

# Should the Serum Concentrations of Cl<sup>-</sup> and TCO<sub>2</sub> Be Measured in Everyday Clinical Practice?

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# Disclosures

None

# The Case of K. M.

PCP: 58 ♂ with headaches and palpitations

PE: BP 158/100, HR 75 no ectopics, otherwise unremarkable

Labs: CBC nl; UA nl, BUN 10, cr 0.7; electrolytes Na<sup>+</sup> 143, K<sup>+</sup> 3.8, Cl<sup>-</sup> 96, TCO<sub>2</sub> 38, AG 9;

TSH nl; ECG including rhythm strip nl

Plan: 1. HTN monitor for now

2. Electrolyte abnormalities, refer to SEMC Nephrology

F/U: 4 weeks

SEMC Nephrology: Final Diagnosis, Primary aldosteronism

## Is More Better?

### Routine Electrolyte Panel USA

Na<sup>+</sup>  
K<sup>+</sup>  
Cl<sup>-</sup>  
TCO<sub>2</sub>  
AG

### Routine Electrolyte Panel Greece

Na<sup>+</sup>  
K<sup>+</sup>

Sx: 58 ♂ headaches, palpitations

Na <sup>+</sup>	143
K <sup>+</sup>	3.8
Cl <sup>-</sup>	96
TCO <sub>2</sub>	38
AG	9

Dx: Primary aldosteronism

# Clinical Utility of Serum Cl<sup>-</sup> Concentration (1)

Changes in serum Cl<sup>-</sup> denote:

- Disorders of water balance
- Disorders of acid-base balance

## Clinical Utility of Serum Cl<sup>-</sup> Concentration (2)

Changes in serum Cl<sup>-</sup> denote:

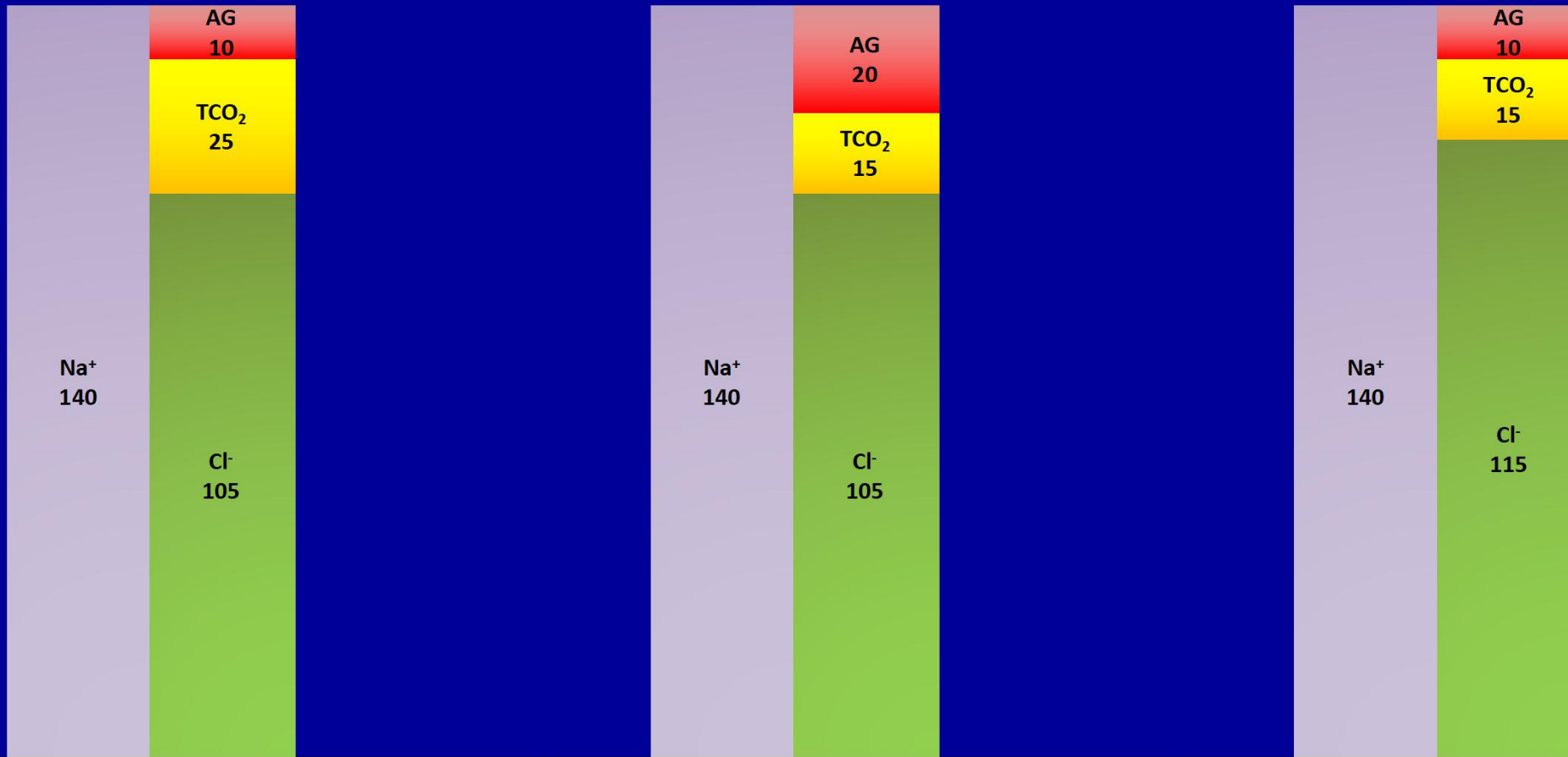
- Disorders of water balance  
Also denoted by proportional changes in serum Na<sup>+</sup>
- Disorders of acid-base balance

# Clinical Utility of Serum Cl<sup>-</sup> Concentration (3)

Changes in serum Cl<sup>-</sup> denote:

- Disorders of water balance  
Also denoted by proportional changes in serum Na<sup>+</sup>
  - Disorders of acid-base balance
    - Hyperchloremic disorders (Na<sup>+</sup> : Cl<sup>-</sup> < 1.34)
      - Hyperchloremic metabolic acidosis
      - Respiratory alkalosis
    - Hypocholemic disorders (Na<sup>+</sup> : Cl<sup>-</sup> > 1.34)
      - Metabolic alkalosis
      - Respiratory acidosis
- 
- Normochloremia occurs in high AG metabolic acidosis

# Electrolyte Patterns in Metabolic Acidosis



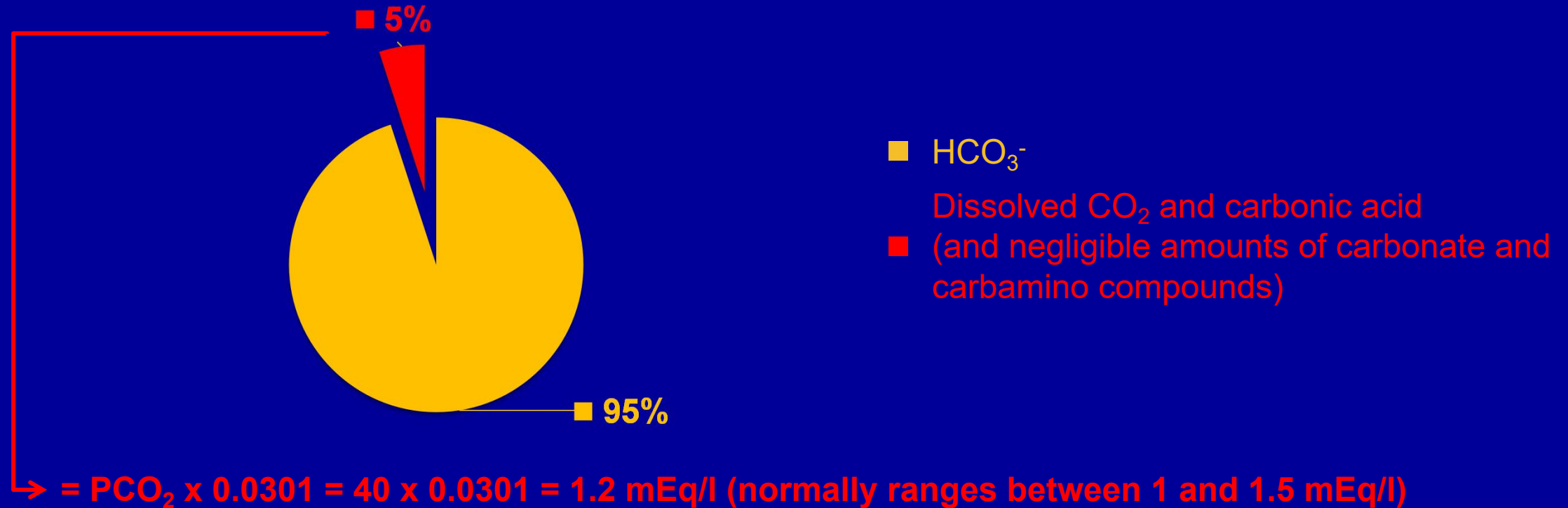
Normal

High Anion Gap Metabolic Acidosis

Normal Anion Gap Metabolic Acidosis



# Serum TCO<sub>2</sub> (a.k.a. bicarbonate or carbon dioxide)



- Measurement of serum TCO<sub>2</sub> is made by first releasing all CO<sub>2</sub> in the sample after addition of strong acid and then utilizing an electrometric or enzymatic method.
- Serum HCO<sub>3</sub><sup>-</sup> is not measured directly but calculated from pH and PCO<sub>2</sub> using the Henderson-Hasselbalch equation.

**Table 1. Secondary responses to alterations in acid-base status**

Disorder	Primary Change	Secondary Response	Mean Slope of the Secondary Response
Respiratory acidosis acute	↑ PaCO <sub>2</sub>	↑ [HCO <sub>3</sub> <sup>-</sup> ]	$\Delta[\text{HCO}_3^-]/\Delta\text{PaCO}_2 = 0.1 \text{ mEq/L per mmHg}$
chronic			$\Delta[\text{HCO}_3^-]/\Delta\text{PaCO}_2 = 0.35 \text{ mEq/L per mmHg}$
Respiratory alkalosis acute	↓ PaCO <sub>2</sub>	↓ [HCO <sub>3</sub> <sup>-</sup> ]	$\Delta[\text{HCO}_3^-]/\Delta\text{PaCO}_2 = 0.2 \text{ mEq/L per mmHg}$
chronic			$\Delta[\text{HCO}_3^-]/\Delta\text{PaCO}_2 = 0.4 \text{ mEq/L per mmHg}$
Metabolic acidosis	↓ [HCO <sub>3</sub> <sup>-</sup> ]	↓ PaCO <sub>2</sub>	$\Delta\text{PaCO}_2/\Delta[\text{HCO}_3^-] = 1.2 \text{ mmHg per mEq/L}$
Metabolic alkalosis	↑ [HCO <sub>3</sub> <sup>-</sup> ]	↑ PaCO <sub>2</sub>	$\Delta\text{PaCO}_2/\Delta[\text{HCO}_3^-] = 0.7 \text{ mmHg per mEq/L}$

The term "acute" refers to a duration of minutes to several hours. The term "chronic" refers to a duration of several days or longer.

