

Metabolic Acid-Base Abnormalities

Jon Palmer, VMD, DACVIM

Director of Neonatal/Perinatal Programs

Graham French Neonatal Section, Connelly Intensive Care Unit

New Bolton Center, University of Pennsylvania

Metabolic Acid-Base Abnormalities

- Pathophysiology
- Metabolic acidosis

SID acidosis

- Lactic Acidosis

SIG acidosis unmeasured anions

Unexplained metabolic acidosis

- Metabolic alkalosis

SID alkalosis

- Cl Responsive
- Cl Resistant

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

Renal Regulation Modifying SID

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

Charges must balance

Excrete as NH_4^+Cl^-

- Renal-Hepatic Interaction

NH_4^+ co-excretion with Cl^-

NH_4^+ produced in the kidney and liver

Renal Regulation Ammoniogenesis

- Hepatic glutaminogenesis
Stimulated by acidosis
- Nitrogen metabolism in liver
→ Urea, glutamine, (NH_4^+)
Glutamine → kidney → $\uparrow \text{NH}_4^+$ → $\uparrow \text{Cl}^-$ excretion
 \uparrow Glutamine → alkalosis by $\downarrow \text{Cl}^-$ relative to Na^+
- Hepatocyte
Cells with urea production capacity
 - Closer to portal vein
 - GI tract nitrogen → urea firstAcidosis inhibits urea formation
 - N to glutamine producing cells → \uparrow Glutamine →
 - Kidney → NH_4^+ → $\uparrow \text{Cl}^-$ loss → compensatory Alk

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 is more important than degree of acidosis
Epiphenomenon

ICU Patients

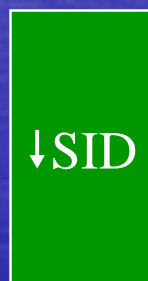
Low albumin \rightarrow \downarrow SID

Neonate \uparrow PO₄ \rightarrow \uparrow SID

Cations



Na⁺



Cl⁻



SID

Anions

Metabolic Acidosis

- ICU patients SID = 30
 - Less reserve
 - $\uparrow \text{Lac}^-$ or $\uparrow \text{NaCl}$ treatment \rightarrow more effect
 - Have lower SID without evidence of acidosis
 - 2ndary to $\downarrow \text{alb}$ \rightarrow $\downarrow \text{A}^-$
 - No compensatory $\downarrow \text{Pco}_2$ for other reasons
 - So must $\downarrow \text{SID}$ to maintain the pH
- $\downarrow \text{SID} \rightarrow \downarrow \text{pH}$ not linear
 - As $\text{SID} < 20 \rightarrow$ greater $\downarrow \text{pH}$
 - As SID approaches 20 \rightarrow small insult $\downarrow \downarrow \downarrow \text{pH}$

