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# Acid Base Disorders

ACOI 2018

Board Review

Case Studies

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# Disclosures

Nothing to declare

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# High Anion Gap Acidosis Case 1

40 yo gentleman presenting to ER with coma

labs : pH 7.14/ pCO<sub>2</sub> 15; Na 138/ K 6.4/ Cl 100/ HCO<sub>3</sub>  
5; BS 100/ BUN 18/ S- OSM 340/ ETOH 0/ALB 4.0

funduscopic showed optic neuritis

How do you approach the differential of this acid base disorder ?

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# Case 1

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory- METABOLIC
3. Compensation appropriate- YES
4. Anion gap – HIGH ( $138 - 105 = 23$ )
5.  $\Delta$  gap =  $\Delta$  HCO<sub>3</sub> - YES
6. Osmolar gap – YES ( $340 - 288 = 52$ )

Corrected anion gap =  $2.5 \times (4 - \text{albumin})$

# High Osmolar Gap Acidosis

when there is a high osmolar gap (>20) as well as a high anion gap the differential includes methanol, ethylene glycol, and propylene glycol intoxication

no other gapped acidosis will increase the osmolar gap to this extent

**osmolar gap = s-osm (meas) - s-osm (calc)**

**ABNORMAL > 10 mosm, PATHOLOGIC > 20**

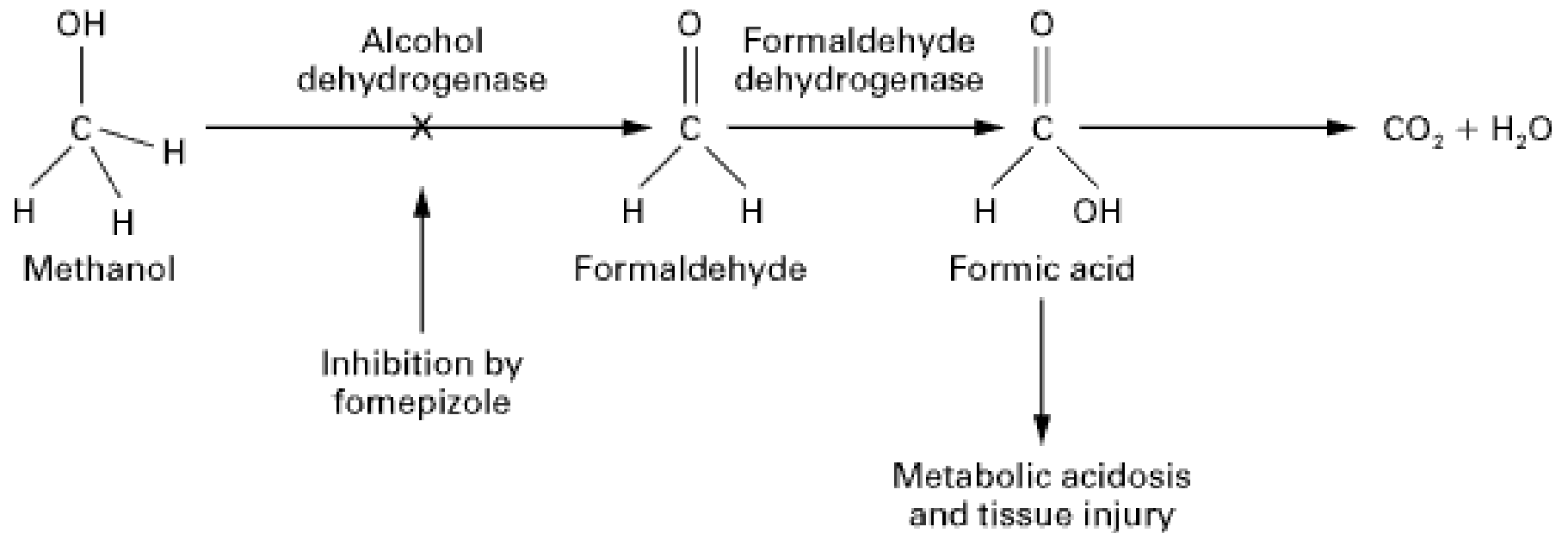
# High Osmolar Gap Acidosis

methanol leads to formic acidosis with CNS and optic toxicity (lethal dose > 15 ml)

ethylene glycol leads to glycolic and oxalic acidosis with renal and CNS toxicity with needle shaped crystals on UA (lethal dose 1-1.5 ml/kg)

treatment of both is ETOH or fomepizole to block alcohol dehydrogenase and/or dialysis

Propylene glycol usually occurs with lorazepam infusion (drug diluent)

