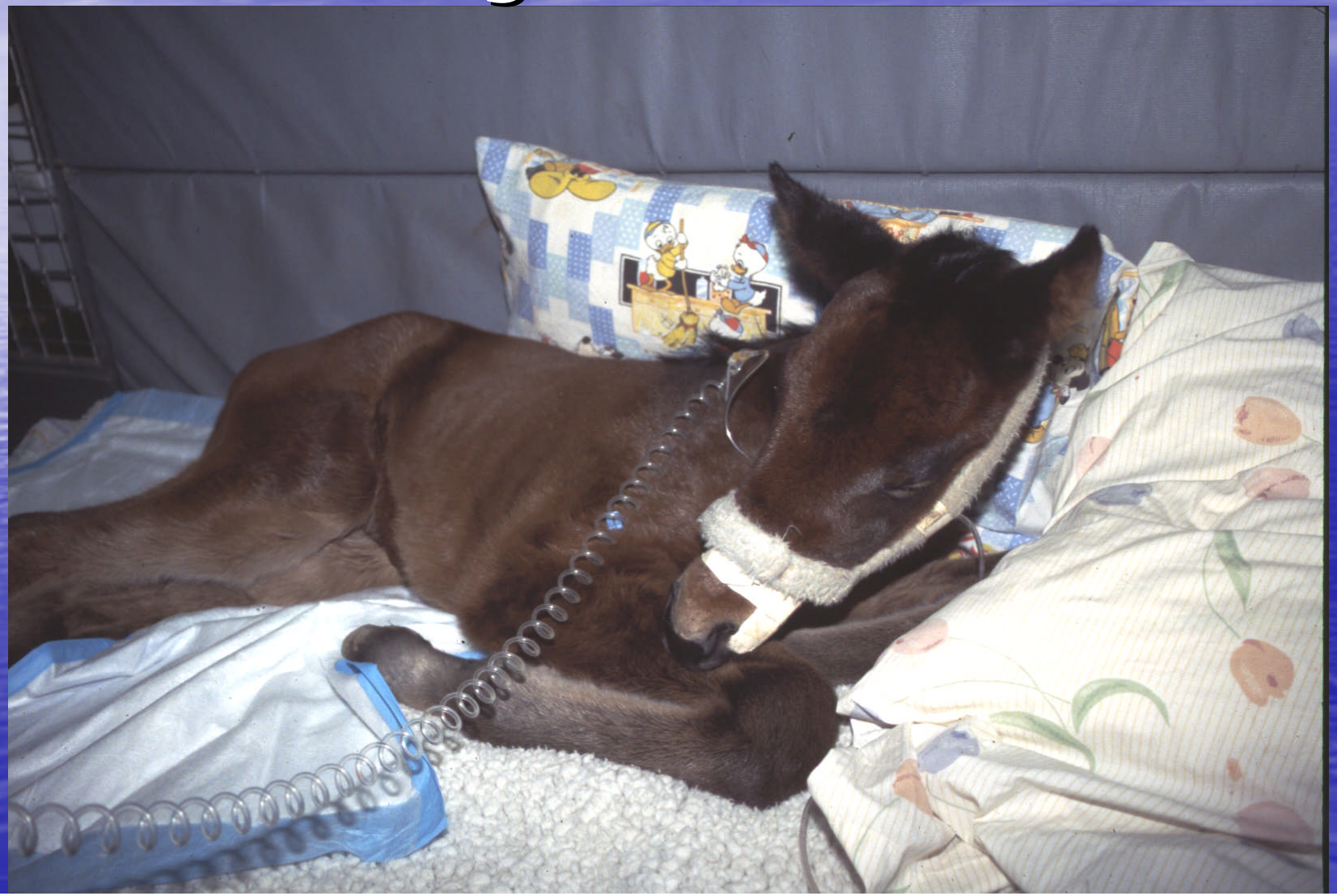
Understanding Strong Ion Difference

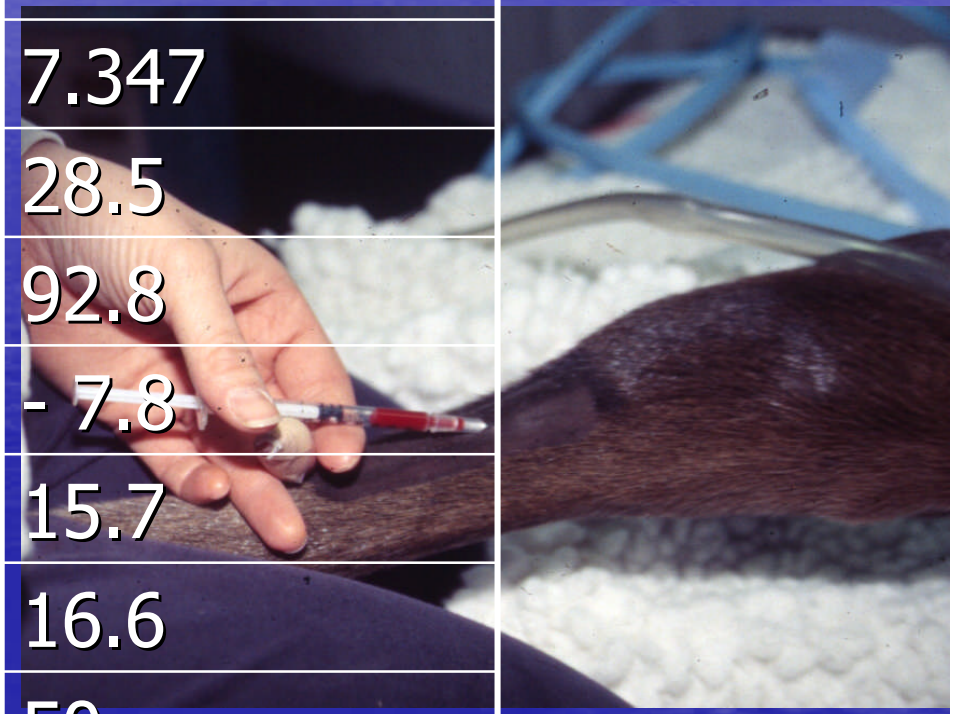


Acid-base
Strong Ion Difference

- Define cations, anions, strong ions
- Determinants of Acid/Base Status
  - Weak ion buffer base, Strong ion difference
- Base Excess, Anion Gap, Strong Ion Gap
- Treatment Guidelines
- Metabolic acid-base control
- Metabolic acidosis
- Metabolic alkalosis

Acid Base measurements Arterial vs. Venous sample

Source	Venous blood	Arterial blood
pH	7.162	7.347
P_{CO2}	59.8	28.5
P_{O2}	28.4	92.8
BE-B	- 7.3	- 7.8
HCO_3	21.5	15.7
TCO_2	23.4	16.6
Dextrose	18	50



Cations and Anions

- Cations

  Na^+ , K^+ , Ca^{++} , Mg^{++}, H^+
- Anions

  Cl^-, Lac^-

  Hgb, Alb, P_i,

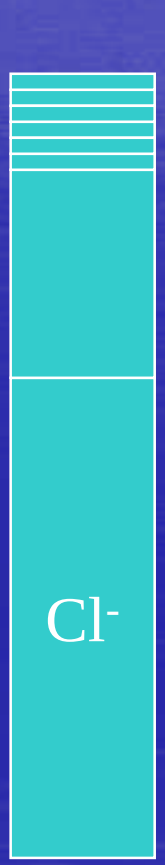
  Ketones, SO_4^{2-}

  Fatty acids, aspirate, glutamate

  $HCO3^-$

Cations/Anions

Cations



Anions

Strong Ions

- Any ion which cannot combine with other ions
  - It is always free
  - Disassociated at physiologic pH
  - Always contributes a charge
- Na^+, K^+, Cl^-
- Not $HCO3^-$
  - Weak ion
  - $HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$
  - Loses its charge
- Lactate is a strong ion
  - Completely disassociated at physiologic pH

Determinants of Acid/Base Status

- CO_2 (Pco_2)
- Nonvolatile weak ion acid buffer (A_{TOT})
- Strong Ion Difference (SID)

Weak Ion Acid Buffer (Buffer Base)

- Buffer takes up or releases H^+
  - in physiologic range of pH changes
- Weak acid buffer
  - Volatile
  - Nonvolatile
- Volatile buffer HCO_3^-
  - Weak ion - can take a H^+
  - Cannot buffer CO_2 (itself)
    - Not prevent acid-base changes caused by CO_2
    - HCO_3^- is not independent

Nonvolatile Weak Ion Acid Buffer

- $A_{Total} = A^- + AH$
  - Hemoglobin
  - Albumin
  - Inorganic phosphates
- A^- changes with SID & Pco_2 – dependent
- A_{Total} not change – independent
- Good buffers
  - Even at extremes of concentrations
- There's no single dissociation constant
  - Large number of buffering sites
  - Most effective near normal pH

Nonvolatile Weak Acid Buffer

- A_{Total} =
  In plasma – Albumin + P_i + SO_4
  In RBC – Hb + P_i
- Estimate A^-
  Using only total protein
  Using albumin & PO_4^{2-}
  - A^- = 0.2 (albumin) + 1.55 (Pi)*
    pH < 7.35
  - A- = pH [(0.116 X albumin) + (1.3 X Pi)] – (0.583 X albumin) – (3.98 X Pi)*

* Albumin in g/L, Pi in mmol/L

Cations/Anions
Weak Ion Acid Buffer

Cations

P_i^- SO_4^{2-}
Alb^- Hb^-

Anions

Acid/Base Balance

- As independent factors change

  CO_2, SID, A_{Total}
- "+" = "-"

