ACID-BASE

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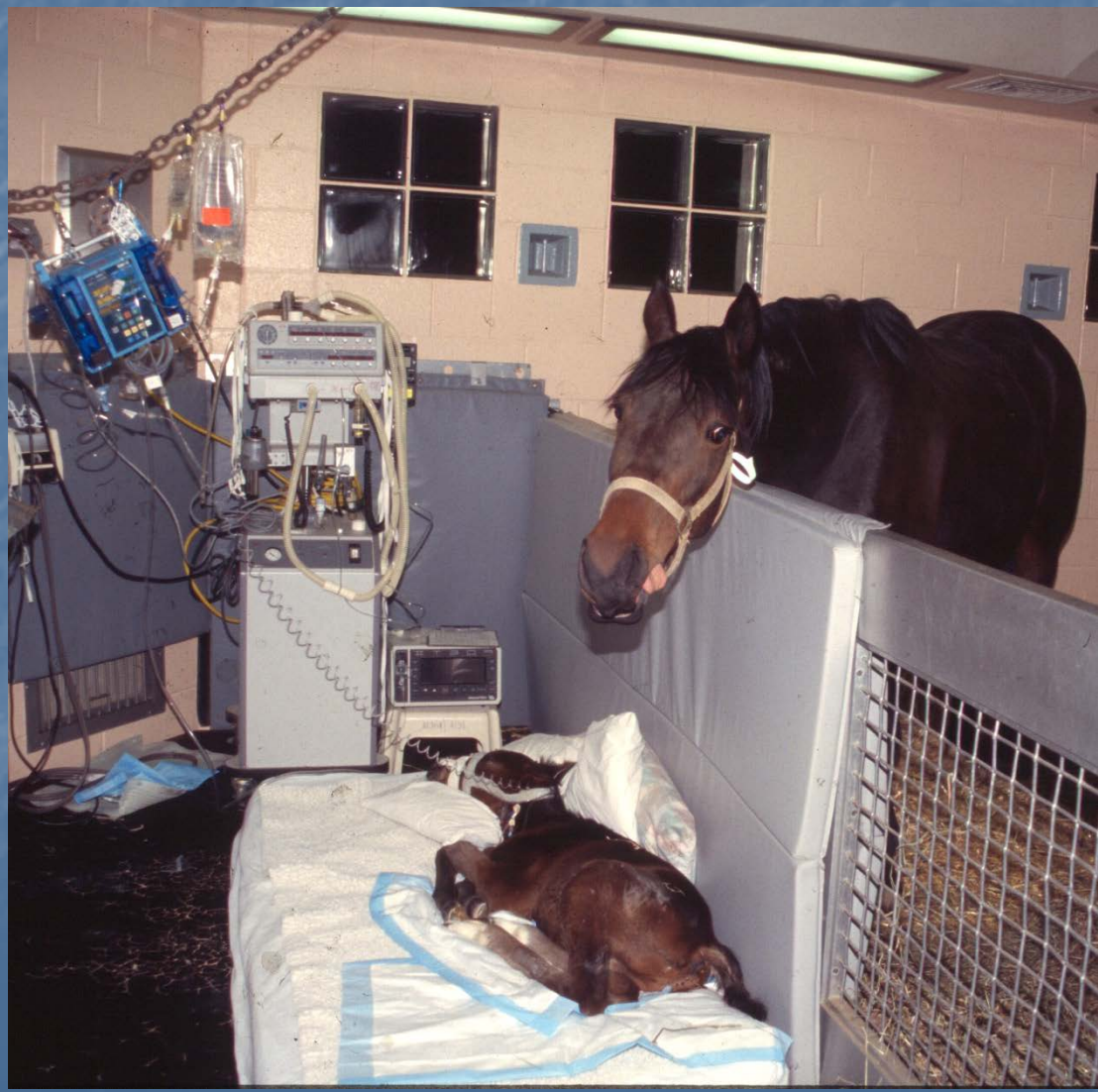
Acid-Base

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

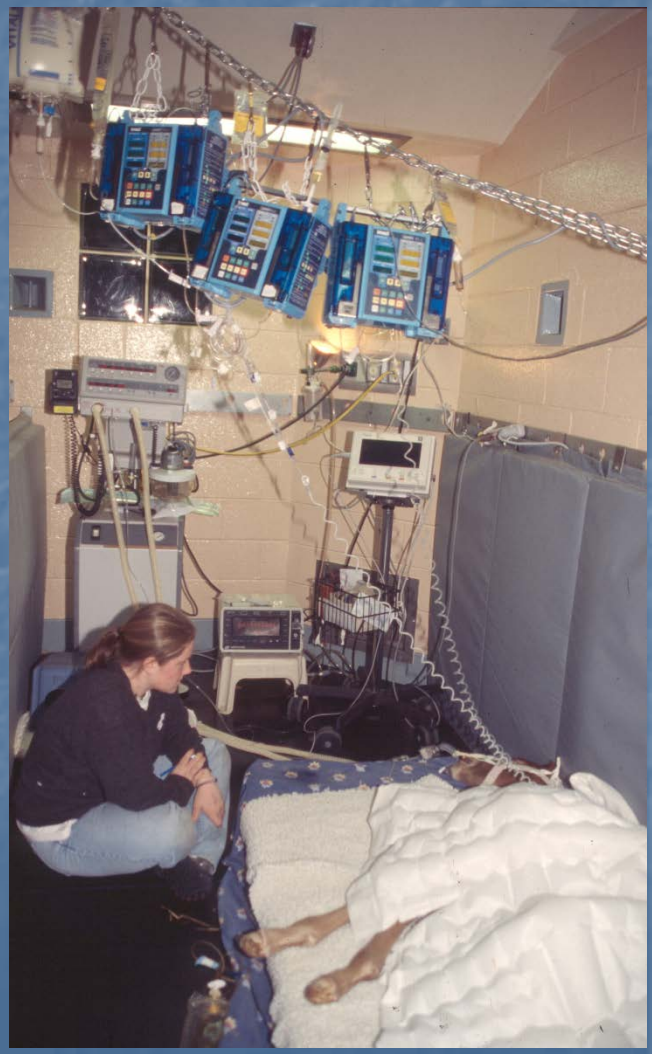
Acid–Base Disorders



Acid-Base Abnormalities

Alterations in acid-base balance

Less important than the pathologic abnormalities causing them



Acid-Base Abnormalities

- Fatal disorders
  - Extreme (eg, 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 - increased adrenergic tone
  - Increase 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

William O'Shaughnessy
Thomas Latta
1832

History Acid-Base Analysis

- Henderson 1909

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

- Hasselbalch 1916

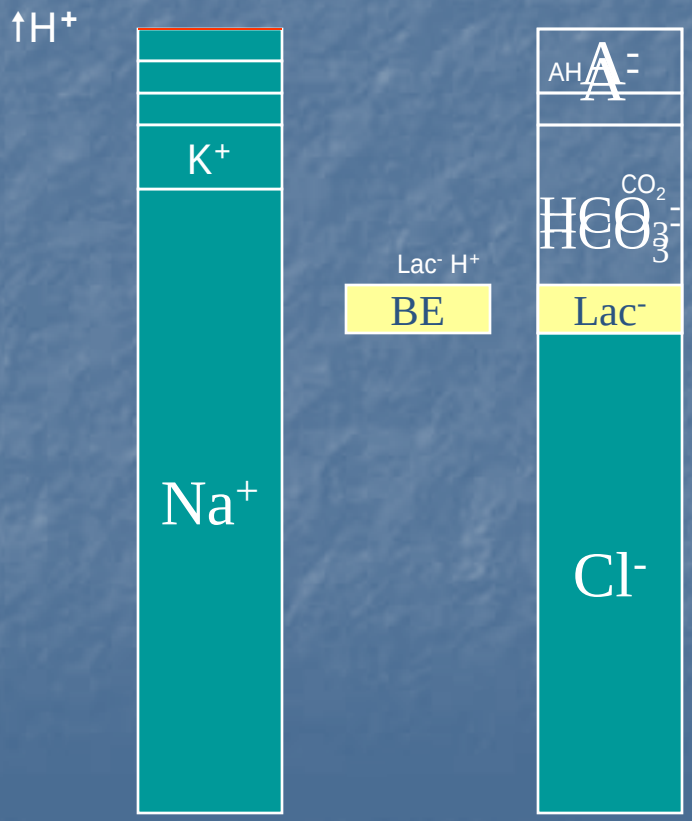
$$pH = 6.1 + \log\left[\frac{HCO_3^-}{P_{co_2} \times 0.03}\right]$$

