

Should the Serum Concentrations of Cl^- and TCO_2 Be Measured in Everyday Clinical Practice?

Nicolaos E. Madias, M.D.
Physician, Division of Nephrology
Department of Medicine
St. Elizabeth's Medical Center
Maurice S. Segal, M.D. Professor of Medicine
Tufts University School of Medicine
Boston, Massachusetts, USA

20th Hellenic Congress of Nephrology
Athens, Greece
May 3-6, 2018

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⁺ 143, K⁺ 3.8, Cl⁻ 96, TCO₂ 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⁺
K⁺
Cl⁻
TCO₂
AG

Routine Electrolyte Panel Greece

Na⁺
K⁺

Sx: 58 ♂ headaches, palpitations

Na ⁺	143
K ⁺	3.8
Cl ⁻	96
TCO ₂	38
AG	9

Dx: Primary aldosteronism

Clinical Utility of Serum Cl⁻ Concentration (1)

Changes in serum Cl⁻ denote:

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

Clinical Utility of Serum Cl⁻ Concentration (2)

Changes in serum Cl⁻ denote:

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

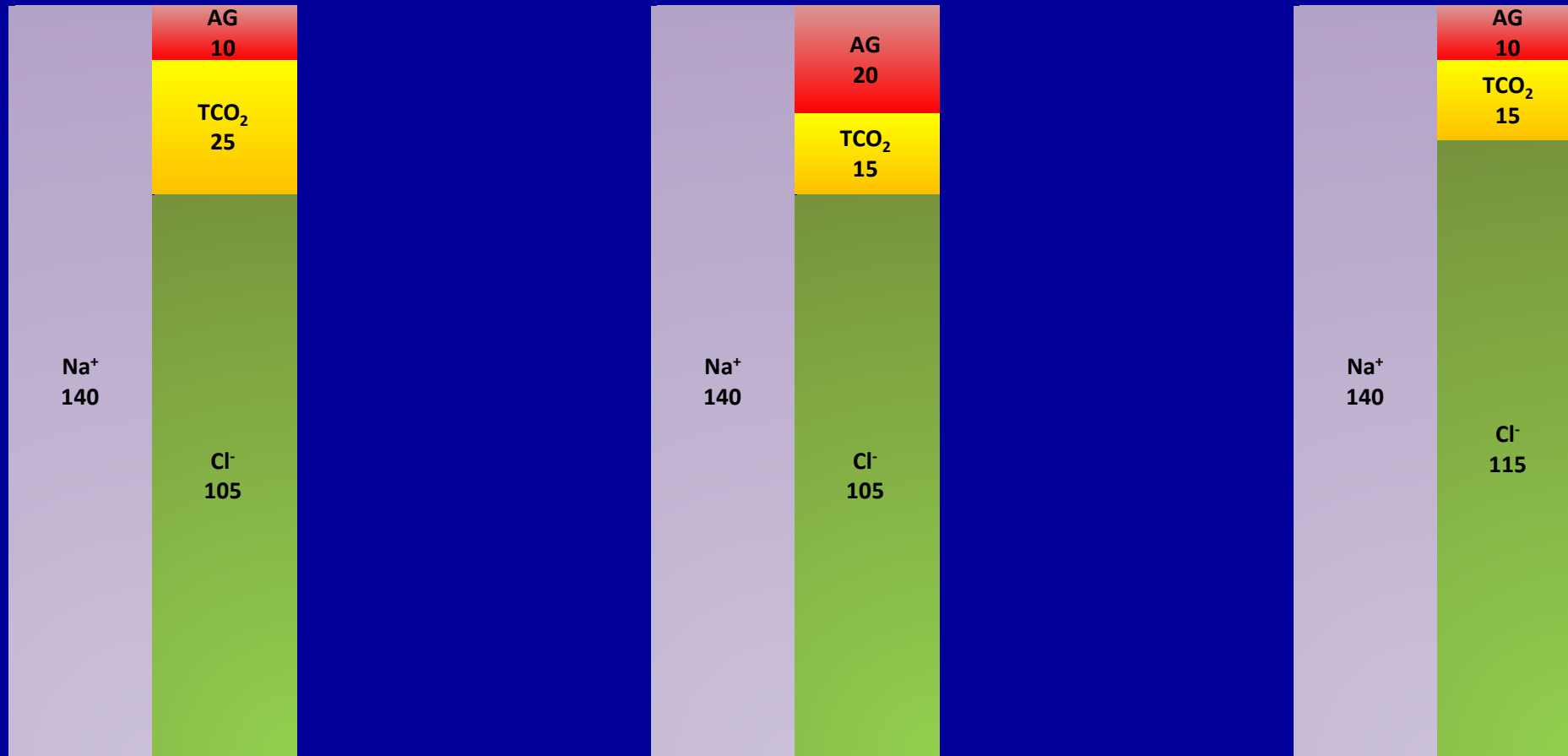
Clinical Utility of Serum Cl⁻ Concentration (3)

Changes in serum Cl⁻ denote:

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

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- Normochloremia occurs in high AG metabolic acidosis