  Charges must remain balanced
- Dependent factors adjust

  To keep charge balanced and maintain pH

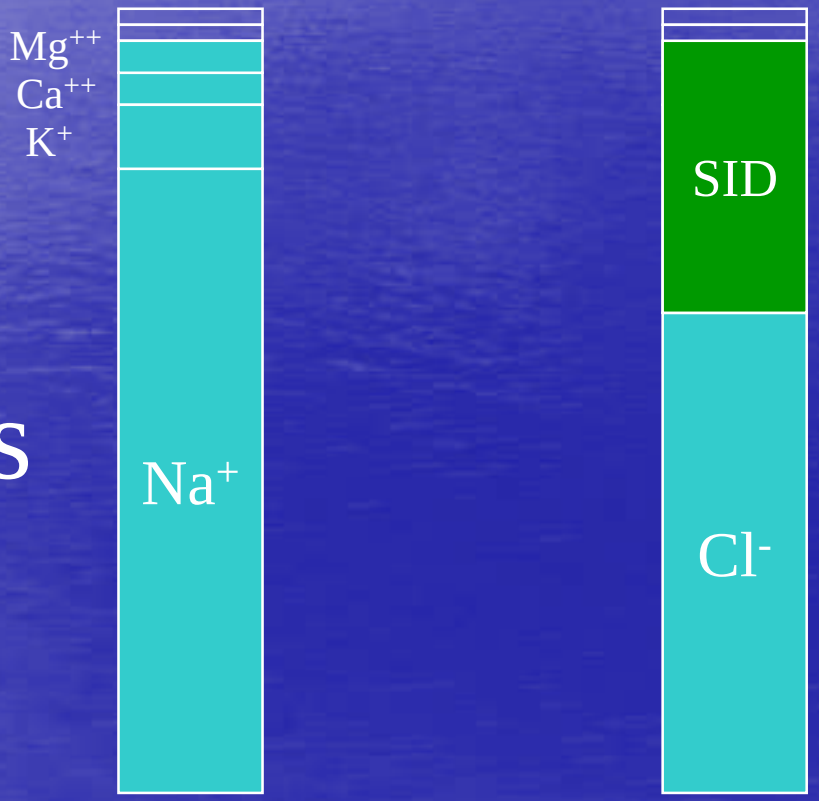
  $A^- + H^+ \longleftrightarrow AH$

  $H^+ + HCO_3^- \longleftrightarrow CO_2 + H_2O$

SID (Strong Ion Difference)

- Old concept - new name
  - Is Buffer Base
  - Change from normal = BE (Standard BE)
- Strong ions
  - Lactate, Hydroxybutyrate, SO_4^{2-} , Na^+, K^+, Cl^-
  - SID = (Na+ + K+ + Ca++) – (Cl + Lac)
  - SID = $HCO3^-$ + A^-
  - SID = 40-42 (ICU patients = 30)

Cations/Anions
SID



Cations

Anions

Base Excess

- Definition

  Blood gas measured pH and P_{co2}

  If adjust P_{co2} = 40

  - pH will change

  If adjusted pH ≠ 7.40

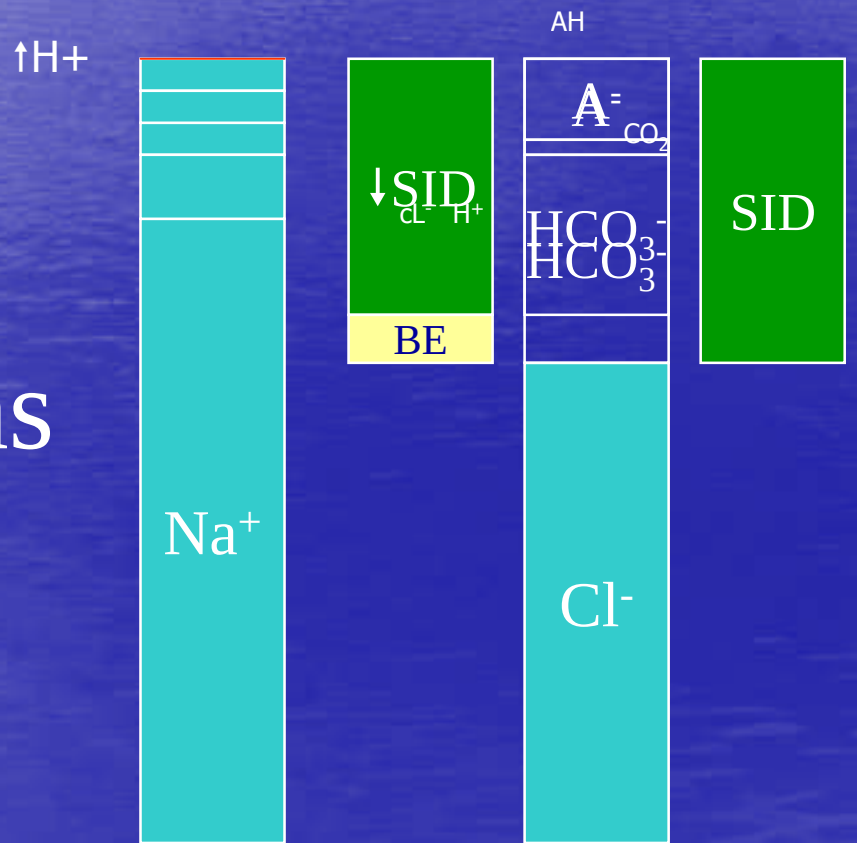
  - Amount of added base needed to pH = 7.40
- It eliminates the respiratory component
- It defines the metabolic derangement

  Causing the abnormal pH

Base Excess

- Base excess =
  Change in A^- + HCO_3^- from normal
  Change in SID from normal
- + BE = metabolic alkalosis
- - BE = metabolic acidosis
- BE = SIDex
- BE from ABG machine
  Calculation assumes
  - A_{TOT} = blood with Hb of 5 g/dl and P_{co2} = 40

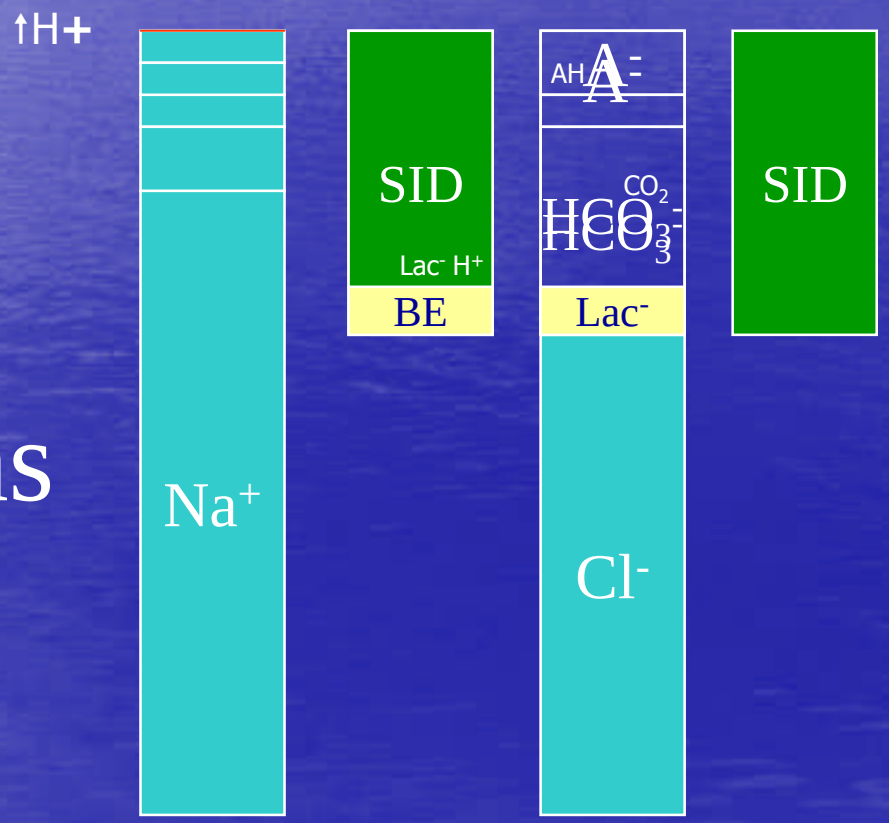
BE
Hyperchloremic Acidosis



Cations

Anions

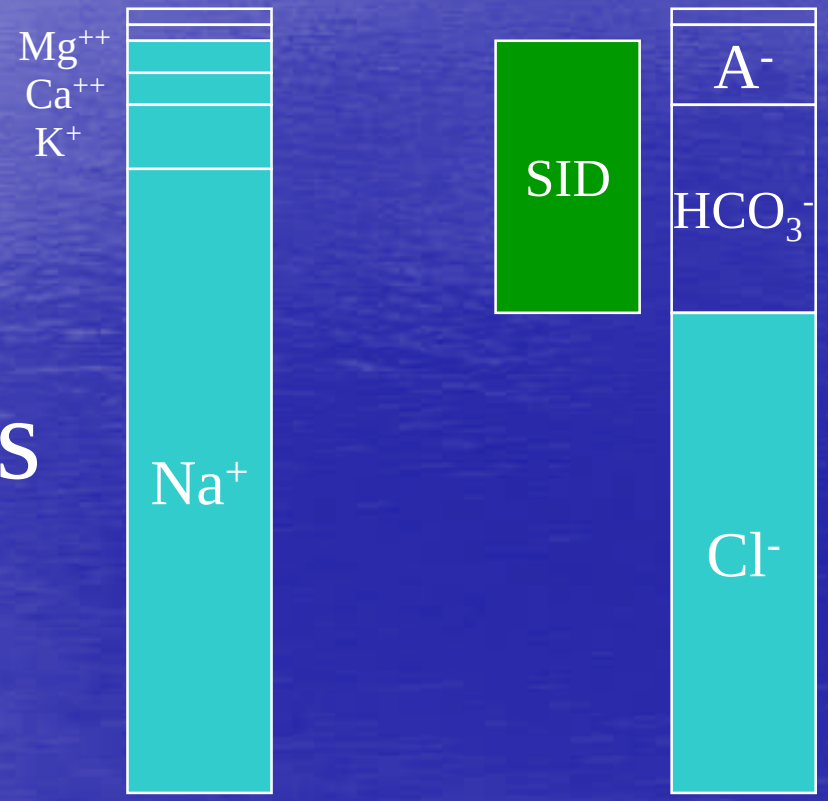
BE
Lactic Acidosis



Standard Base Excess

- If hemoglobin = 1 g/dl – error only 3 mM
- If Pco_2 = 100 – error only 3 mM
- Patients with varying protein buffer conc
  Respond similarly to abnormalities of acid-base
- SBE = SID change required to produce
  pH = 7.4 at $Paco_2$ = 40 with the prevailing A_{TOT}
  Amount $\uparrow P_{Na}$ (with Na bicarbonate) to correct

