Common Acid/Base Disorders: Causes and Consequences

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Disclosure

- I have no financial relationships to disclose
- I will discuss off label use and/or investigational use in my presentation

Goals

- Identify signs and symptoms of common acid/base disorders
- Identify etiology of common acid/base disorders
- Recommend safe and effective pharmacotherapy for common acid/base disorders
- Recommend accurate monitoring for parameters of recommended therapy

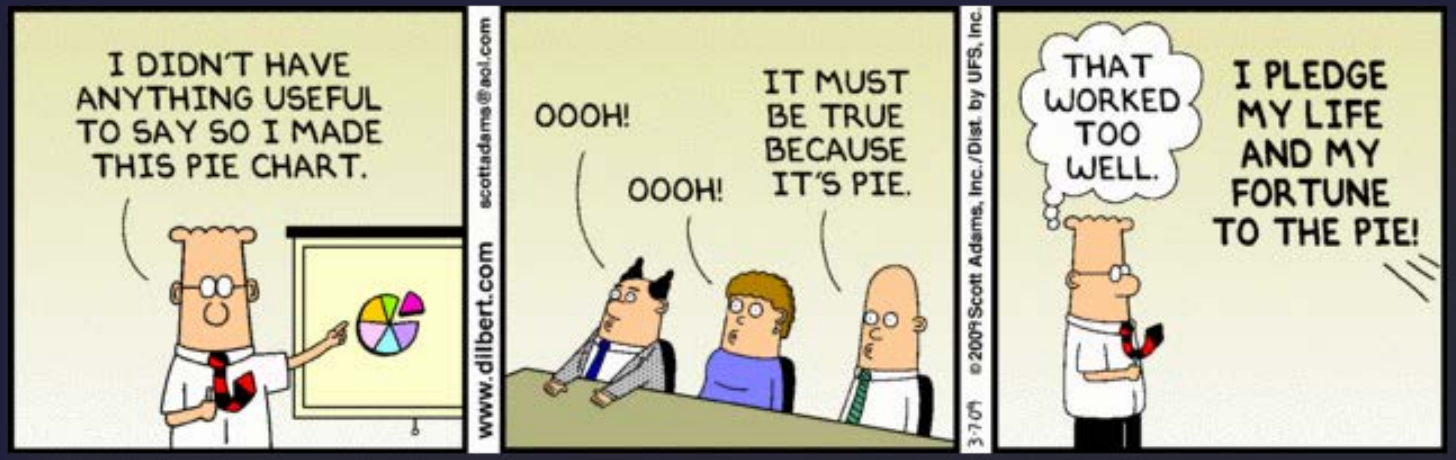
Objectives

- Review available pharmacotherapy for common acid/base disorders
- Discuss appropriate monitoring for parameters of recommended therapy

Acid-Base


I'D LIKE TO START WITH A CARTOON.
www.dilbert.com
IT'S ABOUT A GUY WHO SHOWS A CARTOON BEFORE GIVING A BORING PRESENTATION.
BUT IT DOESN'T WORK BECAUSE THE CARTOON HAS NO PUNCHLINE.