- 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

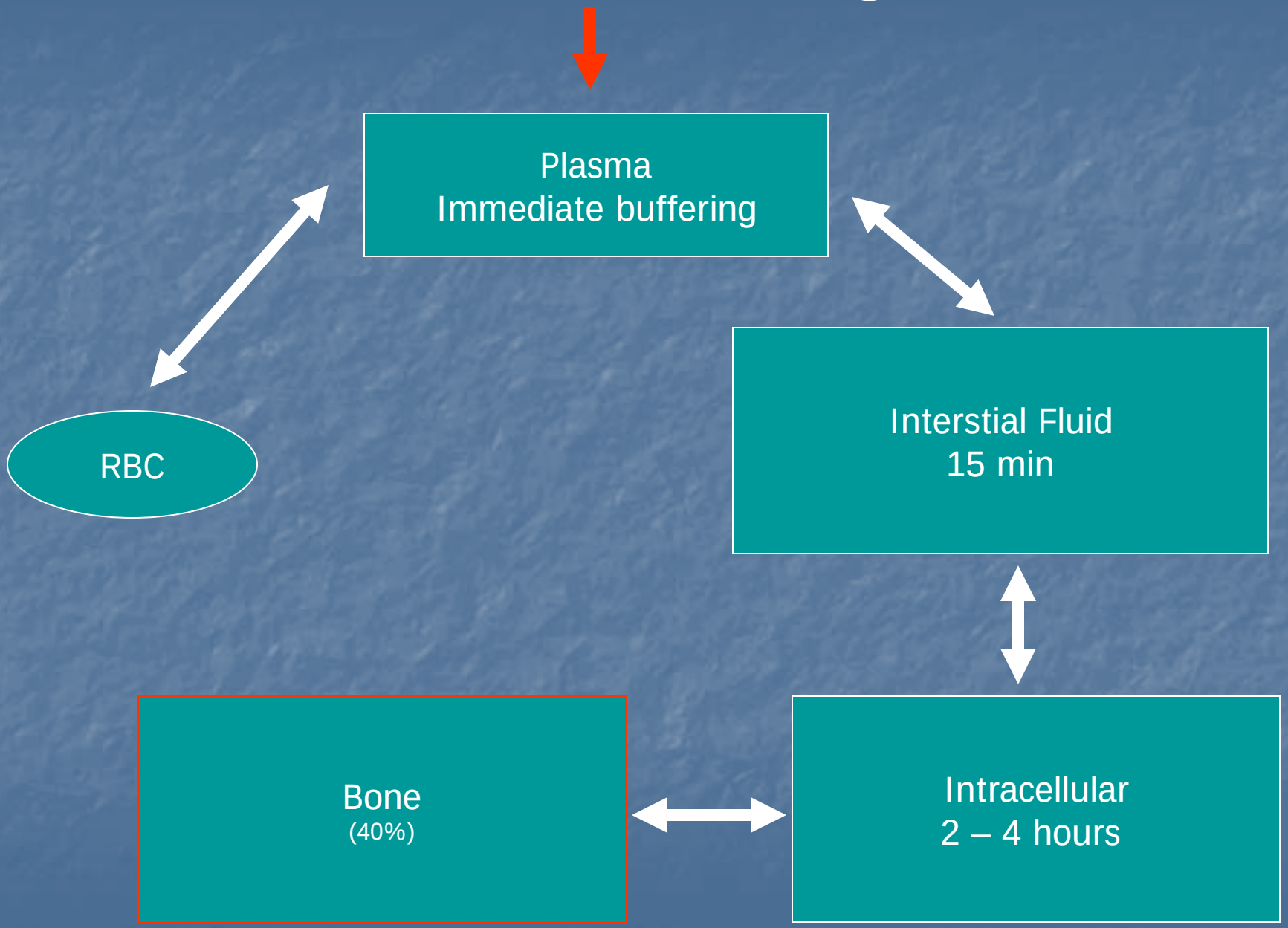
BE
Lactic Acidosis



Cations

Anions

Acid Buffering

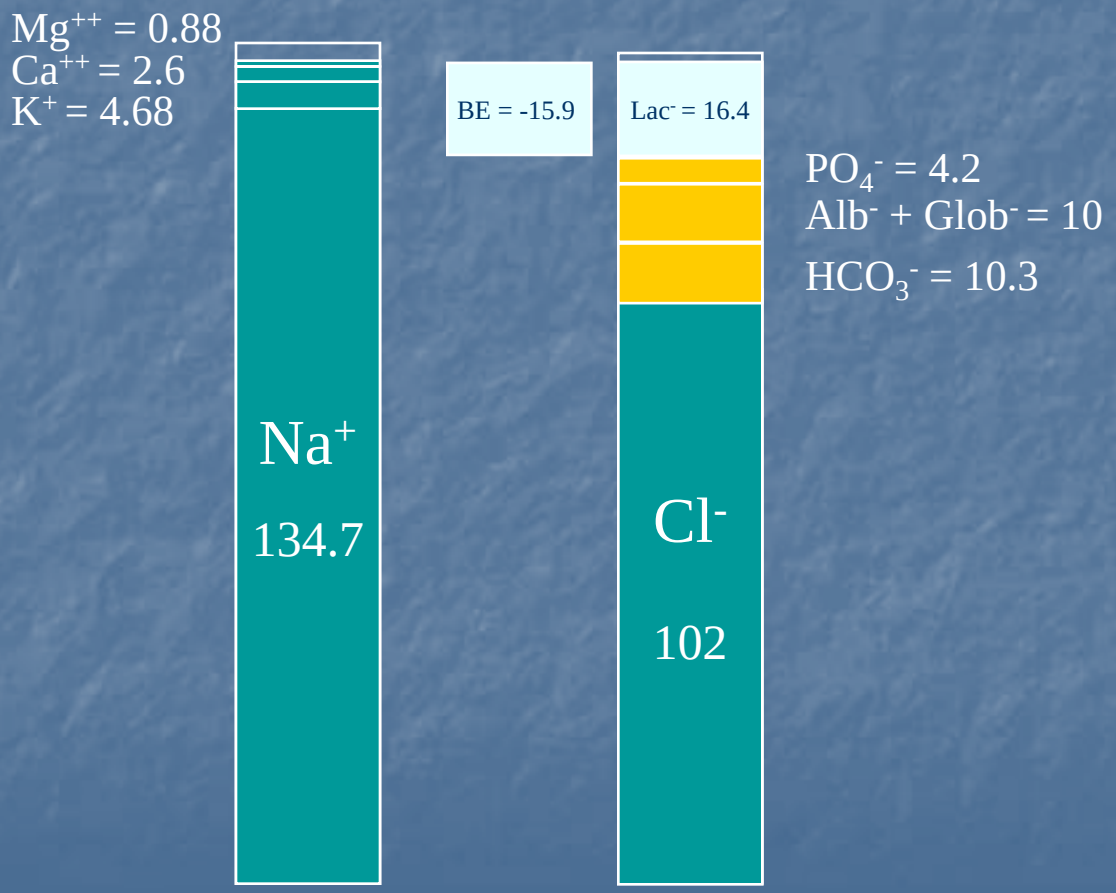


Standard Base Excess

- 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^{++}	5.31 mg/dl	2.6
Mg^{++}	1.08 mg/dl	0.88
Lac	16.4 mmol/l	16.4
PO_4	7.36 mg/dl	4.34
Alb	2.3 g/dl	7.2
Glob	2.0 g/dl	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