Cations/Anions SID



Cations

Anions

Anion Gap

- $Na^+ + K^+ = Cl^- + HCO3^- + A^-$
- $AG = (Na^+ + K^+) - (Cl^- + HCO3^-)$

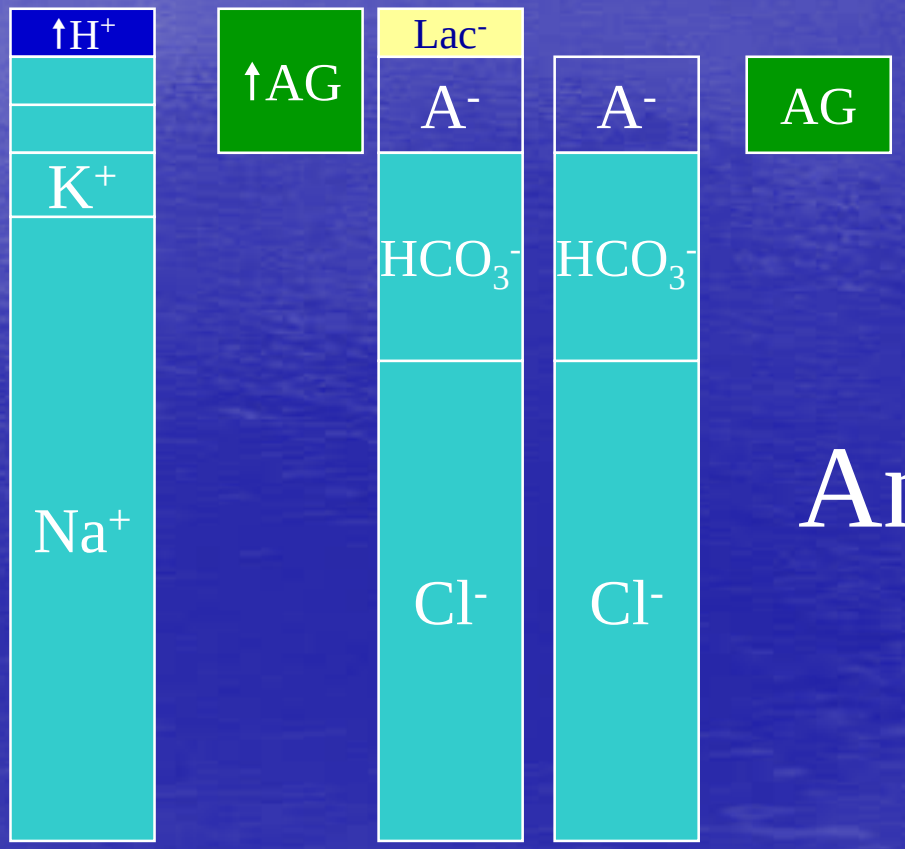
  $AG = A^- =$ ionized albumin + P_i^-
- Normal AG range is large

  Because albumin + P_i range large

  Hypoproteinemia - normal AG with lactic acidosis
- Usually measured in venous blood

  With Tco_2 used to estimated HCO_3

Cations/Anions
Anion Gap



Cations

Anions

Anion Gap Acidosis Artifacts

- Dehydration
  - Concentrating all ions
- Na salts
  - High doses Na penicillin (beta lactams)
  - Na lactate
  - Na acetate
- Decreased unmeasured cations
  - ↓Mg
  - ↓Ca
- Hypoalbuminemia
  - Severe
  - ↓AG by 2.5-3 mEq/l for each 1 g/dl decrease

Anion Gap Acidosis Artifacts

- Respiratory and metabolic alkalosis
  - ↑3-10 mEq/liter in apparent AG
- Parenteral nutrition
  - Formulas with acetate
- Multiple blood transfusions
  - Increased citrate
  - Large volumes
- Unidentified cations

Corrected Anion Gap

- ICU patient
  Albumin and P_i not normal
  Unmeasured anions which make normal gap
- As long as pH < 7.35
  "Normal" AG
  - A^- = 0.2 (albumin) + 1.55 (Pi)*
    pH < 7.35
- Or
  - A- = pH [(0.116 X albumin) + (1.3 X Pi)] – (0.583 X albumin) – (3.98 X Pi)*

* Albumin in g/L, Pi in mmol/L

Strong Ion Difference vs. Anion Gap

- Strong Ion Difference

$$SID = (Na^{+} + K^{+} + Ca^{++} + Mg^{++}) - (Cl^{-} + Lac^{-})$$

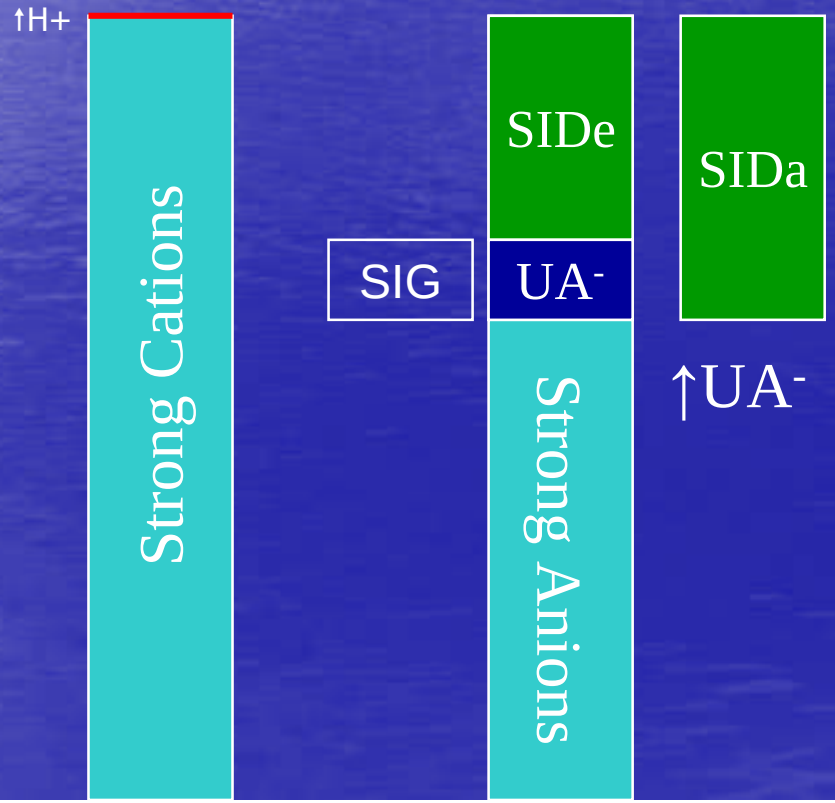
- Anion Gap

$$AG = (Na^{+} + K^{+}) - (Cl^{-} + HCO3^{-})$$

Strong Ion Gap (SIG)

- SID effective
  = A^- + HCO_3^-
  = SIDe
- SID apparent
  = $(Na^+ + K^+ + Ca^{++} + Mg^{++}) - (Cl^- + Lac^-)$
  = SIDa
  = 40-42 (healthy human)
- SIDe = SIDa
  If not there are unmeasured ions
  Difference is SIG

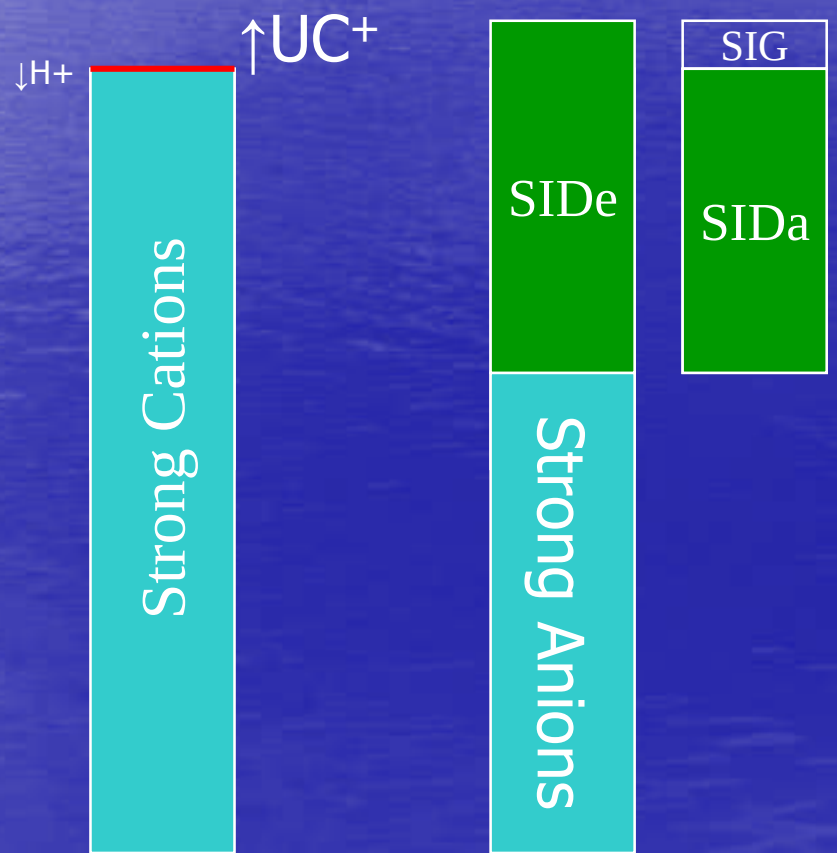
Metabolic Acidosis
Increase in Unidentified Anions
SIG < 0