Acid-Base


I DIDN'T HAVE ANYTHING USEFUL TO SAY SO I MADE THIS PIE CHART.
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OOOH!
OOOH!
IT MUST BE TRUE BECAUSE IT'S PIE.
3-7
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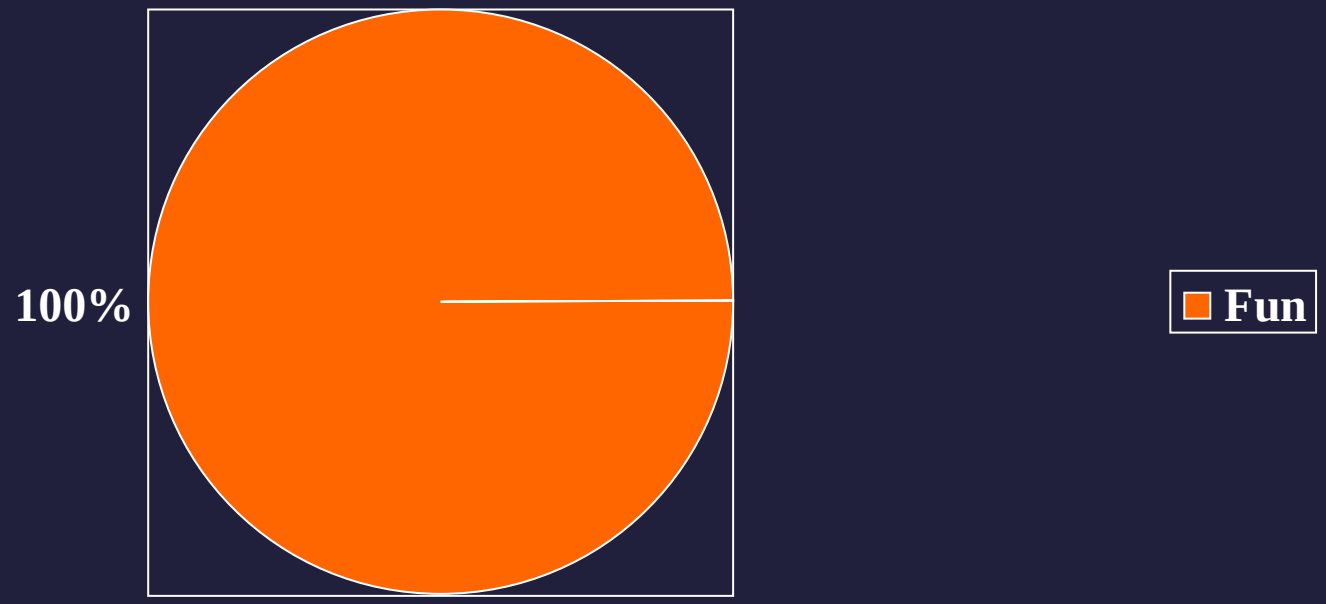
THAT WORKED TOO WELL.
I PLEDGE MY LIFE AND MY FORTUNE TO THE PIE!

Acid-Base



Acid-Base


I COULD HAVE E-MAILED YOU MY POWERPOINT DECK, AND YOU COULD HAVE READ IT IN FIVE MINUTES.
PROJECT EMU
Dilbert.com DilbertCartoonist@gmail.com
BUT I PREFER MAKING YOU SIT HERE FOR AN HOUR WHILE I READ EACH BULLET POINT IN SLOW MOTION.
2-22-10 ©2010 Scott Adams, Inc./Dist. by UFS, Inc.
P-O-I-N-T N-U-M-B-E-R O-N-E. . .
YANK THIS AS HARD AS YOU CAN.

Functions of pH

- Respiratory drive
- Electrolyte levels and availability
  - Potassium
  - Calcium
- Enzyme mediated reactions
- Receptor function

Harrison's Principles of Internal Medicine. 19th edition.

THE BASICS

ABG Normal Values:

- pH 7.35-7.45
- PCO2 35-45 mmHg
- PO2 80-100 mmHg
- HCO_3 20-28 mEq/L

Harrison's Principles of Internal Medicine. 19th edition.

THE BASICS

Acidemia

- high H+, low pH
- result of decreased HCO_3 or increased PCO2

Alkalemia

- low H+, high pH
- result of increased HCO_3 or decreased PCO2

Harrison's Principles of Internal Medicine. 19th edition.

Acidemia

Consequences:

- Cardiovascular
- Respiratory
- Metabolic
- Cerebral

Adrogué, H, et al. Management of Life-Threatening Acid-Base Disorders First of Two Parts. NEJM 1998; 338 (1): 26-34