Cations

PO_4^-
Alb^- Hb^-

Anions

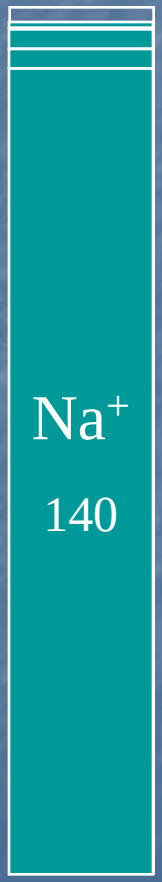
Calculating mEq/l

- Alb^- = (Alb x 10) x ((0.123 x pH) – 0.631)
  - Alb^- = 2.8 x Alb
  - Horse: Alb^- = 2.25 x Alb [g/dl]
  - Horse: $Glob^-$ = 1.40 x glob [g/dl]
- PO_4^- = (PO_4 x 0.323) x ((0.309 x pH) – 0.469)
  - PO_4^- = 0.58 x PO_4
  - Horse: $PO4^-$ = 0.59 x PO4 [mg/dl]

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^{++}	6 mg/dl	3
Mg^{++}	1.1 mg/dl	0.9
Lac	7.1 mmol/l	7.1
PO_4	6.22 mg/dl	3.7
Alb	2.18 g/dl	4.9
Glob	1.62 g/dl	2.3
HCO_3	25.9 mmol/l	25.9

Buffer Base

$Mg^{++} = 0.9$
$Ca^{++} = 3$
$K^{+} = 3.51$



$PO_4^{-} = 3.6$
$Alb^{-} + Glob = 7.2$
$HCO_3^{-} = 25.9$
$Lac^{-} = 7.1$

Anion Gap

Cations = Anions

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

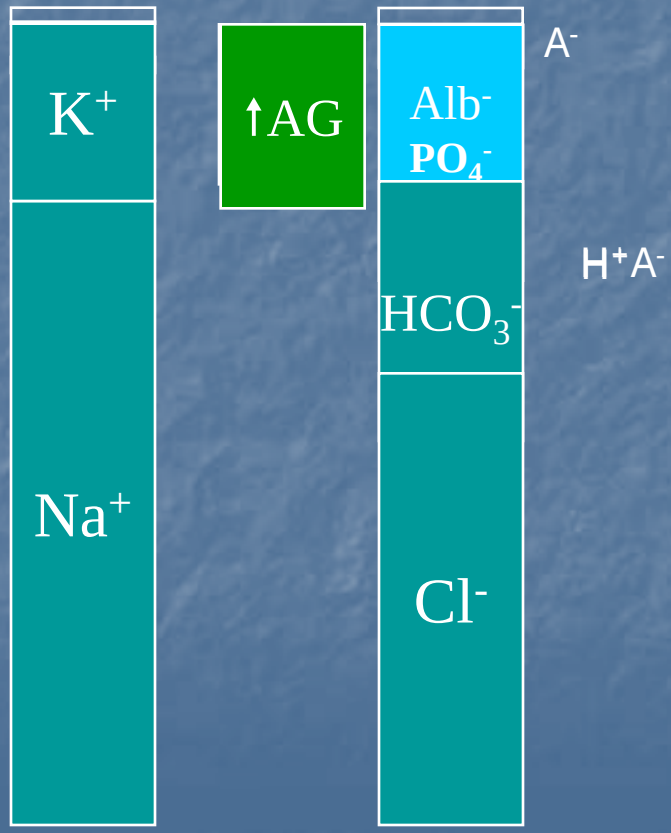
$(Na + K) – (Cl + HCO_3) = (Alb + PO_4 + UA) – (Ca + Mg + UC)$

$(Na + K) – (Cl + HCO_3) = UA - UC$

$(Na + K) – (Cl + HCO_3) = AG$

Cations/Anions
Anion Gap

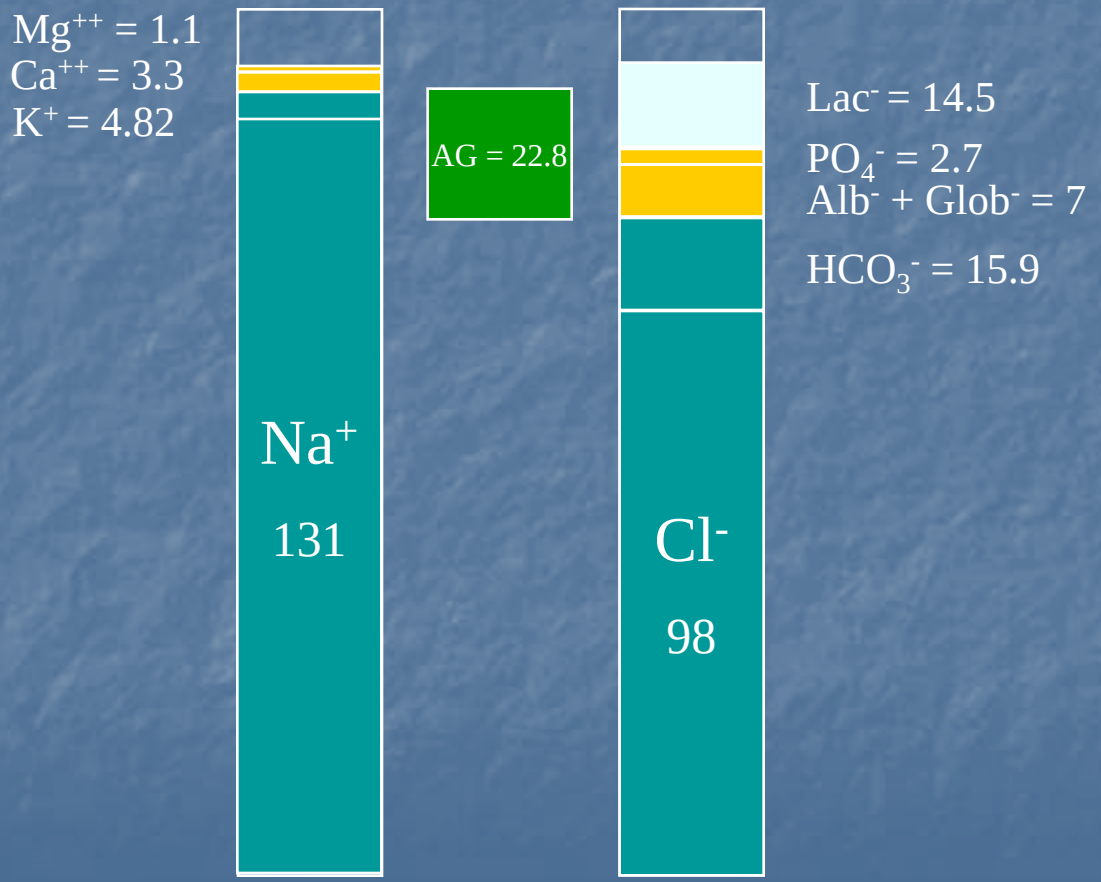
Cations



Anions

Anion Gap

Birth Asphyxia		mEq/l
pH	7.009	
Pco2	62.4	
AG	22.8 mmol/l	
Na	131 mmol/l	131
K	4.82 mmol/l	4.82
Cl	98 mmol/l	98
Ca^{++}	6.58 mg/dl	3.3
Mg^{++}	1.3 mg/dl	1.1
Lac	14.5 mmol/l	14.5
PO_4	4.99 mg/dl	2.9
Alb	2.78 g/dl	6.3
Glob	1.92 g/dl	2.7
HCO_3	15.9 mmol/l	15.9
SBE	-13.3	