Metabolic Alkalosis

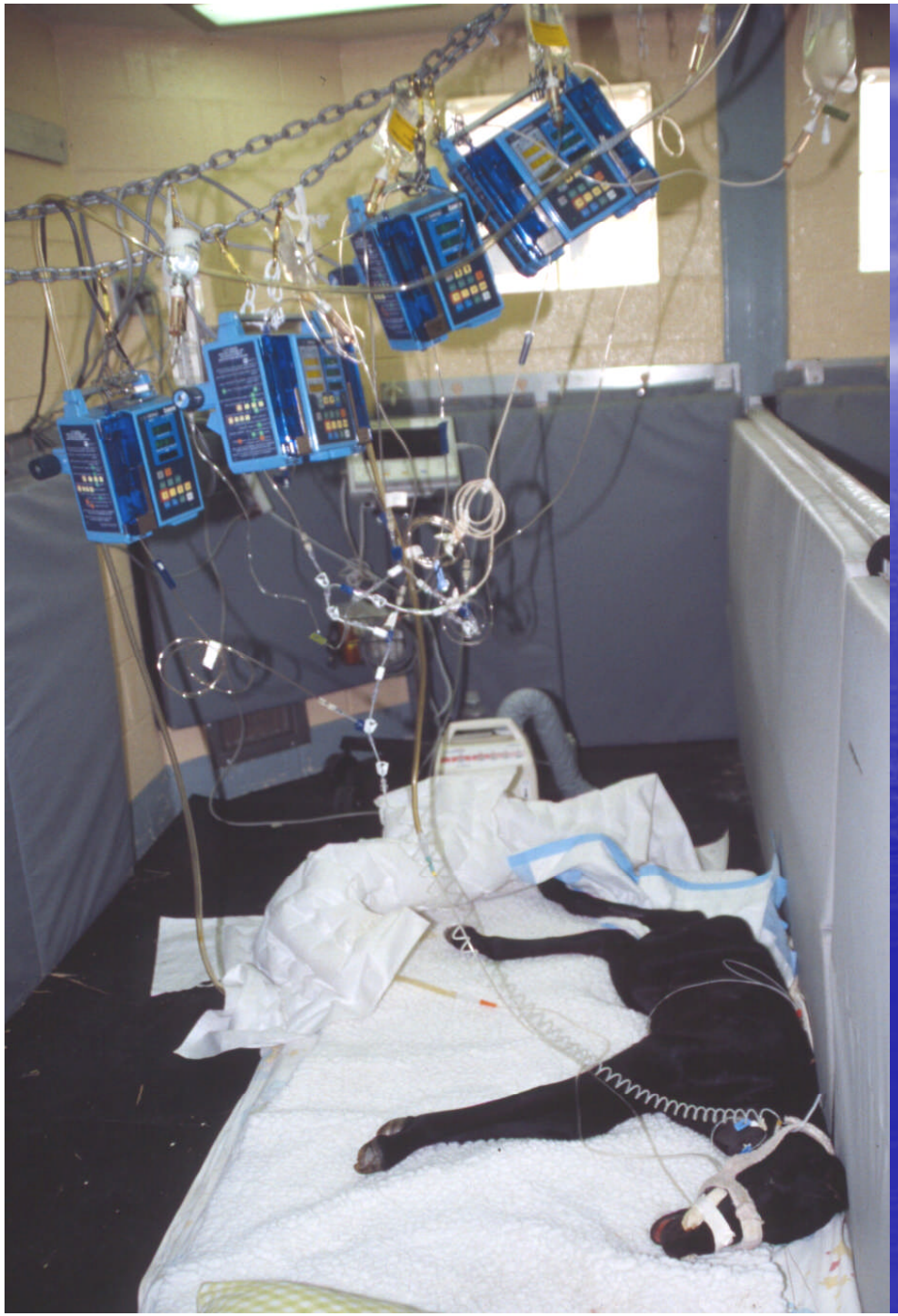
Unidentified Cation Alkalosis

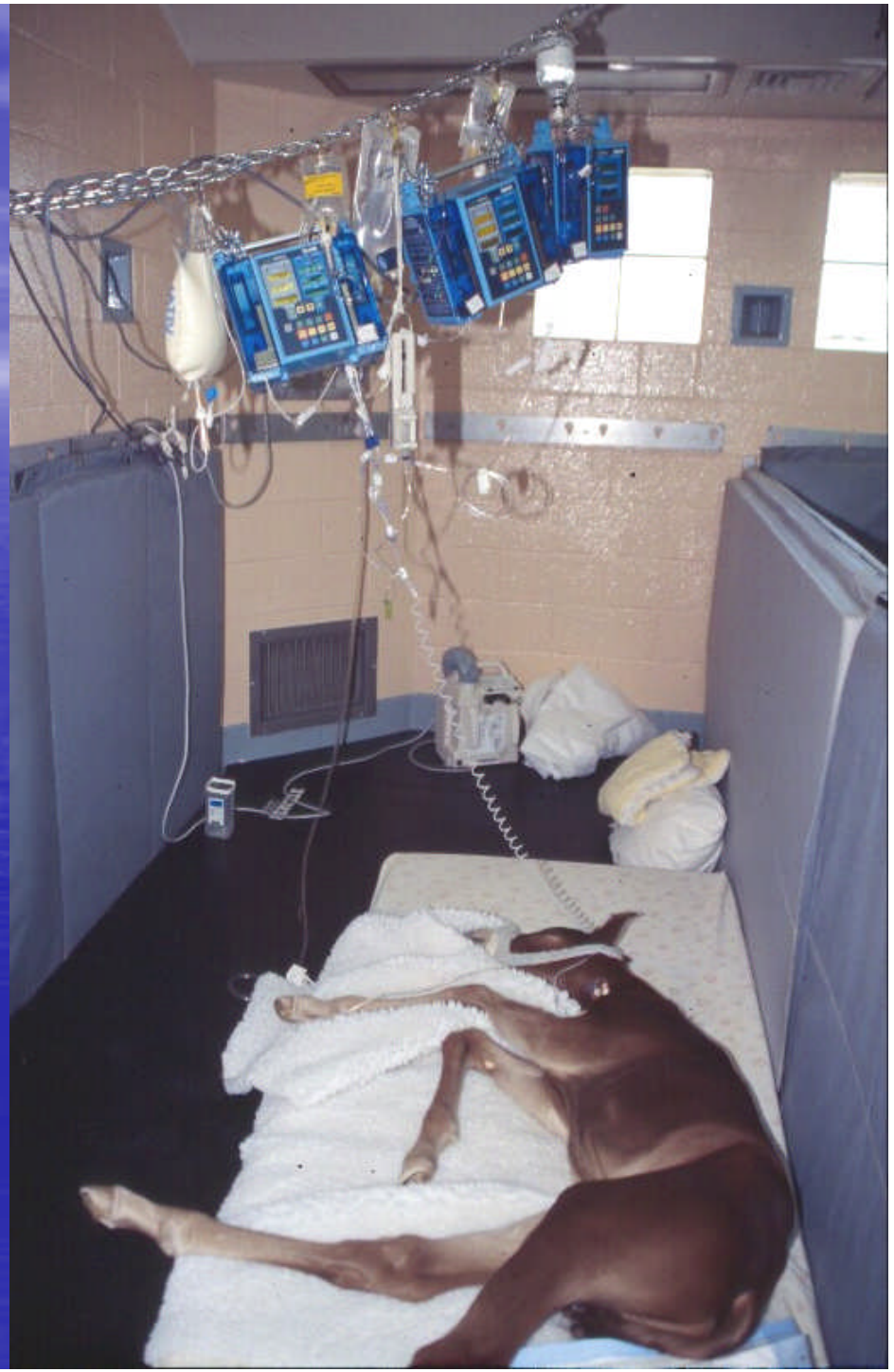
SIG > 0



Strong Ion Gap (SIG)

- SIG = SIDe – SIDa
- SIG < 0 – unmeasured anions
  - Sepsis
  - Liver disease
    - Liver clears unmeasured anions
    - With sepsis, failure → liver releases anions
  - If lactate is not part of SIDa
    - Most common cause of SIG > 0
    - Lactate mmol/l = SIG
- SIG > 0 – increased unidentified cations
- SIG does not change with
  - pH changes
  - Changes in albumin





Metabolic Acidosis

- Metabolic acidosis

  ↓ SID → Results in ↑ free H+ → acidosis

- ↓ SID

  ↑ Organic acids – ↑Lactate, ↑Ketones

  Loss of cations – diarrhea

  Mishandling of ions -- renal tubular acidosis

  Addition of exogenous ions -- iatrogenic, poisoning

- Treat metabolic acidosis

  ↑ Na^+ > ↑Cl^- e.g. $NaHCO_3$

Metabolic Alkalosis

- Metabolic alkalosis
  ↑SID → Results in ↓ free H+ → alkalosis
- ↑SID
  Loss of anions > cations
  Diuretics
  Renal disease
- Treatment
  cations > anions
  Replacing Cl^- e.g. NaCl, KCl, HCl
  Cl resistant alkalosis
  - Only because of ongoing renal loss of Cl - RTA
  - Hyperaldosteronism

Pathophysiology
Disorders of acid-base balance

- Acid-base abnormalities
  - Only occur with failure to compensate
    - Disorders primary regulating organs
    - Exogenous drugs/fluids
      - Alter ability to maintain acid-base balance
    - Abnormal metabolism
      - Overwhelms ability of defense mechanisms
- SID is regulated by the kidneys/GI tract

Acid-Base Balance
Renal Regulation

- Renal excretion strong ions
  - Most reabsorbed automatically
  - Only able to excrete small amounts per min
  - Thus it takes hours for a renal response
- Diet – similar ratios of strong cations/anions
  - Sufficient Cl available to filter
  - If not reabsorbed – ↑SID
- Cl excretion – primary regulating mechanism
  - Na/K handling – other priorities – not acid-base

Pathophysiology
The Kidney - Urine pH

- Independent of plasma pH
- Independent of renal "acid" excretion
- pH = amt H^+

  Not amt NH_4^+

  Not amt other “fixed acids”

  Can have high rate acid excretion

  - But alkaline urine pH

Pathophysiology Ammoniagenesis

- Excrete Cl^- without Na^+ or K^+ - regulate SID

  As $Cl^-NH_4^+$

- Renal-Hepatic Interaction

  NH_4^+ – co -excretion with Cl-

  NH_4^+ produced in the kidney and liver

Pathophysiology Ammoniagenesis

- Hepatic glutaminogenesis

  Stimulated by acidosis

- Nitrogen metabolism in liver

  $\rightarrow$ Urea, glutamine, (NH_4^+)

  Glutamine $\rightarrow$ kidney $\rightarrow$ $\uparrow NH_4^+ \rightarrow \uparrow Cl^-$ excretion

  $\uparrow$Glutamine $\rightarrow$ alkalosis by $\downarrow Cl^-$ relative to Na^+

Pathophysiology Ammoniagenesis

- Hepatocyte with urea production capacity

  Closer to portal vein

  GI tract $NH_4^+ \rightarrow$ urea first

  Acidosis inhibits urea formation

  - NH_4^+ to glutamine producing cells $\rightarrow$ $\uparrow$Glutamine production $\rightarrow$
  - Kidney $\rightarrow$ $NH_4^+ \rightarrow$ $\uparrow Cl^-$ loss $\rightarrow$ compensatory Alk