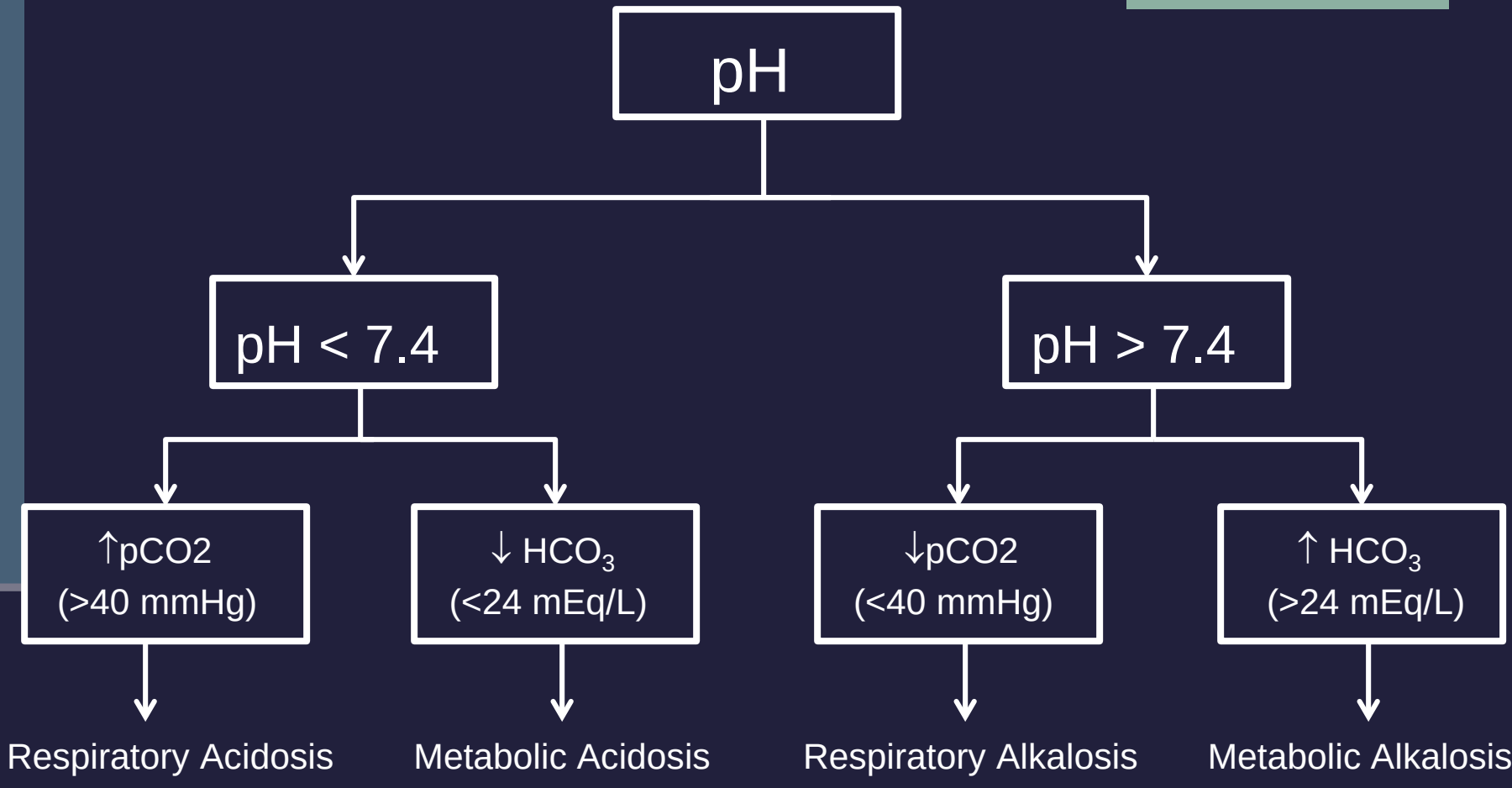
Alkalemia

Consequences:

- Cardiovascular
- Respiratory
- Metabolic
- Cerebral

Adrogué, H, et al. Management of Life-Threatening Acid-Base Disorders Second of Two Parts. NEJM 1998; 338 (2): 107-111

PRIMARY ACID-BASE DISTURBANCES



Harrison's Principles of Internal Medicine. 19th edition.

PRIMARY ACID-BASE DISTURBANCES

Respiratory acidosis

- Primary change: increased PCO2
- Increase in PCO2 due to alveolar hypoventilation or impairment of respiration
- Compensation: enhanced renal H+ secretion (occurs over 3-5 days) resulting in increased plasma HCO_3

Harrison's Principles of Internal Medicine. 19th edition.

Respiratory Acidosis

Respiratory center depression

- Drug-induced
  - Anesthetics
  - Barbituates
  - Benzodiazepines
  - Opiates
  - Parenteral or enteral nutrition (if excessive carbohydrates)
- Sleep apnea
- Obesity
- CNS disease (stroke, infection)

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Respiratory Acidosis

- Neuromuscular disorders:
  - myasthenia gravis, Guillain-Barré syndrome, hypokalemia, myopathy
- Upper airway obstruction
- Pulmonary disease:
  - COPD
  - Asthma
  - Pulmonary edema
  - Pneumothorax
  - Pneumonia
- Mechanical ventilation