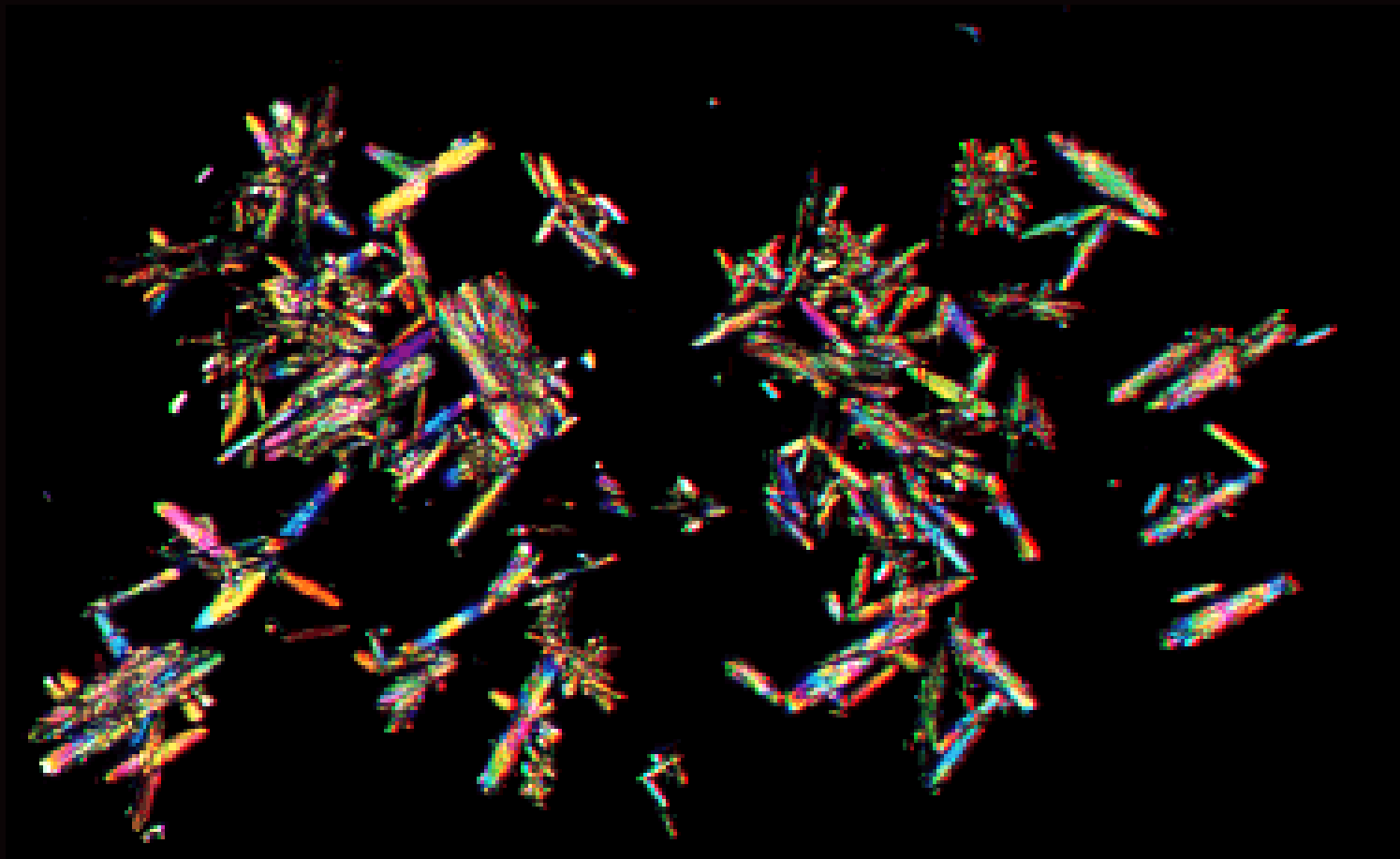


Cost \$ 3000 dollars/treatment

Major alcohol intoxications<sup>a</sup>

Disorder	Substance(s) Causing Toxicity	Clinical and Laboratory Abnormalities	Comments
Alcoholic (ethanol) ketoacidosis	$\beta$ -hydroxybutyric acid Acetoacetic acid	Metabolic acidosis	May be most frequent alcohol-related disorder; mortality low relative to other alcohols; rapidly reversible with fluid administration; increase in SOsm inconsistent
Methanol intoxication	Formic acid Lactic acid Ketones	Metabolic acidosis, hyperosmolality, retinal damage with blindness, putaminal damage with neurologic dysfunction	Less frequent than ethylene glycol; hyperosmolality and high anion gap acidosis can be present alone or together; mortality can be high if not treated quickly
Ethylene glycol intoxication	Glycolic acid Calcium oxalate	Myocardial and cerebral damage and renal failure; metabolic acidosis, hyperosmolality, hypocalcemia	More frequent than methanol intoxication; important cause of intoxications in children; hyperosmolality and high anion gap acidosis can be present alone or together
Diethylene glycol intoxication	2-Hydroxyethoxyacetic acid	Neurological damage, renal failure, metabolic acidosis, hyperosmolality	Very high mortality possibly related to late recognition and treatment; most commonly results from ingestion in contaminated medications or commercial products; hyperosmolality may be less frequent than with other alcohols
Propylene glycol intoxication	Lactic acid	Metabolic acidosis, hyperosmolality	May be most frequent alcohol intoxication in ICU; minimal clinical abnormalities; stopping its administration is sufficient treatment in many cases
Isopropanol intoxication	Isopropanol	Coma, hypotension, hyperosmolality	Hyperosmolality without acidosis; positive nitroprusside reaction





**Calcium oxalate monohydrate crystals** Urine sediment viewed under polarized light showing coarse, needle-shaped calcium oxalate monohydrate crystals. These crystals have a similar appearance to hippurate crystals. Courtesy of W Merrill Hicks, MD.

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# High Anion gap without High Osmolar Gap

**Uremia** - gap 20, GFR < 15ml/min

**Salicylates** - severe respiratory alkalosis, drug levels should always be checked – lactic acidosis

**Lactic acidosis** - diagnosis of exclusion A, B and D

**Pyroglutamic acidosis** – critical illness, females and acetaminophen use. Urine 5-oxoproline

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# High Anion gap without High Osmolar Gap

Ketoacidosis – abnormal glucagon/insulin ratio

**diabetic** - acetone positive, BS > 200

**alcoholic** - during abstinence and BS < 200, acetone may be negative

**starvation** - diagnosis made by history, acetone may be negative

beta hydroxybutyric acid is the major ketone body in all ketoacidosis

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# High Anion Gap Acidosis - Treatment

Treatment of organic acidosis is controversial with physiological data on both sides

Clinically there is no evidence of improved patient survival

Therefore, treatment with bicarbonate is reserved for a pH < 7.1 with refractory hypotension or arrhythmia

