dexamethasone (↳ suppress cortisol production)

C - Licorice → contain glycyrrhetinic acid → inhibit 11-B.. Aldo → Low

D - Bartter → congintal (children) → impaired Na^+ reabsorbtion in thick AL similar to loop diuretics → polyuria / polydipsia / nocturia → contraction Alk → hypokalemia hypo mg / hypo Ca high urinary Ca^{++} + Don't cause HTN

channel $Na^+ K^+ Cl^-$ → thick Ascendy ↓renin ↓Aldo

E - Gitelman Syndrome → channel Na^+/Cl^- → early distal

Defect Na^+ reabsorb distal tubule → similar thiazide diuretic → childhood

polyuria / polydipsia / nocturia → contraction Alk → hypokalemia Low Ca^+ in urine

No HTN ↓↑renin ↓↑Aldo

Normal RR 12-20 breath /min

3] Respiratory Alkalosis

① ↓PCO2 ② ↑PH ③ ↓HCO_3^- compensation secreted in thick Ascending + Intercalated Collecting

Caused by Hyperventilation : >20

1] pain 2] Anxiety 3] Mechanical ventilation

4] High altitude exposure:-

The result:-

Lower atmospher pressure → sea level 760 → PO_2 100 → high Altitude 560 → PO_2 75 → so low O_2 content → lower PO_2 → ↓PO_2 → Hypoxia → ↑RR hyperventilation → ↓PCO_2 → ↑PH

After days → acclimatization → renal response → 24-48 hr kidney excrete HCO_3^- ↓PH

→ Red cell response to hypoxemia → synthesis of 2,3 BPG which cause unloading of O_2 from hemoglobin Polycythemia

5] Aspirin overdose

Resp Alk → HAGMA

PH variable / PCO_2 Low / HCO_3^- low

winters formula predict CO_2 > actual so mixed AB disorder

Diagnosis by serum salicylates Treatment urinary alkalization (sodium bicarb) → will favor ionization of salicylates → excreted

*Treat underlying + inhale in bag to ↑PCO2 cause

4] Respiratory Acidosis:-

↑PCO_2 ↓PH ↑HCO_3^- compensation → excess H^+ secreted / HCO_3^- reabsorb / HCO_3^- generated

by secrete ammonia

↑ from proximal tubules thrown distal

↳ distal tubules + α inter cortical → collecting using phosphate as buffer

NH_3 ⇌ ↳ synthesis HCO_3^-

+ proximal

*Caused by Hypoventilation:-

1] Decreased CNS respiratory drive (opiates, barbiturates)

2] Respiratory muscle diseases (Guillain Barre / polio / multiple sclerosis / Amyotrophic lateral sclerosis)

3] impaired gas exchange (pneumonia, p.edema, ARDS, COPD)

4] Airway obstruction (Aspiration of foreign body, OSA) pickwick Syndrome

↑PCO_2 hypercapnia → ↑ cerebral BF → ↑ICP → anxiety / headach / delirium / coma

tachypnea + sleepy + tachy / sweating

over production in CO_2 hypercatabolic malignant hyperthermia / sepsis + increase CO_2 intake

rebreath ex

*compensation

Acute → intracellular buffer

Chronic → renal compensation

Treat underlying cause

Respiratory acidosis	< 7.35	Compensatory increase	Primary increase
		ΔPCO_2	Δ[HCO_3^-]	pH
Acute R. Acidosis →		↑x10	↑x1	↓0.07
Acute R. Alkalosis →		↓x10	↓x2	↑
Chronic R. Acidosis →		↑x10	↑x3	↓0.03
Chronic R. Alkalosis →		↓x10	↓x4	↑

* intermediate values suggest Mix disorder

Acute: 1–2 mmol/L increase in HCO_3^- for every 10-mm Hg increase in Pco_2

Chronic: 3–4 mmol/L increase in HCO_3^- for every 10-mm Hg increase in Pco_2

Mixed disorder:-

2 disorder at same time

if expected response not meet actual → 2nd

normal PH → mixed

Urine Anion Gap:- used for diagnose M.Acid by renal acid excretion

↑H^+ secreted → ↑NH_4^+ → ↑Cl^- → ↓UAG

↓UAG = $Na^+ + K^+ - Cl^-$ ↑

diarrhea proximal RTA

+ve UAG → Less acid excretion in I RTA + IV RTA

* Renal tubular Acidosis :-

- rare disorder of ion channel in nephrone cause NAGMA (low HCO_3^-) + hypo/hyper kalemia

1] Type I Distal RTA

impaired acidification of urine by distal (a-intercalated cell) nephron → ↓ H^+ excretion acidemia + ↑ K^+ excretion hypokalemia

High urine pH >5.5 alkaline — so low HCO_3^- synthesis ↩ ↳ Less HCO_3^- <10

* Cause Calcium phosphate kidney stones due to urine alkalosis + acidosis cause less Ca^{++} reabsorption

