ACID-BASE

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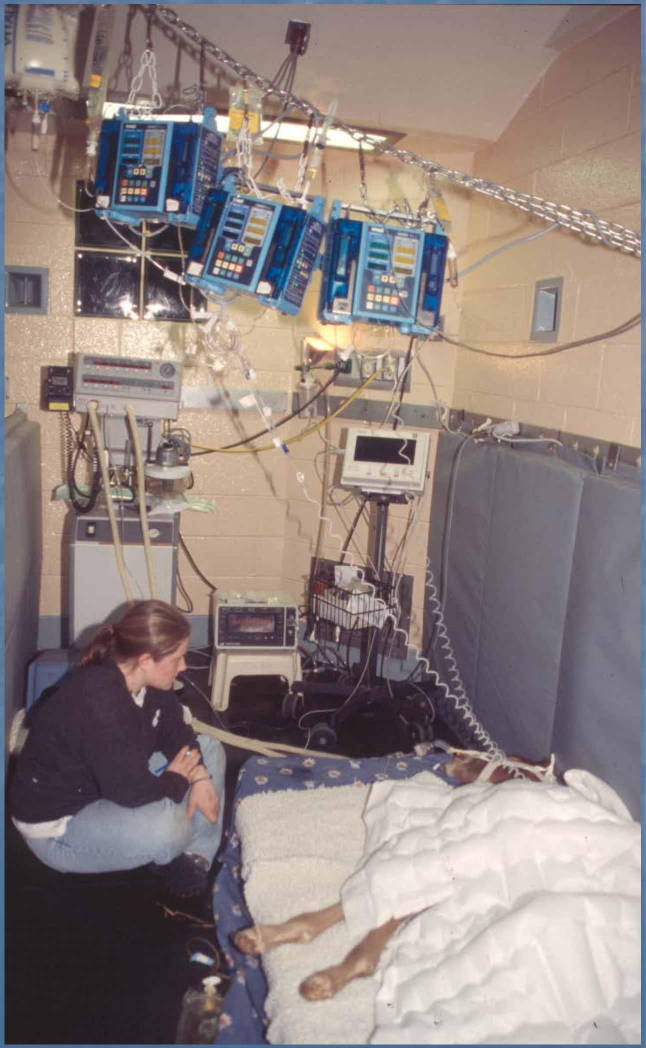
Acid-Base

- Introduction/ historic perspective
- Tools for acid-base analysis
  - Base Excess
  - Buffer base – weak acid buffers
  - Anion Gap
  - Strong ions – SID, SIG
- Metabolic acid-base abnormalities
  - Free water
    - Reflected in [Na]
  - Chloride – inorganic SID
  - Organic anions, Organic cations
  - Albumin level, phosphate level
- Differential diagnosis of metabolic disturbances
- http://ECEIM16.nicuvet.com

Acid-Base Disorders

Acid-Base Abnormalities

- Alterations in acid-base balance
  - Less important than the pathologic abnormalities causing them



Acid-Base Abnormalities

- Fatal disorders
  - Extreme (e.g., pH <7.0 or >7.7)
  - Develops quickly
  - Direct cause of organ dysfunction
- Harm because of the patient’s response
  - Respiratory muscle fatigue
  - Diversion of blood flow from vital organs
  - Acidemia
    - Increases adrenergic tone
    - Increases myocardial oxygen demand

Acid Production

- Primarily CO_2
  - 150 to 250 mEq/kg/d of carbonic acid
  - Hemoglobin is major buffer
    - "Haldane" effect - H^+ bond, HCO_3 to plasma (Cl shift) – 65%
    - CO_2 bound to protein – 27%
    - Pco_2 – 8%
- Strong organic acids
  - 30 to 40 mEq/kg/d
  - Variety of acids
    - Lactic acid
    - Tricarboxylic acids
    - Keto acids
  - Produced/ metabolized to CO_2

Acid Production

- Inorganic acids
  - H_2SO_4
  - H_3PO_4
- Urinary excretion acid
  - 1 to 2 mEq/kg/d anions

History Acid-Base Analysis

- Henderson 1909

$$H^+ \propto \frac{HCO_3^-}{H_2CO_3}$$

- Hasselbalch 1916

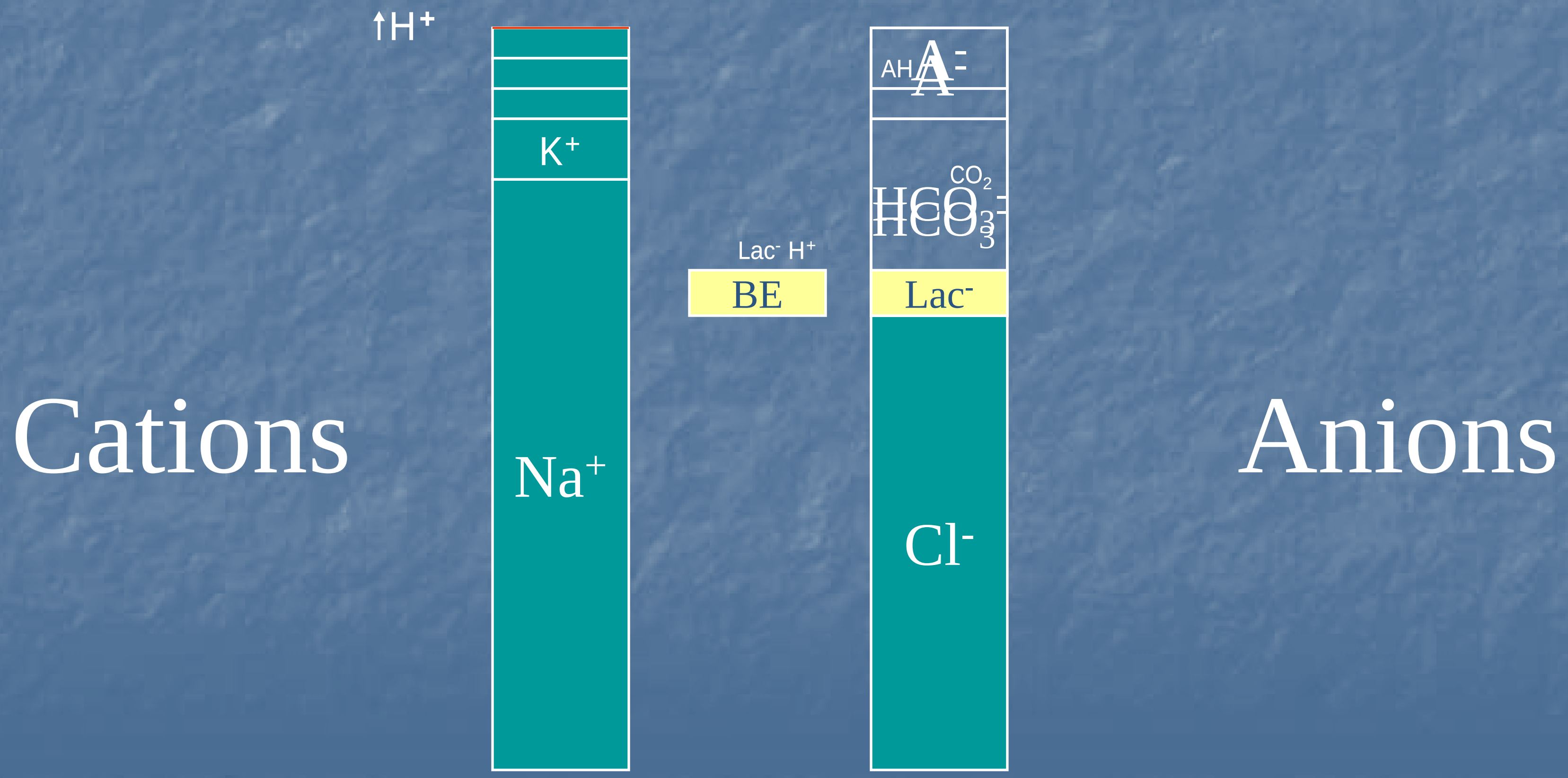
$$pH = 6.1 + \log\left[\frac{HCO_3^-}{P_{co_2} \times 0.03}\right]$$

- 1948 – Buffer Base
- 1957, 1958 – Standard Bicarbonate; Base Excess
- 1977 – Anion Gap
- 1981 – Stewart - Physical Chemistry