Anion Gap

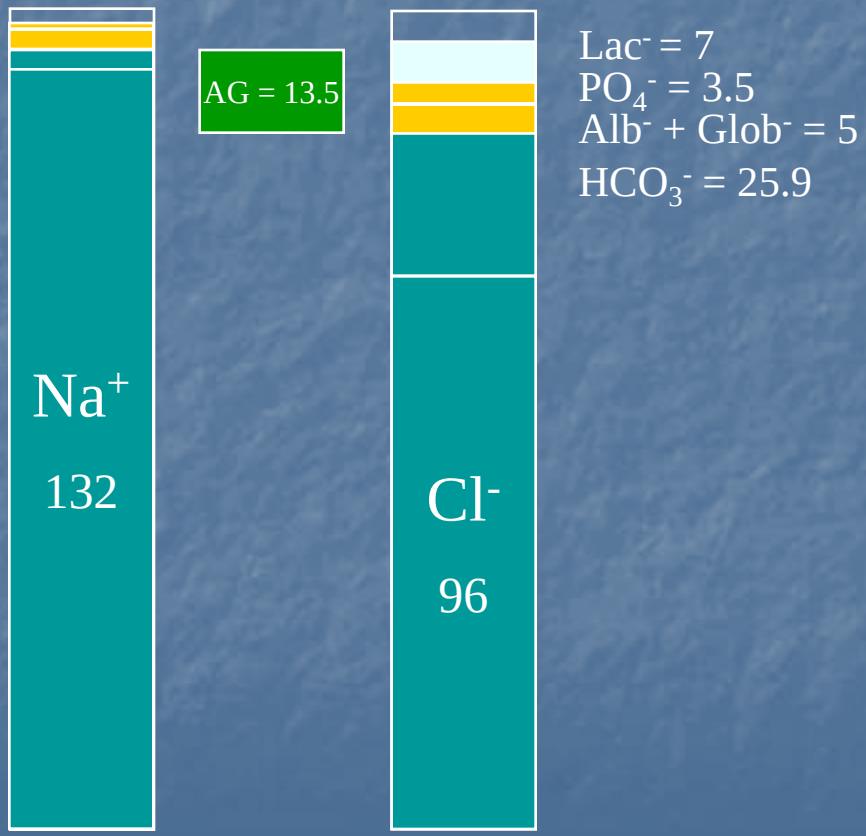
- Unidentified cations
  - Ca^{++}, Mg^{++}
  - Amines, many drugs
- Unidentified anions include Alb, PO_4
  - Low levels could mask presence of UA
  - High levels could mimic presence of UA
- Corrected AG
  - $AG_{Corr} = AG + 2.5 \times (Alb_{ref} - Alb_{measured})$
  - $AG_{corr} = AG - ((2 \times Alb) + (0.5 \times Pi))$
    - Acid pH

Dystocia		mEq/l
pH	7.390	
Pco2	42.6	
AG	13.5 mmol/l	
Na	132 mmol/l	132
K	3.42 mmol/l	3.42
Cl	96 mmol/l	96
Ca^{++}	6.13 mg/dl	3
Mg^{++}	1.4 mg/dl	1
Lac	7 mmol/l	7
PO_4	4.19 mg/dl	2.5
Alb	1.28 g/dl	2.9
Glob	1.52 g/dl	2.1
HCO3	26 mmol/l	26
SBE	1.3	

Anion Gap

$AG_{corr} = AG - (Alb^{-}) + (PO_4^{-})) = 5$

$Mg^{++} = 1$
$Ca^{++} = 3$
$K^{+} = 3.42$



Anion Gap

- HCO_3^-
  - Respiratory influence
- Delta-delta
  - $\Delta AG = AG_{Corr} - AG_{ref}$
  - $\Delta HCO_3^- = HCO_{3\ ref}^- - HCO_{3\ measured}^-$
  - $\Delta AG = \Delta HCO_3^-$ if no respiratory influence
  - But …
    - Non-bicarbonate buffers
    - Volume of distribution
    - Duration of acidosis
  - Normal – (1 to 1.6):1
    - Lactate - 0.8:1 to 1.8:1
    - Ketoacids - 0.8:1 to 1:1
  - Range may hide confounding abnormalities

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

Cations

Anions

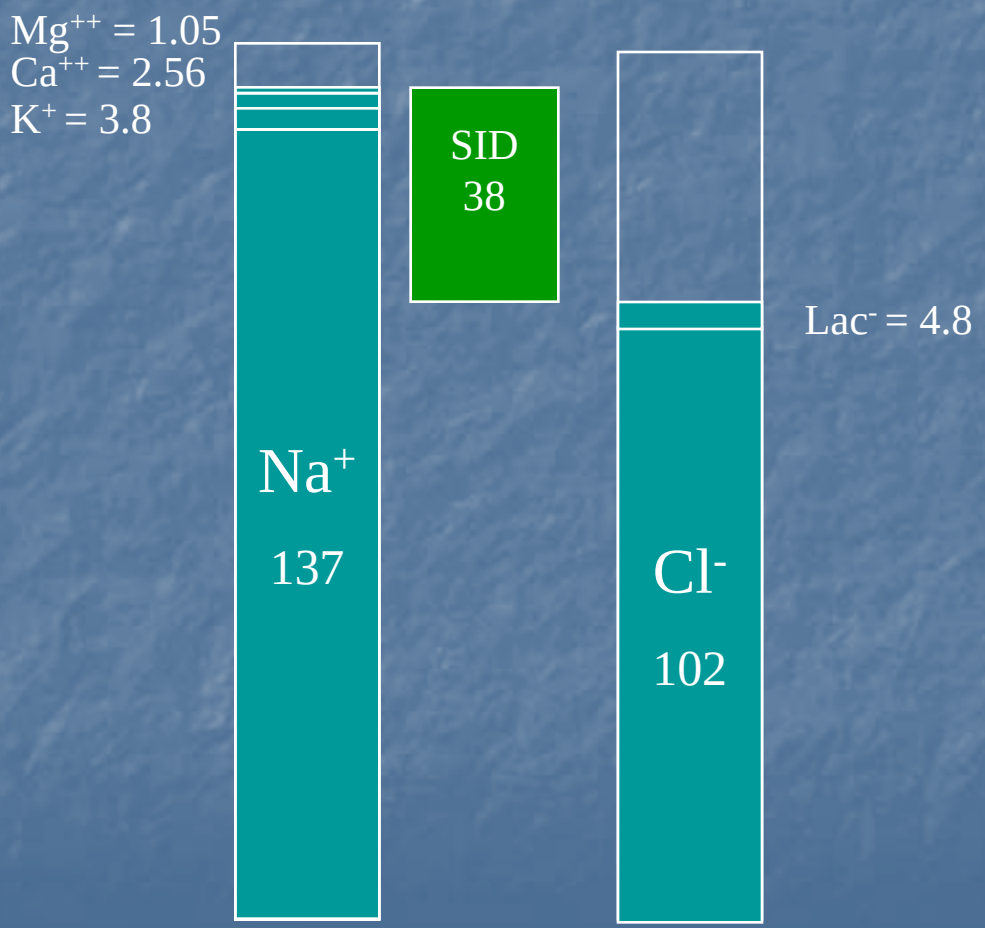
Strong Ions

Cations

Anions

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^{++}	5.11 mg/dl	2.56
Mg^{++}	1.28 mg/dl	1.05
Lac	4.8 mmol/l	4.8
PO_4	4.14 mg/dl	2.4
Alb	4.9 g/dl	11
Glob	0.76 g/dl	1.1
HCO_3	28.6 mmol/l	28.6
SBE	4.7	