* Cause rickets and Osteoprosis due to ↑ Ca from bones

* Associated with auto immune diseases (Sjogren / RA) + Amphotericin + genetic

+v UAG

in NH_4Cl challenge remain urine PH >5.5

NH_4Cl هاد بيستخدموه في M. Acid بس لما نعطيه

↑H^+sec المفروض تزيد ، وتقل حموضة البول

Type I (distal) RTA

- Classic case
  - Patient with Sjogren's disease
  - Recurrent kidney stones
  - Very low bicarb on blood work (< 10)
  - Hypokalemia
  - Urine pH is high (> 5.5)
  - UAG is positive
  - If given NH_4Cl urine remains with high pH
- Treatment: Sodium bicarbonate

2] Type II proximal RTA

defect in HCO_3^- reabsorption in proximal tubules so ↑ HCO_3^- excretion → NAGMA + Hypokalemia

← 12 – 20 ↩ — caused by Less Na^+/H_2O reab → low volume → RAAS → ↑aldosteron ↩

لانو في ↓ H^+ sec → HCO_3^- syn — urine pH < 5.5 because H^+ normally secreted → -ve UAG → No kidney stones

Associated with Fanconi Syndrome + multiple myeloma + metal

Children inherited – failure of proximal tubule urine loss of Phos / Glu / Prot / Bicarb (Fanconi)

(multiple myeloma: can cause)

Drug caused tenofovir (HIV) + ifosfamide (Alkaline)

poisining (lead, Ca, mercury) + Acetazolamide + Topiramate

Acetazolamide: carbonic anhydrase inhibitor [هاد الي بيدخل HCO_3^- ف بعمل ف بنجمه علاج ع Res Alk

Topiramate: ↳ anti seizure, Carbonic anhydrase inhibitors

Type II (proximal) RTA

- Sample Case
  - No symptoms : routine blood work
  - Mild weakness (low K)
  - Mildly reduced HCO_3^- (12 – 20)
  - Hypokalemia
  - Urine pH is low (< 5.3)
- Treatment: Sodium bicarbonate

3] Type IV Hyperkalemia RTA

Hyperkalemia → inhibit NH_3 Syn in proximal → decrease NH_4^+ excretion so less H^+ excretion → pH urine < 5.5

NAGMA HCO_3^- >17

Causes :- Hyporeninemic hypoaldosteronism in Diabetes + NSAIDs

RAAS drugs ACEI / ARBs / Aliskiren (Direct renin inhibitor)

Aldosteron resistance K^+ sparing drugs + TMP / SMX

Type IV RTA

- Classic case:
  - Diabetic with renal insufficiency
  - Unexplained hyperkalemia
- Treatment usually aimed at potassium
- Hyporeninemic hypoaldosteronism treated with **fludrocortisone**
  - Mineralocorticoid

Type	Key Features
I	Distal; High urine pH; kidney stones; very low HCO3-
II	Proximal; mild acidosis; Fanconi's
IV	Aldosterone; hyperkalemia; ammonium

Type	Plasma K+	Urine pH	HCO_3^-
I	Low (< 3.5)	High (> 5.4)	<10
II	Low (< 3.5)	Low (< 5.4)	12-20
IV	High (> 5.0)	Low (< 5.4)	>17

Variable	Normal	Normal Range(2SD)
pH	7.40	7.35 - 7.45
pCO2	40	35-45
Bicarbonate	24	22-26
Anion gap	12	10-14
Albumin	4	4

What is the pH? Acidemia or Alkalemia?
2.What is the primary disorder present?

3.Is there appropriate compensation?

Metabolic acidosis :
Expected Pco2 = (1.5*Hco3)+8 (+2)

Metabolic alkalosis
Expected PCO2= 40+ change of PcO2
Change of PCO2= 0.7*change of HCo3 (+2)

Respiratory acidosis

For every 10 Increase of PCO2 = increase HCo3 (1) in acute and (3.5) in chronic (added to normal Hco3 (24)

Respiratory alkalosis

For every 10 decrease of Pco2 = decrease Hco3 (2) in acute and (5) in chronic (removed from 24)

4.Is the compensation acute or chronic? In (respiratory pathology)

5.Is there an anion gap?