Metabolic Acidosis

Strong Ion Acidosis

Decrease SID



$\uparrow H^+$

Strong Cations

SID

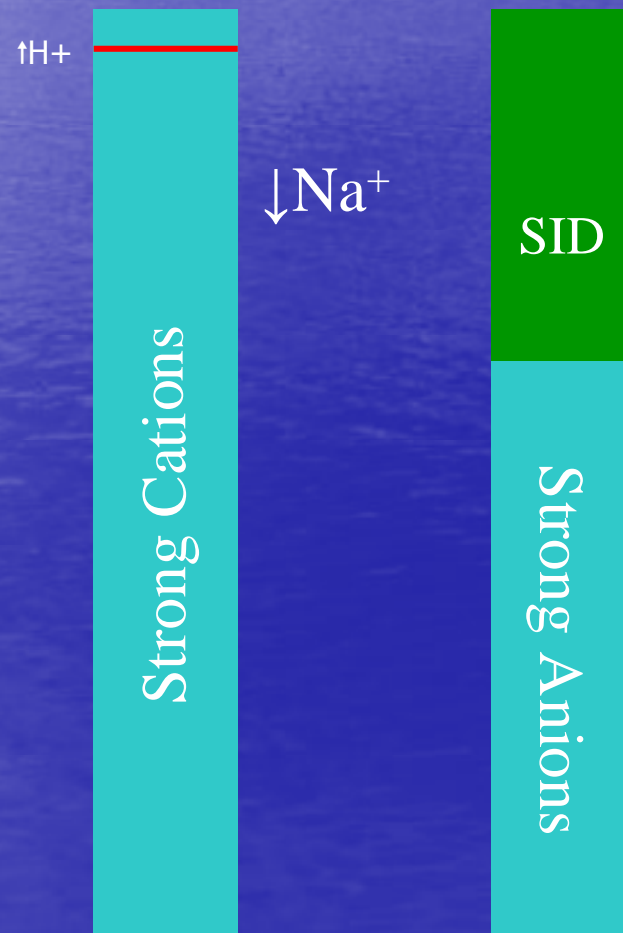
Strong Anions

$\uparrow Cl^-$

Metabolic Acidosis

Strong Ion Acidosis

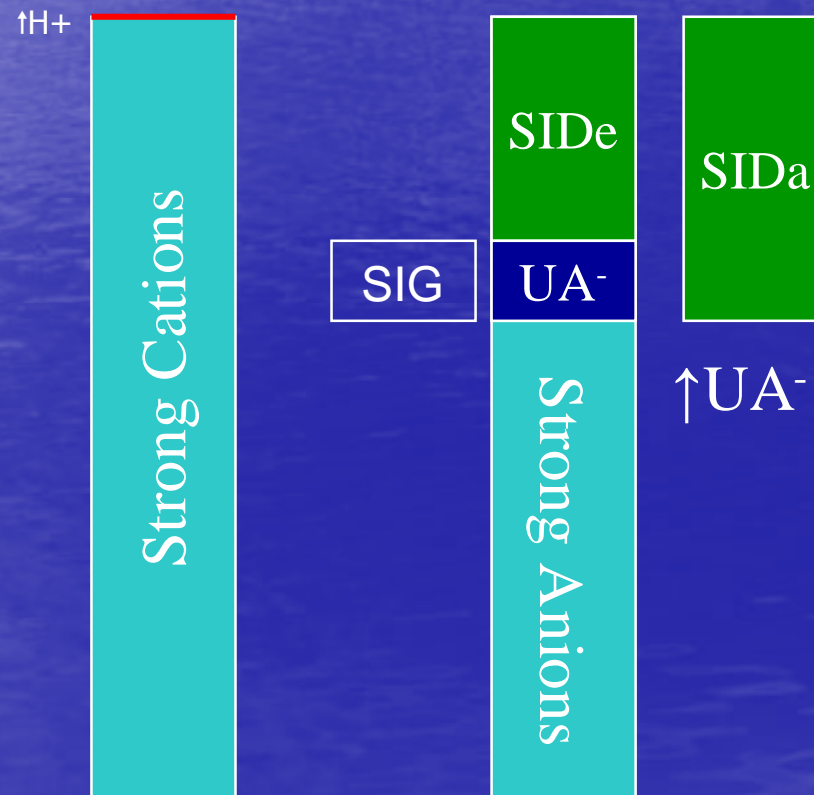
Decrease SID



Metabolic Acidosis

Increase in Unidentified Anions

$SIG < 0$



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