SID

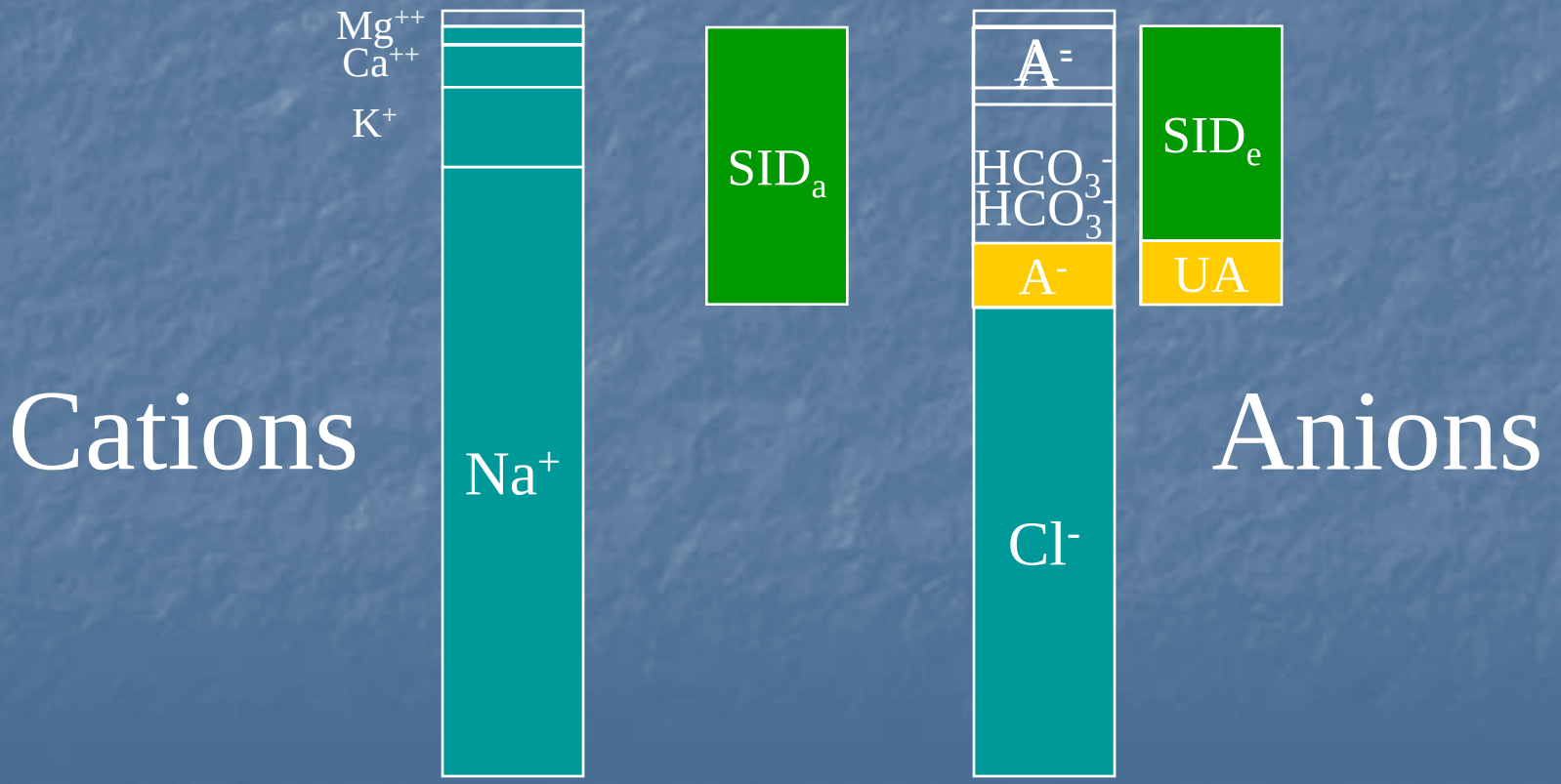
- Approximately 40±2
- Strong ion balance
  - SID > 40 - alkalizing
  - SID < 40 - acidifying
- Quantitate
- Hyper/hypochloremia - relative
  - Decrease Cl < decrease Na – acidosis
  - Decrease Cl > decrease Na – alkalosis

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

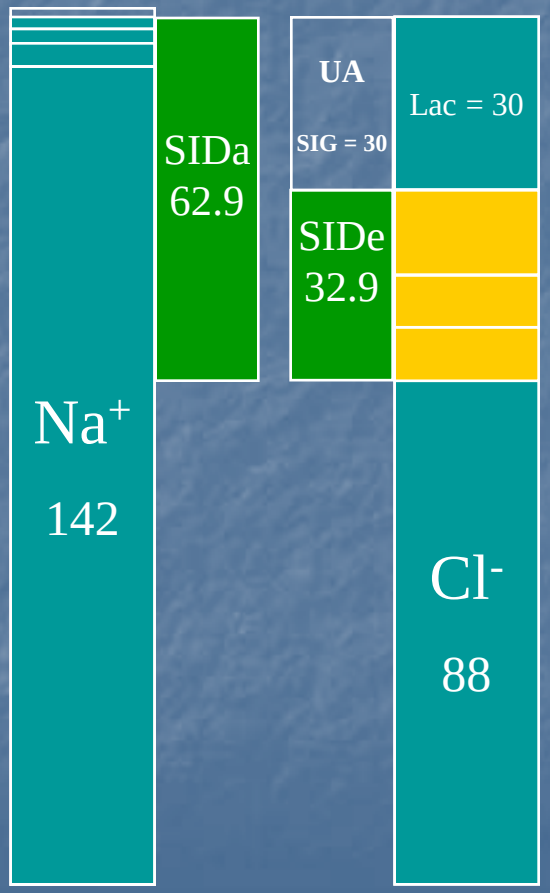
Intrauterine distress Birth asphyxia		mEq/l
pH	6.791	
Pco_2	59.6	
SIDa	62.9	
SIDe	32.9	
SIG	30	
Na	142 mmol/l	142
K	4.13 mmol/l	4.13
Cl	88 mmol/l	88
Ca^{++}	5.49 mg/dl	2.74
Mg^{++}	2.49 mg/dl	2.04
Lac	?? mmol/l	??
PO_4	27.8 mg/dl	16.4
Alb	2.97 g/dl	6.7
Glob	1.73 g/dl	2.4
HCO_3	9.2 mmol/l	9.2
SBE	-22.5 mEq/l	-22.5