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# High Anion Gap Acidosis - Summary

The presence of a high anion gap as well as a high osmolar gap leads to the diagnosis of intoxication with ethylene glycol or methanol

The treatment of both are the same (ETOH, fomepizole and dialysis)

Optic neuritis is seen in methanol intoxication

Propylene glycol occurs only in inpatients

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# High Anion Gap Acidosis

Recent reports

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# Pyroglutamic Acidosis – Acquired Form

Pyroglutamic acid accumulates during times of glycine deficiency (critical illness, pregnancy and malnutrition) which will deplete glutathione

Usually occurs in women (urine 5-oxoproline)

Glutathione is also depleted by acetaminophen use

Syndrome – unexplained high anion gap acidosis, use of acetaminophen and change in mental status in the setting of critical illness

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# Propylene Glycol Intoxication

Propylene glycol (PG) is a solvent used in IV medications (lorazepam)

Use of lorazepam infusions at  $> 0.1$  mg/kg/hr may cause accumulation of PG leading to a high osmolar high anion gap acidosis (lactic acidosis)

Treat with fomepizole

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# Propafol Infusion Syndrome

Occurs in critically ill patients

Myocardial failure, rhabdomyolysis, metabolic acidosis  
hypertriglyceridemia and renal failure

Anion gap may be elevated (?? lactic acidosis)

Risk related to duration (> 48 h) and intensity of  
infusion

Infusion > 4mg/kg/hr

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# Diethylene Glycol

Substitute for glycerol by disreputable companies  
selling to developing nations

Causes CNS and PNS symptoms

Causes AKI

Generation of 2-hydroxyethylacetate (HEAA)

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# Drug induced Lactic Acidosis

Linezolid – usually occurs with prolonged therapy (5-6 weeks)

Metformin – occurs in patients with contraindications given the drug (liver disease, > Stage 3 CKD, CHF, critical illness, peri-operative state, and IV contrast)

HAART HIV – chronic use of many drugs have been implicated (didanosine, stavudinw

Misc – mangosteen, clenbuteral

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# D-LACTIC ACIDOSIS

Recent reports of gapped metabolic acidosis in patients with short bowel syndrome

Occurs after ingesting a large CHO load

Confusion, gapped metabolic acidosis and negative lactate levels

Treatment – antibiotics and NPO

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## Case 2 - Hyperchloremic Metabolic Acidosis

an elderly man present with tachypnea, diarrhea and weakness

labs - pH 7.24/ pCO<sub>2</sub> 24; Na 140/ K 6.7/ Cl 120/ HCO<sub>3</sub> 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?

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## Case 2

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory- METABOLIC
3. Compensation appropriate - YES
4. Anion gap – NORMAL (10)
5.  $\Delta$  gap =  $\Delta$  HCO<sub>3</sub> - YES
6. Osmolar gap - NONE

# Urine Anion Gap

HCO<sub>3</sub> is either resorbed (prox) or regenerated (distal)

To regenerate HCO<sub>3</sub> - NH<sub>4</sub> is formed distally

In an acidic urine **Na+K+NH<sub>4</sub> = Cl**

NH<sub>4</sub> can not be measured therefore

**Cl > Na+K** if NH<sub>4</sub> is present NL DISTAL FX

If Cl < or = Na+K then distal urinary acidification is impaired (UAG abnormal)

# 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.) ( $\text{Cl} > \text{Na} + \text{K}$ )

Abnormal UAG - CKD (lack of  $\text{NH}_4$  production), distal RTA Type I and IV or aldosterone deficiency) ( $\text{Cl} \leq \text{Na} + \text{K}$ )



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# Hyperchloremic Metabolic Acidosis

Normal Urine  $\text{NH}_4$  ( $\text{Cl} > \text{Na} + \text{K}$ )

this is due to  $\text{HCO}_3$  loss with normal distal tubular function

**GI** - loss of  $\text{HCO}_3$  due to diarrhea, urinary diversion or pancreatic fistulae

**Renal** - proximal RTA (type 2) leads to renal  $\text{HCO}_3$  loss with normal distal regeneration. May be associated with other proximal defects (Fanconi's), hypergammaglobulinemia, drugs (toluene, toperimate, zonisamide, tenofovir, acetazolamide) or multiple myeloma

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# Hyperchloremic Metabolic Acidosis