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Respiratory Acidosis

Treatment

- Correct underlying disorders
- Hold or discontinue any respiratory depressant drugs
- Improve ventilation/respiration
- Reverse effects of respiratory depressants if present:
  - Opiates: Naloxone 0.4-2 mg SQ/IV/IM q 2-3 min prn (should see response within 10 minutes)
  - Benzodiazepines: Flumazenil 0.2 mg IV q1 min prn (max 5 doses per series, may repeat series at 20 minute intervals)

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Respiratory Acidosis

- ABG every 2-5 hours initially
- ABG every 12-24 hours as pH improves
- Basic Metabolic Panel
- Respiratory status

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PRIMARY ACID-BASE DISTURBANCES

Metabolic Acidosis

- Primary change: decreased HCO_3
- Decrease in plasma HCO_3 due to HCO_3 loss or accumulation of acid
- Compensation: fall in PCO2 resulting from alveolar hyperventilation

Harrison's Principles of Internal Medicine. 19th edition.

Diagnostics

Anion Gap

- $[Na+] – \{[Cl-] + [HCO_3]\}$
- Normal: 10-14
- High AG indicates overproduction of acid or presence of renal failure
- Low AG signifies hypoalbuminemia, halide intoxication, multiple myeloma

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GAP Metabolic Acidosis

- Lactic Acidosis
- Ketoacidosis
- Endstage Renal Failure
- Methanol ingestion
- Ethylene Glycol ingestion
- Salicylates

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GAP Metabolic Acidosis

Methanol

Uremic acid

Diabetic Ketoacidosis

Propylene glycol

I (Infection, Iron, Isoniazid)

Lactic acidosis

Ethylene glycol

Salicylates

GAP Metabolic Acidosis

Methanol

Uremia

Lactic Acidosis

Ethylene glycol

Propylene Glycol

Aspirin

Ketoacidosis

Lactic Acidosis

Risk factors

- hypoxia
  - hypotension
  - sepsis
  - cardiovascular shock
  - anemia
  - ischemia
  - diabetes
- leukemia

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Lactic Acidosis

Drug Induced:

- APAP
- catecholamines
- NRTIs (ddI, d4T, ddC)
- Ibuprofen
- Iron overdose
- Isoniazid overdose
- Linezolid
- Metformin
- Neuroleptic malignant syndrome
- Nitroprusside (secondary to cyanide toxicity)

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Lactic Acidosis

Drug Induced cont.

- Propylene glycol
- Propofol
- Salicylate overdose (mixed disorder: metabolic acidosis with respiratory alkalosis)
- Streptozocin
- Sorbitol and Xylitol
- Theophylline overdose

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Lactic Acidosis

Treatment

- Optimize hemodynamics
  - MAP
  - HR
  - CVP
- O_2 delivery
  - Hb
  - Arterial O_2 saturation
  - Central venous O_2 saturation

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Lactic Acidosis

Treatment

- pH correction
  - Sodium Bicarbonate
    - V_d 50% body weight
  - THAM
    - Tromethamine (mL of 0.3 M solution) = body weight (kg) x base deficit (mEq/L) x 1.1
  - HD
    - Continuous HD preferred, controlled studies needed

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Acetaminophen Overdose

- Stage III
- Liver failure
- Decreased lactate clearance
- Treatment
  - Standard APAP overdose treatment and supportive care

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Metformin

- Mechanism
  - Increased serum levels of metformin
  - Interference with oxidative phosphorylation
  - Suppression of hepatic gluconeogenesis
- Treatment
  - Supportive Care
  - Hemodialysis
- Contraindicated with renal dysfunction?

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Propylene Glycol

- d-Lactate and l-lactate are normal products of metabolism
- May occur with or without oxidative phosphorylation impairment

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Propylene Glycol

- diazepam
- digoxin
- esmolol
- etomidate
- hydralazine
- lorazepam
- MVI injection
- nitroglycerine
- pentobarbital
- phenobarbital
- phenytoin
- trimethoprim/ sulfamethoxazole

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Propylene Glycol

Treatment

- Discontinue drug
- Optimize hemodynamics
- O_2 delivery
- pH correction

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Aspirin Overdose

- Interference with oxidative phosphorylation
- Hyperlactatemia is usually minimal
- Commonly presents as a mixed disorder
- Treatment:
  - Activated charcoal
  - Sodium bicarbonate to pH greater than 7.45
  - HD in patients with renal failure