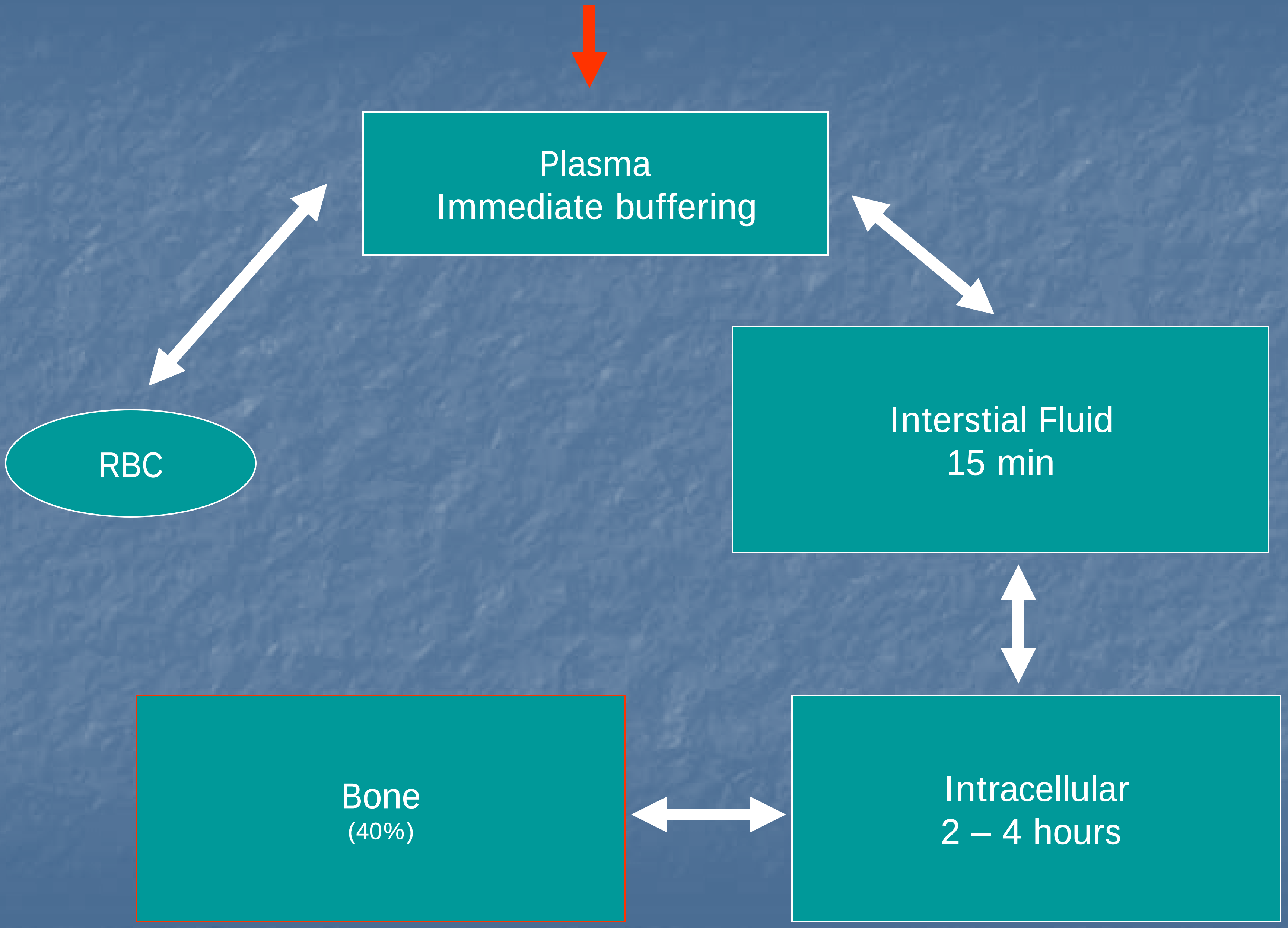
Base Excess

- Copenhagen Approach
  - Change in blood buffers
- Amount of acid/base added to whole blood
  - Return pH to 7.4
  - Assumptions
    - Pco_2 of 40 mm Hg
    - Temperature 37°C
    - Normal hemoglobin
    - Fully saturated blood
- Titration experiments
  - Nomograms
  - Formulas

BE
Lactic Acidosis



Acid Buffering

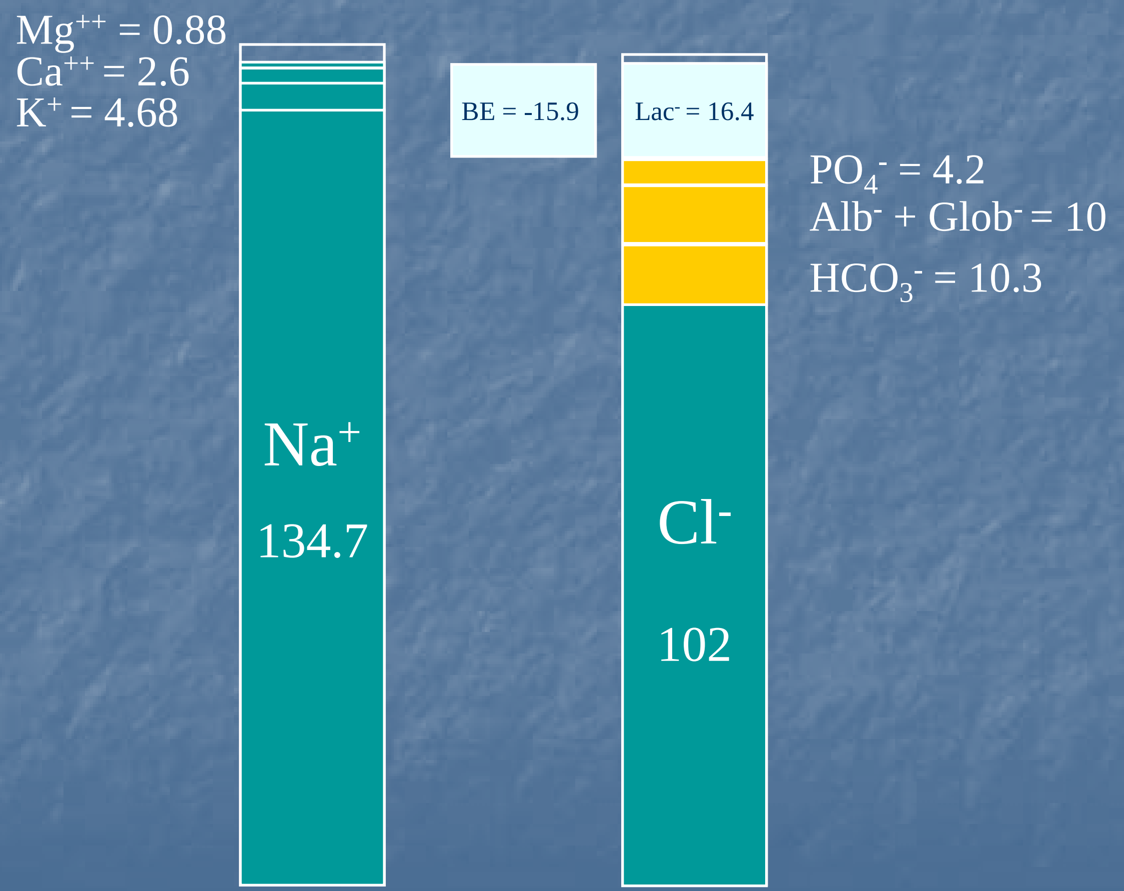


Standard Base Excess

- Buffer space
  - 1/3 normal hemoglobin
- Assumptions
  - Normal hemoglobin
  - Normal vascular/ECF ratio
  - Normal nonvolatile buffer
    - SBE_{corr} – Albumin, PO_4

Base Excess

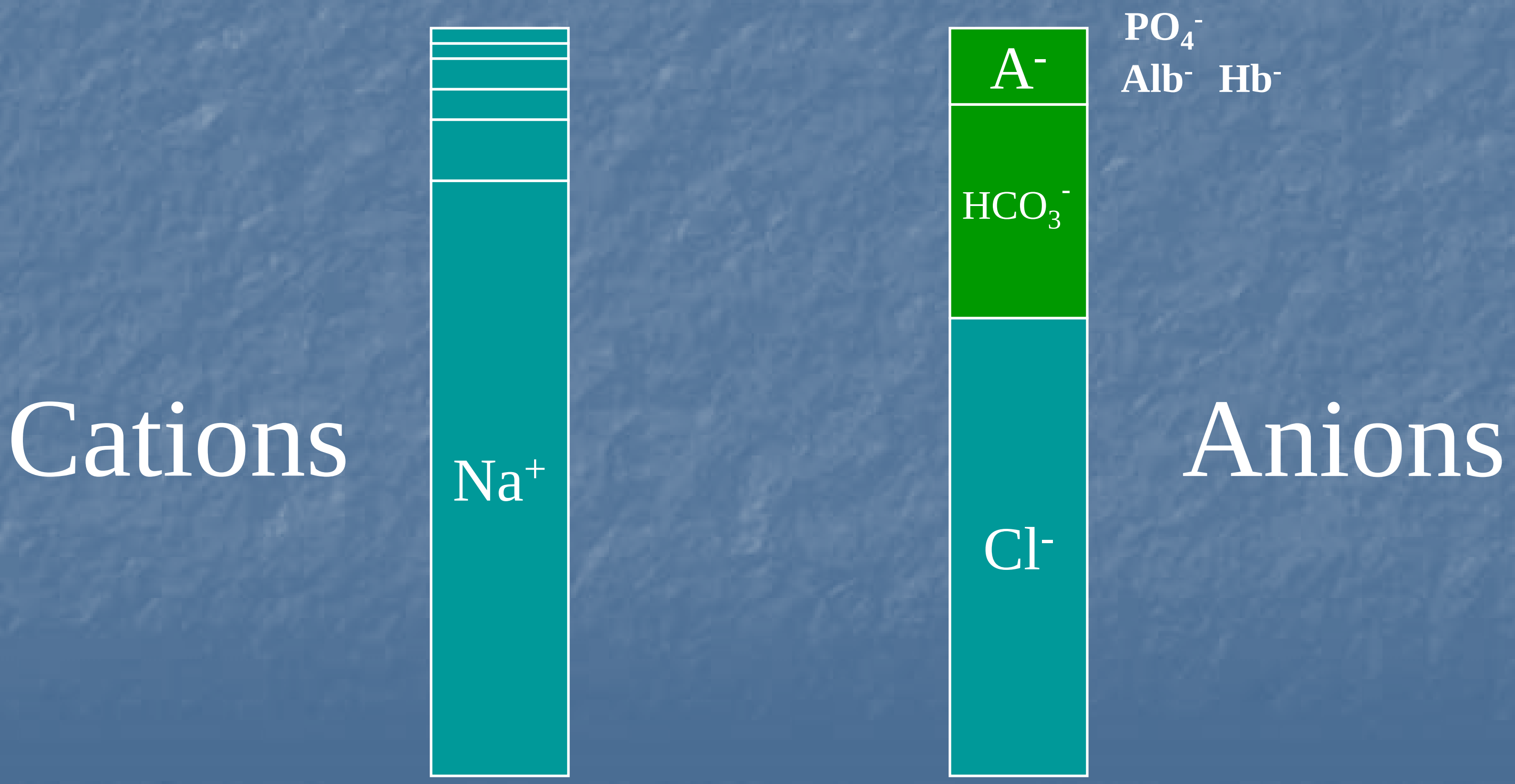
Septic shock, NE		mEq/l
pH	7.195	
Pco_2	26.4	
SBE	-15.9 mmol/L	-15.9
Na	134.7 mmol/L	134.7
K	4.68 mmol/L	4.68
Cl	102 mmol/L	102
Ca^{++}	1.3 mmol/L	2.6
Mg^{++}	0.44 mmolL	0.88
Lac	16.4 mmol/L	16.4
PO_4	2.38 mmolL	4.34
Alb	23 g/L	7.2
Glob	20 g/L	2.8
HCO_3	10.3 mmol/L	10.3