## Clinical Utility of Serum TCO<sub>2</sub> Concentration (2)

- Changes in serum TCO<sub>2</sub> denote disorders of acid-base balance

Low serum TCO<sub>2</sub>

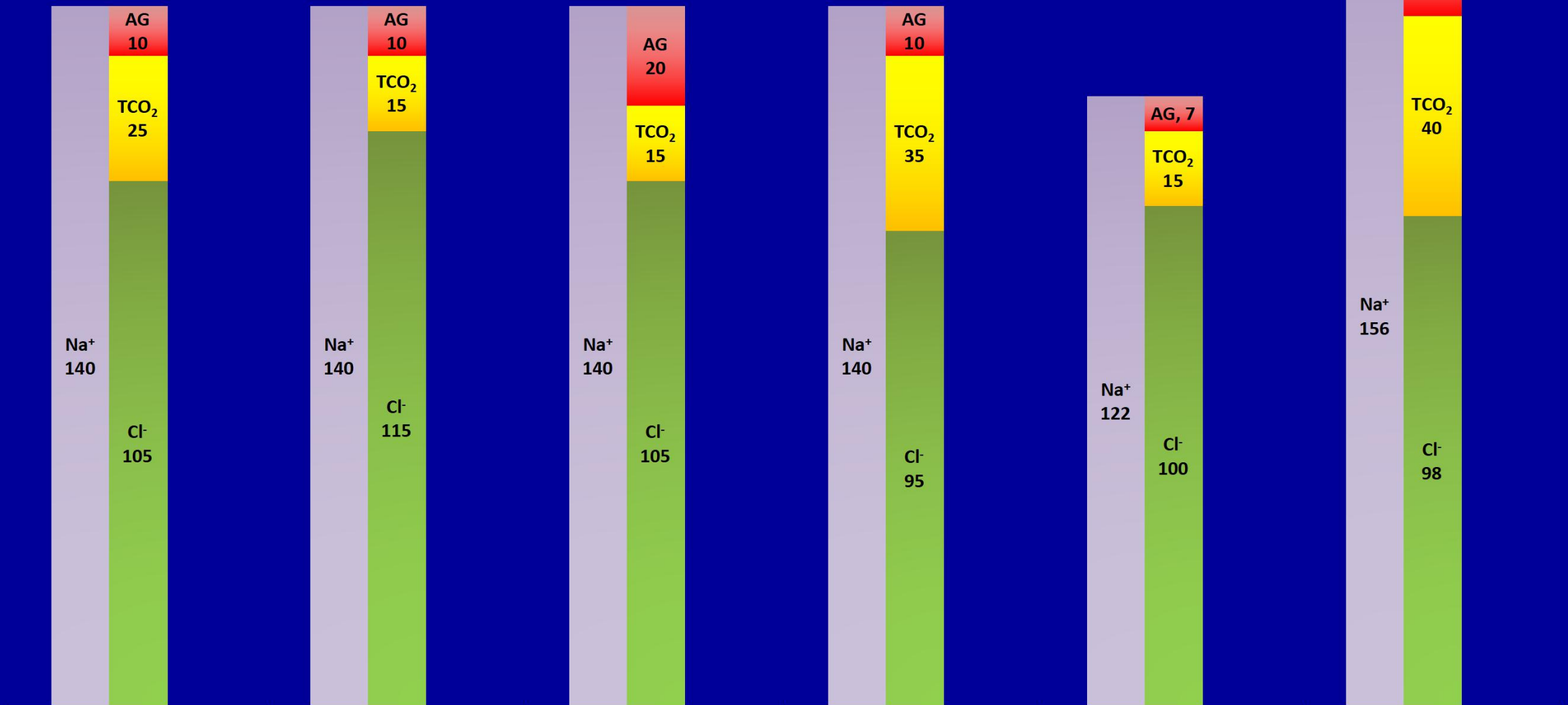
Metabolic acidosis

Respiratory alkalosis

High serum TCO<sub>2</sub>

Metabolic alkalosis

Respiratory acidosis



Normal

Normal Anion Gap...

High Anion Gap...

Metabolic Alkalosi...

Hyponatremia &...

Hypertatremia &...

# Does Serum TCO<sub>2</sub> Supersede Serum Cl<sup>-</sup> ?

Sx: 63 ♂ T2DM, HTN

Na<sup>+</sup> 140  
K<sup>+</sup> 5.2  
Cl<sup>-</sup> 113  
TCO<sub>2</sub> 17  
AG 10

Dx: Type 4 RTA  
Diabetic nephropathy

Sx: 32 ♀ anxiety, paresthesias

Na<sup>+</sup> 140  
K<sup>+</sup> 4.6  
Cl<sup>-</sup> 112  
TCO<sub>2</sub> 17  
AG 11

Dx: Panic disorder  
Chronic hyperventilation

Sx: 23 ♀ depression, insomnia

Na<sup>+</sup> 141  
K<sup>+</sup> 3.8  
Cl<sup>-</sup> 106  
TCO<sub>2</sub> 16  
AG 19

Dx: Starvation ketosis  
Eating disorder

Sx: 54 ♂ obesity, somnolence

Na<sup>+</sup> 143  
K<sup>+</sup> 4.2  
Cl<sup>-</sup> 97  
TCO<sub>2</sub> 36  
AG 10

Dx: Obesity-hypoventilation  
syndrome

Sx: 67 ♀ HF

Na<sup>+</sup> 138  
K<sup>+</sup> 3.6  
Cl<sup>-</sup> 92  
TCO<sub>2</sub> 34  
AG 12