 - ↑ Exogenous ions -- iatrogenic, poisoning

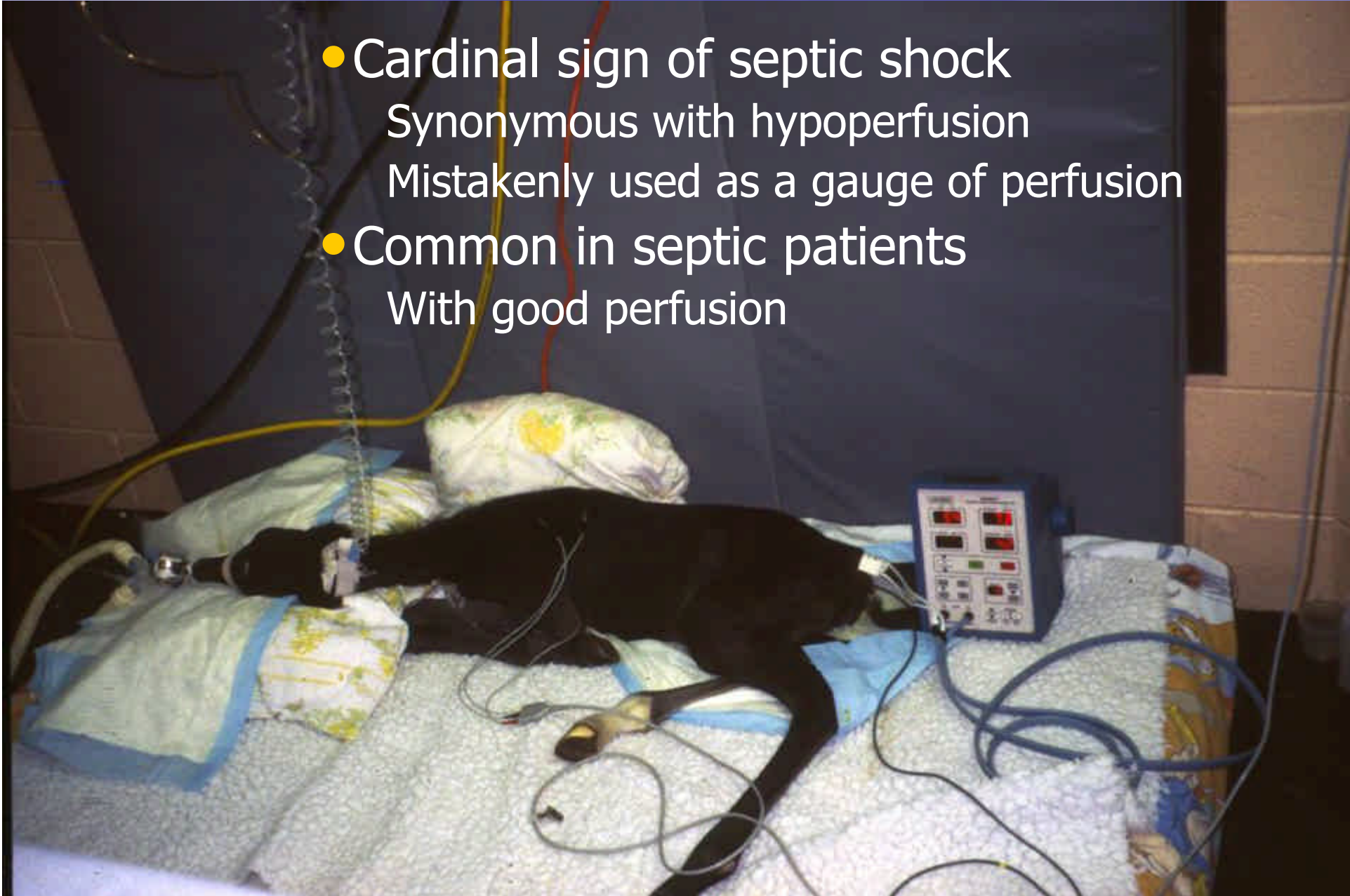
Metabolic Acidosis

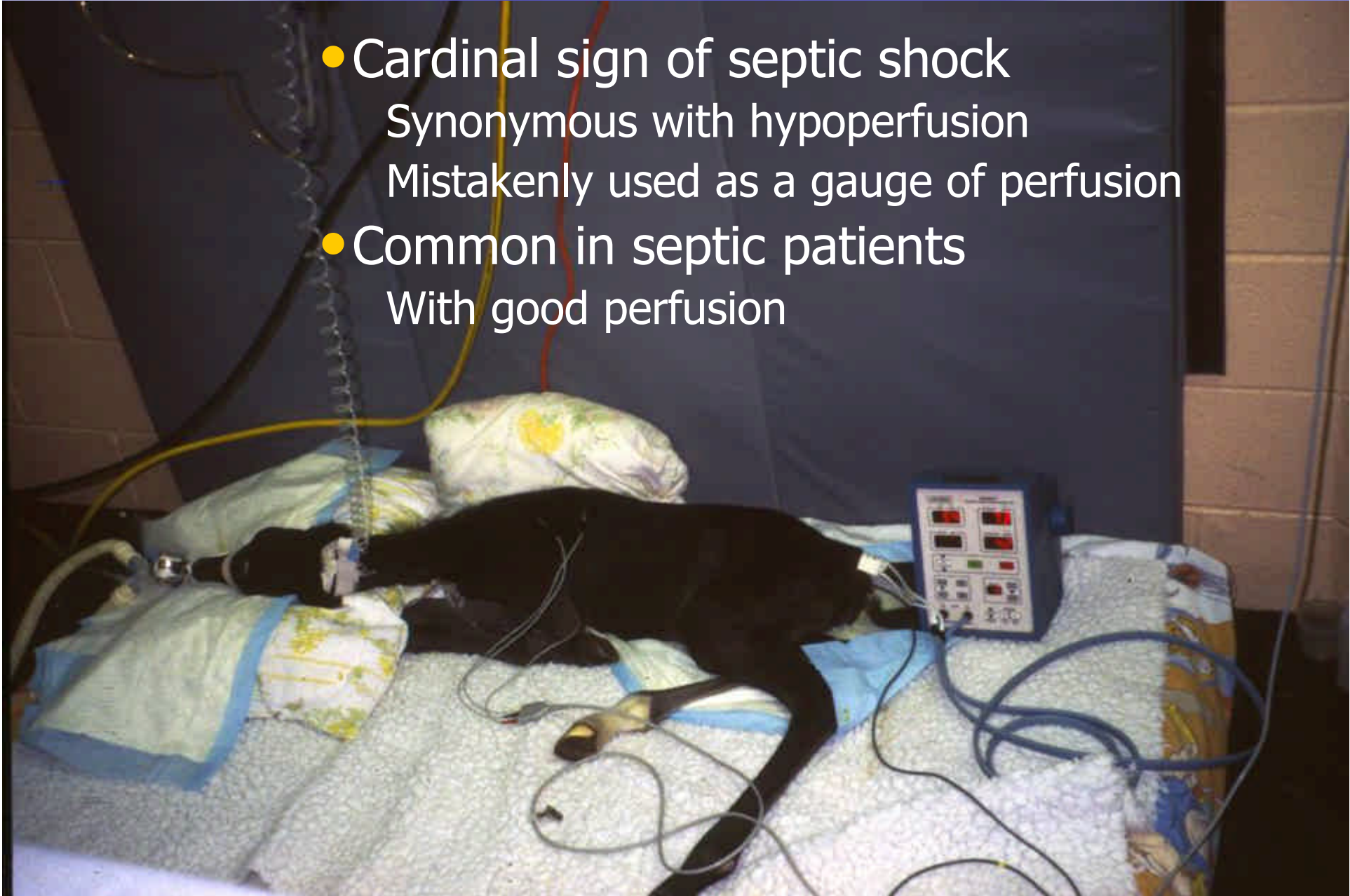
Strong ion acidosis

- 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
- 
- A black dog is lying on a hospital bed, appearing to be under medical care. The dog is positioned horizontally across the frame. It has several medical tubes and wires attached to it, including a large yellow tube near its head and a blue tube near its tail. A small electronic device with multiple red and green lights is connected to the dog's tail area. The bed is covered with a white sheet and a patterned blanket. The background shows a dark blue curtain and a light-colored wall.