Electrolyte Patterns in Metabolic Acidosis

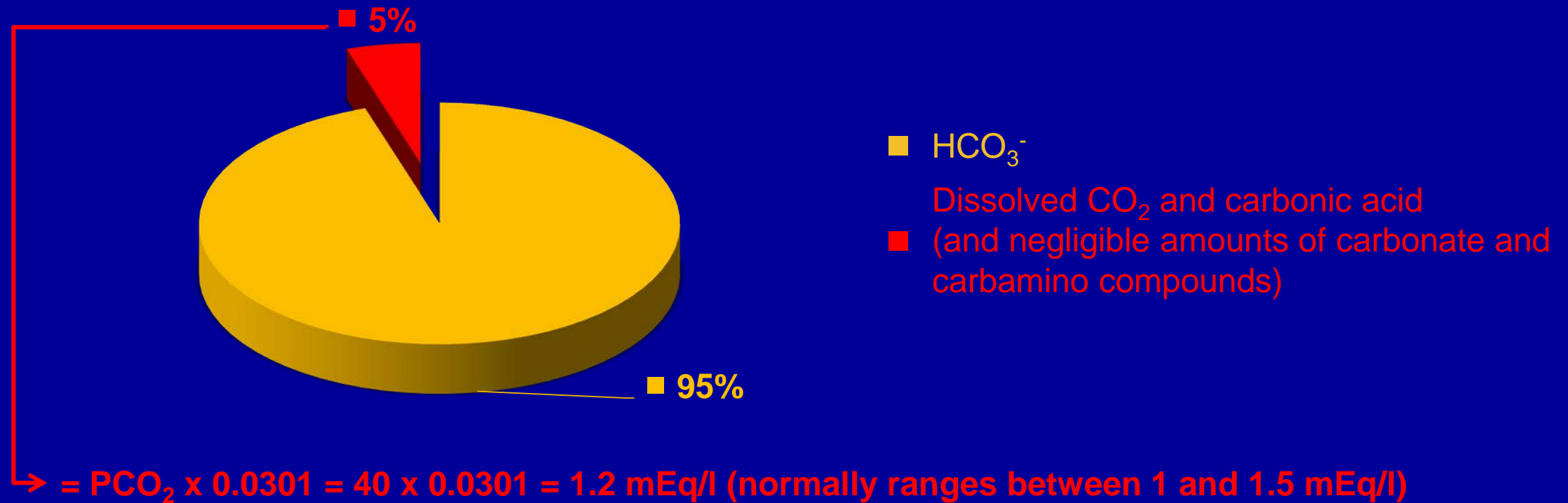


Normal

High Anion Gap Metabolic Acidosis

Normal Anion Gap Metabolic Acidosis

Serum TCO₂ (a.k.a. bicarbonate or carbon dioxide)



- Measurement of serum TCO₂ is made by first releasing all CO₂ in the sample after addition of strong acid and then utilizing an electrometric or enzymatic method.
- Serum HCO₃⁻ is not measured directly but calculated from pH and PCO₂ 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 ₂	↑ [HCO ₃ ⁻]	Δ[HCO ₃ ⁻]/ΔPaCO ₂ = 0.1 mEq/L per mmHg
chronic			Δ[HCO ₃ ⁻]/ΔPaCO ₂ = 0.35 mEq/L per mmHg
Respiratory alkalosis acute	↓ PaCO ₂	↓ [HCO ₃ ⁻]	Δ[HCO ₃ ⁻]/ΔPaCO ₂ = 0.2 mEq/L per mmHg
chronic			Δ[HCO ₃ ⁻]/ΔPaCO ₂ = 0.4 mEq/L per mmHg
Metabolic acidosis	↓ [HCO ₃ ⁻]	↓ PaCO ₂	ΔPaCO ₂ /Δ[HCO ₃ ⁻] = 1.2 mmHg per mEq/L
Metabolic alkalosis	↑ [HCO ₃ ⁻]	↑ PaCO ₂	ΔPaCO ₂ /Δ[HCO ₃ ⁻] = 0.7 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 TCO₂ Concentration (2)