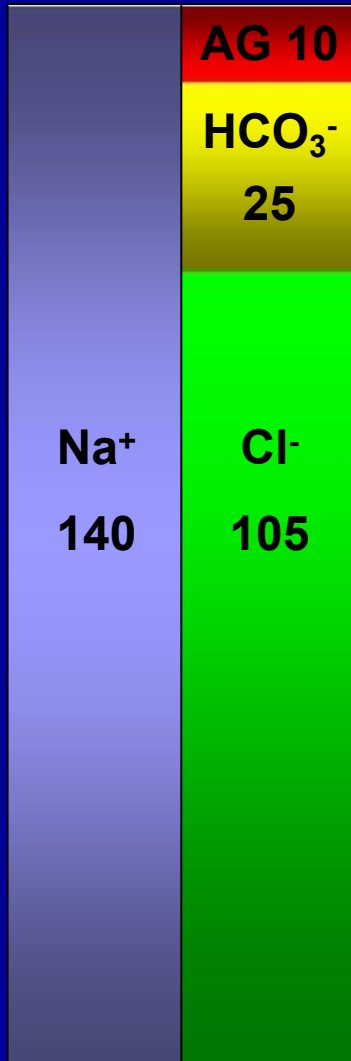
Dx: Furosemide-induced  
metabolic alkalosis

Sx: 54 ♀ alcoholic, vomiting

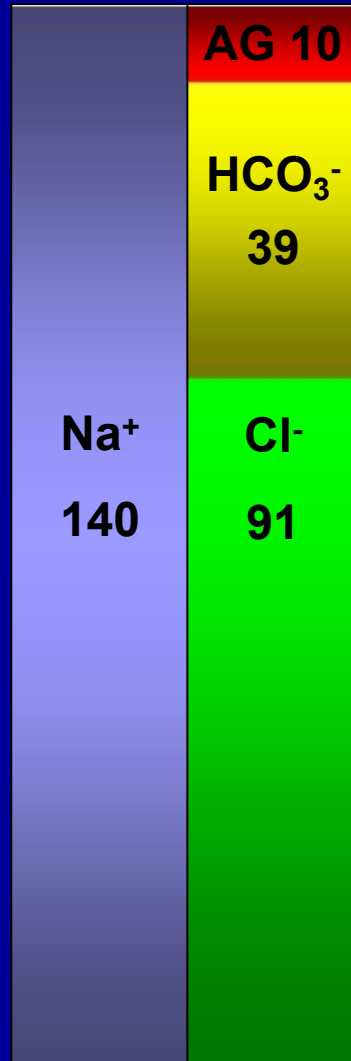
Na<sup>+</sup> 140  
K<sup>+</sup> 3.7  
Cl<sup>-</sup> 91  
TCO<sub>2</sub> 25  
AG 24

Dx: Metabolic alkalosis and  
alcoholic ketoacidosis

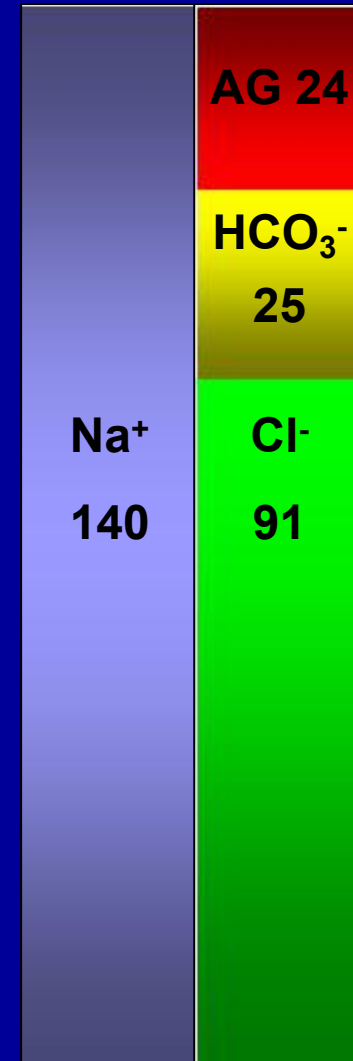
Normal



Metabolic Alkalosis



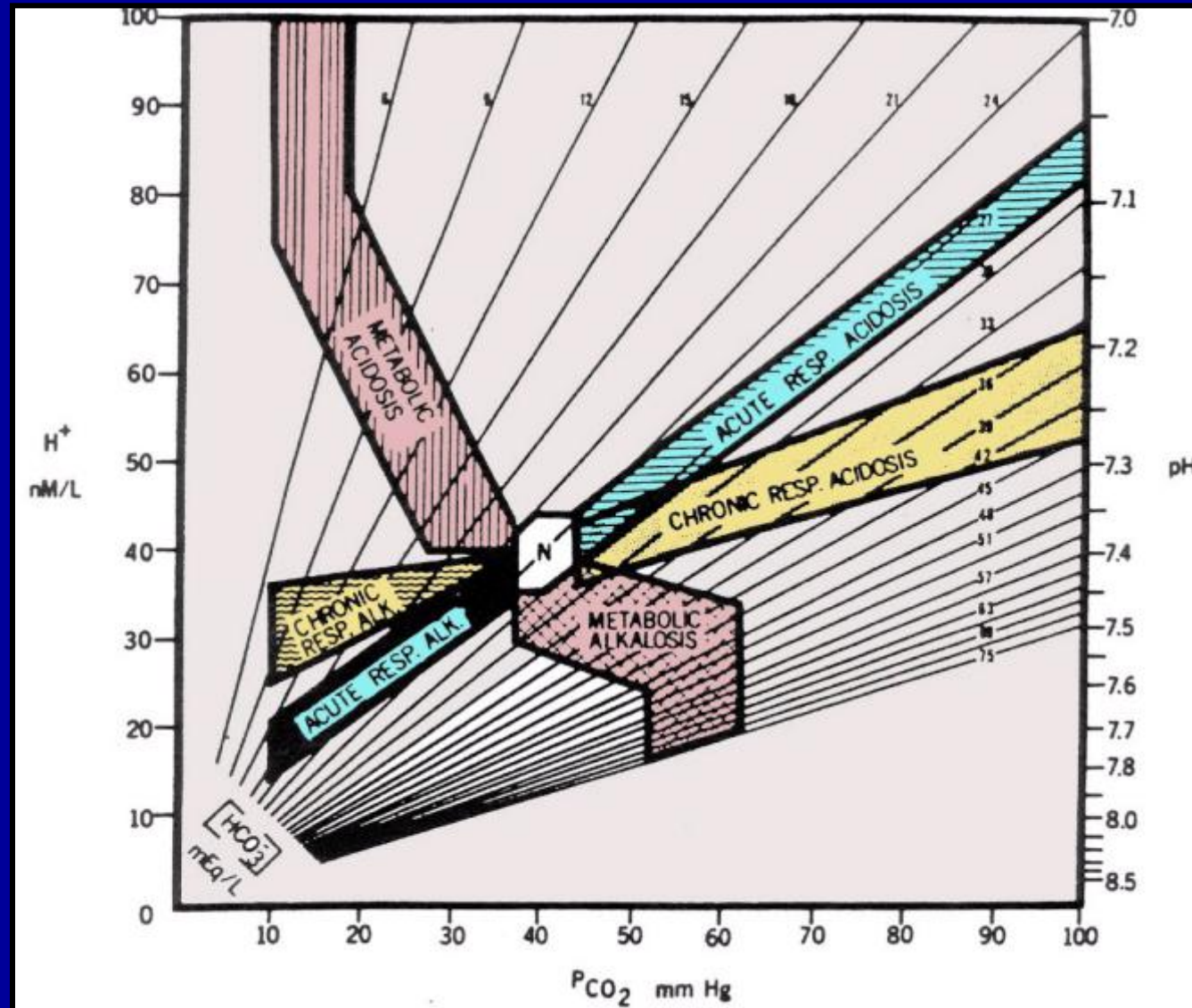
Metabolic Alkalosis and High Anion Gap Metabolic Acidosis