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Propofol Infusion Syndrome

- Interference with oxidative phosphorylation
- Lactic acidosis can be seen with prolonged high-dose infusion (>5 mcg/kg/min for > 48 h)
- Treatment:
  - Discontinuation
  - Supportive Measures

Kraut J, et al. Lactic Acidosis. NEJM 2014;371:2309-19

Diabetic Ketoacidosis

- Diabetes Mellitus
  - Infection
  - Myocardial infarction
  - Gestational Diabetes
  - Initial presentation/insufficient insulin
- Breakdown of fatty acids/production of ketones
- Treatment
  - Insulin
  - Fluid/electrolytes
  - Sodium bicarbonate for pH < 7.1

Gap Metabolic Acidosis

Treatment

- Increased AG Acidosis: treat underlying disorder
  - Renal Failure
    - Hold or discontinue any suspected drugs
    - Consider oral alkali therapy if no improvement in acidosis within 1-3 days or if symptomatic

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Gap Metabolic Acidosis

Monitoring

- Hemodynamics
- O_2 delivery
- Basic Metabolic Panel
- Lactic Acid

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Acid-Base


UH—OH. MY AUDIENCE HAS FALLEN INTO A POWERPOINT COMA.
THE ONLY THING I CAN DO NOW IS PUT THEM IN FUNNY POSES AND LEAVE.
IT LOOKS LIKE HIS FINGER HIT BRAIN.
Dilbert.com DilbertCartoonist@gmail.com
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Non-Gap Metabolic Acidosis

Risk Factors

- Cirrhosis
- CHF
- Diabetes
- renal dysfuntion
- ECF volume depletion
- cholestyramine + aldosterone antagonists
- cummulative dose of amphotericin B > 2-3 g

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Non-Gap Metabolic Acidosis

- Renal HCO_3- loss
  - Carbonic Anhydrase Inhibitors
  - Renal Tubular Acidosis (RTA)
- Gastrointestinal HCO_3 loss
  - Diarrhea
  - Pancreatic, biliary or small bowel fistulas or drainage
  - Cholestyramine, laxative abuse
- Dilutional (rapid administration of IV fluids)

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Non-Gap Metabolic Acidosis

Renal Tubular Acidosis (RTA)

Proximal RTA (Type II)	Distal RTA (Type I)	Hyperkalemia-associated Distal RTA (Type IV)
Acetazolamide	Amphotericin B	Aldosterone deficiency or resistance
Sulfamethoxazole	Cisplatin	Heparin
Topiramate		ACEIs and ARBs
AMGs		Amiloride
Arginine		Lithium
Cidofovir		Trimethoprim
Ifosfamide		Triamterene
Tetracycline (expired)		Foscarnet
Streptozotocin		Tacrolimus

Non-Gap Metabolic Acidosis

Treatment

pH < 7.1

- Discontinue any suspected drugs
- IV fluids
- Calculate bicarbonate deficit
  (0.5L/kg x Weight (kg) x $[HCO_3]_{desired} - [HCO_3]_{observed}$
- Give 30-50 % of calculated dose over 30 minutes to several hours
- Reassess need for additional replacement with ABG 30 minutes after end of infusion (target pH 7.15-7.20, plasma bicarbonate 8-10 mEq/L)
- Hemodialysis if renal failure present or insufficient response

Non-Gap Metabolic Acidosis

Treatment

- Proximal RTA
  - 10-25 mEq alkali/kg/24 hr in 3 divided doses
  - prefer potassium citrate or potassium/sodium citrate combination

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Non-Gap Metabolic Acidosis

Treatment

- Distal RTA
  - 1-2 mEq alkali/kg/24 hr in 3 divided doses
  - sodium bicarbonate preferred
  - titrate to serum HCO_3 20-24 mEq/L

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Non-Gap Metabolic Acidosis

Treatment

- Hyperkalemic Distal RTA
  - reduce serum potassium using following order of intervention
    - Kayexylate 15-30 g po 1-4x/d ± dietary potassium restriction
    - Addition of furosemide 60-80 mg po daily
    - Addition of fludrocortisone 0.1-0.2 mg po daily (monitor for s/sx of fluid retention)