Buffer Base

- Weak Acid Buffer
- Volatile Weak Acid
  - $H_2CO_3 \Leftrightarrow H^+ + HCO_3^-$
- Nonvolatile Weak Acids, A_{TOT}
  - Hemoglobin
  - Albumin (& Globulin)
  - Inorganic phosphate
- Weak acids
  - pK_a act as buffers

Cations/Anions
Weak Ion Acid Buffer



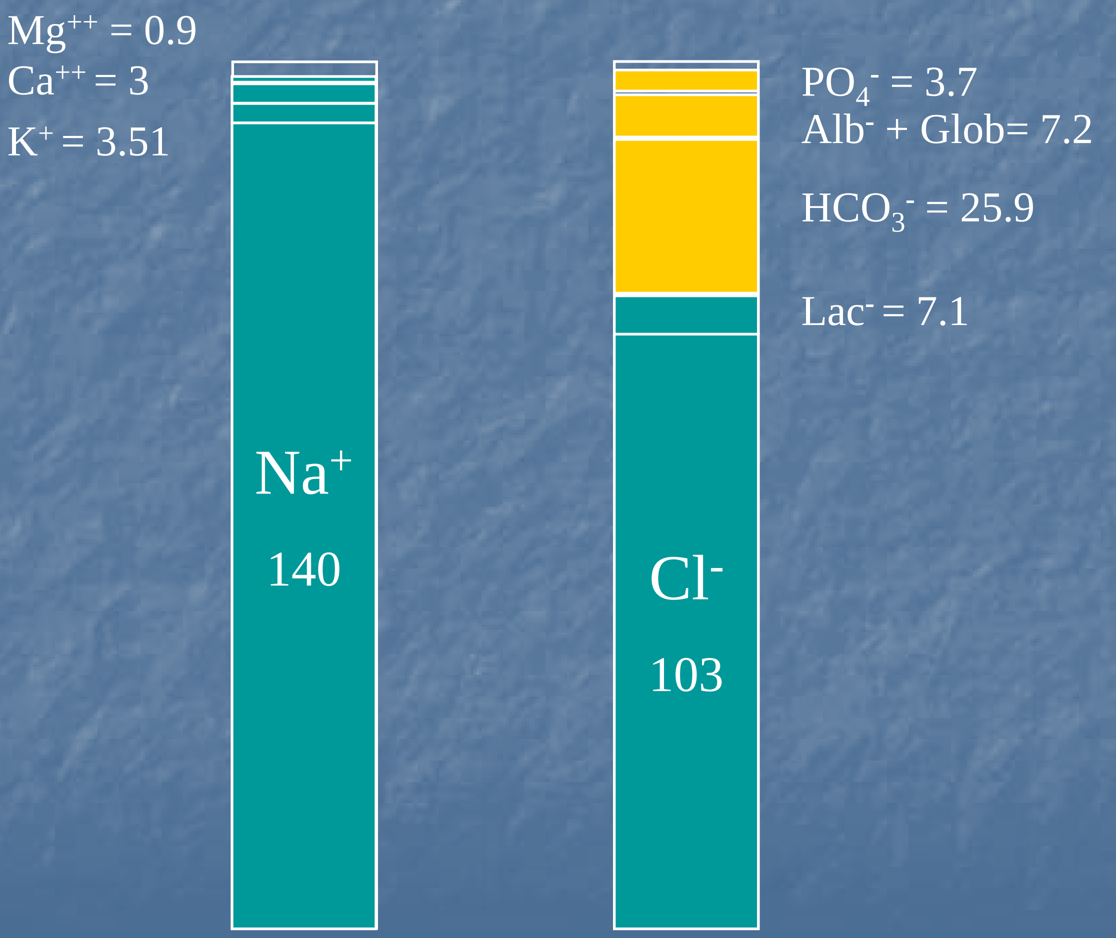
Calculating mEq/l

- $Alb^- = (Alb) \times ((0.123 \times pH) - 0.631)$
  - $Alb^- = 0.28 \times Alb$
  - Horse: $Alb^- = 0.225 \times Alb$ [g/L]
  - Horse: $Glob^- = 0.14 \times glob$ [g/L]
- $PO_4^- = PO_4 \times ((0.309 \times pH) - 0.469)$
  - Horse: $PO4^- = 1.83 \times PO4$ [mmol/L]

Acid-base calculator

Neonatal Encephalopathy		mEq/l
pH	7.295	
Pco_2	52.7	
SBE	1.2	1.2
Na	140 mmol/l	140
K	3.51 mmol/l	3.51
Cl	103 mmol/l	103
Ca^{++}	1.5 mmol/L	3
Mg^{++}	0.45 mmolL	0.9
Lac	7.1 mmol/l	7.1
PO_4	2.0 mmolL	3.7
Alb	21.8 g/L	4.9
Glob	16.2 g/L	2.3
HCO_3	25.9 mmol/l	25.9

Buffer Base



Anion Gap

Cations = Anions

$$Na + K + Ca + Mg + UC = Cl + HCO_3 + Alb + PO_4 + UA$$

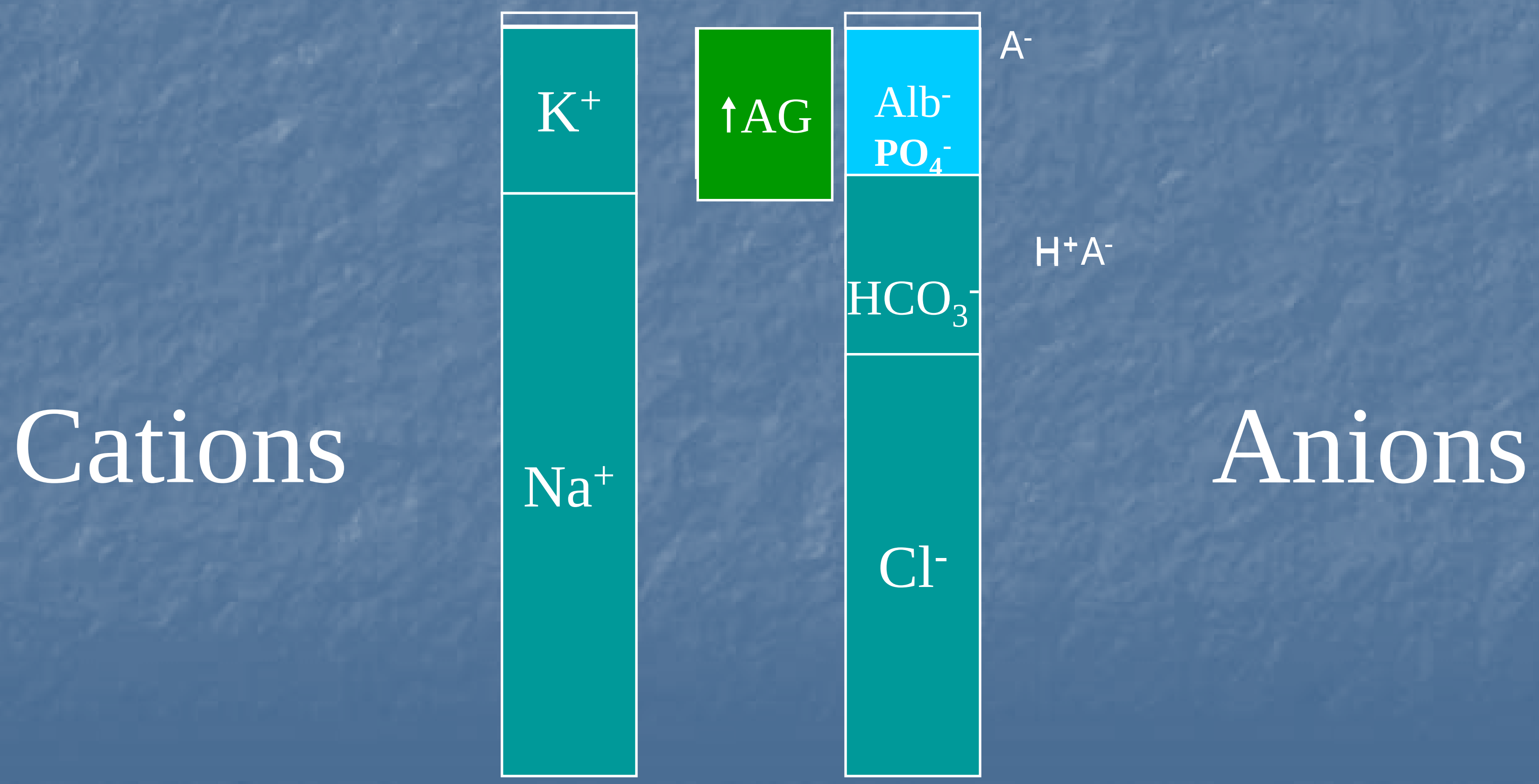
$$(Na + K) – (Cl+HCO_3) = (Alb + PO_4 + UA) – (Ca + Mg + UC)$$