## Clinical Utility of Serum TCO<sub>2</sub> Concentration (3)

- Most acid-base disorders are first recognized by clinicians through abnormalities in serum TCO<sub>2</sub>
- Assessment of TCO<sub>2</sub> is complemented by evaluation of the serum Cl<sup>-</sup> and, thus, the serum AG

# Acid-Base Template





# **How Common Are Acid-Base Disorders in the Outpatient Practice?**

**What is the Normal Range for Serum TCO<sub>2</sub>?**

## Normal Range of Serum TCO<sub>2</sub> (1)

- Longstanding concern about substantial variability and wide limits of normal reported by clinical laboratories often on the order of 10-13 mEq/l, e.g., *20-31 mEq/l*
- Have encountered many patients who had serum TCO<sub>2</sub> within the lower or upper end of reported normal range, in whom assessment of blood gases revealed data consistent with a cardinal acid-base disorder

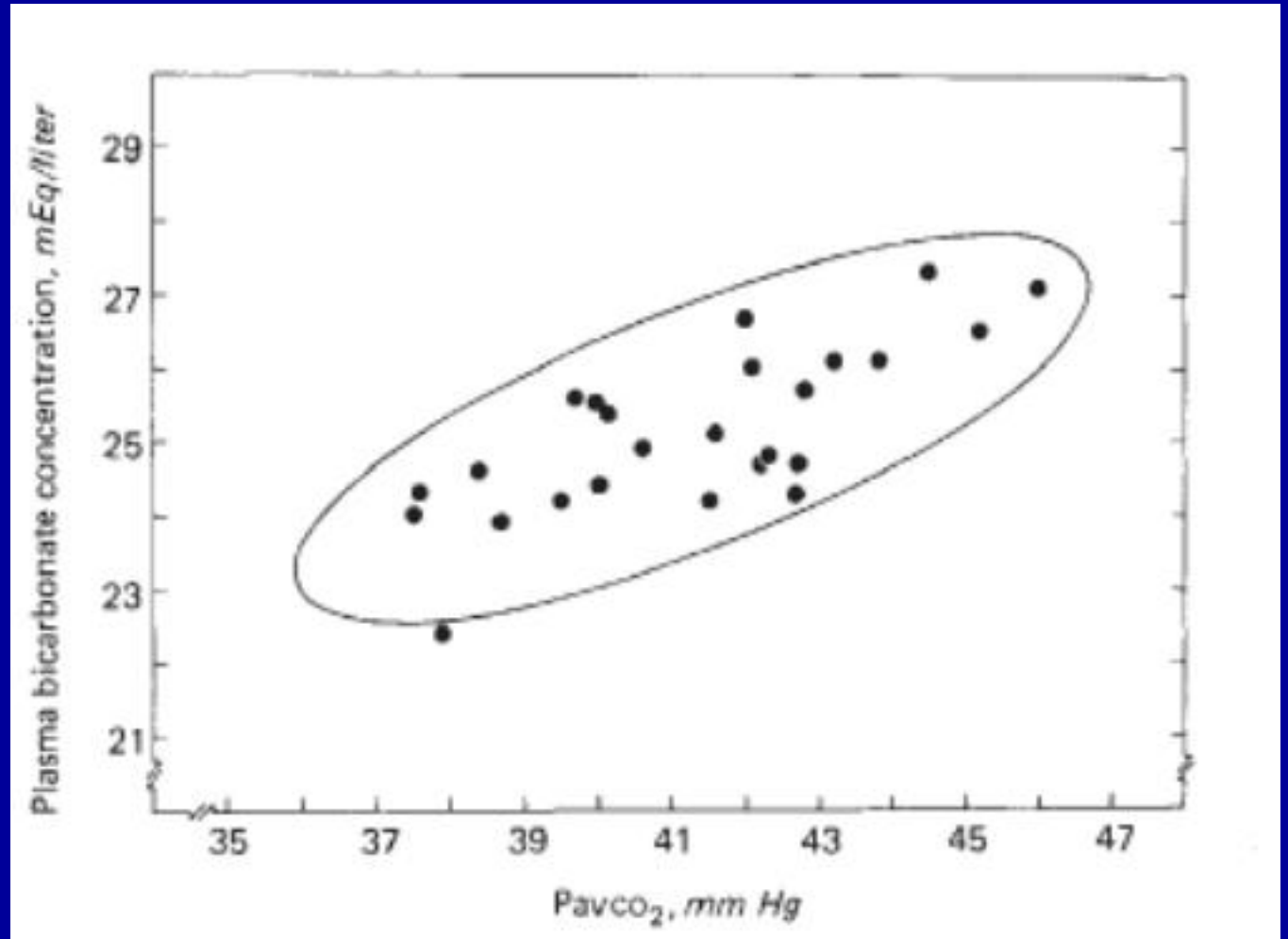
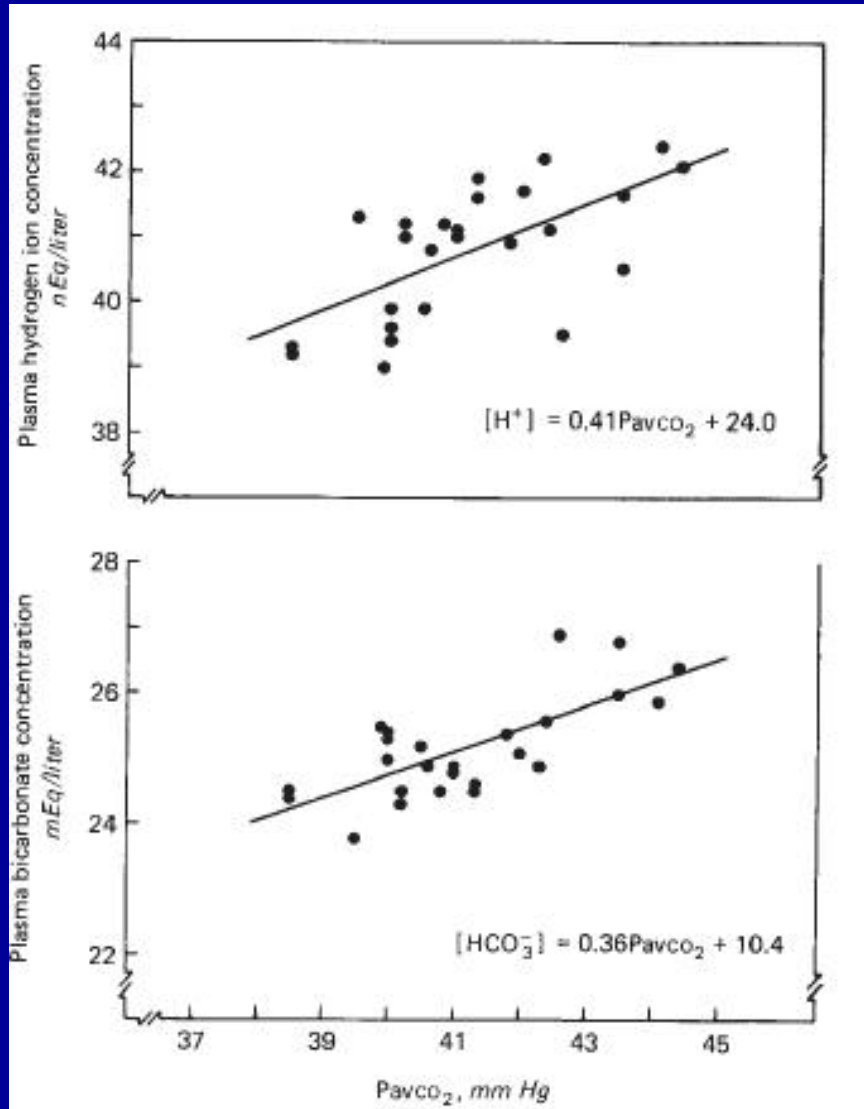
## Normal Range of Serum TCO<sub>2</sub> (2)

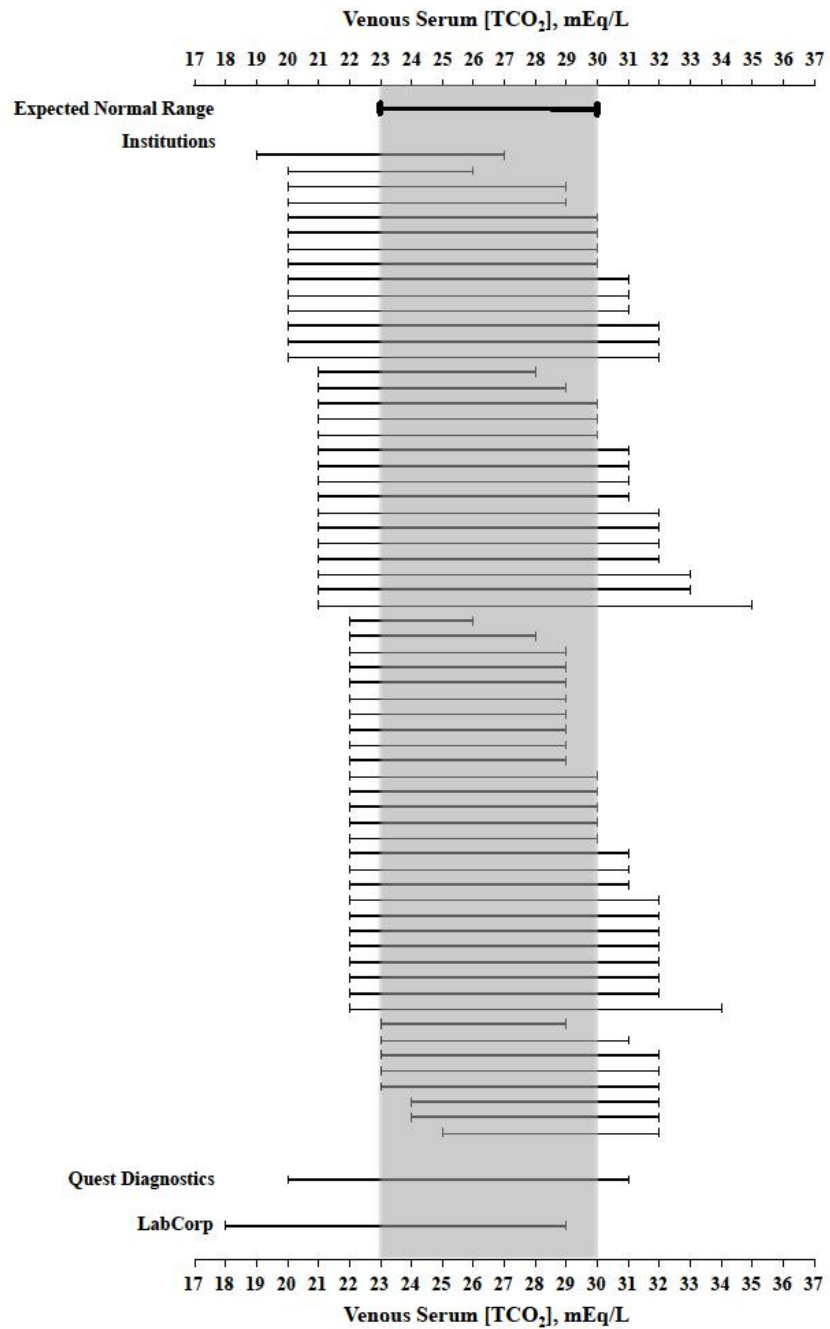
- 37-year-old woman with Sjögren syndrome referred for evaluation of active nephrolithiasis