Pathophysiology Gastrointestinal tract

- Important cause of acid-base imbalance
- *Stomach* – Cl^- pumped out of plasma →
  - ↓SID in gastric juices → acid
  - ↑SID in plasma → "Alkaline tide" with meal
- *Duodenum* – Cl^- is reabsorbed →
  - Return SID of plasma
- Reflux → loss of Cl^- → alkalosis (↑SID)
- *Pancreas* -- fluid has ↑SID (↓Cl^-) →
  - Plasma ↓SID → peaks after meal (counter act alkaline tide)
  - If reflux → plasma remains acidotic (↓SID – ↑Cl^-)

Pathophysiology Gastrointestinal tract

- *Colon* -- fluid ↑SID
  - Most of Cl^- removed in small intestine
  - Na+/K+ left in lumen
  - Should absorb Na+ and water
    - If diarrhea → lose Na^+/K^+ relative to Cl^- → acidosis
- Can GI tract compensated in acidosis/alkalosis??
  - Not been studied
  - Endotoxemia may remove anions →
    - ↑SID in plasma → ↑alkalosis

Clinical Effects Of Metabolic Acidosis

- Brief exposure to acidosis well tolerated
  - Exercise - pH < 7.15, lactate > 20 mEq/liter
- Chronic mild acidosis (pH < 7.35)
  - Metabolic bone disease
  - Protein catabolism
- Critically ill patients
  - Not tolerate even brief acidosis
- Metabolic acidosis patients
  - Poorer outcome than respiratory acidosis
  - Cause more important than degree of acidosis
  - Epiphenomenon

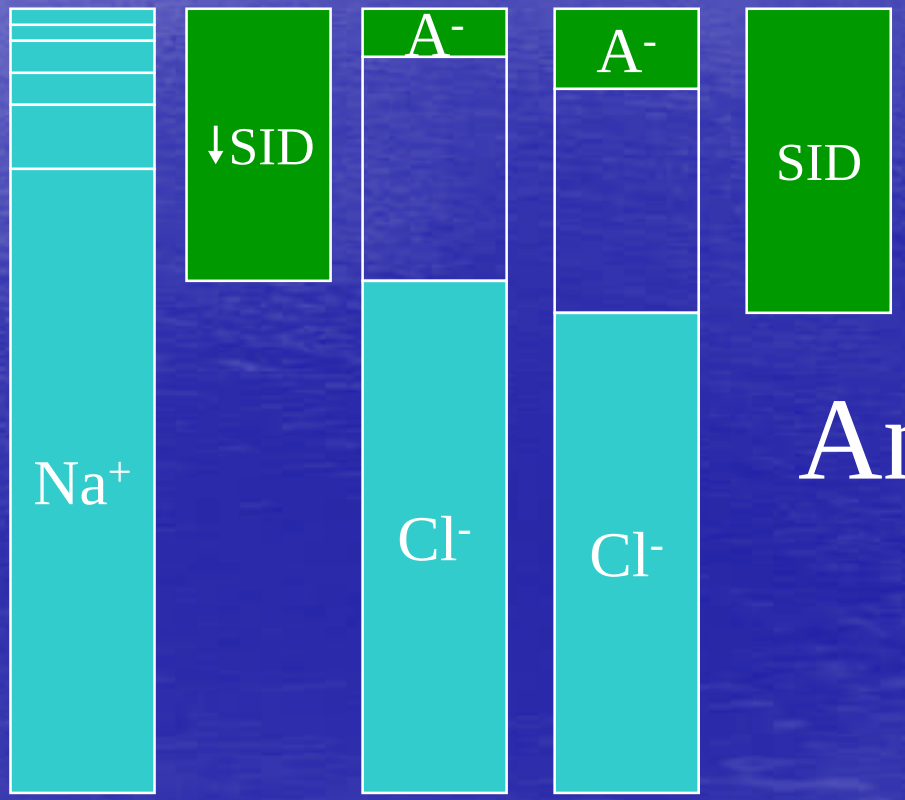
Potential Clinical Effects of Metabolic Acidosis

- Cardiovascular
  - ↓Inotropy
  - Conduction defects
  - Arterial vasodilation
  - Venous vasoconstriction
- 0_2 Delivery
  - ↓Oxyhemoglobin binding
  - ↓ 2,3-DPG (late)
- Electrolytes
  - ↑K, ↑Ca
  - Hyperuricemia

Potential Clinical Effects of Metabolic Acidosis

- Neuromuscular
  - Respiratory depression
  - Decreased sensorium
- Metabolism
  - Protein wasting
  - Bone demineralization
  - Insulin resistance
  - Catecholamine stimulation
  - PTH stimulation
  - Aldosterone stimulation

ICU Patients



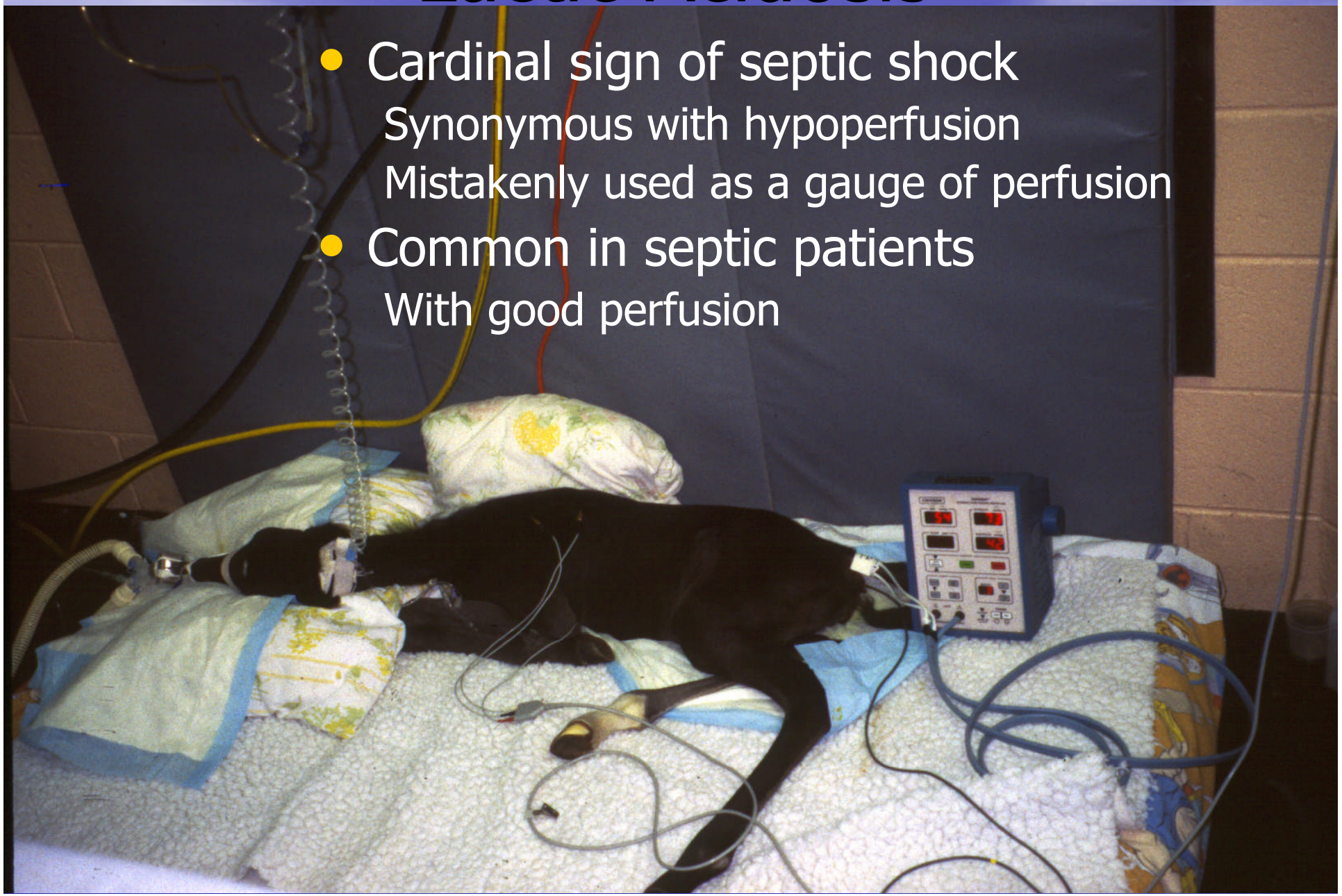
Metabolic Acidosis

- ICU patients SID = 30
  - Less reserve
  - ↑Lac^- or ↑NaCl treatment → more effect
  - Have lower SID without evidence of acidosis
  - 2ndary to ↓alb → ↓A^-
  - No compensatory ↓Pco2 for other reasons
  - So must ↓SID to maintain the pH
- ↓SID → ↓pH not linear
  - As SID < 20 → greater ↓pH
  - As SID approaches 20 → small insult ↓↓↓pH