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

Normally

Glucose

Glucose

glycolysis

Lactate

Lactate

Pyruvate

Pyruvate dehydrogenase

Acetyl-CoA

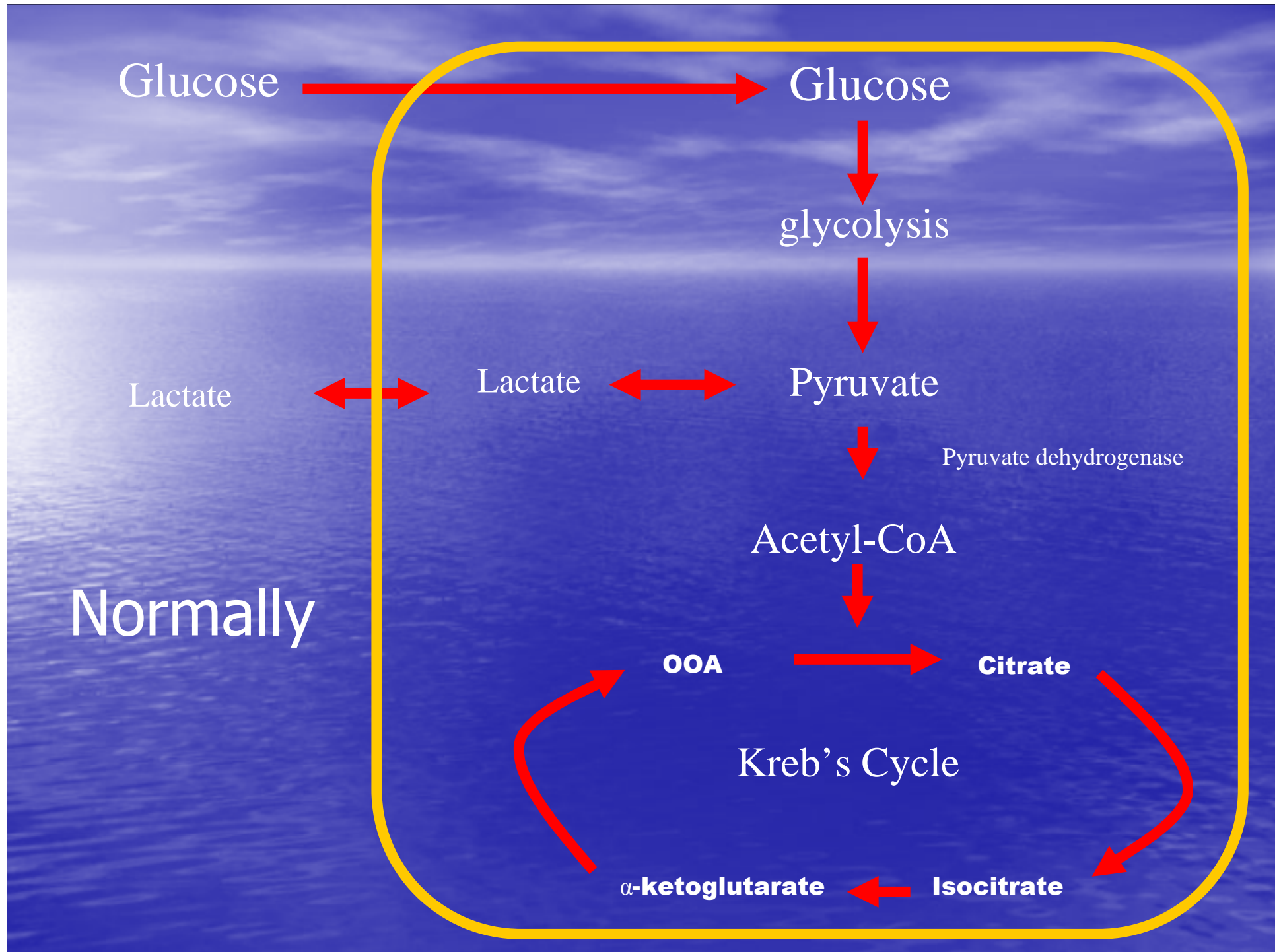
OOA