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Alkali Therapy

Generic Name	Trade Name	mEq Alkali
Shohl's solution (sodium citrate/citric acid)	Bicitra	1 mEq Na/ml = 1 mEq bicarbonate/mL
Sodium bicarbonate	Various	325 mg tablet = 3.9 mEq bicarbonate/tablet 650 mg tab = 7.8 mEq bicarbonate/tablet
Potassium citrate	Urocit-K	5 mEq citrate/tablet
Potassium bicarbonate/ Potassium citrate	K-Lyte K-Lyte DS	25 mEq bicarbonate/tablet 50 mEq bicarbonate/tablet
Potassium citrate/ Citric acid	Polycitra-K	2 mEq K/ml = 2 mEq bicarbonate/mL 30 mEq bicarbonate/packet
Sodium citrate/potassium citrate/citric acid	Polycitra	1 mEq K/mL, 1 mEq Na/mL = 2 mEq bicarbonate/mL

Non-Gap Metabolic Acidosis

Treatment

- pH > 7.1
  - Discontinue any suspected drugs
  - IV fluids
  - Hemodialysis if renal failure or insufficient response

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Non-Gap Metabolic Acidosis

Monitoring

- ABG
- Basic Metabolic Panel (especially K+)
- Ins and outs

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Acid-Base


AS YOU CAN CLEARLY SEE IN SLIDE 397...
GAAAAH!
"POWERPOINT" POISONING.

PRIMARY ACID-BASE DISTURBANCES

Respiratory Alkalosis

- Primary change: decreased PCO2
- Decreased PCO2 resulting from hyperventilation
- Compensation: small decrease in NH4+ excretion leading to decreased plasma HCO_3 with plasma pH (usually) in normal range

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Respiratory Alkalosis

- Hypoxemia:
  - Pulmonary disease
  - Anemia
  - Heart failure
  - High altitude
- Respiratory center stimulation
- Pulmonary disease: pneumonia, edema, emboli, interstitial fibrosis
- Mechanical hyperventilation

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Respiratory Alkalosis

Respiratory center stimulation

- Drug-induced:
  - Salicylates (mixed metabolic acidosis and respiratory alkalosis)
  - Progesterone
  - Theophylline overdose
  - Catecholamies
- Pregnancy
- Psycogenic
- CNS disorders
- Liver failure
- Gram-negative sepsis

Adrogué, H, et al. Management of Life-Threatening Acid-Base Disorders Second of Two Parts. NEJM 1998; 338 (2): 107-111

Respiratory Alkalosis

Treatment

- Identify and correct underlying disorders
- Hold or discontinue any suspected drugs
- Initiate oxygen therapy in patients with severe hypoxemia ($pO_2 < 40$ mmHg) or change ventilator settings as needed
- Treat theophylline and salicylate overdoses appropriately

Adrogué, H, et al. Management of Life-Threatening Acid-Base Disorders Second of Two Parts. NEJM 1998; 338 (2): 107-111

Respiratory Alkalosis

Monitoring

- Arterial Blood Gas
- Basic Metabolic Panel
- Respiratory status

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PRIMARY ACID-BASE DISTURBANCES

Metabolic Alkalosis

- Primary change: increased HCO_3
- Increase in plasma HCO_3 due to H+ loss or HCO_3 gain
- Compensation: rise in PCO2 resulting from decreased alveolar ventilation

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Metabolic Alkalosis

- ECF volume contraction, normotension, hypokalemia, secondary hyperaldosteronism

- ECF volume expansion, hypertension, hypokalemia, mineralcorticoid excess

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Metabolic Alkalosis

Volume Contraction

- Drug-induced
  - nonreabsorbable anions (ampicillin, nafcillin, penicillin, ticarcillin)
  - Diuretics
  - Gentamicin
  - Laxative abuse
  - Co-administration of sodium polystyrene sulfonate and AlOH or MagOH

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Metabolic Alkalosis

Volume Contraction

- GI: vomiting, gastric aspiration, villous adenoma
- Edematous states
- Mg or K depletion
- Recovery from lactic acidosis or ketoacidosis
- Post-hypercapnic states

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Metabolic Alkalosis

Volume Expansion

- Drug-induced:
  - Fludrocortisone
  - Glycyrrhizic acid (black licorice, chewing tobacco)

Metabolic Alkalosis

Volume Expansion

- Renal artery stenosis
- Hypertension
- Renin-secreting tumor
- Primary aldosterism
- Adrenal enzyme defects
- Cushing's syndrome
- Liddle's syndrome