Serum	Na <sup>+</sup>	138
	K <sup>+</sup>	3.4
	Cl <sup>-</sup>	108
	TCO <sub>2</sub>	20 (nl, 19-30)
	AG	10

- VBG revealed pH 7.32, PvCO<sub>2</sub> 38 mm Hg, and HCO<sub>3</sub><sup>-</sup> 19 mEq/L. Additional tests established the diagnosis of type 1 RTA. Treatment with potassium citrate reversed the activity of nephrolithiasis

# Normal Acid-Base Equilibrium in Man



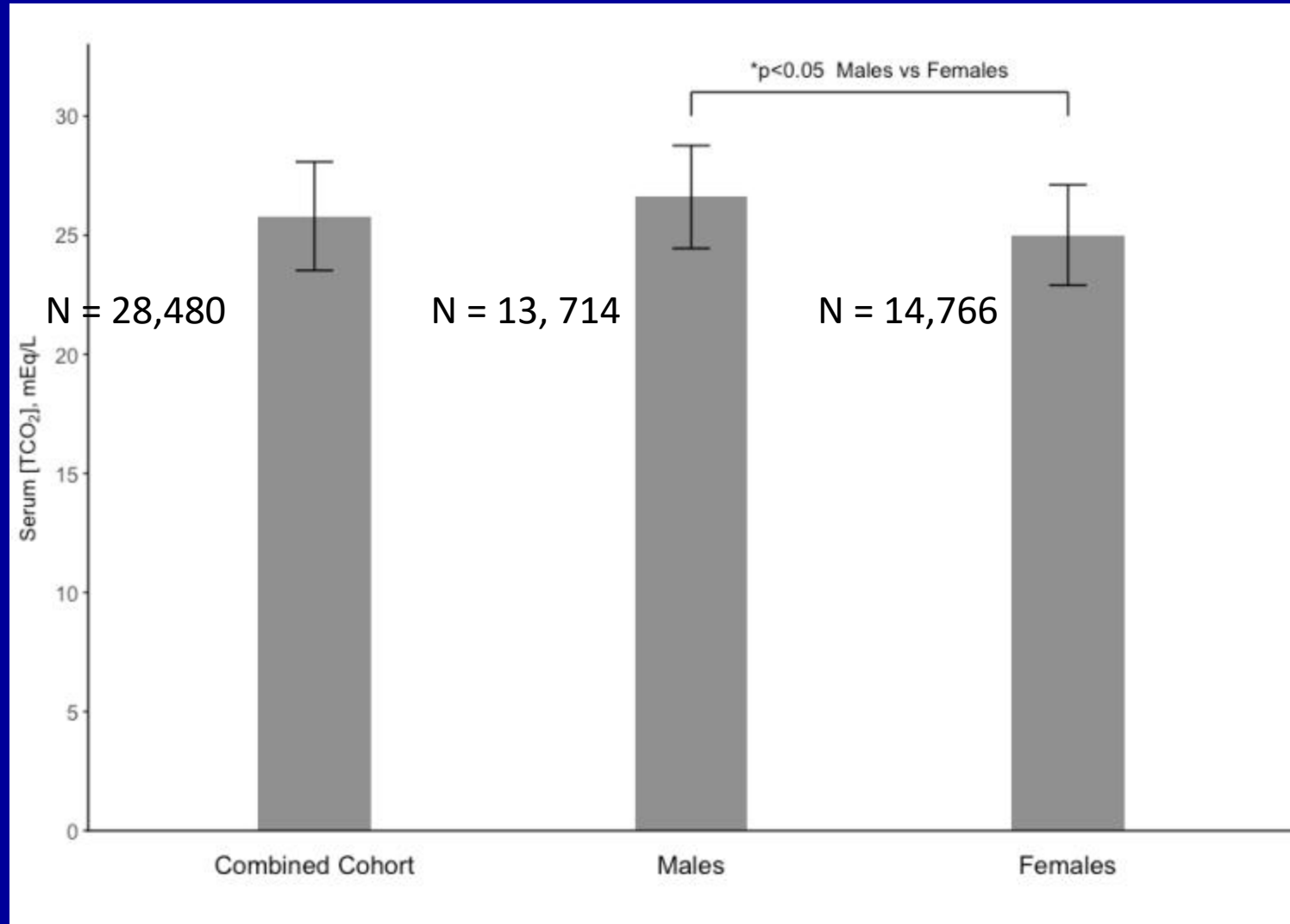


## Reported vs Expected Serum TCO<sub>2</sub>

# External Validation of Proposed Normal Range of Serum TCO<sub>2</sub>

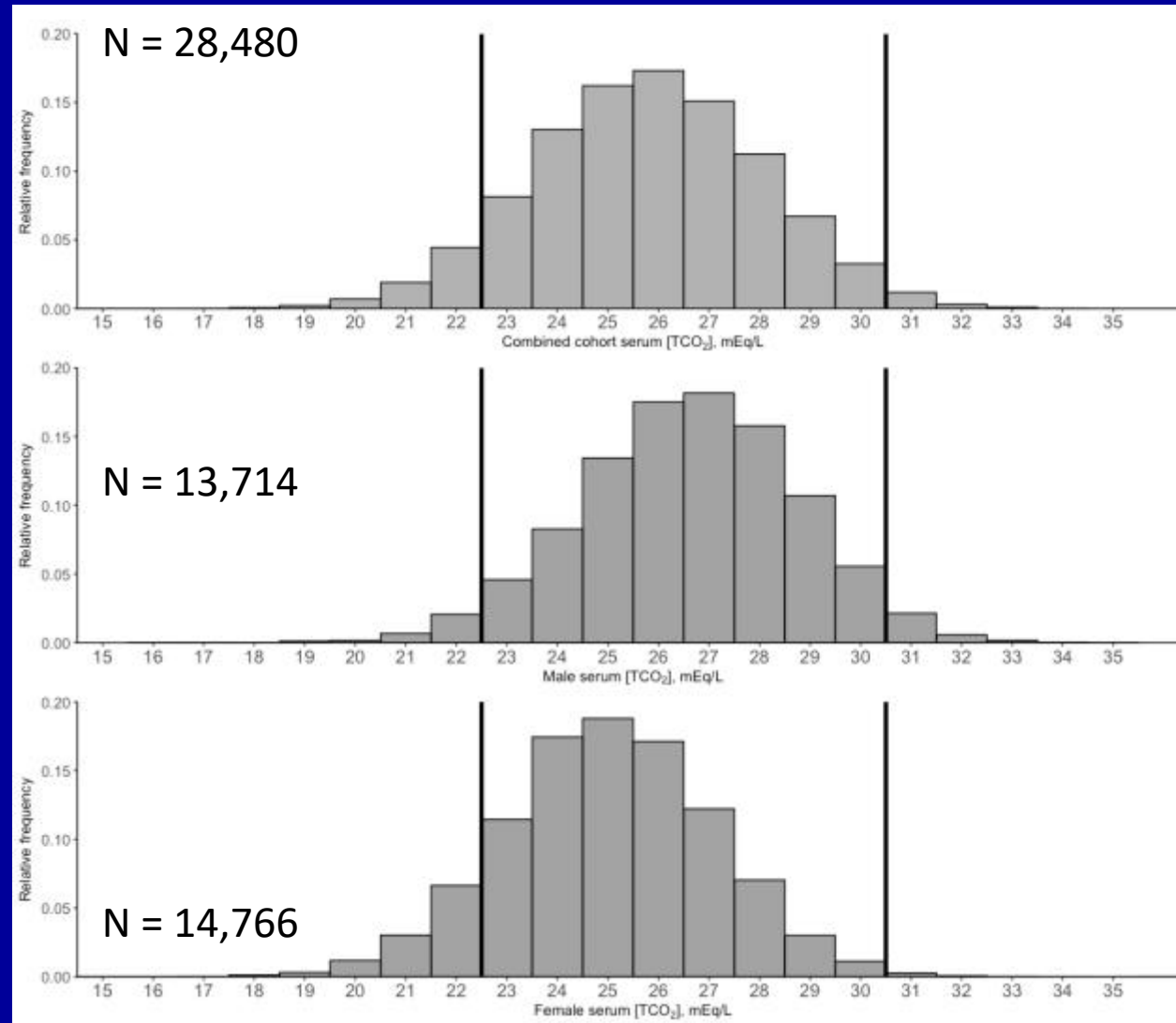
- We queried UCLA's xDR, a database containing records of ~4.5 million patients cared for at UCLA's hospitals and clinics
- Inclusion criteria:
  - Adults aged 18-40 years seen as outpatients for routine medical examination or immunization
  - Absence of kidney disease, pulmonary disease, heart failure, liver disease, cancer, diabetes mellitus, gastrointestinal disease, vomiting, diarrhea, or pregnancy
  - Not taking diuretics, base-containing substances, converting enzyme inhibitors, angiotensin receptor blockers, carbonic anhydrase inhibitors, or steroids

# Mean ( $\pm$ SD) Serum TCO<sub>2</sub> in Venous Blood in Apparently Healthy Younger Adults





# Relative Frequency of Values for Serum TCO<sub>2</sub> in Venous Blood in Apparently Healthy Younger Adults



Combined cohort

Males

Females

# Clinical States with High Prevalence of Acid-Base Disorders

- Heart failure
- COPD
- Asthma
- Hypertension
- Cirrhosis
- Gastrointestinal disorders
- Eating disorders
- Chronic alcoholism
- Diabetes mellitus
- Cancer
- CKD
- Organ transplantation

## Key Points

- Acid-base disorders have major implications for patient outcomes
- Acid-base disorders are highly prevalent in many disease states
- An expansive serum electrolyte panel that includes  $\text{Cl}^-$  and  $\text{TCO}_2$  is required for screening for acid-base disorders and for monitoring previously diagnosed acid-base disorders