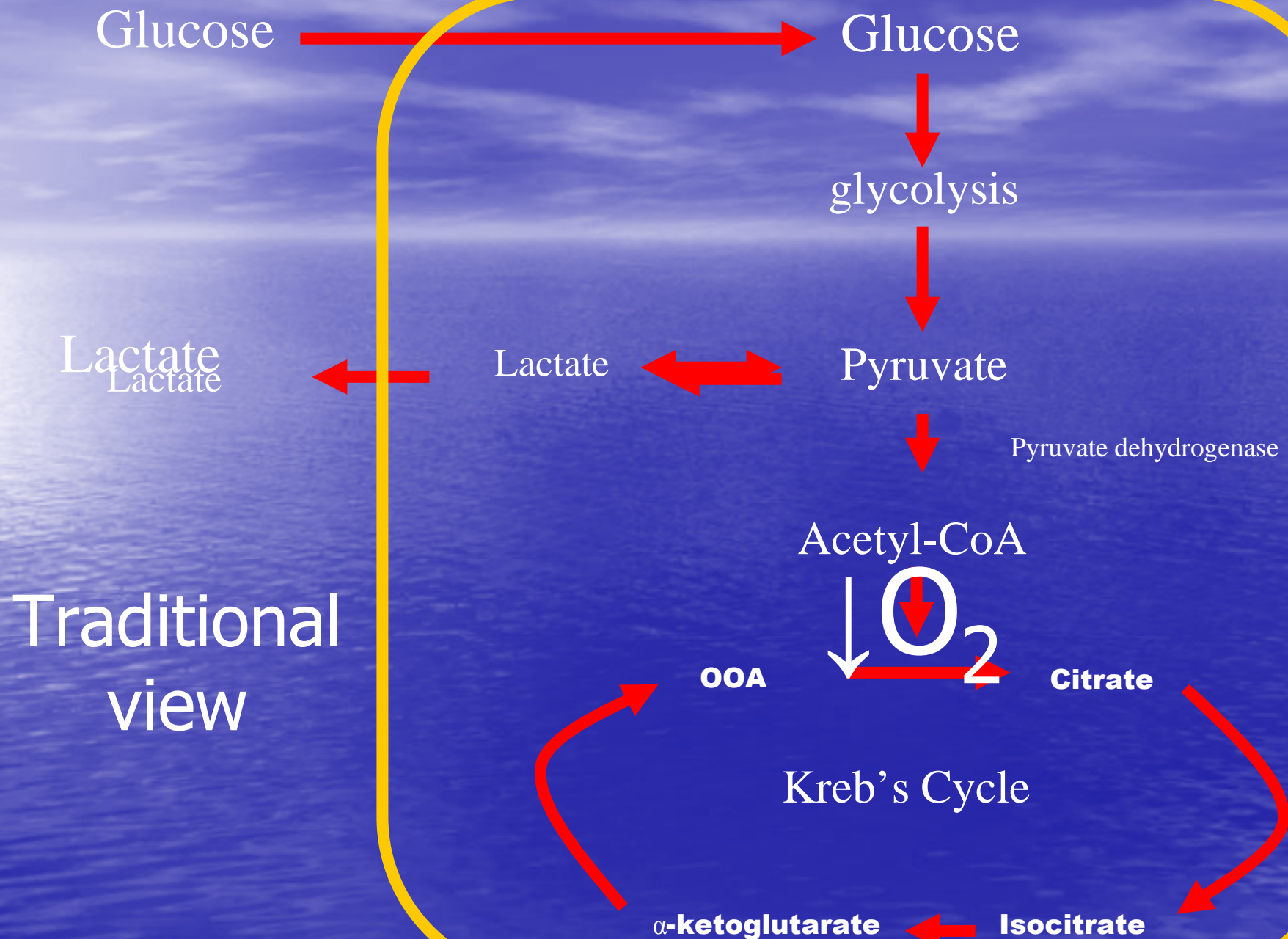
Citrate

Kreb's Cycle

α -ketoglutarate

Isocitrate





Glucose

Glucose

glycolysis

Lactate
Lactate

Lactate

Pyruvate

Pyruvate dehydrogenase

Acetyl-CoA

But ...