$$(Na + K) – (Cl + HCO_3) = UA - UC$$

$$(Na + K) – (Cl + HCO_3) = AG$$

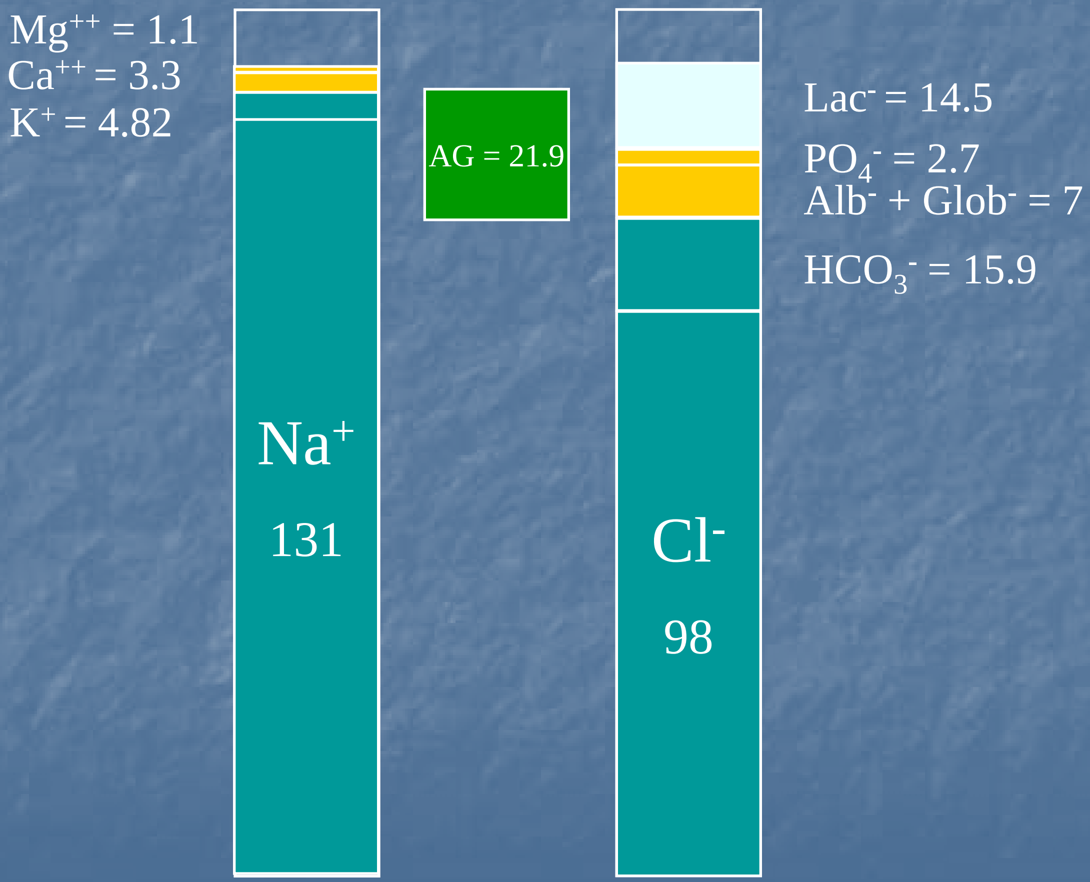
Cations/Anions
Anion Gap

$(Na + K) – (Cl + HCO_3) = AG$



Anion Gap

Birth Asphyxia		mEq/l
pH	7.009	
Pco2	62.4	
AG	21.9 mmol/L	
Na	131 mmol/L	131
K	4.82 mmol/L	4.82
Cl	98 mmol/L	98
Ca^{++}	1.65 mmol/L	3.3
Mg^{++}	0.53 mmol/L	1.1
Lac	14.5 mmol/L	14.5
PO_4	1.61 mmol/L	2.9
Alb	27.8 g/L	6.3
Glob	19.2 g/L	2.7
HCO_3	15.9 mmol/L	15.9
SBE	-13.3	



Anion Gap

- Unidentified cations
  - Ca^{++}, Mg^{++}
  - Amines, many drugs
- Unidentified anions include Alb, PO_4
  - Low levels could mask presence of UA
  - High levels could mimic presence of UA
- Corrected AG
  - Corrected for Alb and Pi values
    - Acid pH

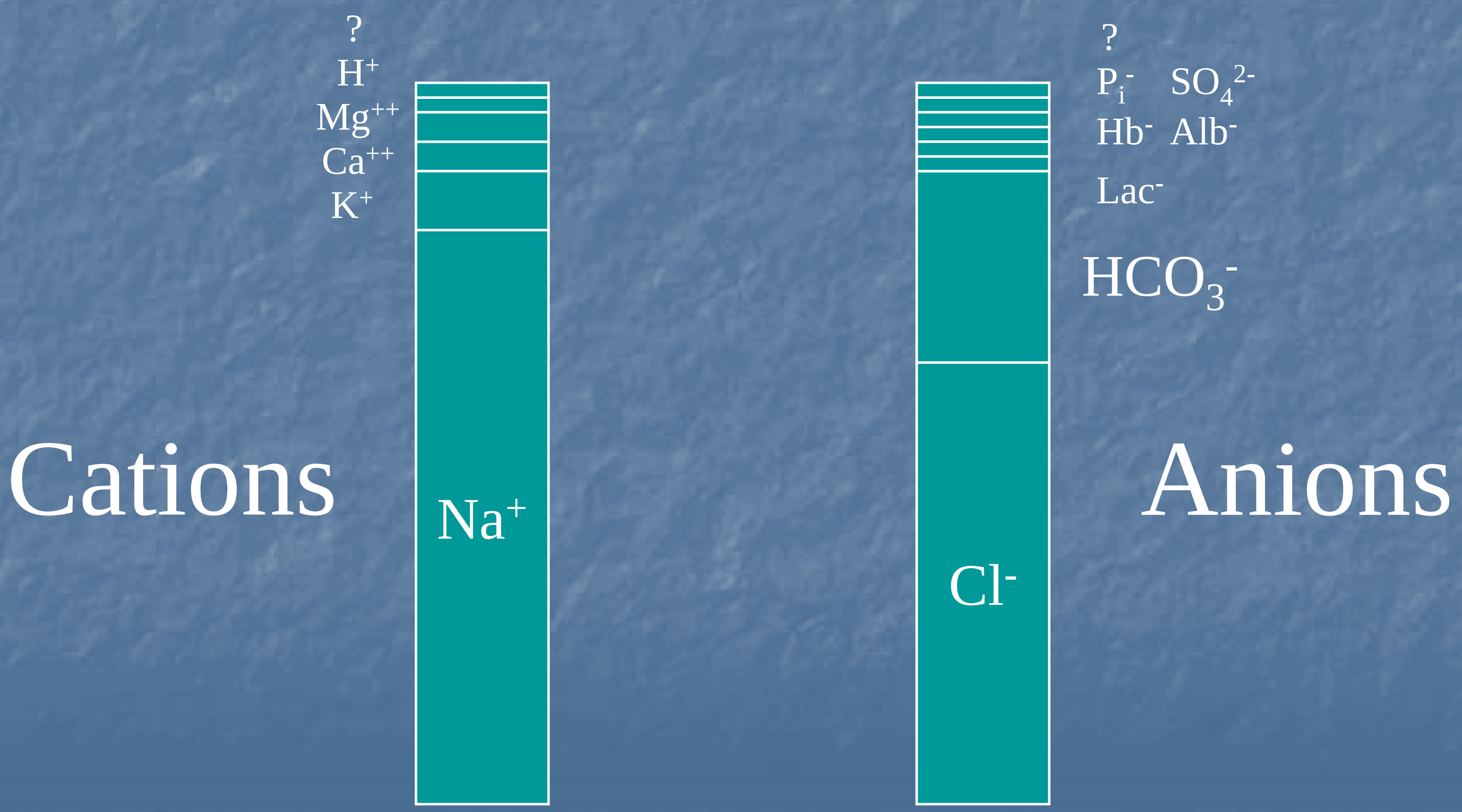
Stewart Approach

- Principles of physical chemistry
  - Electrical neutrality
  - Dissociation equilibriums
  - Conservation of mass
- Independent variables
  - SID
  - Weak acids (A_{TOT}) – buffer base
  - P_{CO2}

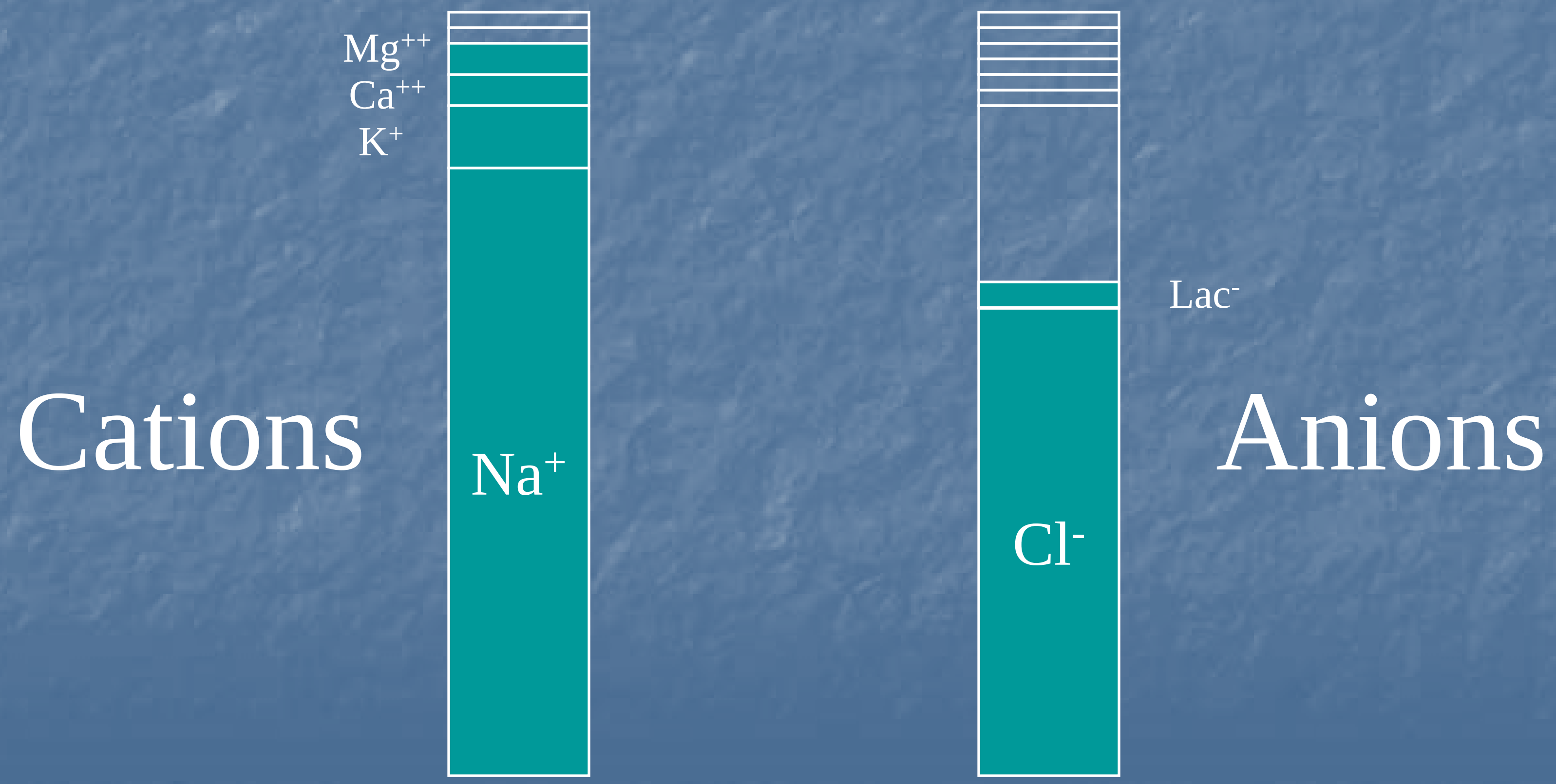
Strong Ions

- Inorganic
  - Na^+, Cl^-, K^+, $SO4^{--}$, Ca^{++}, and Mg^{++}
- Organic
  - Lactic acids
  - Tricarboxylic acids
  - Keto acids
- Strong organic anion
  - “footprint” or “ghost” of the strong acid