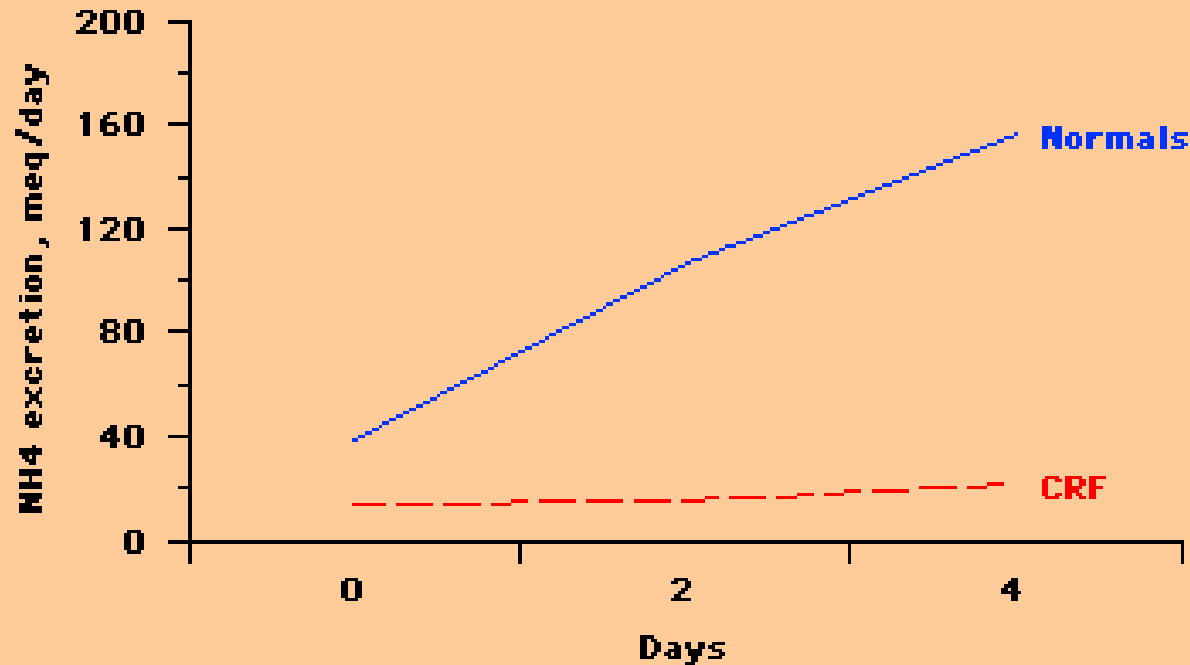
## Abnormal $\text{NH}_4$

**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 aldosterone sensitive collecting duct leads to acidosis and hyperkalemia with preserved renal acidification (**Type 4**) (obstruction, aldosterone resistance)

**$\text{NH}_3$  Defect** - CKD leads to abnormal  $\text{NH}_3$  production with preserved urinary acidification (GFR  $< 30$ )

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**Impaired ammonium excretion in chronic renal failure.** Urinary excretion of ammonium (NH<sub>4</sub>) in normals (solid line) and patients with chronic renal failure (dashed line) at baseline and after an acid load. The plasma bicarbonate concentration fell from 27 to 22 meq/L in normals and from 22 to 14 meq/L in CRF following the acid load. Ammonium excretion rose markedly in normal subjects, but was low at baseline and did not increase in the patients with CRF despite a greater degree of metabolic acidosis. (Data from Welbourne, T, Weber, M, Bank, N, J Clin Invest 1972; 51:1852.)

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# Hyperchloremic Metabolic Acidosis

## Summary

the patient had a hyperchloremic metabolic acidosis  
with an abnormal urine anion gap - no  $\text{NH}_4$  excretion  
despite acidosis

urinary acidification was preserved eliminating Type 1  
RTA (U pH < 6.5)

hyperkalemia was consistent with a Type 4 RTA

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

Figure 4. Correlation between central venous and arterial blood gas values for pH

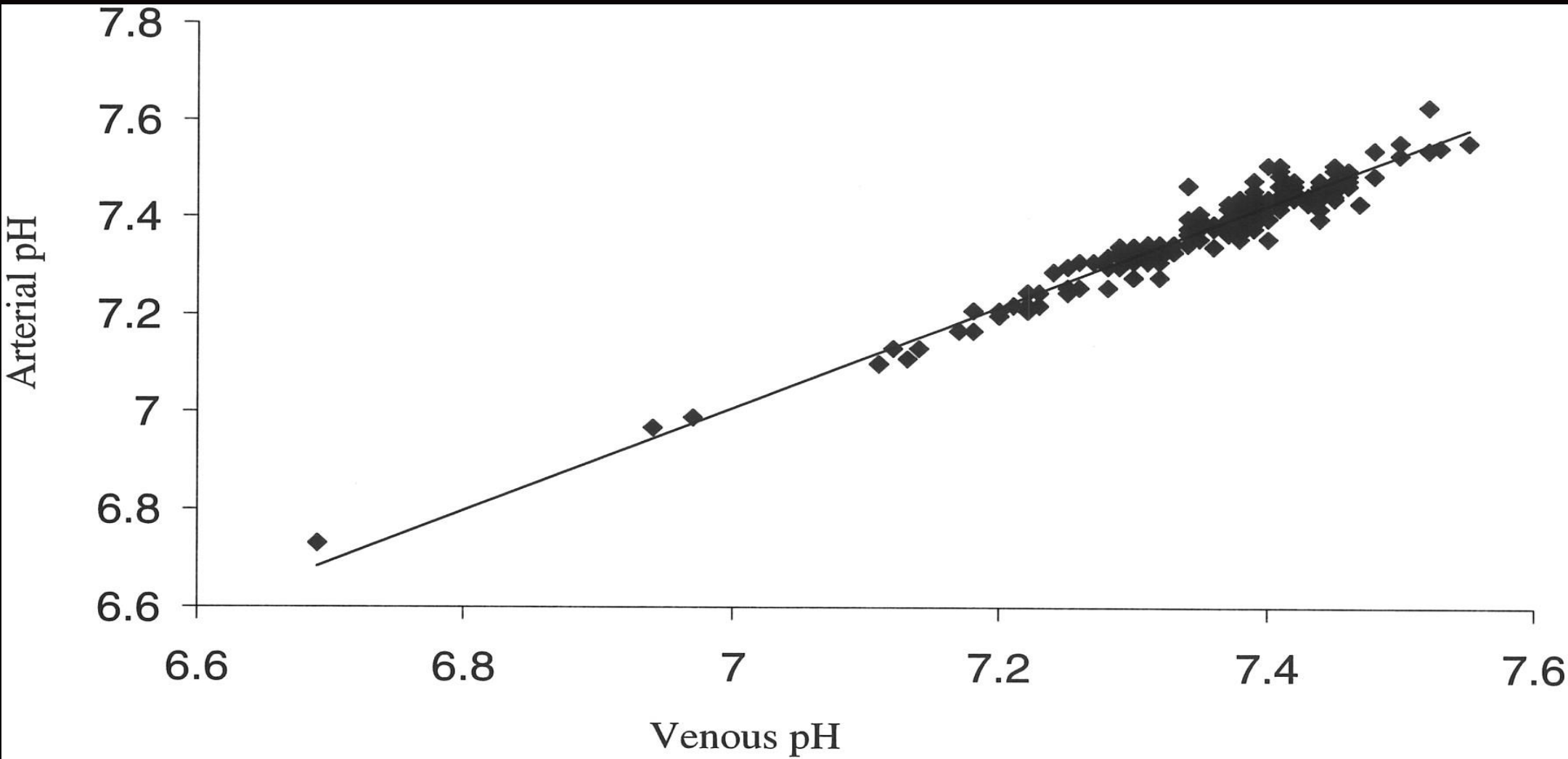


Figure 5. Correlation between central venous and arterial blood gas values for PCO<sub>2</sub>