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Metabolic Alkalosis

Treatment

- Correct underlying disorder, hold or discontinue any suspected drugs
- If ECF volume contracted:
  - NS at appropriate rate for degree of volume depletion
- Replace potassium as needed
- If ECF volume overload:
  - If no renal insufficiency: Acetazolamide: 250-375 daily or BID
  - If ARF or ESRD: hemodialysis or peritoneal dialysis (reduced bicarbonate bath)

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Metabolic Alkalosis

Treatment

- If severe alkalemia (pH > 7.7) with ECF volume excess or renal failure:
  - Calculate HCl dose required:
    - Males:[0.5L/kg x weight (kg)] x [103 mEq/L-observed serum chloride]
    - Females: [0.6L/kg x weight (kg)] x [103 mEq/L-observed serum chloride]
  - Administer dose HCl in D5W or NS via central vein at rate of 10-25 mEq/hr
- Hypoaldosteronism: spironolactone or amiloride

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Metabolic Alkalosis

Monitoring

- Arterial Blood Gas
- Respiratory Status
- Basic Metabolic Panel

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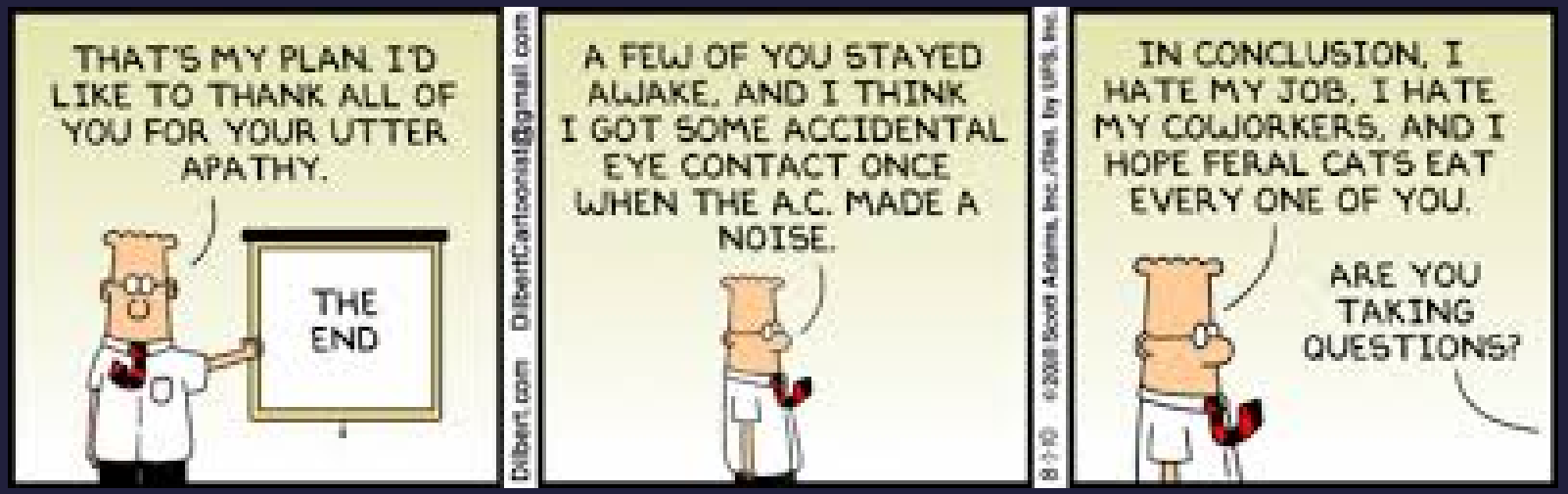
Conclusion

- Verify disorder
- Hold or discontinue any suspected drugs
- Supportive Care
- Correct pH if disorder severe
- Monitor

Questions


THAT'S MY PLAN. I'D LIKE TO THANK ALL OF YOU FOR YOUR UTTER APATHY.
THE END
A FEW OF YOU STAYED AWAKE. AND I THINK I GOT SOME ACCIDENTAL EYE CONTACT ONCE WHEN THE A.C. MADE A NOISE.
IN CONCLUSION, I HATE MY JOB, I HATE MY COWORKERS, AND I HOPE FERAL CATS EAT EVERY ONE OF YOU.
ARE YOU TAKING QUESTIONS?