Cations/Anions

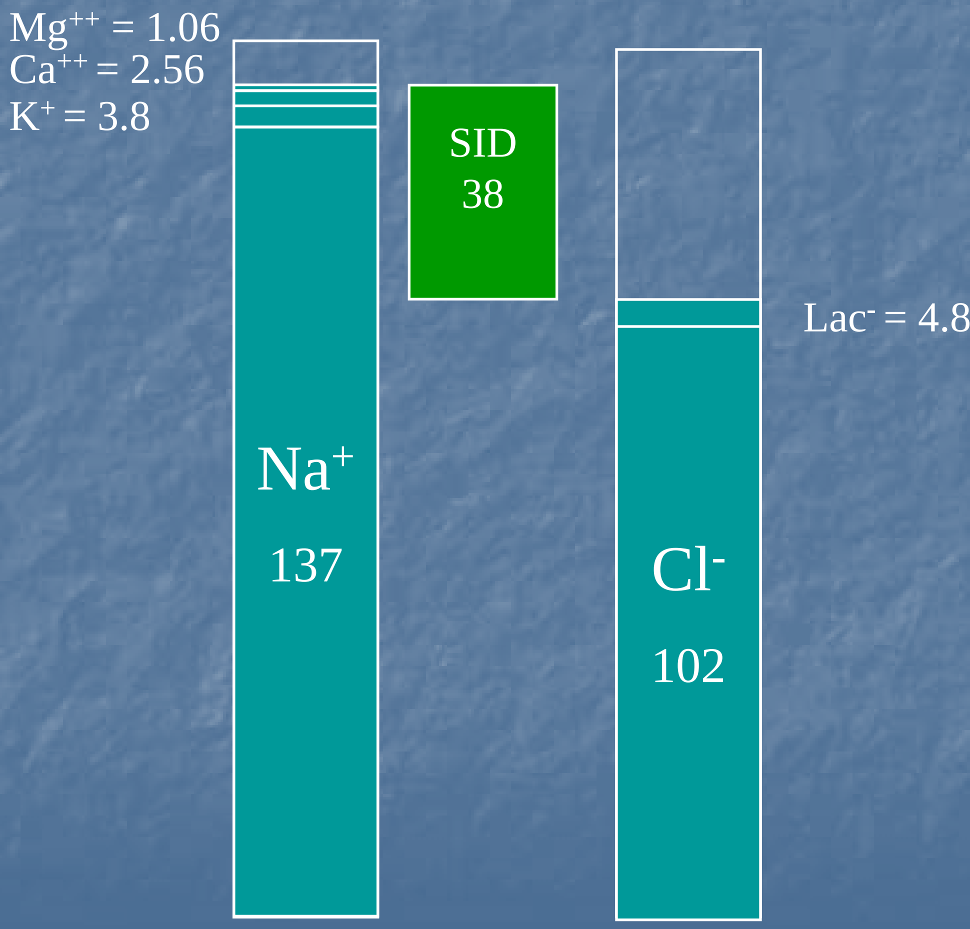


Strong Ions



Strong Ions

FIRS, Sepsis		mEq/l
pH	7.46	
Pco_2	39.8	
SID	38	
Na	137 mmol/L	137
K	3.8 mmol/L	3.8
Cl	102 mmol/L	102
Ca^{++}	1.28 mmol/L	2.56
Mg^{++}	0.53 mmol/L	1.06
Lac	4.8 mmol/L	4.8
PO_4	1.34 mmol/L	2.4
Alb	49 g/L	11
Glob	7.6 g/L	1.1
HCO_3	28.6 mmol/L	28.6
SBE	4.7	



SID

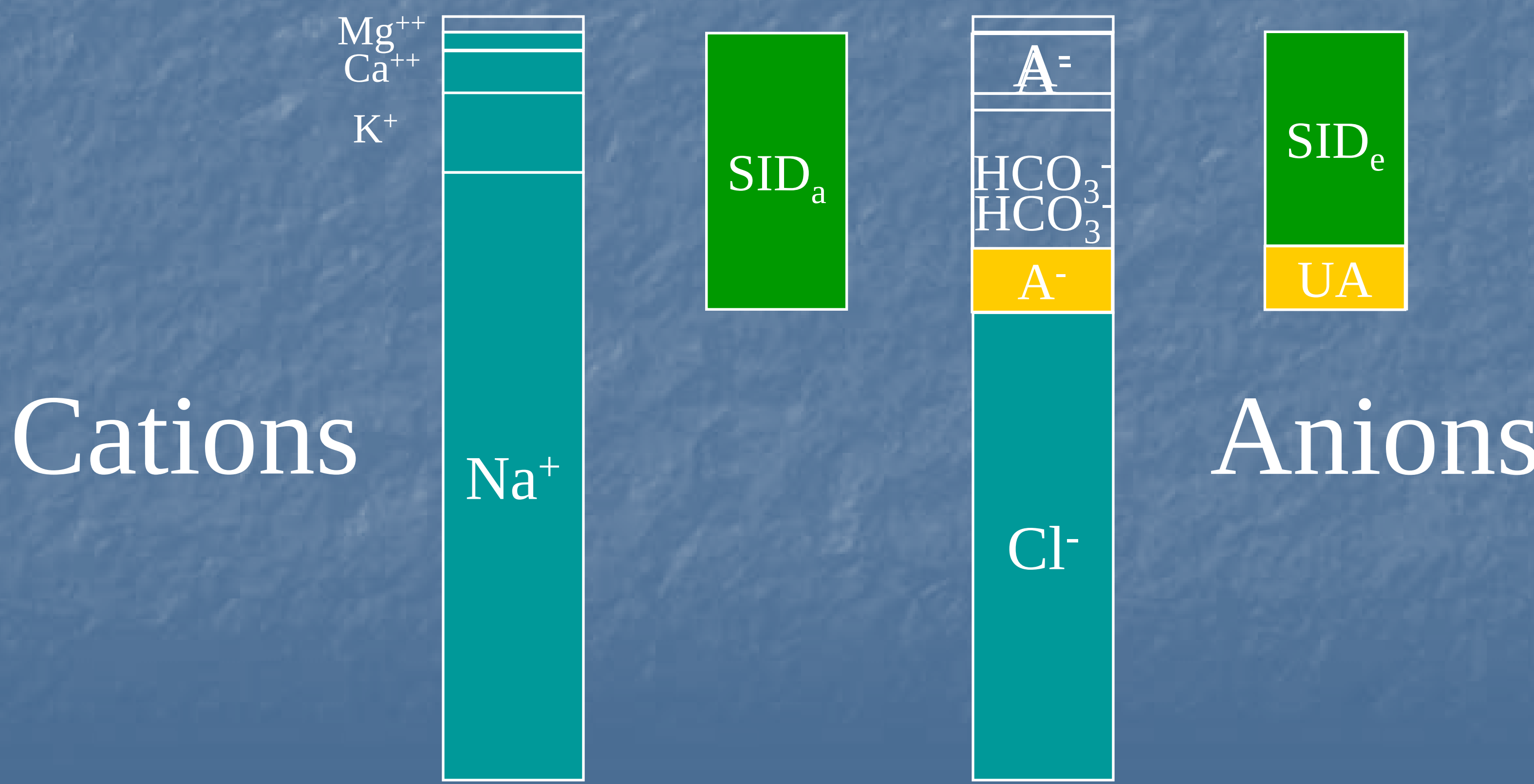
- Approximately 40±2
- Strong ion balance
  - SID > 40 - alkalizing
  - SID < 40 - acidifying
- Quantitate
- Hyper/hypochloremia - relative
  - Decrease Cl < decrease Na – acidosis
  - Decrease Cl > decrease Na – alkalosis