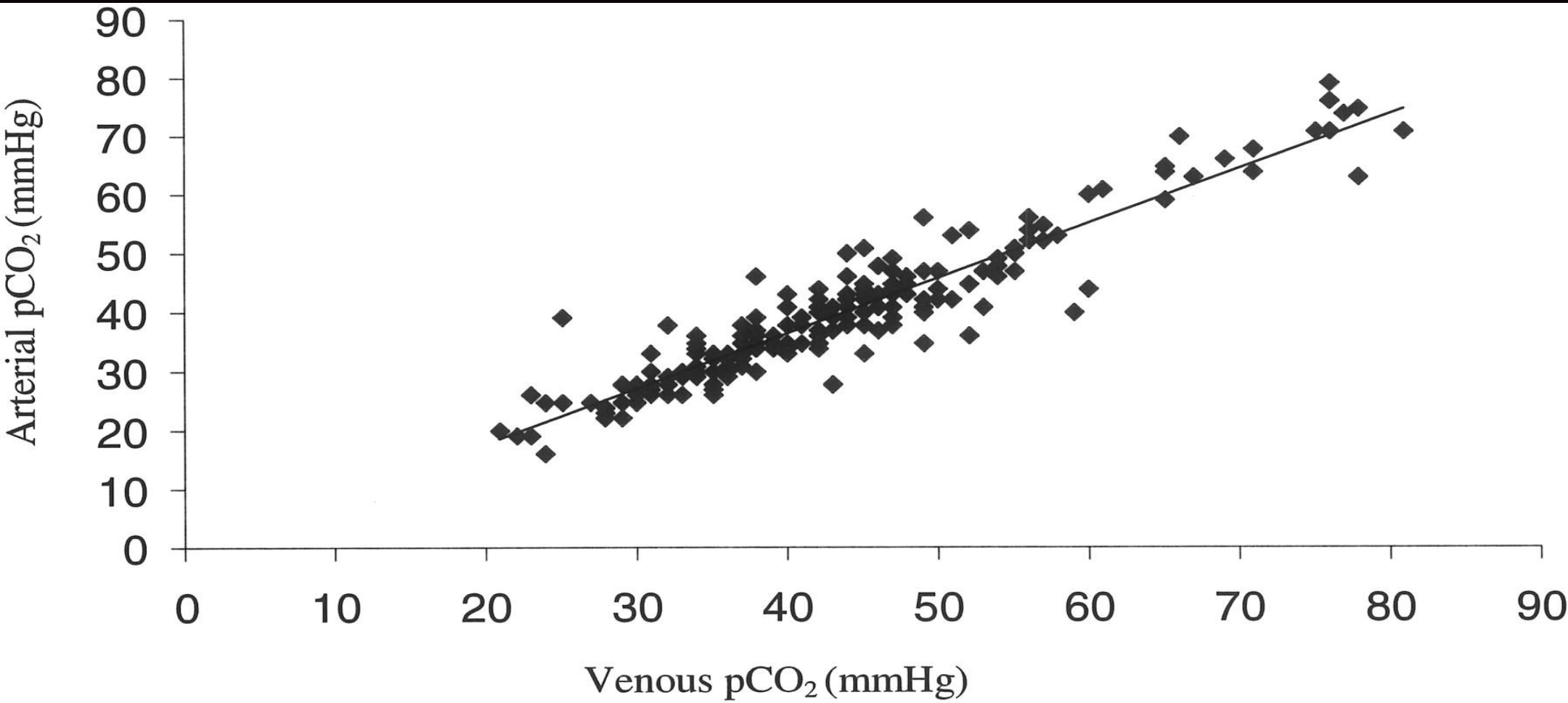
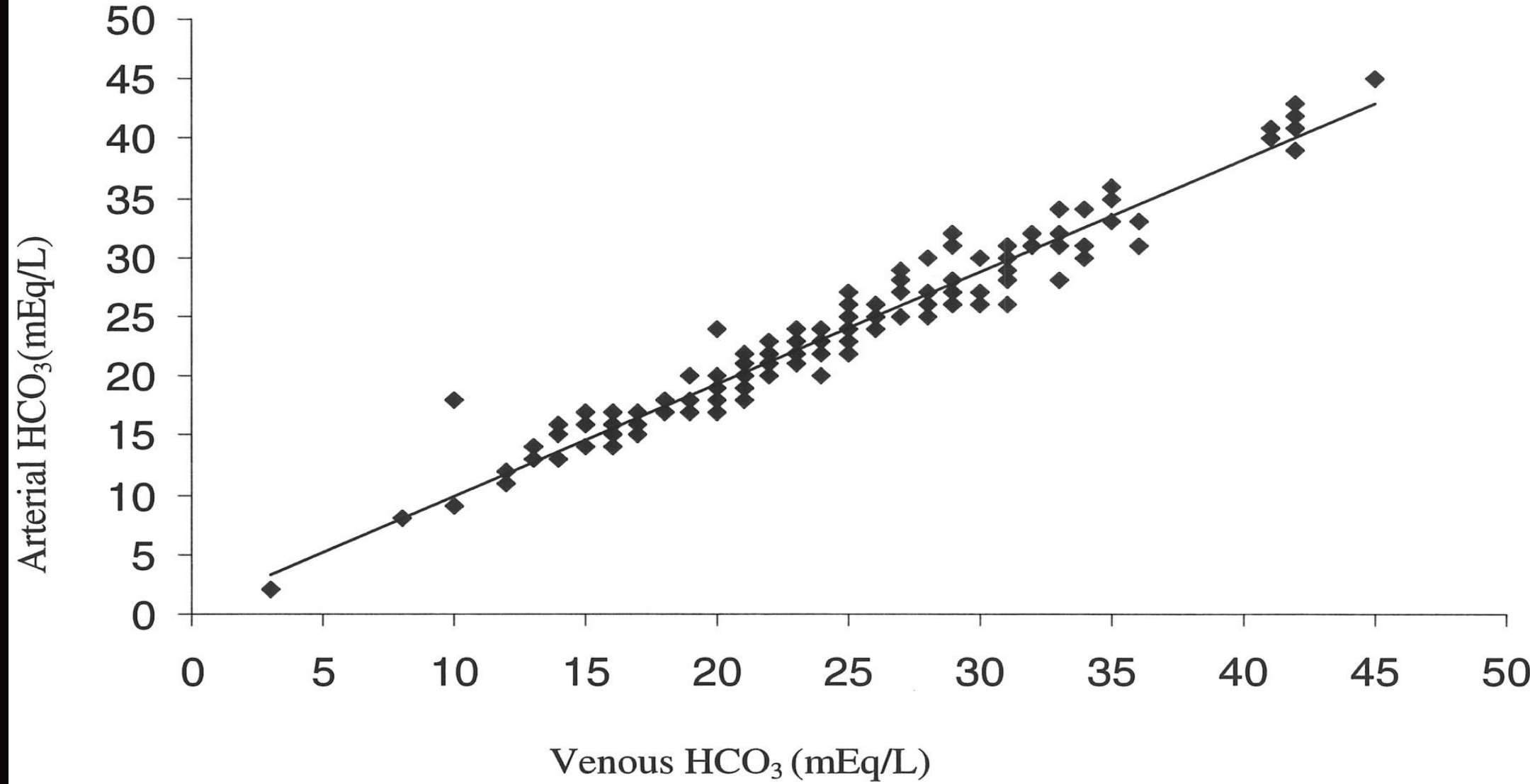