SIG – UA

Mg^{++} = 2.04

Ca^{++} = 2.74

K^{+} = 4.13



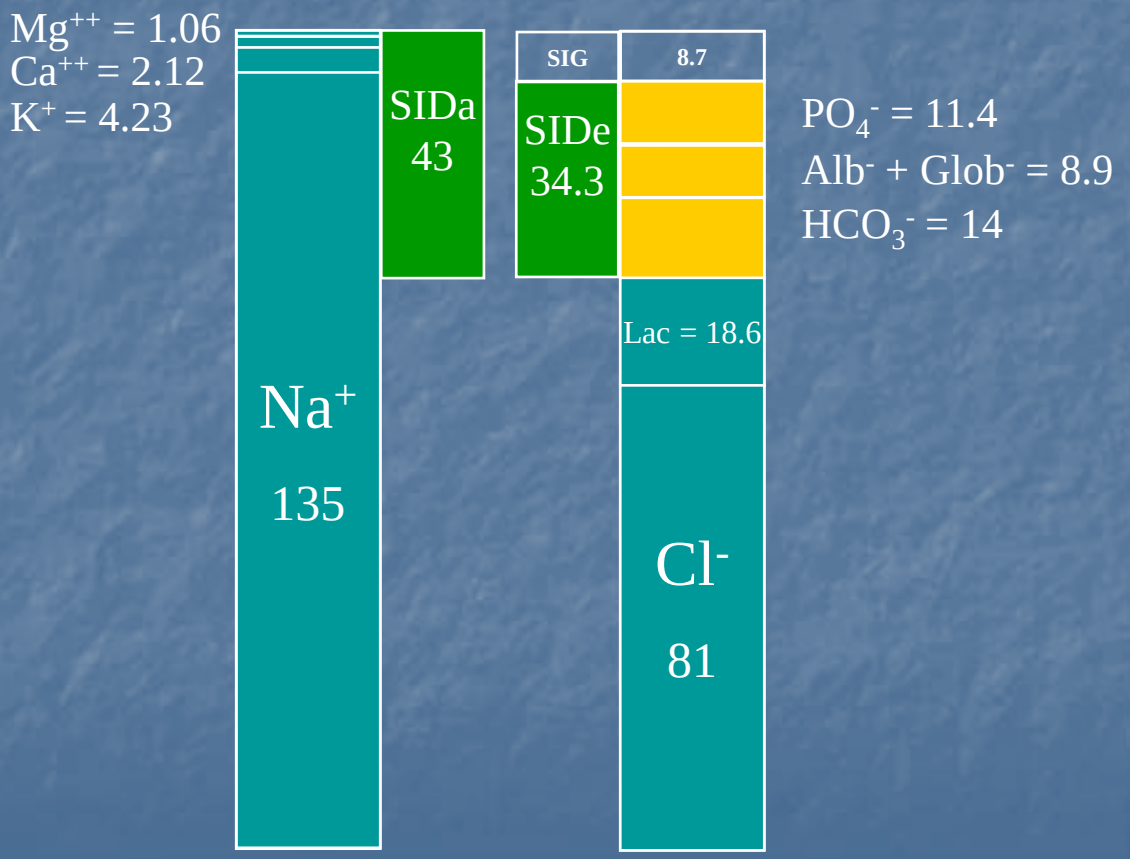
PO_4^{-} = 14.6

Alb^{-} + $Glob^{-}$ = 9.1

HCO_3^{-} = 9.2

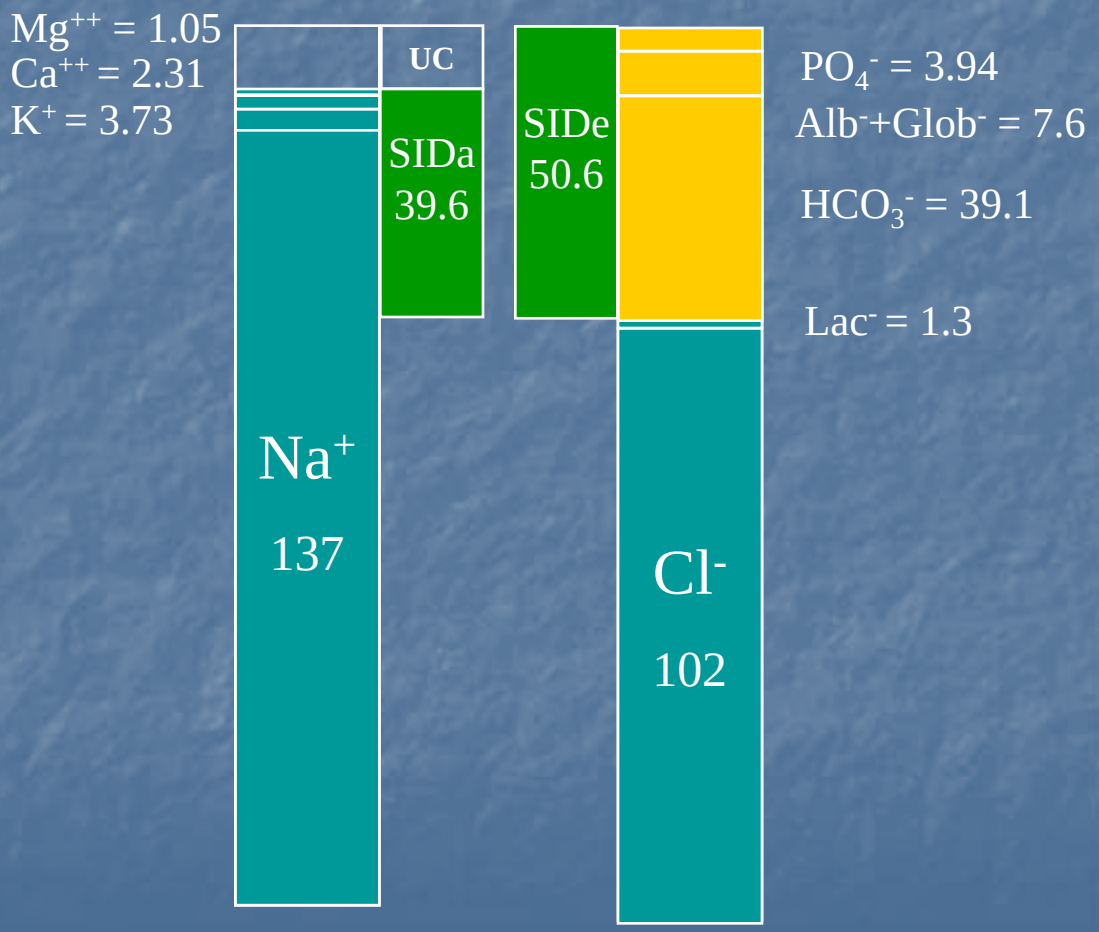
Case 91645		mEq/l
pH	7.088	
Pco_2	45.9	
SIDa	43	
SIDe	34.3	
SIG	8.7	
Na	135 mmol/l	135
K	4.23 mmol/l	4.23
Cl	81 mmol/l	81
Ca^{++}	4.23 mg/dl	2.12
Mg^{++}	1.23 mg/dl	1.06
ssLac	18.6 mmol/l	18.6
PO_4	20.53 mg/dl	12.1
Alb	2.89 g/dl	6.5
Glob	1.71 g/dl	2.4
HCO_3	14 mmol/l	14
SBE	-15.2 mEq/l	-15.2

SIG – UA



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^{++}	4.62 mg/dl	2.31
Mg^{++}	1.03 mg/dl	0.84
Lac	1.3 mmol/l	1.3
PO_4	6.75 mg/dl	3.98
Alb	1.82 g/dl	4.1
Glob	2.48 g/dl	3.5
HCO_3	39.1 mmol/l	39.1
SBE	13.1	

SIG - UC



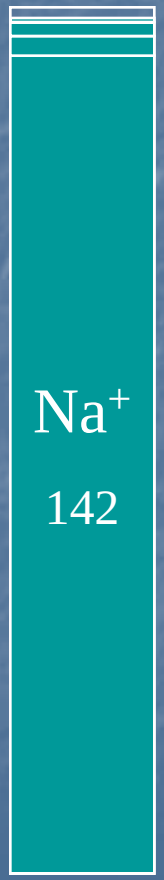
Modified BE Method

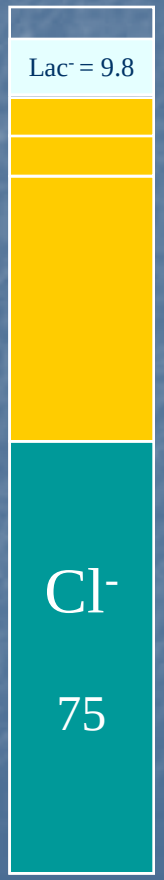
- Combining BE and Stewart's approach
  - Free water (deficit or excess)
  - Changes in Cl
  - Changes in A^- (Nonvolatile buffer base)
  - Presence of organic UA
- $BE_{lab} = BE_{fw} + BE_{Cl} + BE_{alb} + BE_{UA}$
  - $BE_{fw} = 0.3 \text{ X } (Na_{measured} - Na_{ref})$
  - $BE_{Cl} = Cl_{ref} - Cl_{Corr}$
    - $Cl_{corr} = (Na_{ref} / Na_{measured}) \text{ x } Cl^-_{measured}$
  - $BE_{alb} = 3.4 \ (Alb_{ref} - Alb_{measured})$
  - $BE_{UA} = BE_{lab} - (BE_{fw} + BE_{Cl} + BE_{alb})$

Modified Base Excess

IUGR, FIRS, NEC		mEq/l
pH	7.424	
Pco_2	69.8	
SBE	20.5	
Na	142	142
K	3.4	3.4
Cl	75	75
Ca^{++}	4.69	2.3
Mg^{++}	0.78	0.64
Lac	9.8	9.8
PO_4	11.5	6.8
Alb	2.45	6.25
Glob	3.05	4.27
HCO_3	46.1	46.1