SIG

$SID_a = (Na + K + Ca + Mg) – (Cl + Lac)$

$SID_e = Alb^- + PO_4^- + HCO_3^-$

$SIG = SID_a – SID_e = UA – UC = 0$

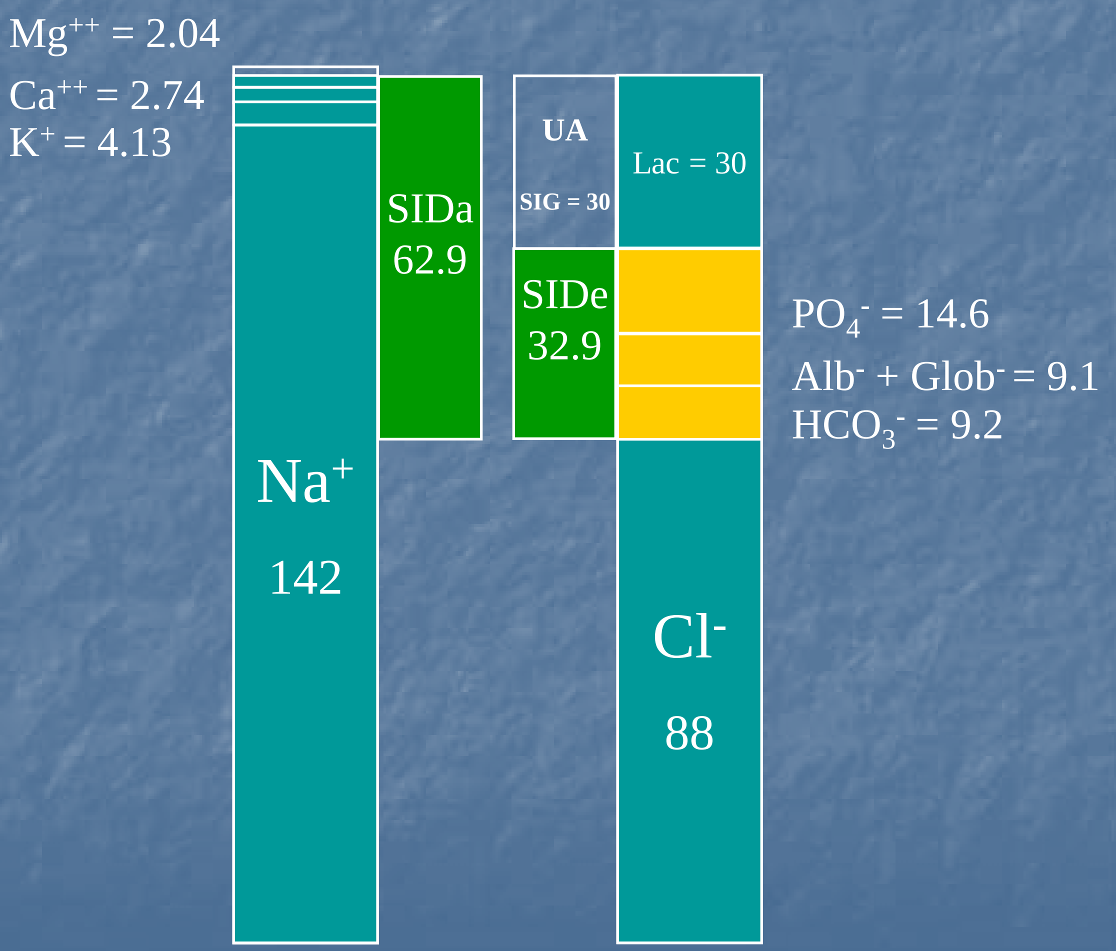


SIG

- SIG = SIDa – SIDe
- SIG > 0 – unmeasured anions
  - Sepsis
  - Liver disease
  - If lactate is not part of SIDa, D-Lac
    - Most common cause of SIG > 0
    - Lactate mmol/l = SIG
- SIG < 0 – increased unidentified cations
- Can have mixed picture but UC very rare
- SIG does not change with
  - pH, Pco_2 changes
  - Changes in albumin, phosphate

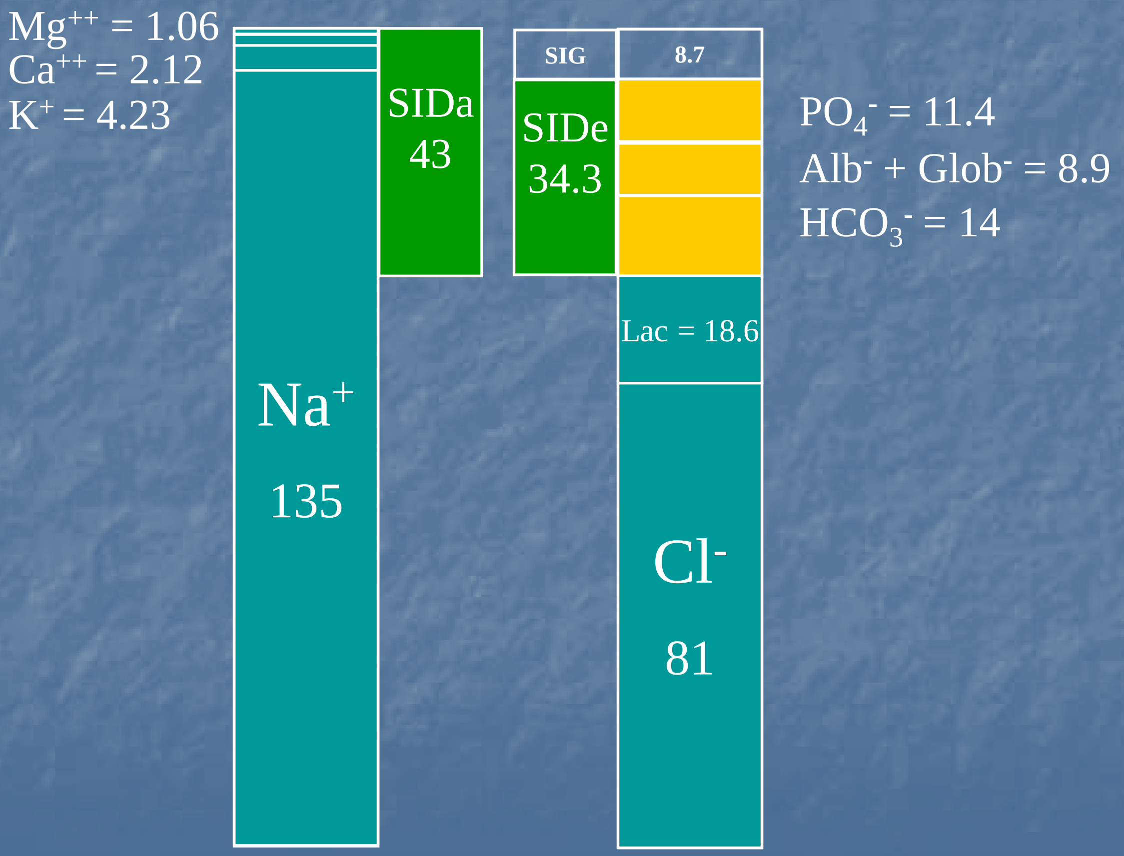
SIG – UA

Intrauterine distress Birth asphyxia		mEq/l
pH	6.791	
Pco_2	59.6	
SIDa	62.9	
SIDe	32.9	
SIG	30	
Na	142 mmol/L	142
K	4.13 mmol/L	4.13
Cl	88 mmol/L	88
Ca^{++}	1.37 mmol/L	2.74
Mg^{++}	1.02 mmol/L	2.04
Lac	?? mmol/L	??
PO_4	8.98 mmol/L	16.4
Alb	29.7 g/L	6.7
Glob	17.3 g/L	2.4
HCO_3	9.2 mmol/L	9.2
SBE	-22.5 mEq/L	-22.5



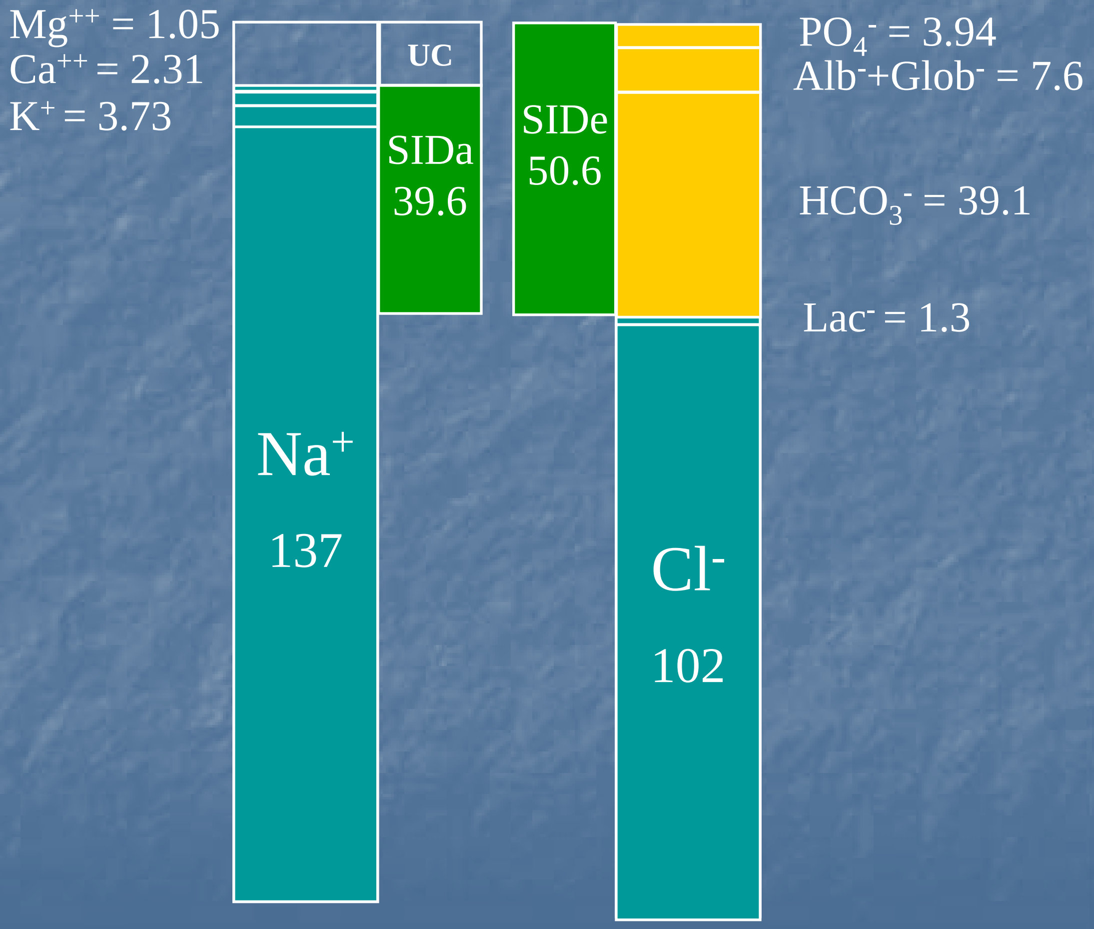
SIG – UA

Case 91645		mEq/l
pH	7.088	
Pco_2	45.9	
SIDa	43	
SIDe	34.3	
SIG	8.7	
Na	135 mmol/L	135
K	4.23 mmol/L	4.23
Cl	81 mmol/L	81
Ca^{++}	1.06 mmol/L	2.12
Mg^{++}	0.53 mmol/L	1.06
ssLac	18.6 mmol/L	18.6
PO_4	6.63 mmol/L	12.1
Alb	28.9 g/L	6.5
Glob	17.1 g/L	2.4
HCO_3	14 mmol/L	14
SBE	-15.2 mEq/L	-15.2



SIG - UC

FIRS, Sepsis		mEq/l
pH	7.361	
Pco_2	68.3	
SIDa	39.6	
SIDe	50.6	
SIG	-11	
Na	137 mmol/L	137
K	3.73 mmol/L	3.73
Cl	102 mmol/L	102
Ca^{++}	1.16 mmol/L	2.31
Mg^{++}	0.42 mmol/L	0.84
Lac	1.3 mmol/L	1.3
PO_4	2.18 mmol/L	3.98
Alb	18.2 g/L	4.1
Glob	24.8 g/L	3.5
HCO_3	39.1 mmol/L	39.1
SBE	13.1	