Figure 6. Correlation between central venous and arterial blood gas values for  $\text{HCO}_3^-$





# Arterial and central venous blood gas values ( $n = 190$ )

Parameter	Arterial	Venous	Difference
pH	7.37	7.34	.027
pCO <sub>2</sub>	38.4	42.3	-3.8
HCO <sub>3</sub>	22.4	23.2	-0.80

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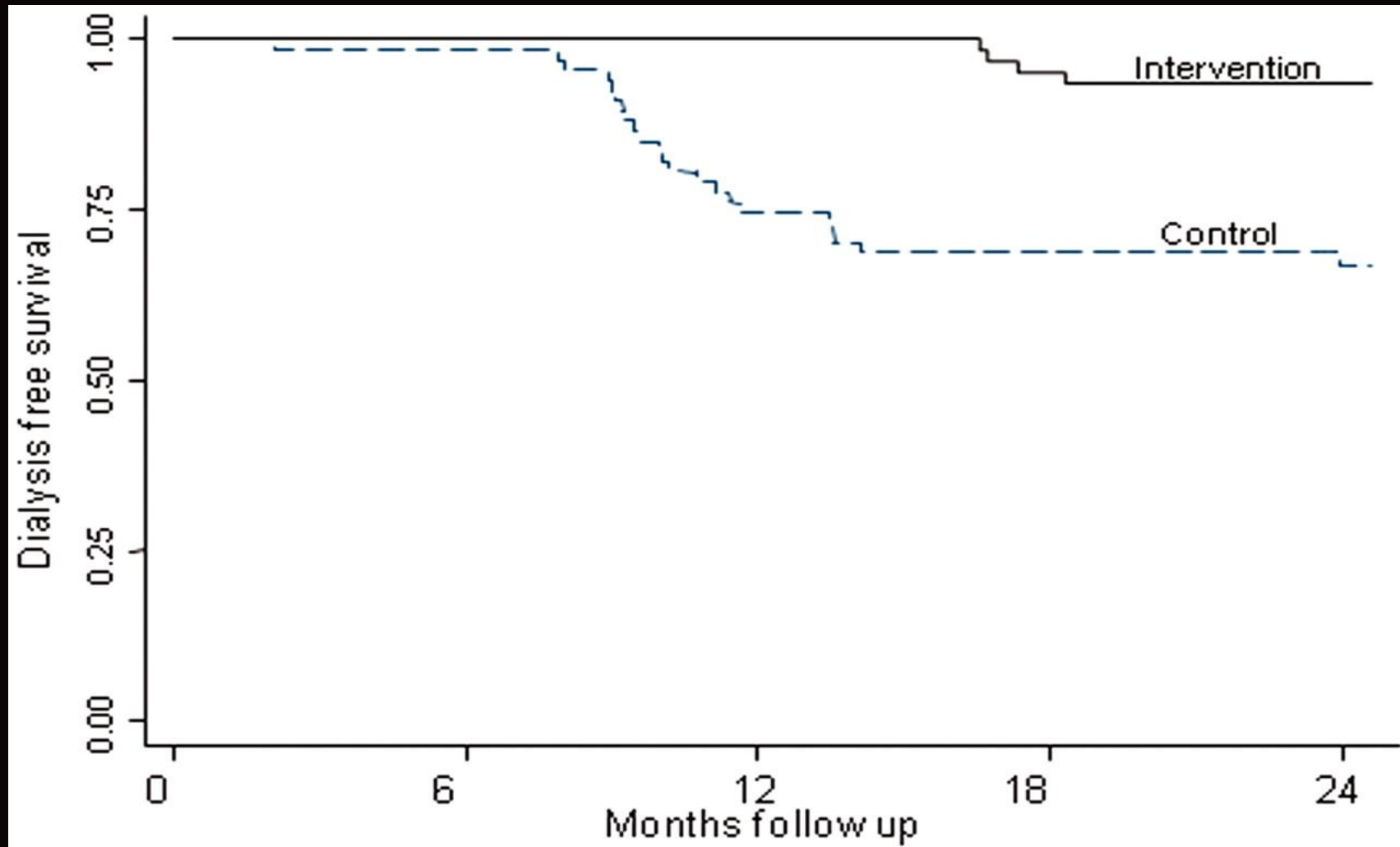
# Venous Blood Gas