- Changes in serum TCO₂ denote disorders of acid-base balance

Low serum TCO₂

Metabolic acidosis

Respiratory alkalosis

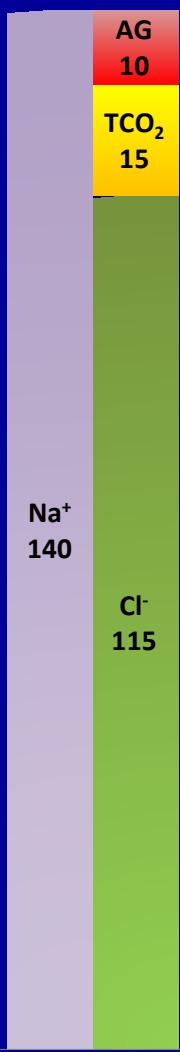
High serum TCO₂

Metabolic alkalosis

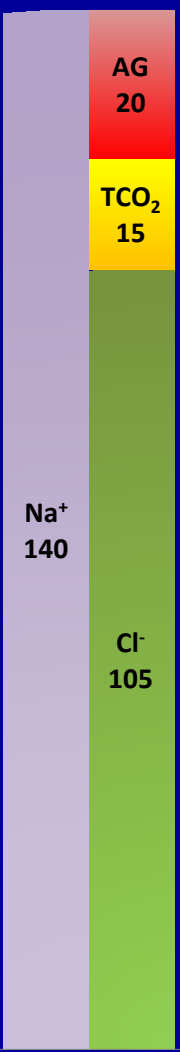
Respiratory acidosis



Normal



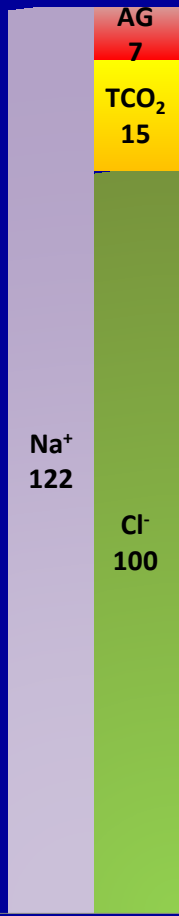
Normal Anion Gap
Metabolic Acidosis or
Respiratory Alkalosis



High Anion Gap Metabolic
Acidosis



Metabolic Alkalosis or
Respiratory Acidosis



Hyponatremia & Normal
Anion Gap Metabolic
Acidosis or Respiratory
Alkalosis



Hypernatremia & Metabolic
Alkalosis or Respiratory
Acidosis

Does Serum TCO₂ Supersede Serum Cl⁻ ?

Sx: 63 ♂ T2DM, HTN

Na⁺ 140
K⁺ 5.2
Cl⁻ 113
TCO₂ 17
AG 10

Dx: Type 4 RTA
Diabetic nephropathy

Sx: 32 ♀ anxiety, paresthesias

Na⁺ 140
K⁺ 4.6
Cl⁻ 112
TCO₂ 17
AG 11

Dx: Panic disorder
Chronic hyperventilation

Sx: 23 ♀ depression, insomnia

Na⁺ 141
K⁺ 3.8
Cl⁻ 106
TCO₂ 16
AG 19

Dx: Starvation ketosis
Eating disorder

Sx: 54 ♂ obesity, somnolence

Na⁺ 143
K⁺ 4.2
Cl⁻ 97
TCO₂ 36
AG 10

Dx: Obesity-hypoventilation
syndrome

Sx: 67 ♀ HF

Na⁺ 138
K⁺ 3.6
Cl⁻ 92
TCO₂ 34
AG 12

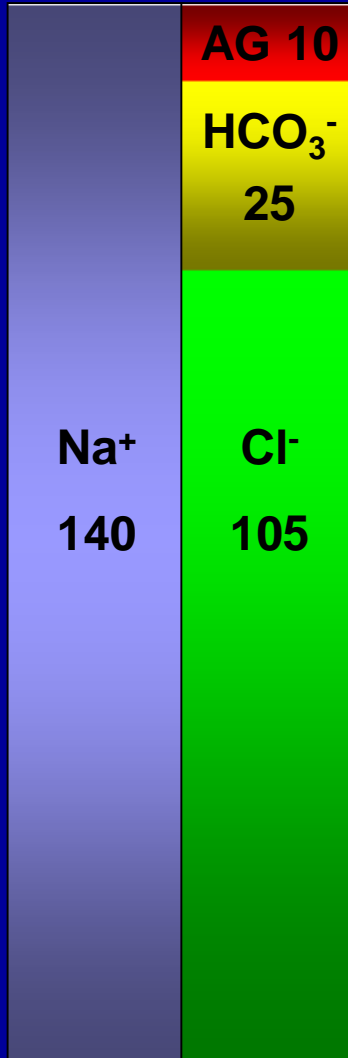
Dx: Furosemide-induced
metabolic alkalosis