Metabolic Acidosis
Strong ion acidosis

- Lactic acidosis
- Hyperchloremic acidosis

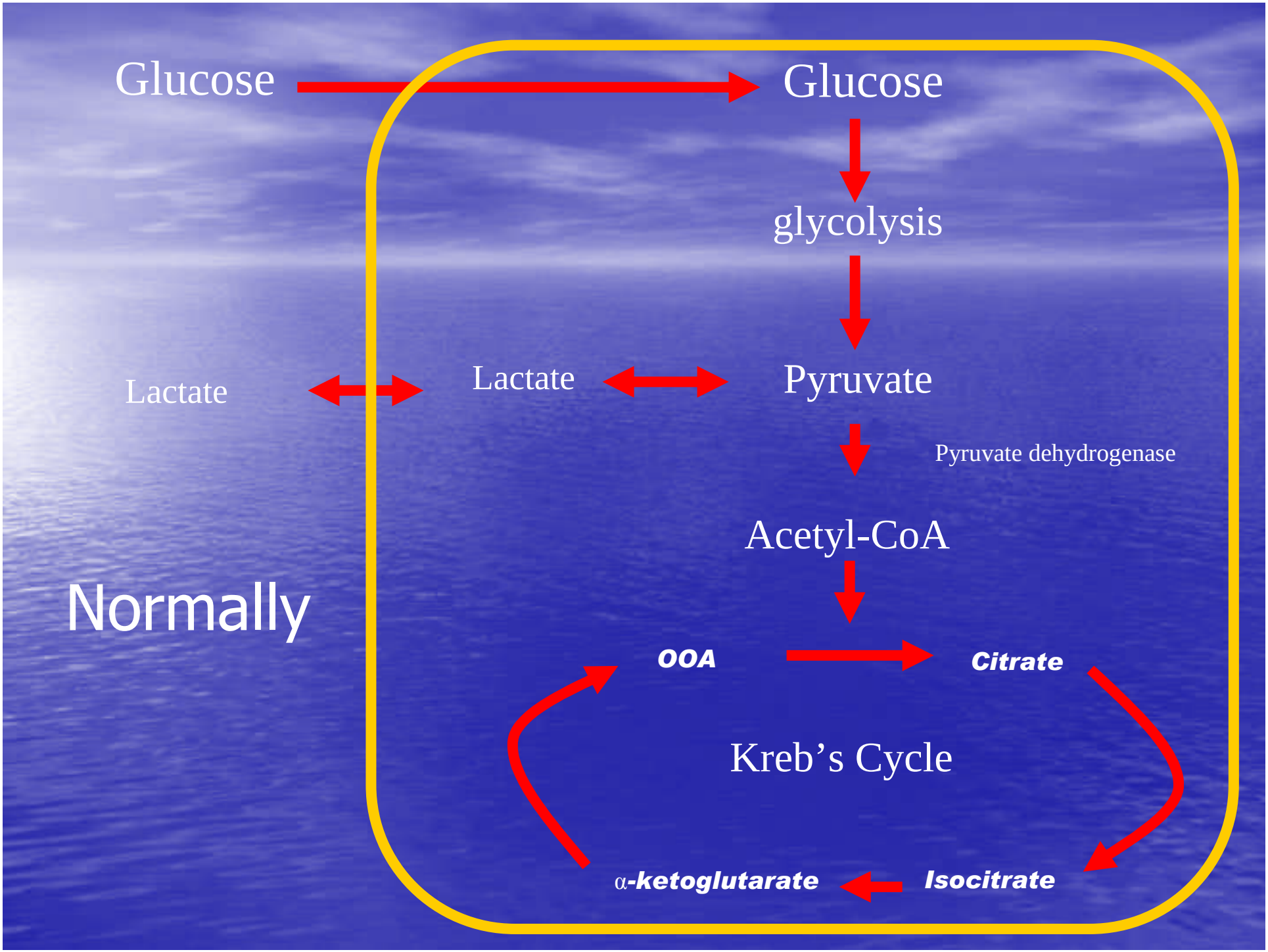
Lactic Acidosis



- Cardinal sign of septic shock
  - Synonymous with hypoperfusion
  - Mistakenly used as a gauge of perfusion
- Common in septic patients
  - With good perfusion

Source of Lactate in Sepsis

- Septic shock
  - Increase ATP requirement
  - Anaerobic metabolism
  - Rapid increase lactate levels
- Sepsis without shock
  - "Stress" lactic acidosis
  - Cytokine mediated
    - IL-1beta, IL-6 and TNF alpha


Glucose
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glycolysis
Lactate
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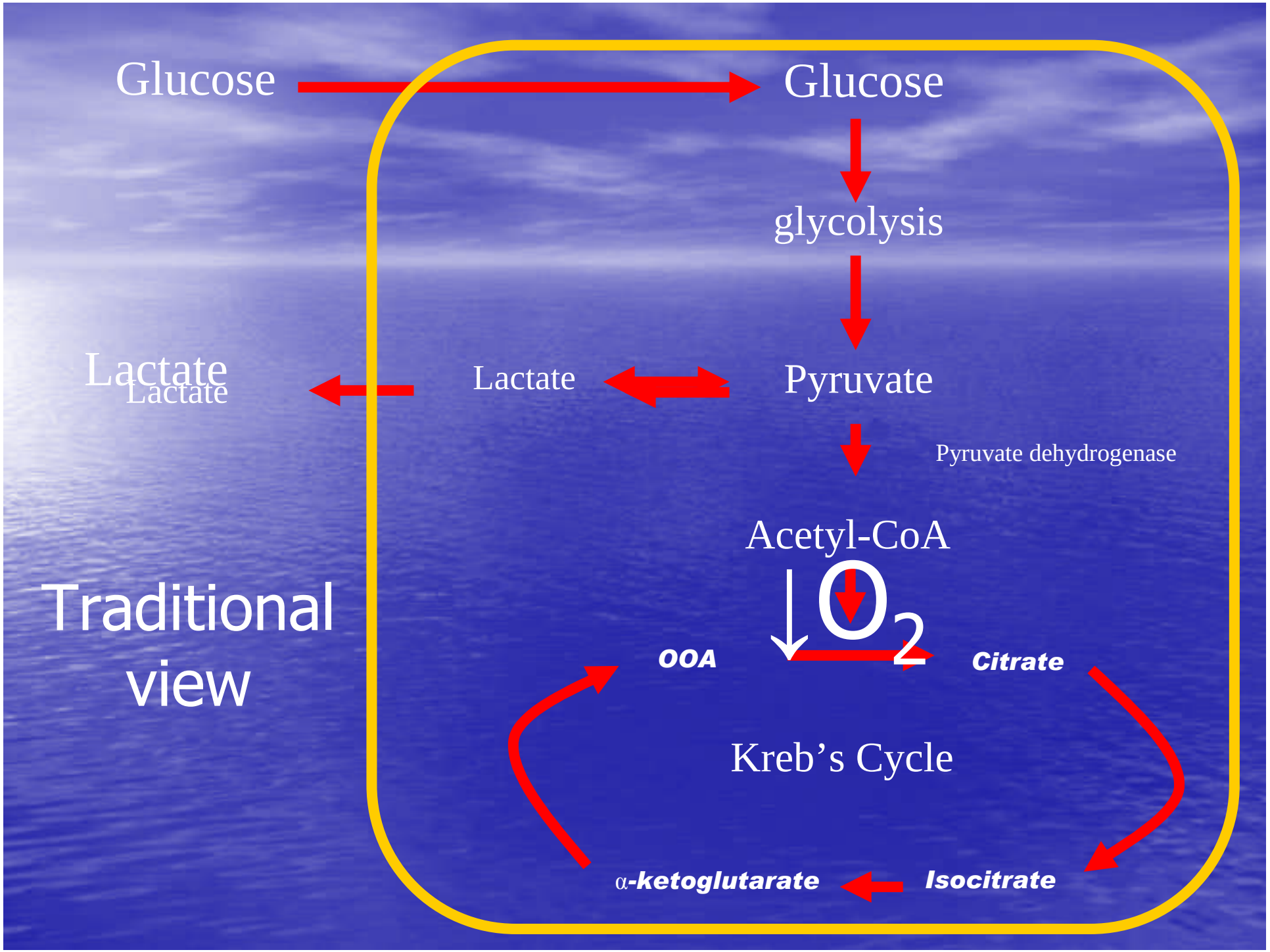
Pyruvate
Pyruvate dehydrogenase
Acetyl-CoA
Normally
OOA
Citrate
Kreb's Cycle
α-ketoglutarate
Isocitrate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Traditional view
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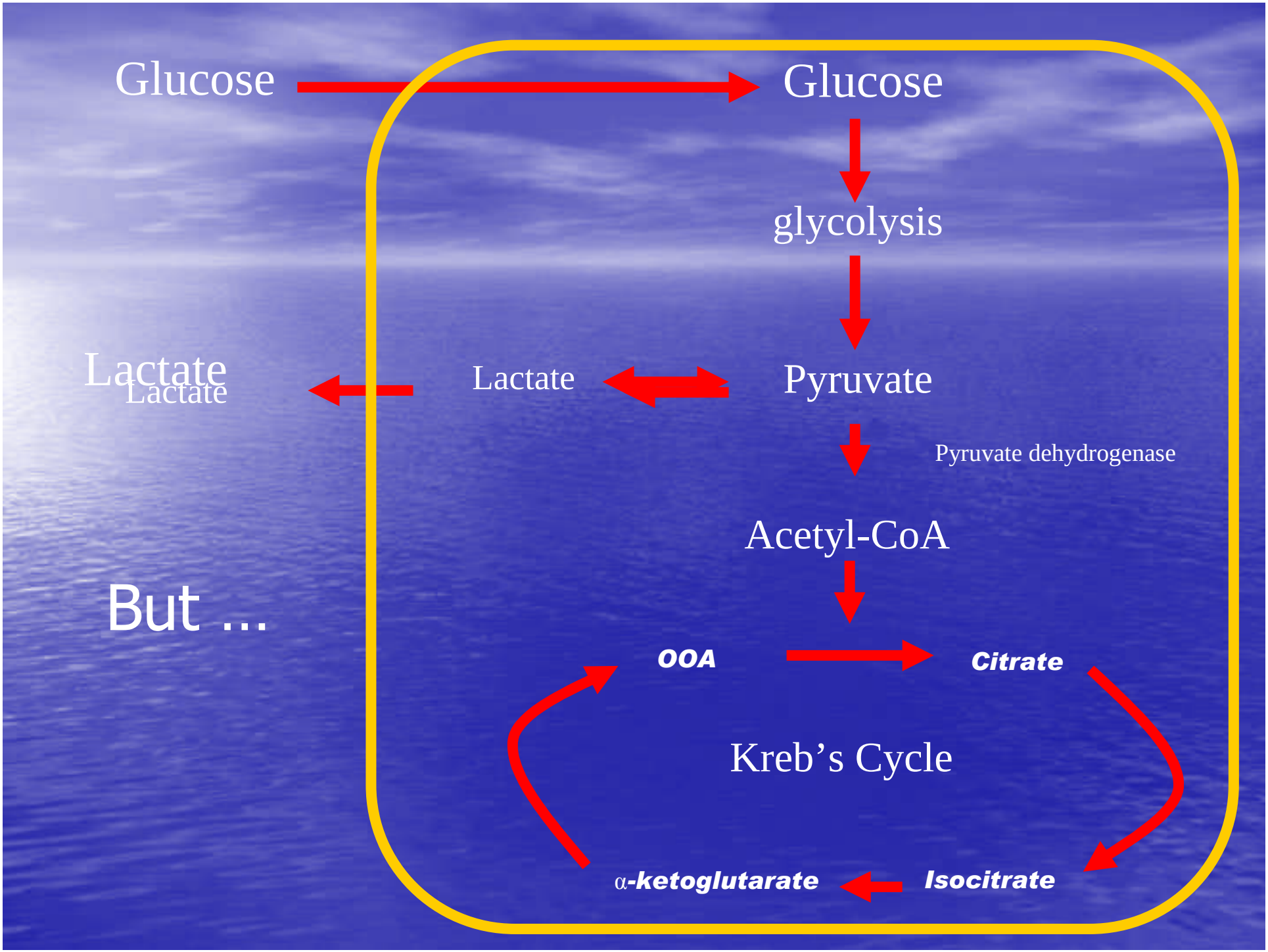
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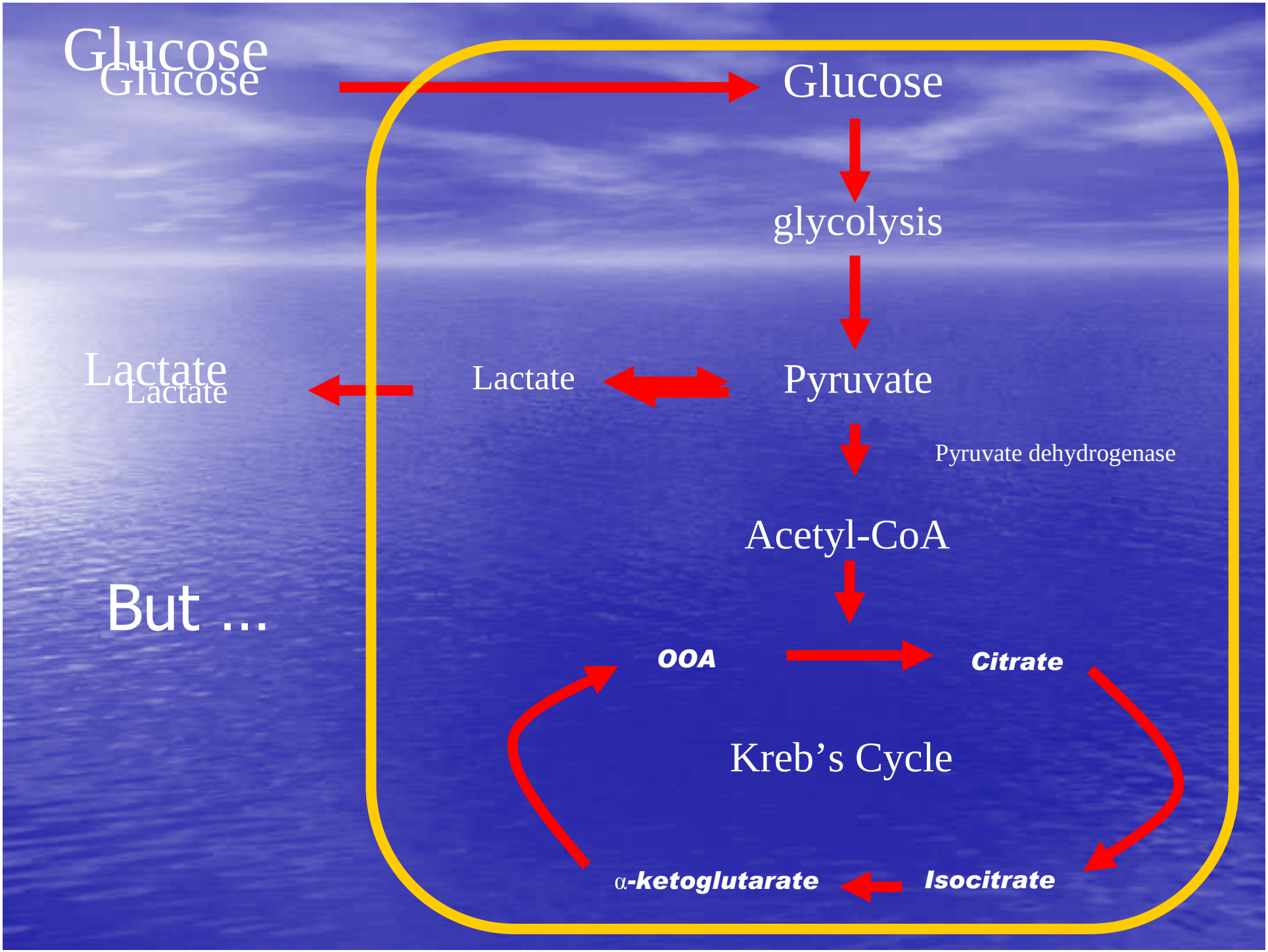
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Lactate Sources