Results in same clinical outcomes as ABGs

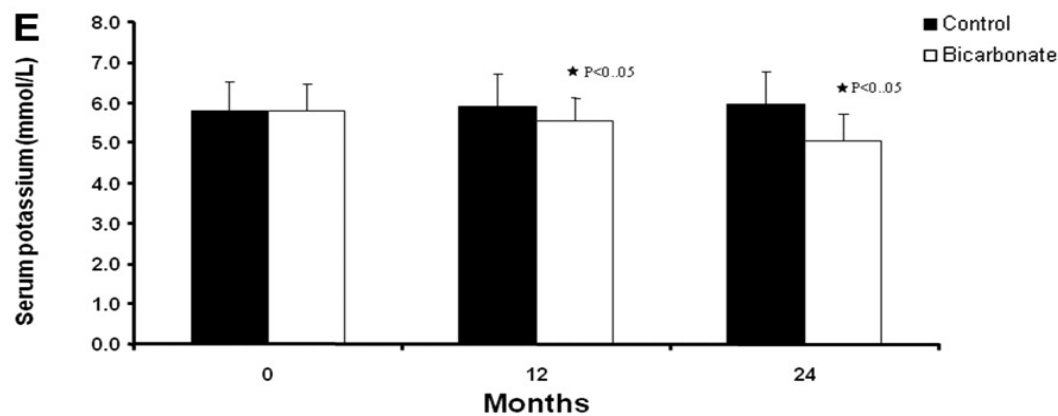
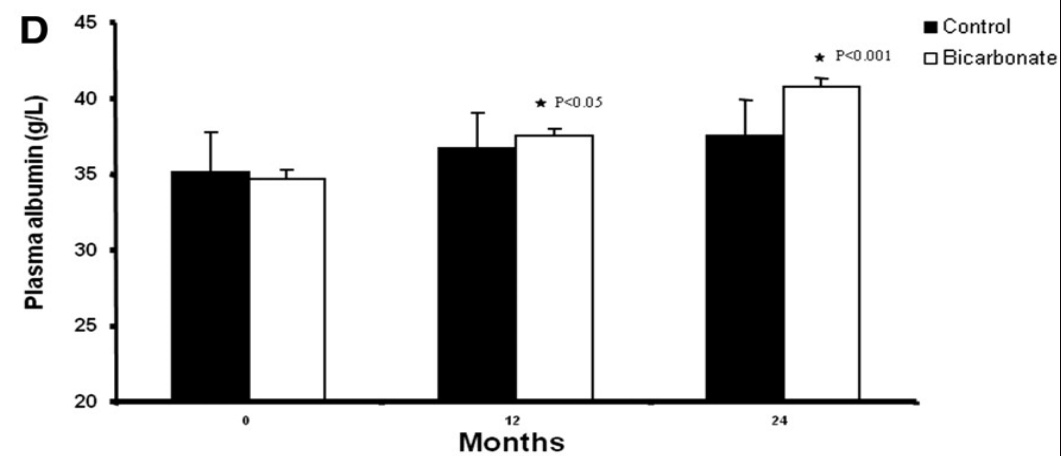
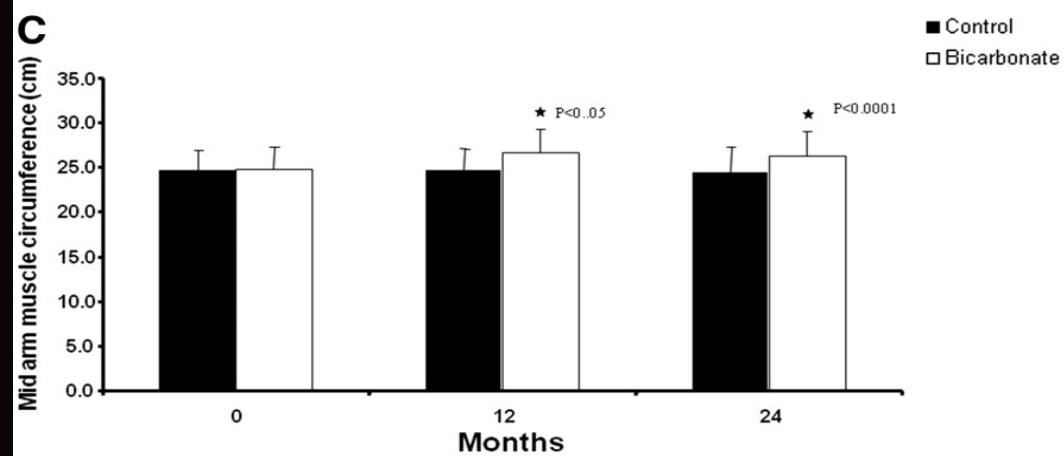
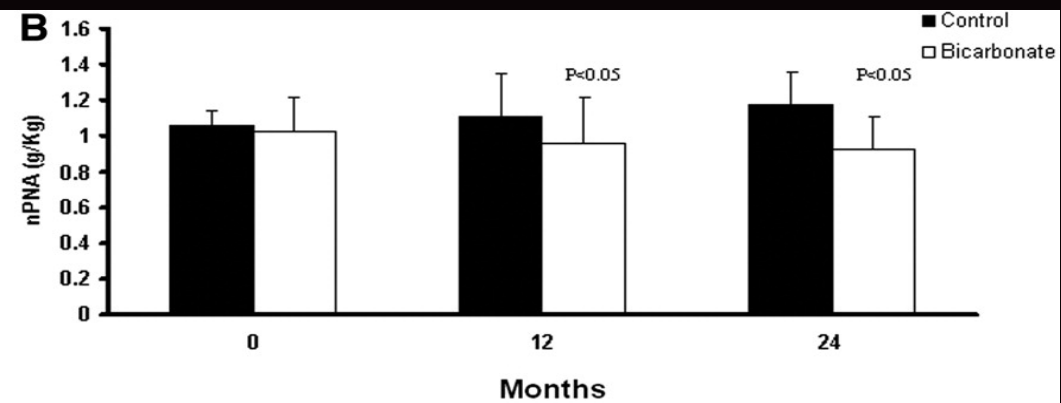
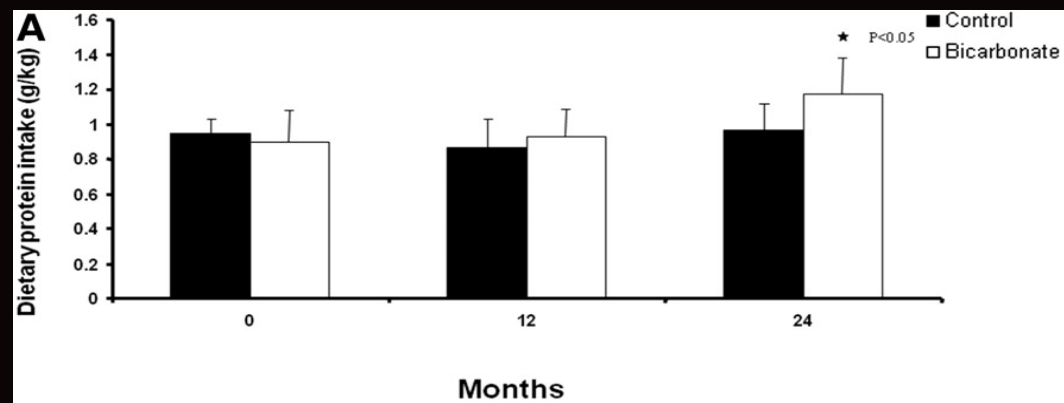
Low CO widens the difference