Sx: 54 ♀ alcoholic, vomiting

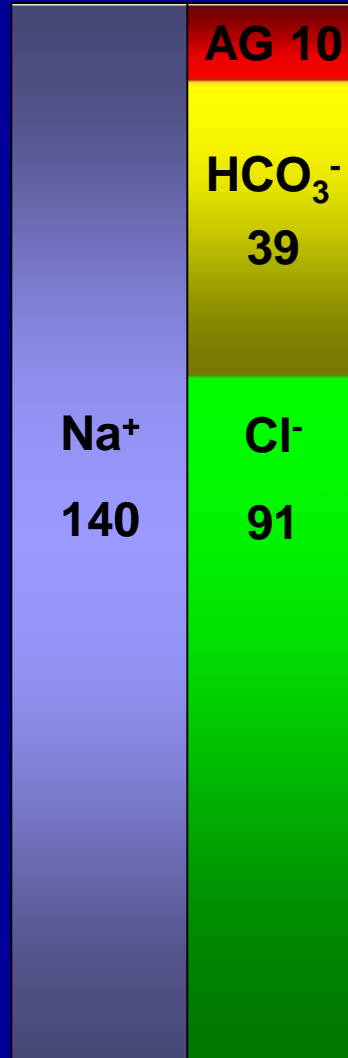
Na⁺ 140
K⁺ 3.7
Cl⁻ 91
TCO₂ 25
AG 24

Dx: Metabolic alkalosis and
alcoholic ketoacidosis

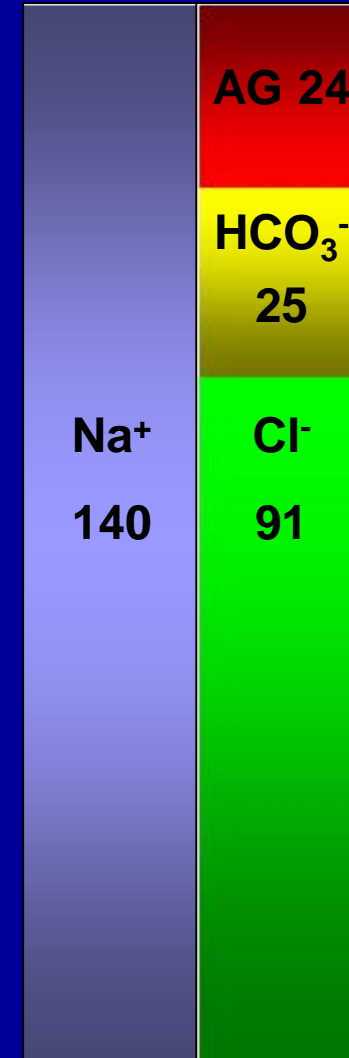
Normal



Metabolic Alkalosis



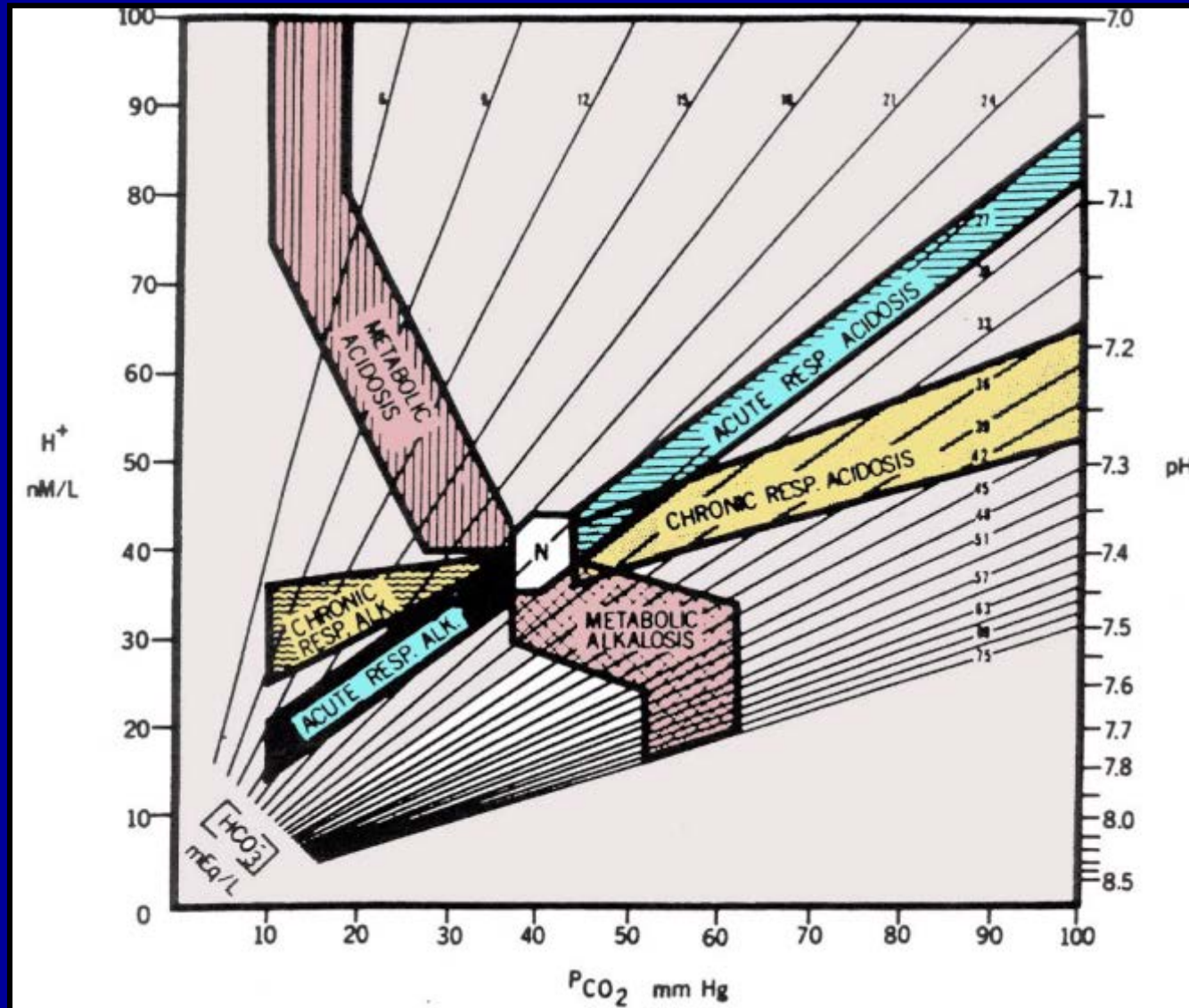
Metabolic Alkalosis and High Anion Gap Metabolic Acidosis