- Tissue Hypoxia
  - Hypodynamic shock
  - Organ ischemia
- Hypermetabolism
  - Increased aerobic glycolysis
  - Increased protein catabolism
  - Increased muscle activity – shivering
- Decreased Clearance of Lactate
  - Shock – poor liver perfusion
  - Cytokine-mediated
  - Liver failure
- Inhibition of Pyruvate Dehydrogenase
- Activation of Inflammatory Cells

Source of Lactate in Sepsis

- Pyruvate dehydrogenase block
  - Cytokine down-regulation
  - Relative thiamine deficiency
  - Forces glucose → lactate production
- SIRS Hypermetabolism
  - Increase cellular glucose uptake
  - Stress hormone mediated
    - Epinephrine
  - Cytokine-mediated modulation of glucose transporter
    - ↑ synthesis
    - ↑ activity
    - ↑ distribution
  - ↑ glucose entry into cells
    - Mass action → ↑ glycolytic flux → ↑lactate production

Source of Lactate in Sepsis

- Phagocytes major cellular source
  - Required energy for respiratory burst
  - Occurs where macrophages are active
    - Damaged organ or site of trauma
    - Liver, spleen, gut, lung, wound
- Decreased hepatic lactate clearance
  - Sepsis impairs liver clearance

Lactate Accumulation Epinephrine Surge

- After injury, in sepsis, at birth
- Stimulates Na^+:K^+ ATPase

  ↑↑Aerobic glycolysis →↑lactate production

  Coupled to Na^+:K^+ ATPase activity in muscle

  - At rest , < 10% of its total Na^+:K^+ ATPase

    Maintain Na:K gradients

Lactate Accumulation Epinephrine Surge

- ↑Activity Na^+:K^+ ATPase
  - ↑Lactate production
    - Under well-oxygenated conditions
  - One cause of ↓K
- Inhibition of β2-adrenoreceptors
  - Prevents muscle associated lactate increase
  - Confirms mechanism Epinephrine increase lactate
- Epinephrine results in
  - Lactatemia
  - Hypokalemia

Lactate Accumulation Clearance by Tissues

- Liver
  - Large capacity for lactate removal
- Other organs
  - Kidneys
  - GI tract
  - Muscles
- Lactate clearance reduced by
  - Sepsis
  - Alkalosis
  - Acidosis (pH < 7.20)
  - Liver failure

Hyperlactatemia without acidemia

- Large quantities of Na lactate administered
  - Alkalemia occurs as lactate is metabolized
- Chronic lactate accumulation
  - Chloride ions move out of the vascular space
  - Compensatory increase SID
- Endogenous hyperlactatemia
  - Initially always associated acidosis
  - Normal pH or alkalosis
    - Suggests relative chronicity
    - Hypochloremic increase SID

Lactic Acidemia

- Nonspecific marker of hypoperfusion
- Important marker of tissue distress

  Malmetabolism

Lactate Levels Hypoperfusion

- Traditionally
  - Increased blood lactate = hypoxia/hypoperfusion
  - Tissue hypoxia → MODS/death
- Fundamental goal of therapy
  - Restoration of cellular oxygen delivery
- Reliable indicators of adequate perfusion
  - Warm legs
  - Strong peripheral pulses
  - Organ function - Urine output, Mental status, Borborygmi
- Lactate levels elevated
  - With hypoperfusion
  - With normal perfusion
- Decrease lactate levels
  - A goal of cardiovascular support
  - Not exclusive goal
  - Pressor therapy may cause significant increase lactate

Lactate Levels Hypoperfusion

- Blood lactate
  - Guide to resuscitation
- Epinephrine surge
  - Occurs
    - Normal birth
    - SIRS - Sepsis/septic shock
    - Hypoxic ischemic asphyxial insult
  - Greatly accelerate aerobic glycolysis and lactate production
    - Coupled to Na+: K+ ATPase activity in skeletal muscle
- Significant proportion ↑ blood lactate
  - Unrelated to poor tissue perfusion
  - Not respond to supranormal oxygen delivery
- Increased Na+: K+ ATPase activity
  - →↑lactate production under well-oxygenated conditions
  - Erythrocytes, vascular smooth muscle, neurons, skeletal muscle

Lactate
Enteric Bacteria

- Lactate produced by enteric bacteria
  Absorbed, produce lactic acidosis
  D-lactate
    - Endogenous lactate is L-lactate
- D-lactic acidosis
  Detection
    - Some assays for lactate only report L-lactate
    - Some assays report total lactate
    - Special D-lactate assays
  Will appear as unidentified anion if not assayed
- Metabolism
  Will be catabolized through L-lactate pathway
  Clearance is slower than D-lactate

Lactate
"High-octane" Fuel During Sepsis

- High energy fuel for heart
  - Allows maintenance of CO
  - Blocking lactate production:
    - Pronounced low flow state
    - Profound hypotension
  - Heart is a "metabolic omnivore"
    - Fatty acids (60-90%), glucose, lactate, and other
- Energy for CNS during HI insults
  - Protective – prevents lesions
  - Maintains CNS metabolism
  - High levels toxic to neurocytes
- Lactate production
  - Adaptive event in response to energetic crisis

SIG acidosis
Anion gap acidosis
Unmeasured anions

- Renal failure
- Ketoacidosis
  - Starvation
  - Metabolic errors
- Toxins
  - Ethylene glycol
  - Salicylates
- Sepsis/endotoxemia
  - Lactic acidosis
  - Other
- Liver disease

Non SIG acidosis
Non anion gap acidosis
SID acidosis

- Hyperchloremic acidosis
  - ↑Cl^- relative to Na^+
  - Loss of cation relative to Cl^-
- Renal Acidosis – often some role
  - Renal response →↑Cl^- excretion in urine
  - Kidney must be source of acidosis since
    - ↑plasma Cl^- rather than ↓plasma Cl^-
- Extrarenal Acidosis (↑Cl^-)
  - From treatment with Cl^- (NaCl)
  - Lower GI tract cation loss without loss of Cl^-