$Mg^{++} = 0.64$
$Ca^{++} = 2.3$
$K^{+} = 3.4$





$PO_4^{-} = 6.8$
$Alb^{-} = 6.9$

$HCO_3^{-} = 46.1$

BE	
SBE	20.5
BEfw	1.2
BEcl	27.1
BEalb	-0.51
BE_{UA}	-7.29

Metabolic Acid-Base Abnormalities

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

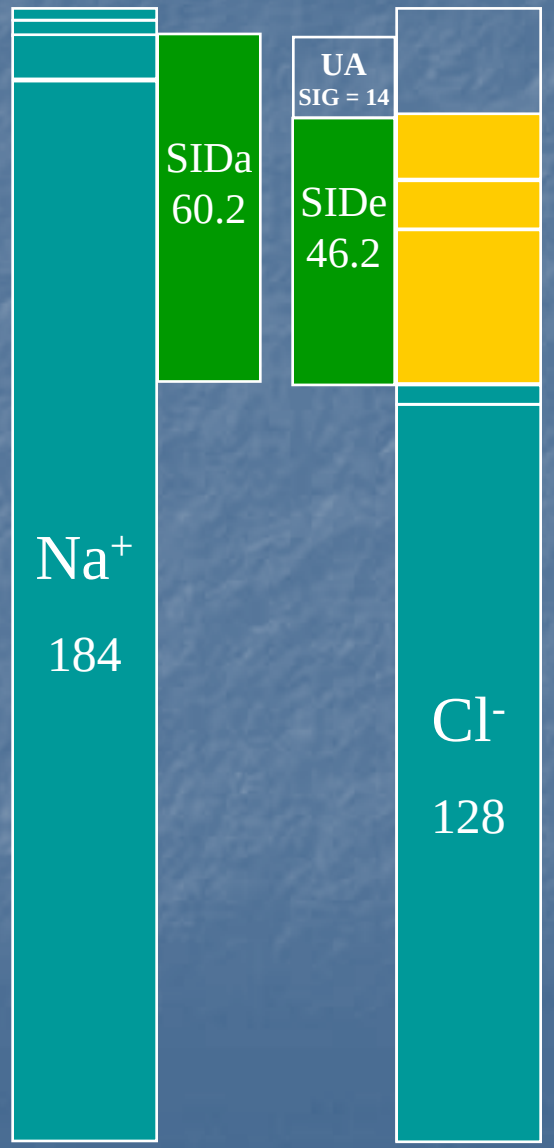
Albumin/Phosphate Concentrations

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

Maggie's Cria

Intrauterine distress Birth asphyxia		mEq/l
pH	7.568	
Pco_2	22.2	
SIDa	60.2	
SIDe	46.2	
SIG	14	
Na	184 mmol/l	184
K	7.71 mmol/l	7.71
Cl	128 mmol/l	128
Ca^{++}	? mg/dl	?
Mg^{++}	? mg/dl	?
Lac	3.5? mmol/l	3.5?
PO_4	19.03 mg/dl	11.23
Alb	3.02 g/dl	8.46
Glob	3.08 g/dl	?
HCO_3	26.5 mmol/l	26.5
SBE	-1.5 mEq/l	-1.5

Mg^{++} = ??
Ca^{++} = ??
K^+ =7.71

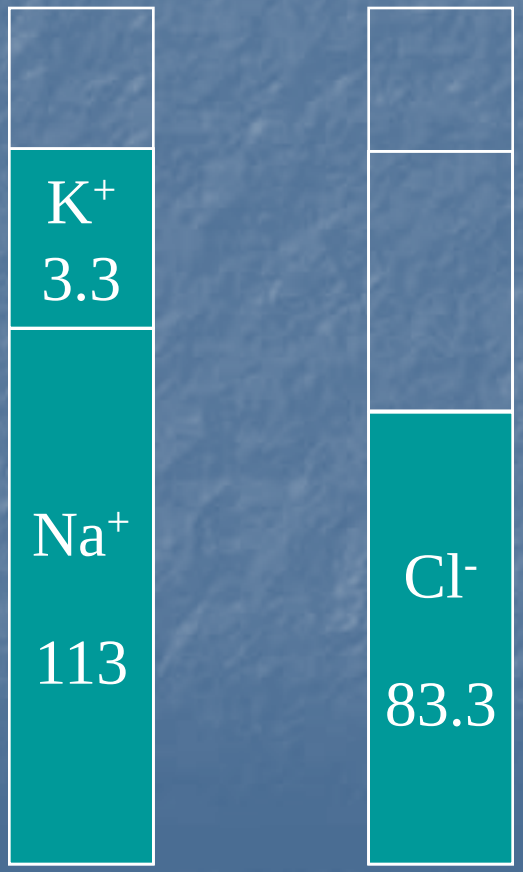


PO_4^- = 11.23
Alb^- = 8.46
HCO_3^- = 26.5

Lac = 3.5?

Dilutional Acidosis
Free Water

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



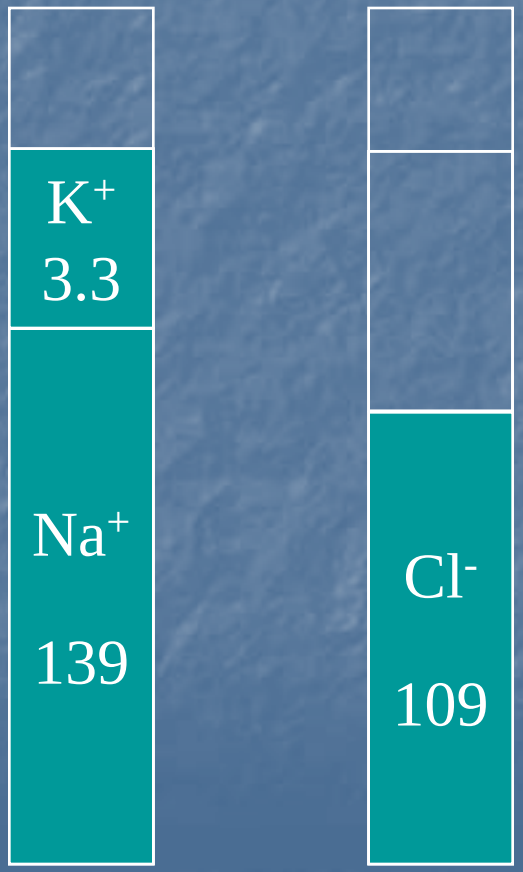
Add 20% water
Na = 113
K = 3.3
Cl = 83.3
SID = 33

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

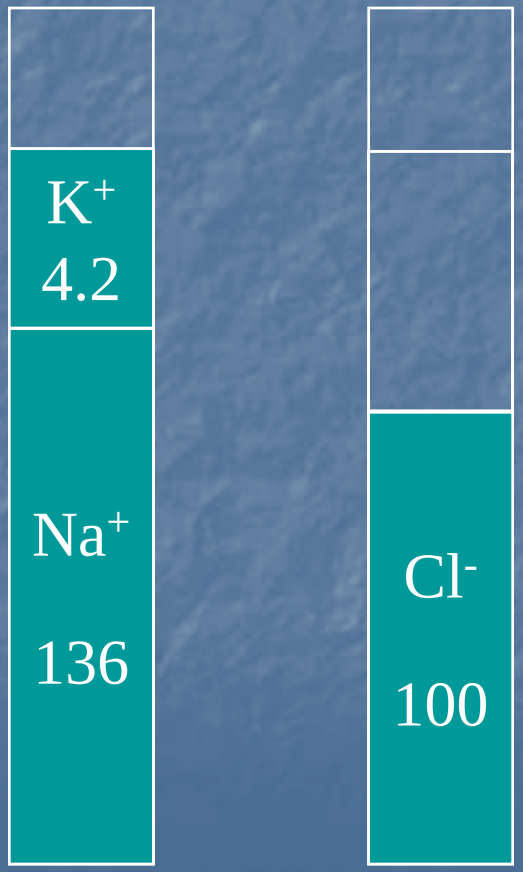
Na = 136
K = 4
Cl = 100
SID = 40



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

Dilutional Acidosis
Add SID balance fluid

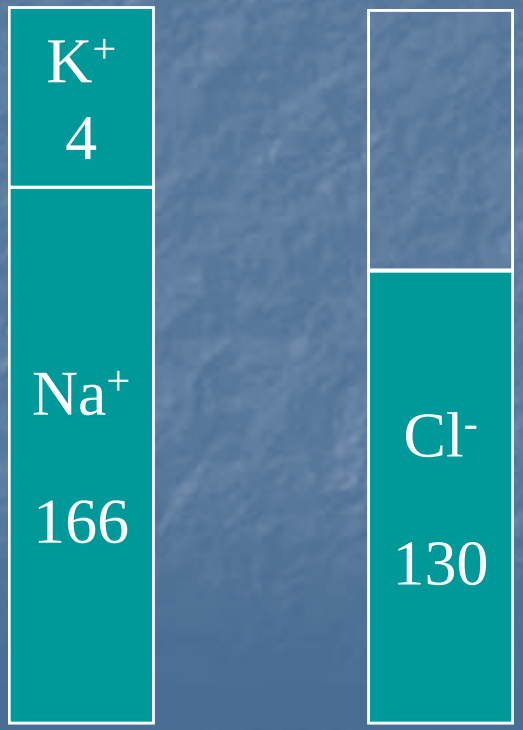
Na = 136
K = 4
Cl = 100
SID = 40



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



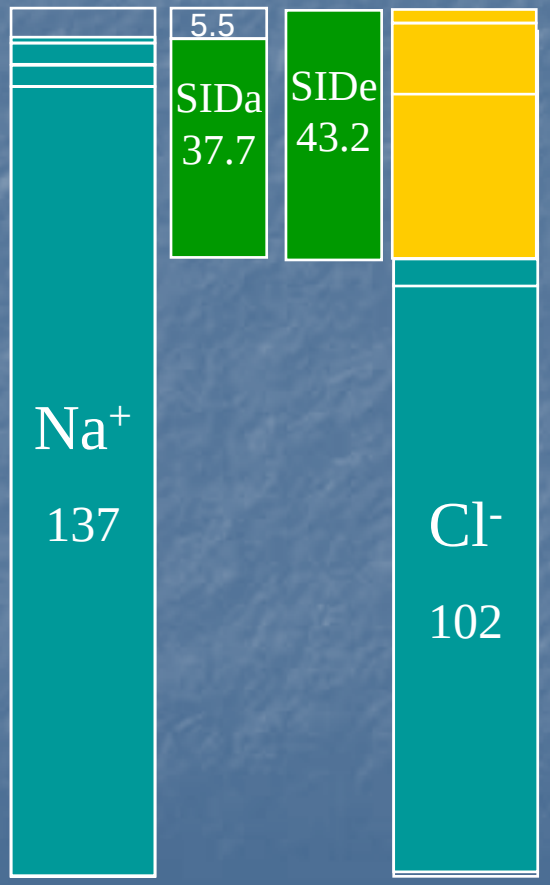
Add 30 mEq
Na = 166
K = 4
Cl = 130
SID = 40