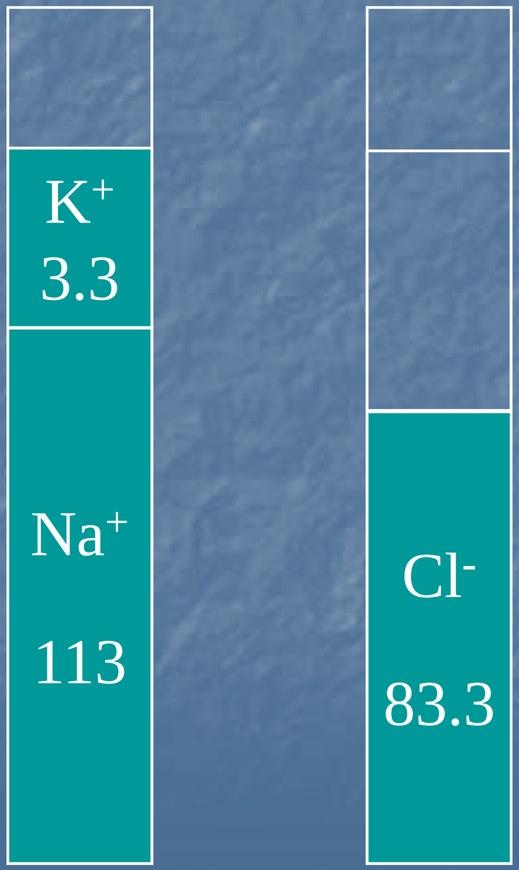



Metabolic Acid-Base Abnormalities

- Free water
  - Dilutional Acidosis
  - Contraction Alkalosis
- Hypochloremia/ Hyperchloremia
- Unidentified Anions/ Unidentified Cations
- Albumin/Phosphate concentrations

Dilutional Acidosis
Free Water

Na = 136
K = 4
Cl = 100
SID = 40



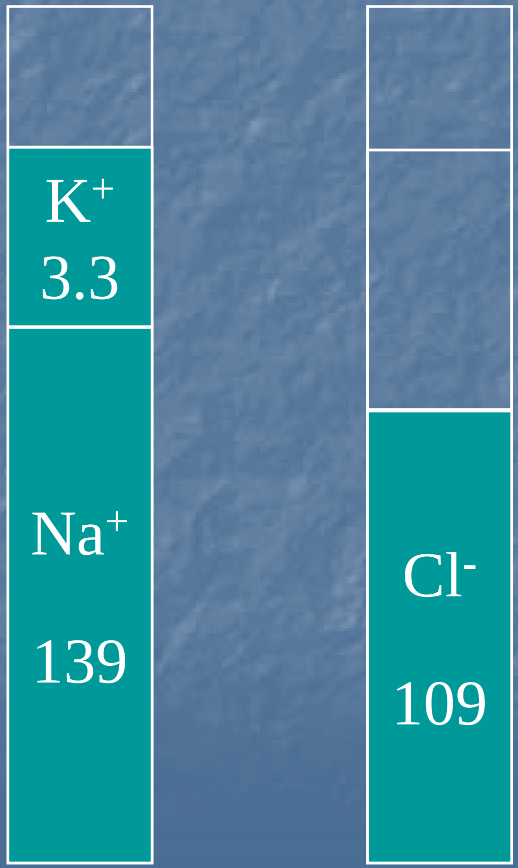
Add 20% water
Na = 113
K = 3.3
Cl = 83.3
SID = 33

Dilutional Acidosis

- Addition of free water (hyponatremia)
  - Will cause a decrease SID
  - Dilutional acidosis
    - Any osmotically active particle
      - Increase volume of ECF, no change in charge
      - Mannitol (before the diuresis)
      - Hyperglycemia
      - Ethylene glycol or methanol poisoning

Dilutional Acidosis
Saline

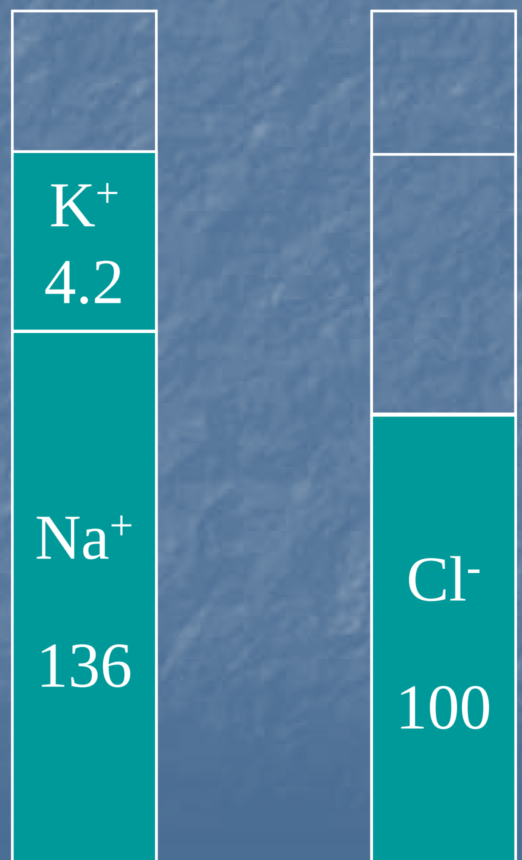
Na = 136
K = 4
Cl = 100
SID = 40



Add 20% saline
Na = 139
K = 3.3
Cl = 109
SID = 33.3

Dilutional Acidosis
Add SID balance fluid

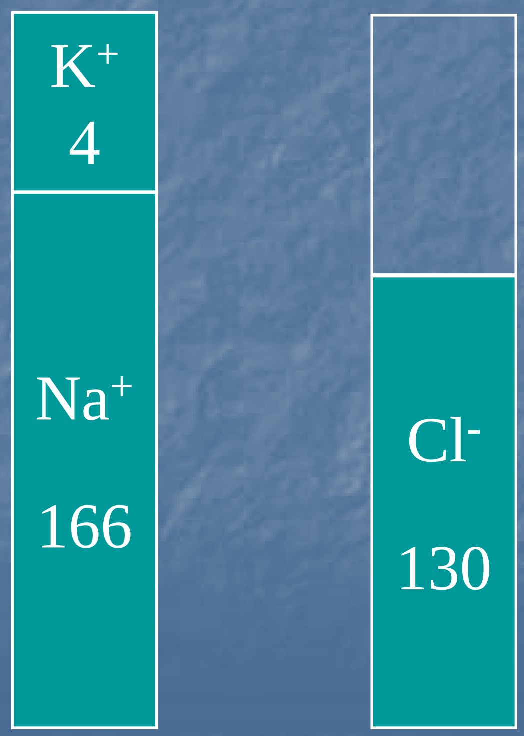
Na = 136
K = 4
Cl = 100
SID = 40



Add 20% Normisol R
Na = 137
K = 4.2
Cl = 100
SID = 41

Dilutional Acidosis
Add NaCl – no volume

Na = 136
K = 4
Cl = 100
SID = 40



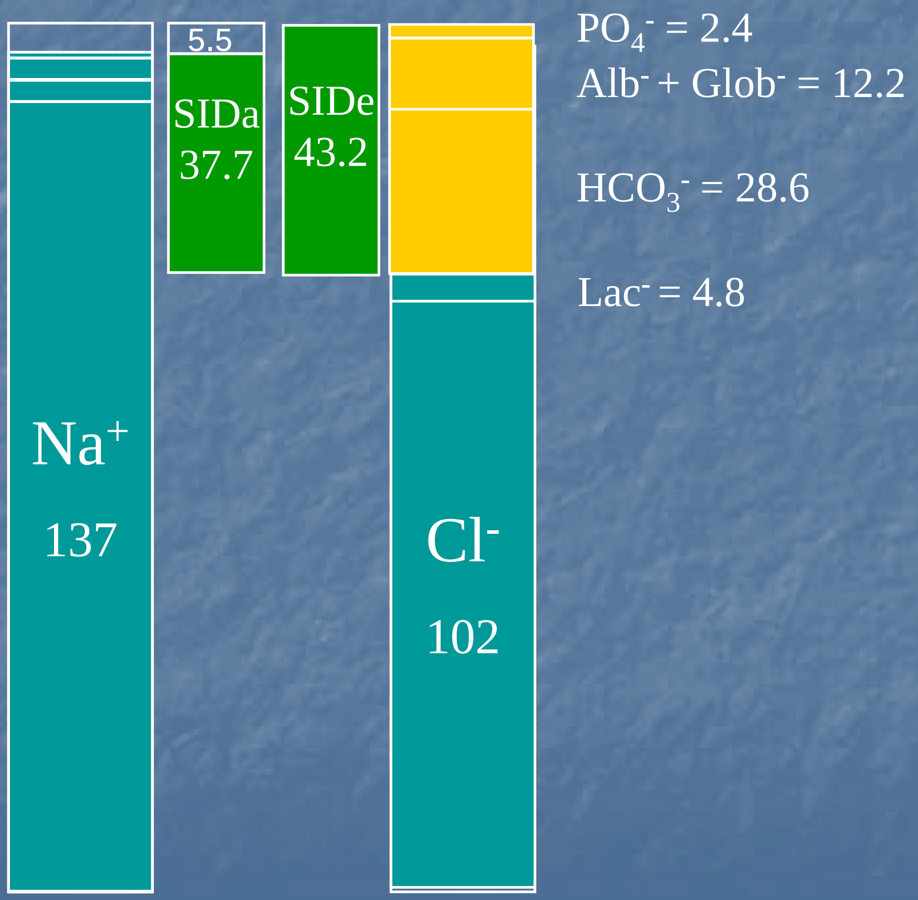
Add 30 mEq
Na = 166
K = 4
Cl = 130
SID = 40

Dilutional Acidosis

- Dilution effect
  - Depends on the SID of added fluid
  - Amount of fluid added
- How much of the SID is from free water?
- To correct for the free water effect
  - $Na_{ref}/Na_{measured}$
  - $Cl_{Corr} = (Na_{ref} / Na_{measured}) \times Cl^{-}_{measured}$
- Not that simple – in real life
  - Dilute Alb, PO_4
  - Alkalizing effect