Clinical Utility of Serum TCO₂ Concentration (3)

- Most acid-base disorders are first recognized by clinicians through abnormalities in serum TCO₂
- Assessment of TCO₂ is complemented by evaluation of the serum Cl⁻ 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 TCO₂?

Normal Range of Serum TCO₂ (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 TCO₂ 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

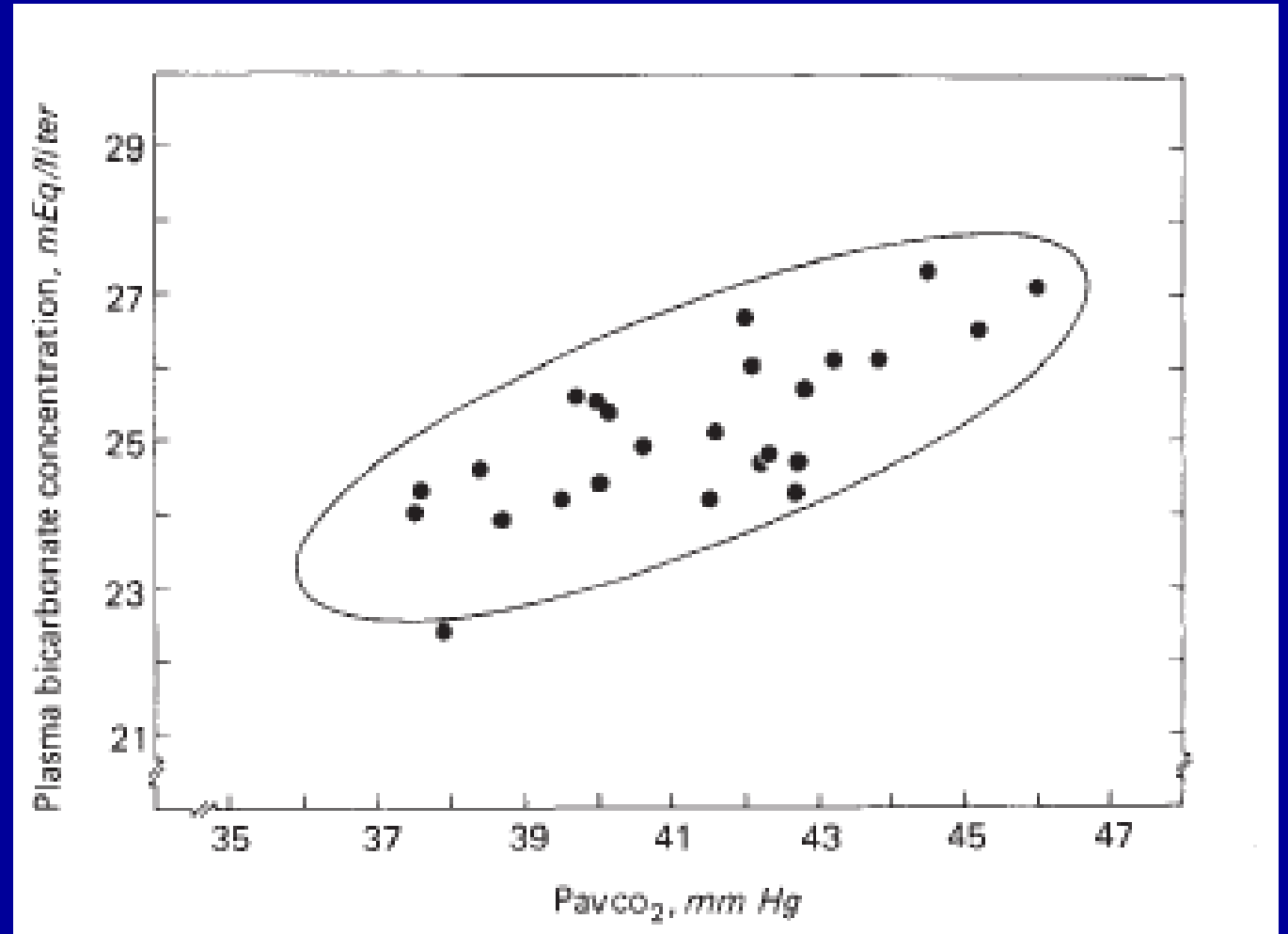
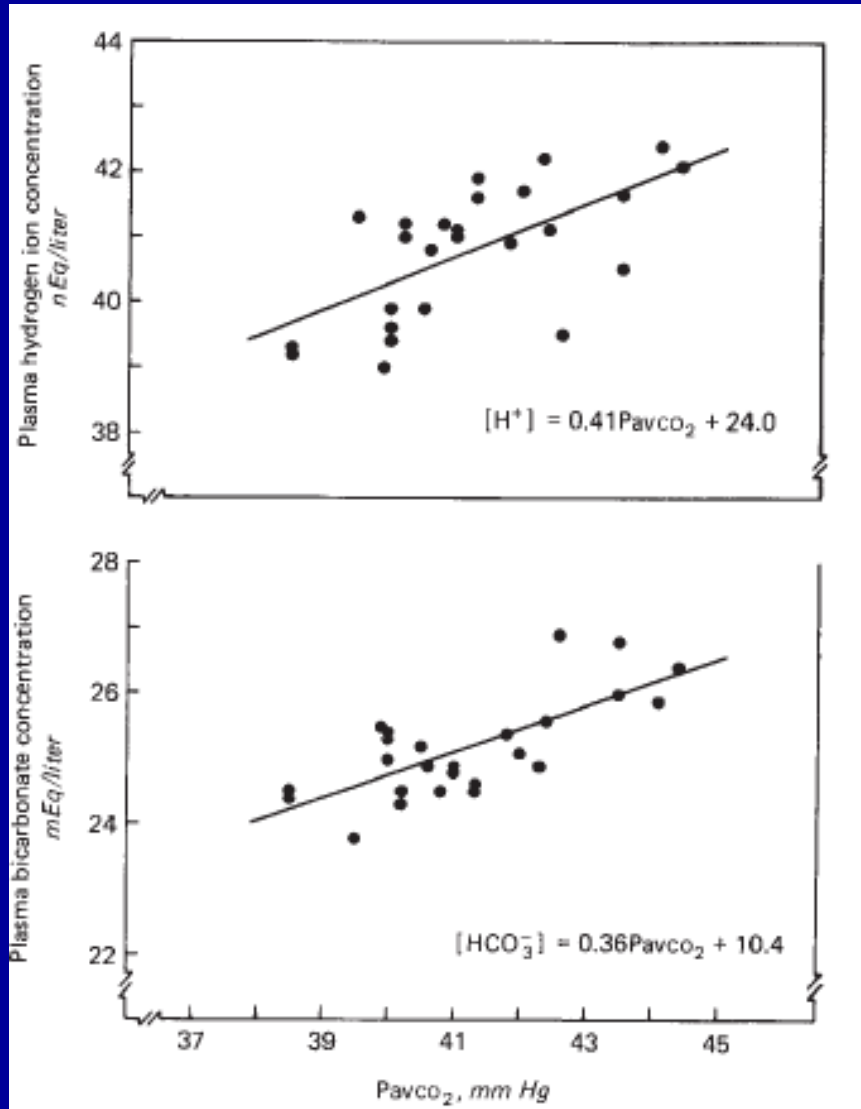
Normal Range of Serum TCO₂ (2)