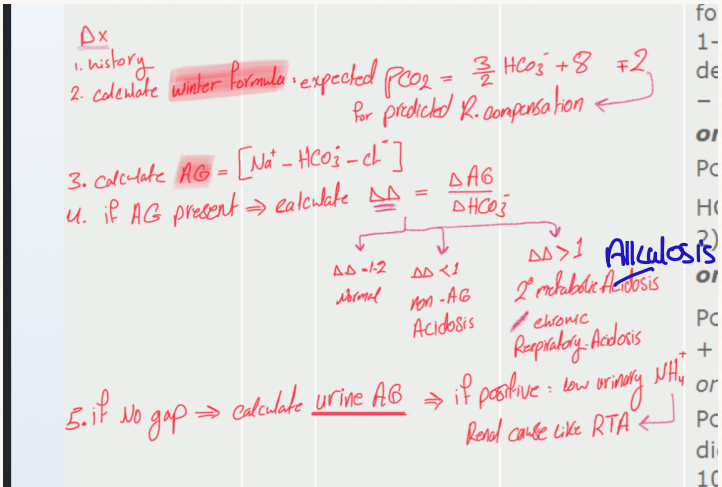
Na- (Cl +Hco3)

6.If there is a AG check the delta gap?

Delta gap = Change in AG ÷ change in HCO3

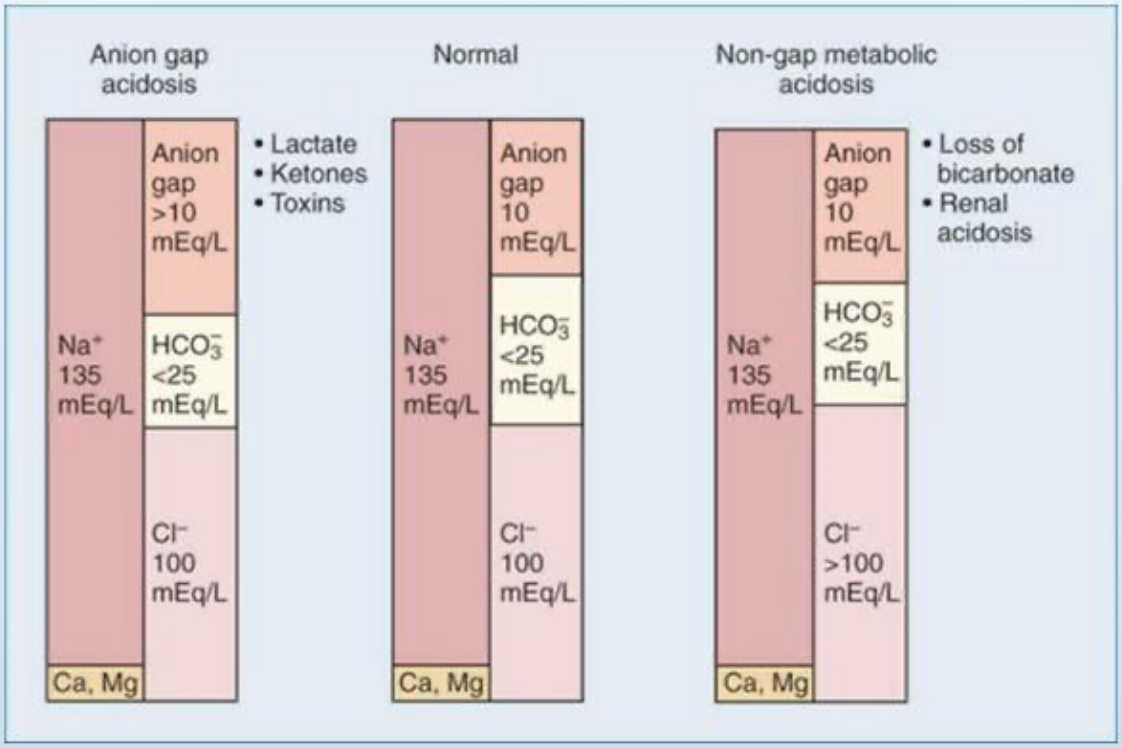
- if delta gap > 6 there is combined AGMA with metabolic alkalosis
- if delta gap <- 6 there is combined AGMA with NAGMA

7.What is the differential for the clinical processes?



What disorder is present?	pH	pCO2	HCO3
Respiratory Acidosis	pH low	high	high
Metabolic Acidosis	pH low	low	low
Respiratory Alkalosis	pH high	low	low
Metabolic Alkalosis	pH high	high	high

This will you to determine what is the primary process !
If no AG ,
Every 1 meq/l increase of chloride there should be a 1 mEq/L decrease in HCO3 (+_5) , if HCo3 decrease is less than predicted, then there is metabolic alkalosis in addition to NAGMA


Anion gap acidosis
Anion gap >10 mEq/L
HCO_3^- <25 mEq/L
Cl^- 100 mEq/L
Na^+ 135 mEq/L
Ca, Mg
• Lactate
• Ketones
• Toxins
Normal
Anion gap 10 mEq/L
HCO_3^- <25 mEq/L
Cl^- 100 mEq/L
Na^+ 135 mEq/L
Ca, Mg
Non-gap metabolic acidosis
Anion gap 10 mEq/L
HCO_3^- <25 mEq/L
Cl^- >100 mEq/L
Na^+ 135 mEq/L
Ca, Mg
• Loss of bicarbonate
• Renal acidosis