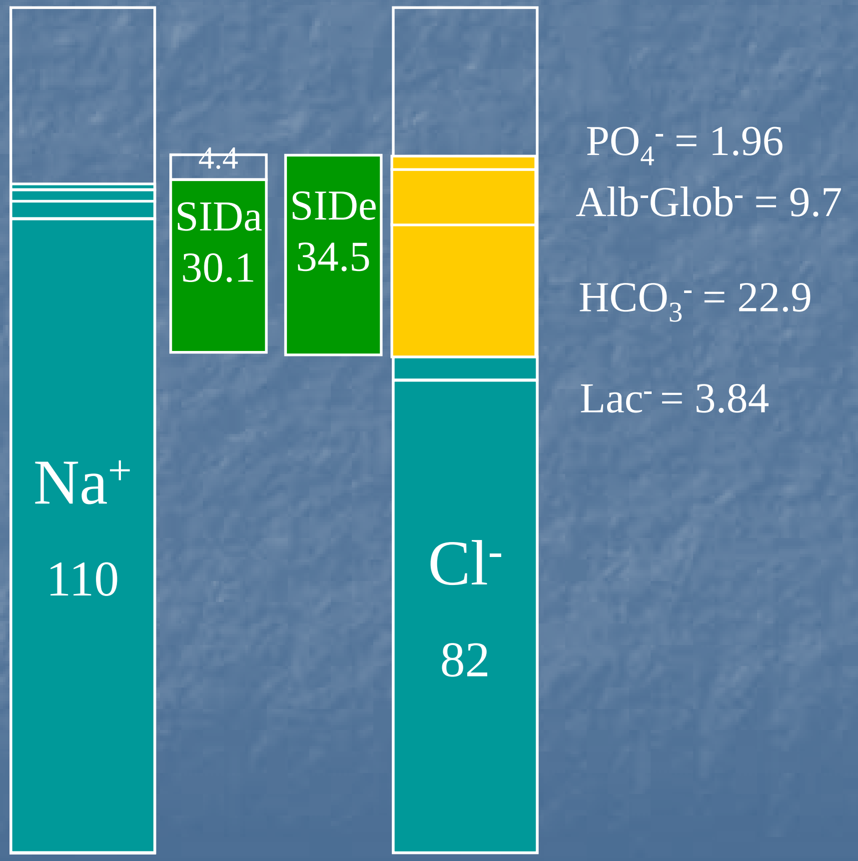
Free Water

FIRS, Sepsis		mEq/l
SIDa		37.7
SIDe		43.2
SIG		-5.5
Na	137 mmol/L	137
K	3.8 mmol/L	3.8
Cl	102 mmol/L	102
Ca^{++}	1.28 mmol/L	2.56
Mg^{++}	0.53 mmol/L	1.05
Lac	4.8 mmol/L	4.8
PO_4	1.34 mmol/L	2.44
Alb	49 g/L	11
Glob	7.6 g/L	1.1
HCO_3	28.6 mmol/L	28.6
SBE	4.7	



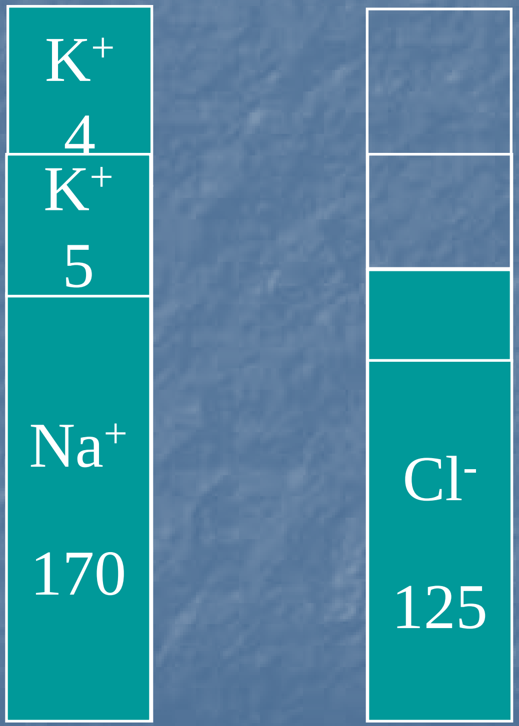
Free Water +20% water

FIRS, Sepsis		mEq/L	mEq/L
SIDa		37.7	30.1
SIDe		43.2	34.5
SIG		-5.5	-4.4
Na	137 mmol/L	137	110
K	3.8 mmol/L	3.8	3.04
Cl	102 mmol/L	102	82
Ca^{++}	1.28 mmol/L	2.56	2.04
Mg^{++}	0.53 mmol/L	1.05	0.88
Lac	4.8 mmol/L	4.8	3.84
PO_4	1.34 mmol/L	2.44	1.95
Alb	49 mg/L	11	8.8
Glob	7.6 g/L	1.1	0.88
HCO_3	28.6 mmol/l	28.6	22.9
SBE	4.7		



Contraction Alkalosis

Na = 136
K = 4
Cl = 100
SID = 40



Contract 20%
Na = 170
K = 5
Cl = 125
SID = 50

Hypochloremia Hyperchloremia

- Normal renal handling of Cl
  - Renal acid-base control
  - Adjust SID by excreting Cl without Na
  - Diet – equal Na and Cl
- Abnormal renal handling of Cl
  - Renal Tubular Acidosis
  - Renal tubular disease

Hypochloremia Hyperchloremia

- Hyperchloremic acidosis
  - Non-renal
    - GI losses Na
    - Excessive saline therapy
  - Renal
    - Renal compensation
    - RTA
- Hypochloremic alkalosis
  - Renal compensation
  - Chloriuresis (furosemide)
  - GI loss Cl
  - Contraction alkalosis (loss of free water)
    - Glucose diuresis

Unidentified Anions
Unidentified Cations

- Unidentified anions
  - L-lactate
  - D-lactate
  - Endogenous unidentified anions
    - Ketoacids
    - VFA
    - Sulfates
  - Exogenous organic unidentified anions
    - Salicylates
    - Methanol
    - Ethylene glycol

Unidentified Anions Unidentified Cations

- Unidentified cations
  - Endogenous organic cations
    - Amines
  - Exogenous organic cations
    - Toxins
    - Drugs
- Detect unidentified anions/cations
  - Numbers don't "add up"
  - "Gap"
    - AG
    - SIG
  - Occurrence of unidentified cations
    - Can mask the presence of unidentified anions

Albumin/Phosphate Concentrations

- A_{TOT}, Buffer Base, weak acids
- Metabolic acidosis
  - Hyperphosphatemia
    - Renal failure, catabolism
  - Hyperalbuminemia
    - Hemoconcentration
    - Plasma/albumin therapy
- Metabolic alkalosis
  - Hypoalbuminemia
- Neonates
  - Hypoalbuminemia
  - Hyperphosphatemia

Differential Diagnosis Metabolic Acid-Base Disturbances

- Free water
  - Reflected in [Na]
- Chloride – inorganic SID
- Organic anions
- Organic cations
- Albumin level
- Phosphate level

Changes SIDa

- SID acidosis
  - Renal tubular acidosis
  - GIt - Diarrhea
  - Iatrogenic
- SID alkalosis
  - GIt
  - Diuretics/diuresis
  - Compensation for respiratory acidosis
  - Pathologic renal loses
  - Na loading – iatrogenic

SIG Acidosis

- Multiple sources
  - D-lactate
  - Intermediary metabolites
    - Ketones
    - Sulfates
  - Exogenous administered
    - Gelatins
    - Acetate, gluconate*, citrate
  - Acute phase proteins
  - Other inflammatory proteins
    - Cytokines
    - Chemokines
    - Other mediators

SIG Acidosis

- Accumulate - renal and liver dysfunction
  - Magnitude of the inflammatory response
  - Presence of organ dysfunction
- Prognostic significance
  - Lactic acidosis
  - SIG acidosis
  - Hyperchloremia
  - Respiratory acidosis

Mixed Acid Base Disorders

- One obvious disturbance
  - Inappropriate compensation
  - Separate primary disorder
- pH can be normal
  - Disorders cancel other's effects
- Compensation
  - P_{aCO2} and HCO_3 change in the same direction
  - Could be a mixed disorder
  - Excessive, insufficient, or appropriate

Mixed Acid Base Disorders

- Common in critically ill patients
  - Can lead to dangerous extremes of pH
- Four factors that determine pH
  - SIDa excluding lactate
  - Lactate plus and other organic anions (UA)
  - Abnormalities in the buffer base
  - Respiratory component

Mixed Acid Base Disorders

- Abnormalities of the SIDa (not lactate)
  - Chronic – time to develop and correct
  - Appropriate renal compensation
  - Primary abnormality
  - Na+K and Cl concentrations
    - Renal
    - Placental
    - Gastrointestinal

Mixed Acid Base Disorders

- Lactate, other organic anions (UA)
  - Abnormal intermediary metabolism
  - Can develop rapidly and resolve rapidly
  - Imply underlying pathophysiologic forces
- Abnormalities in the buffer base
  - Levels of plasma proteins and phosphate
  - Reflect underlying pathophysiology

Mixed Acid Base Disorders

- Respiratory component
  - Normal respiratory compensation
  - Underlying neuro-respiratory abnormalities
- Examining each part of the puzzle
  - Why pH is normal or abnormal
  - Understand underlying pathophysiology

Acid Base Disorders

- Prognosis
  - Underlying cause more important than degree
  - Not all acidosis equal
    - Dilution
    - Poisoning
    - Hyperchloremia
    - Saline infusions
    - Dysox - lactate production
    - Sepsis - lactate production

Metabolic Acid-Base Disturbances

Abnormality	Acidosis	Alkalosis
Abnormal SIDa		
Free water excess/deficit	Water excess = dilutional ↓ SID +↓$[Na^+]$	Water deficit = contraction ↑ SID ↑$[Na^+]$
Chloride	↓ SID ↑$[Cl^-]$	↑ SID +↓$[Cl^-]$
UA (e.g. D-lactate, keto acids)	↓ SID ↑$[UA^-]$	—
UC (e.g. organic cations)	—	↑ SID ↑$[UC^+]$
Abnormal Buffer Base, SIDe		
Albumin [Alb]	↑[Alb]	↓[Alb]
Phosphate [Pi]	↑[Pi]	↓[Pi]