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**Kaplan-Meier analysis to assess the probability of reaching ESRD for the two groups.  
Bicarbonate Supplementation Vs. Control**



de Brito-Ashurst J et al. JASN 2009;20:2075-2084



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# Metabolic Alkalosis

A normotensive ice skater presents with weakness

Labs : pH 7.54/ pCO<sub>2</sub> 45; Na 140/ K 2.8/ Cl 95/ HCO<sub>3</sub>  
38; U Cl 50 U Na 70

Repeat U Cl < 20

How do you approach the differential of this acid base disorder?

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## Case 3

1. Acidosis or alkalosis - ALKALOSIS
2. Metabolic or respiratory - METABOLIC
3. Compensation appropriate – YES
4. Anion gap – NORMAL (7)
5.  $\Delta$  gap =  $\Delta$  HCO<sub>3</sub> – YES
6. Osmolar gap - NONE

# Metabolic Alkalosis

**Generation** - loss of HCl from kidneys or GI tract

**Maintenance** - because of prerenal state, hyperaldosteronism, and hypokalemia the body is unable to excrete  $\text{HCO}_3^-$

**Cl responsive** - when Cl is given it will shut off the maintenance phase and allow the kidney to excrete  $\text{HCO}_3^-$  by restoring volume and normalizing aldosterone production

**Cl unresponsive** - even when Cl is given it will not shut off aldosterone production

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# Cl Responsive Alkalosis

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  $\text{HCO}_3$

Treatment - administration of NaCl and KCl

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# Metabolic Alkalosis 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

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# Milk Alkali Syndrome

Historically due antacids and large quantities of milk to treat PUD

Modern –large amount of Ca carbonate and Vit D leading to alkalosis, hypercalcemia and AKI

Calcium acts like a loop diuretic

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# Cl Unresponsive Alkalosis

This group of disorders 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

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# Metabolic Alkalosis Cl Unresponsive

**Primary aldo excess** - pharmacologic or primary aldosteronism

**Secondary aldo excess** - CHF, cirrhosis, RAS, ?Barter's, hypomagnesemia

**Primary renal Cl loss** - Barter's syndrome (furosemide pump), Gitelman's syndrome (thiazide pump), Liddle's syndrome and diuretics

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# Metabolic Alkalosis - Summary

Patient had a metabolic alkalosis with high urine Cl initially due to diuretic abuse

Stopping the diuretic stopped the loss of urinary Cl

She had an eating disorder – Diuretic abuse

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# Metabolic Alkalosis Update

Permissive hypercapnic ventilation – current recommendations for ventilation in the setting of acute lung injury. Use of  $\text{HCO}_3^-$  for  $\text{pH} < 7.2$ . This may lead to posthypercapnic alkalosis

Performance enhancement – use of  $\text{NaHCO}_3$  pre exercise will enhance performance

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