SID acidosis

- GI tract

  Diarrhea

  - Diarrhea fluid Na^+ > Cl^- similar to plasma
  - If treat with a NaCl → ↑Cl^- →↓SID
  - If treat with SID balanced fluids

    Will not happen

  Small intestinal disease

SID acidosis

- Iatrogenic

  TPN/PPN

  - Contains balance of weak anions (e.g. acetate) + Cl^-

    If acetate<< Cl^- then plasma Cl^- ↑ →↓SID

  Saline – dilutional acidosis

  - Critical patient - already have lactic acidosis, can't change ventilation to compensate, have ↓A_{TOT} (↓albumin)
  - Treated 5-10X plasma volume → significant acidosis
  - Unlike normal patient treated with NaCl

Renal Acidosis

- Renal failure

  Uncomplicated renal failure no acidosis

  Hyperchloremic acidosis ↓SID

  - Na wasting > Cl excretion
  - Failure of Cl excretion without Na

  Chronic ↑sulfates ↓SID

- Treat with $NaHCO_3$ → ↑SID

  If Na^+ concentration is too high treat with Ca^{++}

  But little ↑SID because of small normal range Ca

- Renal tubular acidosis

Renal Tubular Acidosis

- Defect in all types of RTA

  Inability to excrete Cl^- in proportion to Na^+

- RTA type I – distal

  Impaired Na^+ transport cortical collecting ducts

  Treat NaHCO3 → respond

  K^+ deficient/hyperkalemic form

Renal Tubular Acidosis

- RTA type II - proximal

  Na^+ & K^+ reabsorption defect

  - Franconi Syndrome – glu, PO_4, urate, aa reabsorption defects

  Treat Na HCO3 → just ↑losses and not work

- RTA type IV

  Aldosterone deficiency or resistance

  ↑serum K and low urine pH (< 5.5)

  Often caused by NSAIDs, heparin, K sparing diuretics

  Discontinue drugs

Unexplained metabolic acidosis

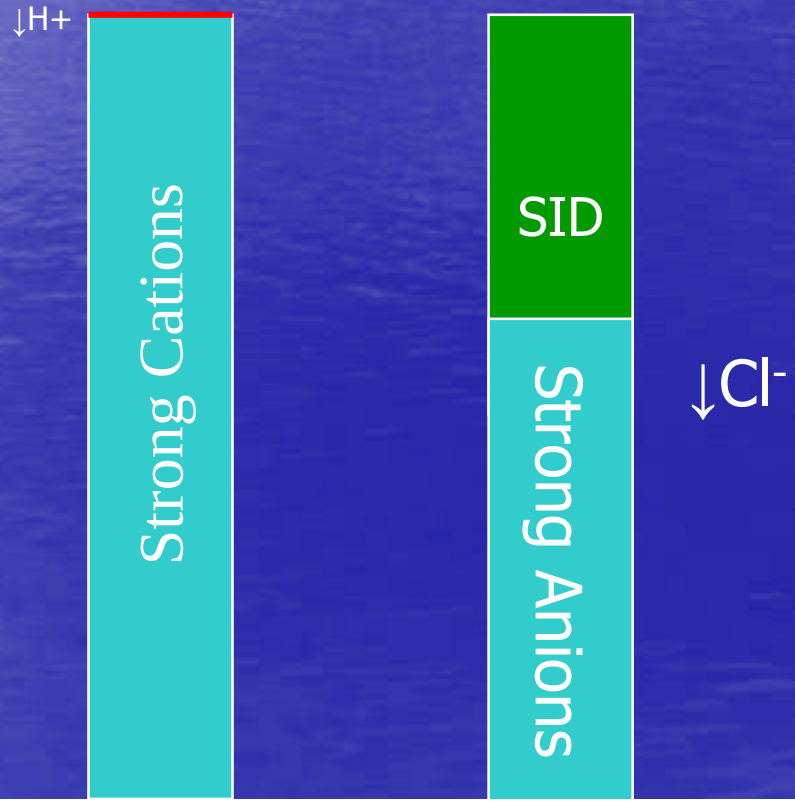
- Lactic acidosis
  - More acidotic than explained by lactate level
- Sepsis
  - Acidosis without ↑ lactate
    - Could be D-lactate
  - May be secondary to ↑ Cl^-
  - Unexplained anions released from liver
    - Normally liver clears unmeasured anions
- Often ⅓ of acidosis is unexplained
  - Loss of Donnan equilibrium of plasma
  - Capillary leak – loss of albumin from vascular space
  - Cl^- moves into vascular space to balance loss
  - Hyperchloremic acidosis with ↓ SID

Metabolic Alkalosis

Metabolic Alkalosis

Strong Ion Alkalosis

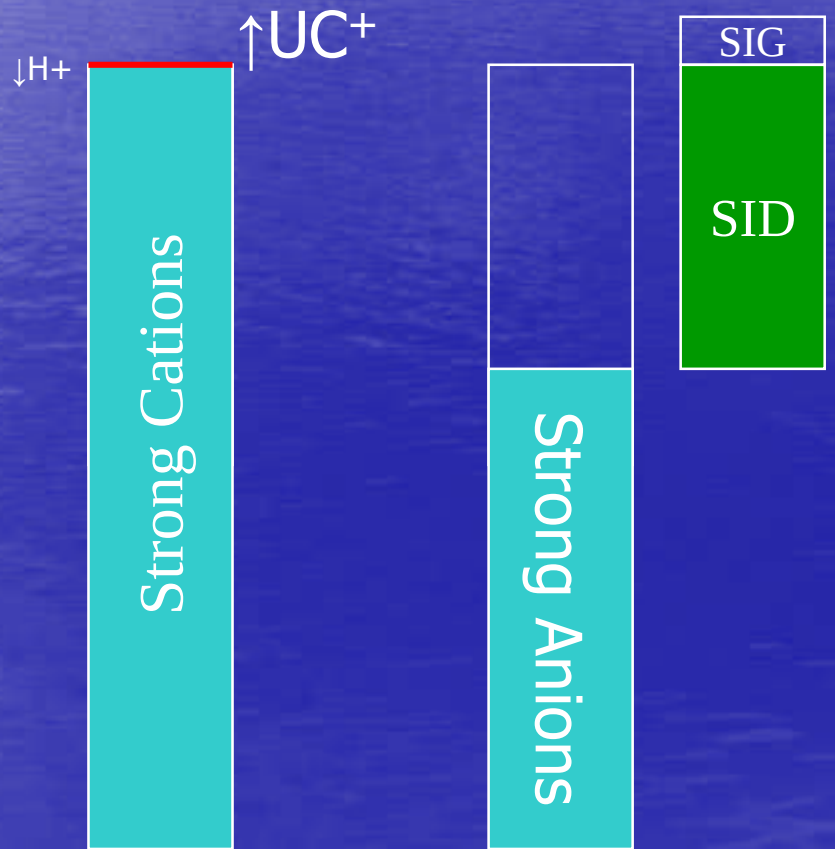
Increased SID



Metabolic Alkalosis

Unidentified Cation Alkalosis

SIG > 0



Metabolic Alkalosis

- Metabolic alkalosis

  ↑SID → Results in ↓ free H+ → alkalosis

- ↑SID

  Loss of anions > cations

  Diuretics

  Renal disease

Metabolic alkalosis

- ↑SID

  Loss of Cl^- -- ↓anions

  - or from ↑cations (rare)

  Cl^- loss > Na

- **Cl^- Responsive**
- **Cl^- Resistant**

Potential Clinical Effects of Metabolic Alkalosis

- Cardiovascular
  - ↑Inotropy (Ca^{++} entry)
  - Altered coronary blood flow (↑/↓)
  - Digoxin toxicity
- 0_2 Delivery
  - ↑Oxyhemoglobin affinity
  - ↑2,3-DPG (delayed)

Potential Clinical Effects of Metabolic Alkalosis

- Neuromuscular
  - Neuromuscular excitability
  - Encephalopathy
  - Seizures
- Metabolic Effects
  - ↓K
  - ↓Ca
  - ↓PO4
  - Impaired enzyme function

Metabolic alkalosis
Cl Responsive

- Cl^- loss easily treated

  Cl^- loss > Na^+

  Temporary loss – compensation

  Not ongoing (Ucl low)

- Gastrointestinal

  Reflux, Cl wasting diarrhea

Metabolic alkalosis Cl Responsive

- Post diuretic
  - Volume contraction →↑aldosterone →↑Na reabsorption
  - But also ↑K and Cl^- loss → alkalosis
- Post chronic lactic acidosis
  - ↓Cl^- as compensation for acidosis
  - Lactic acidosis may resolve quickly
  - Residual hypochloremic alkalosis
- Post hypercapnia – metabolic compensation
  - Hypercapnea resolves quickly
  - Residual hypochloremic alkalosis

Metabolic alkalosis
Cl Responsive

- Treatment

  Replace Cl with NaCl, KCl

- Dehydration usually present

  ↑ SID – corrected with saline

  ↑ SID – corrected with balanced fluids

Metabolic Alkalosis
Cl Resistant

- Renal dysfunction
- Cl^- loss is ongoing (Ucl high)

  Hormonal mechanisms
  - Mineralocorticoid excess
  - Primary/secondary hyperaldosteronism
  - Cushing syndrome
  - Liddle's syndrome
  - Bartter's syndrome
  - Excessive corticoids
  - Excessive licorice intake (mimics aldosterone)

  Ongoing diuretic use

Metabolic Alkalosis
Cl Resistant

- Only temporarily correct with Cl^- therapy
  - Urine Cl^- > 20 mmol/l
  - Saline therapy may temporarily correct SID
- Ongoing renal loss results in return ↑ SID
  - ↑ Mineralocorticoid activity

Metabolic acid-base therapy

- If Na/Cl levels normal

  Don't use Na/Cl in therapy

- If Na/Cl abnormal

  ↑ Na – $NaHCO_3$

  ↑ Cl – NaCl

- If ↑ lactate (↑ SIG, ↑ AG)

  ↑ metabolic clearance

  ↓ epinephrine levels

  ↓ hypermetabolism

  Don't treat with $NaHCO_3$

  - After lactate ↓ - Na remains - ↑ SID
  - But pH < 7.20 liver may not clear lactate well