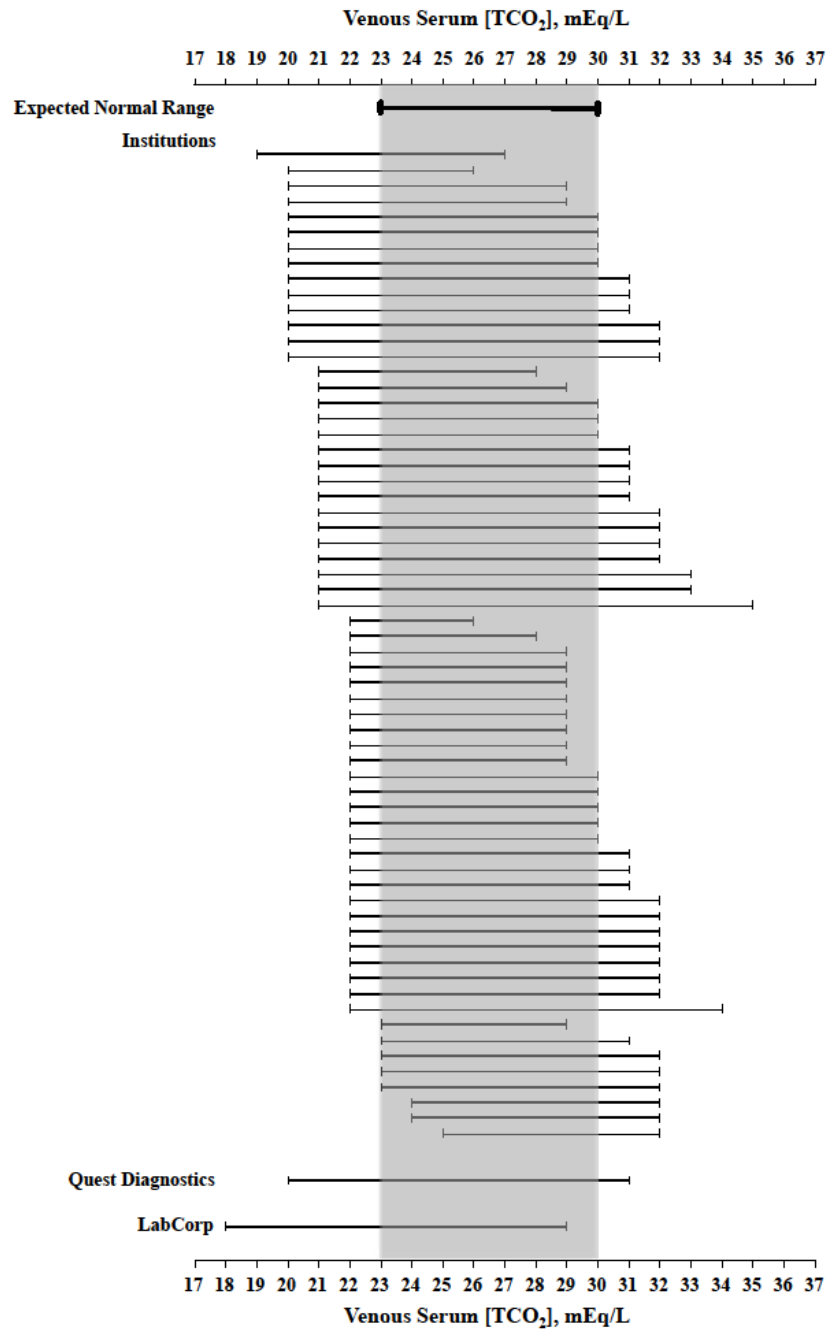
- 37-year-old woman with Sjögren syndrome referred for evaluation of active nephrolithiasis