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
pH	7.46	
Pco_2	39.8	
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^{++}	5.11 mg/dl	2.56
Mg^{++}	1.28 mg/dl	1.05
Lac	4.8 mmol/l	4.8
PO_4	4.14 mg/dl	2.44
Alb	4.9 g/dl	11
Glob	0.76 g/dl	1.1
HCO_3	28.6 mmol/l	28.6
SBE	4.7	



PO_4^- = 2.4

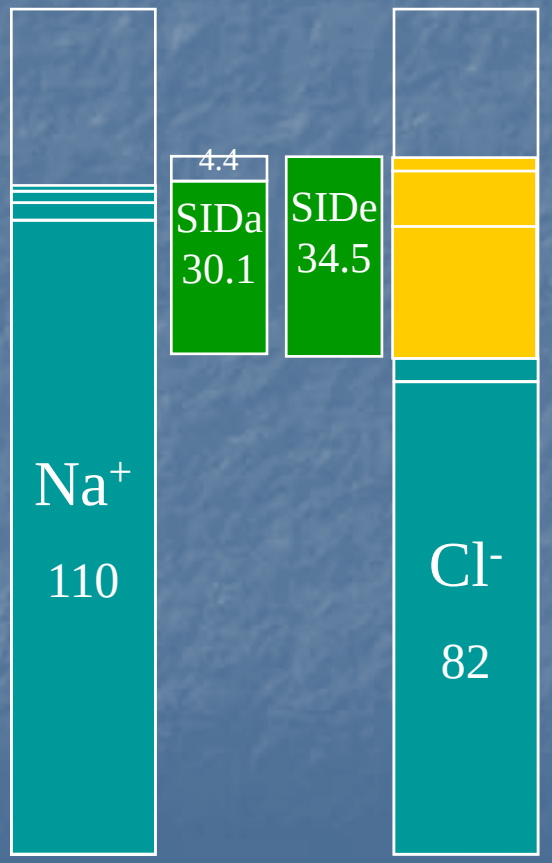
$Alb^- + Glob^-$ = 12.2

HCO_3^- = 28.6

Lac^- = 4.8

Free Water

FIRS, Sepsis		mEq/l	
pH	7.46		
Pco_2	39.8		
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^{++}	5.11 mg/dl	2.56	2.04
Mg^{++}	1.28 mg/dl	1.05	0.88
Lac	4.8 mmol/l	4.8	3.84
PO_4	4.14 mg/dl	2.44	1.95
Alb	4.9 mg/dl	11	8.8
Glob	0.76 g/dl	1.1	0.88
HCO_3	28.6 mmol/l	28.6	22.9
SBE	4.7		



PO_4^- = 1.96

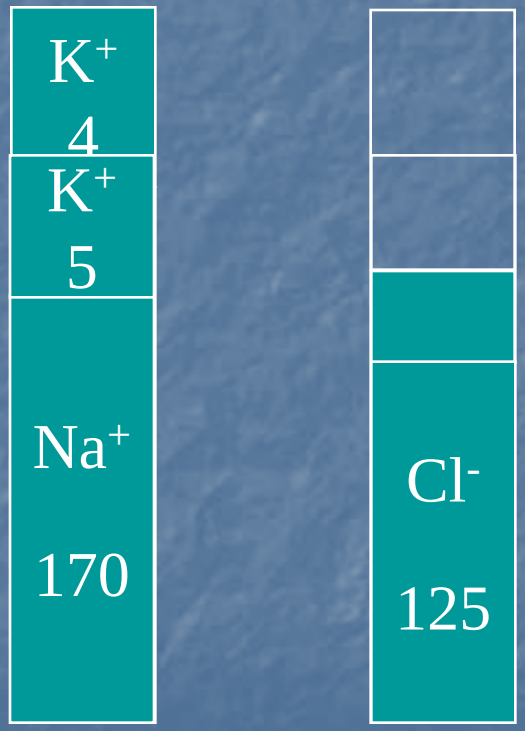
Alb^- = 9.7

HCO_3^- = 22.9

Lac^- = 3.84

Contraction Alkalosis

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



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

Maggie's Cria

Intrauterine distress Birth asphyxia		mEq/l
pH	7.568	
Pco_2	22.2	
SIDa	60.2	
SIDe	46.2	
SIG	14	
Na	184 mmol/l	184
K	7.71 mmol/l	7.71
Cl	128 mmol/l	128
Ca^{++}	? mg/dl	?
Mg^{++}	? mg/dl	?
Lac	3.5? mmol/l	3.5?
PO_4	19.03 mg/dl	11.23
Alb	3.02 g/dl	8.46
Glob	3.08 g/dl	?
HCO_3	26.5 mmol/l	26.5
SBE	-1.5 mEq/l	-1.5

Mg^{++} = ??

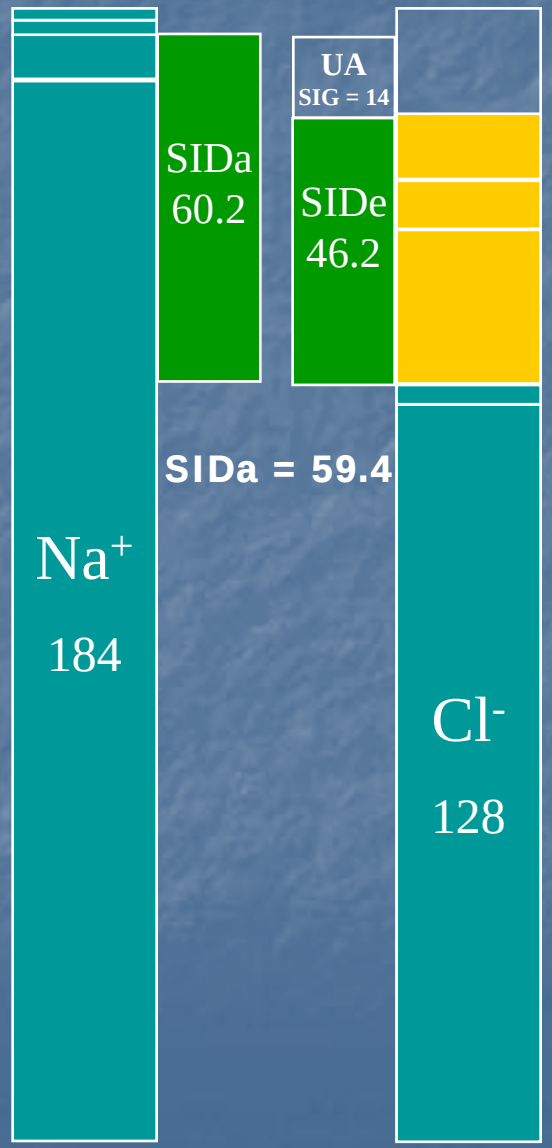
Ca^{++} = ??

K^+ =7.71

K = 4.8
K = 6.4

25% contraction

Na = 140
Na = 186



SIDa = 59.4

PO_4^- = 11.23
Alb^- = 8.46
HCO_3^- = 26.5

Lac = 3.5

Cl =100
Cl = 133

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

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

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

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]