Serum	Na ⁺	138
	K ⁺	3.4
	Cl ⁻	108
	TCO ₂	20 (nl,19-30)
	AG	10

- VBG revealed pH 7.32, PvCO₂ 38 mm Hg, and HCO₃⁻ 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



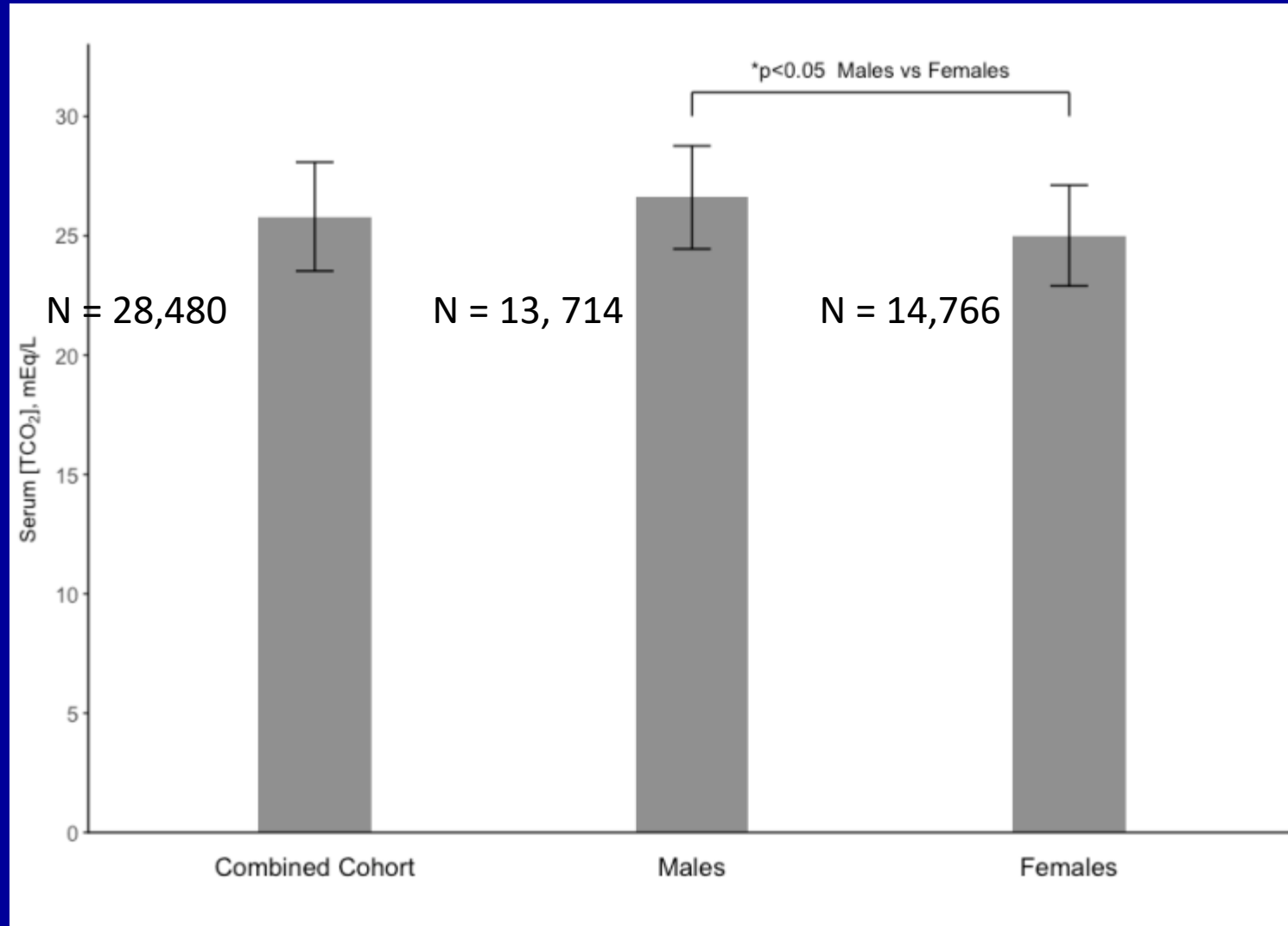


Reported vs Expected Serum TCO₂

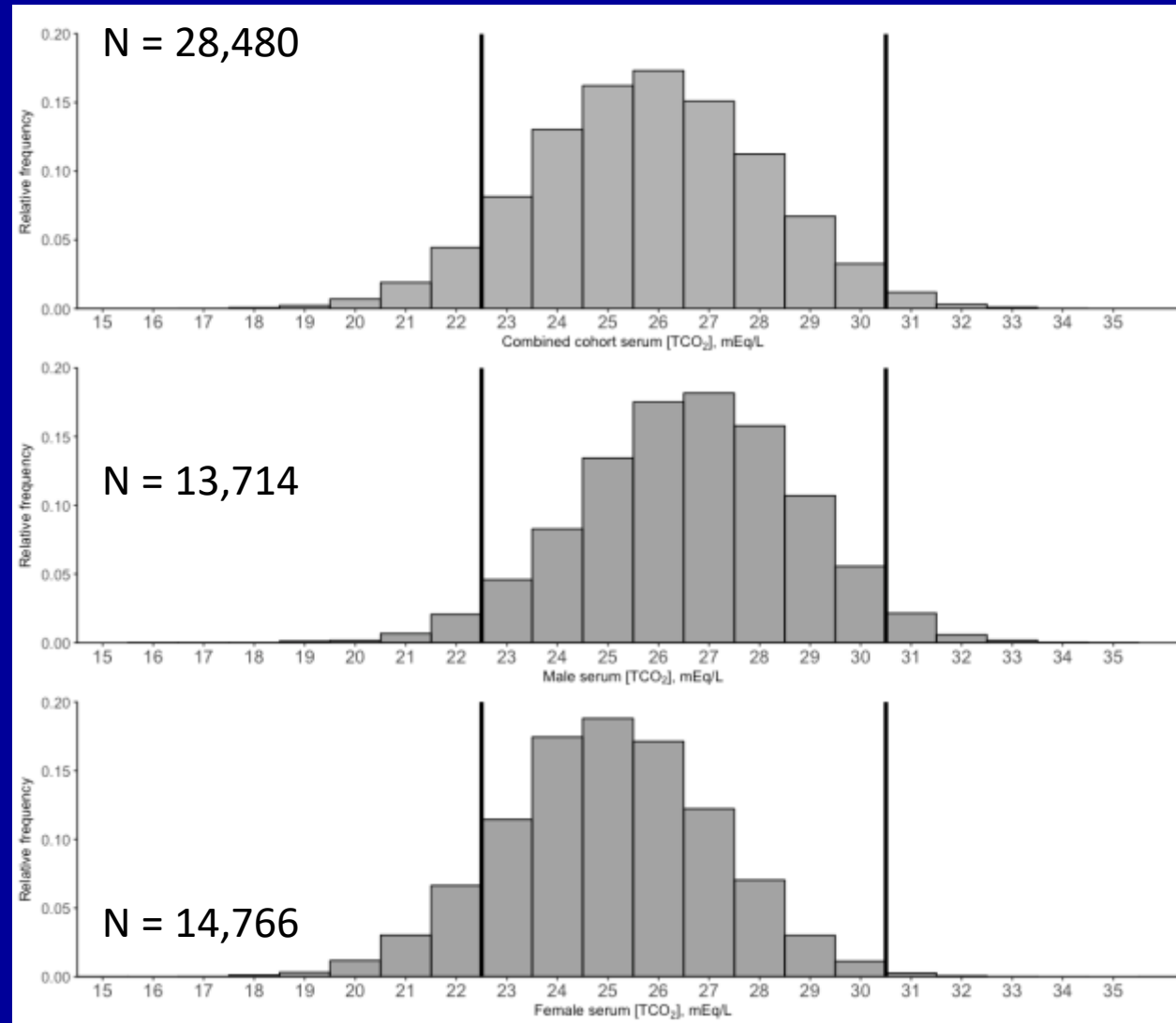
External Validation of Proposed Normal Range of Serum TCO₂

- 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 TCO₂ in Venous Blood in Apparently Healthy Younger Adults



Relative Frequency of Values for Serum TCO₂ 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 Cl^- and TCO_2 is required for screening for acid-base disorders and for monitoring previously diagnosed acid-base disorders