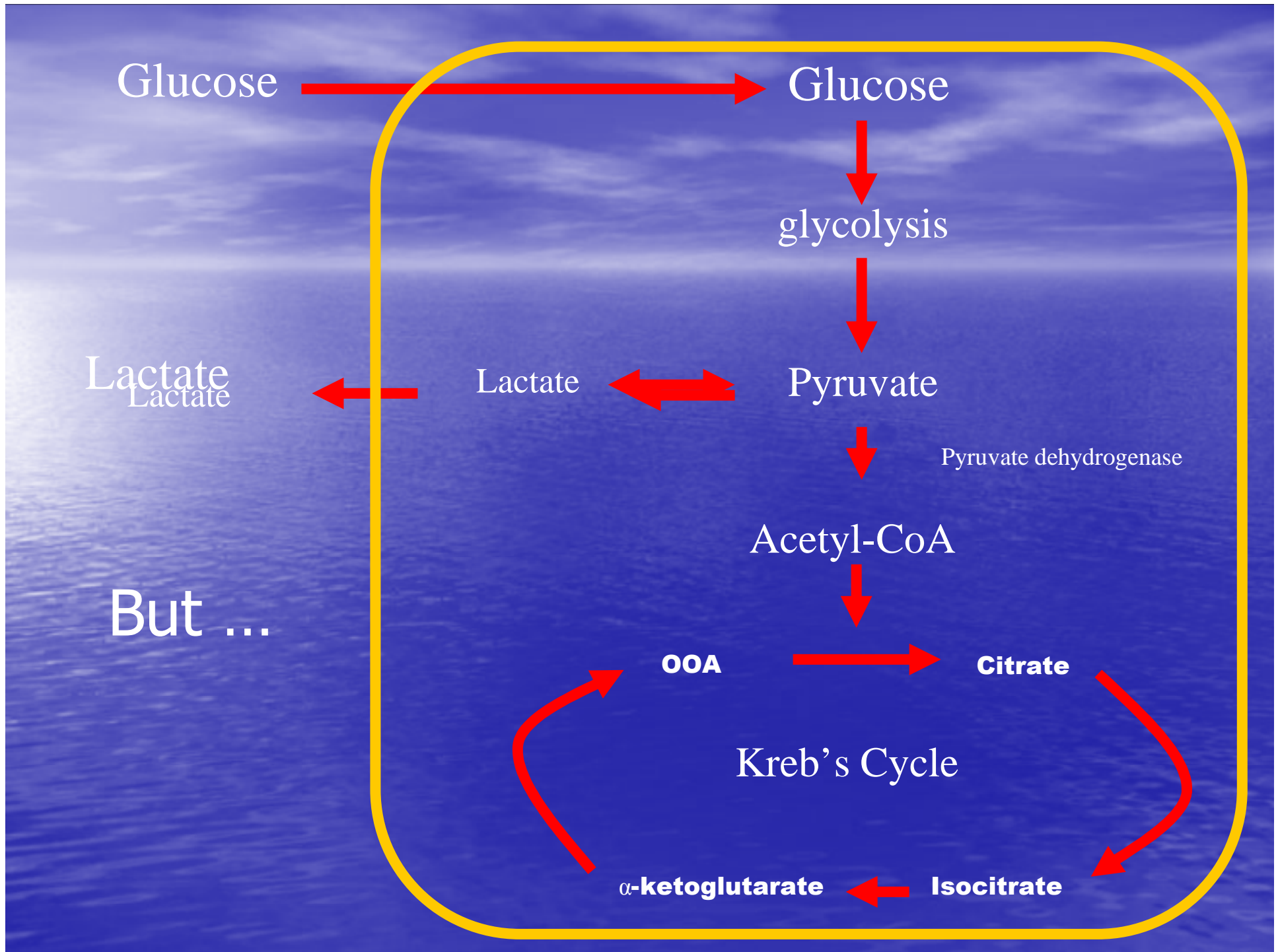
OOA

Citrate

Kreb's Cycle

α -ketoglutarate

Isocitrate



Glucose
Glucose

Glucose

glycolysis

Lactate
Lactate

Lactate

Pyruvate

Pyruvate dehydrogenase

Acetyl-CoA

But ...

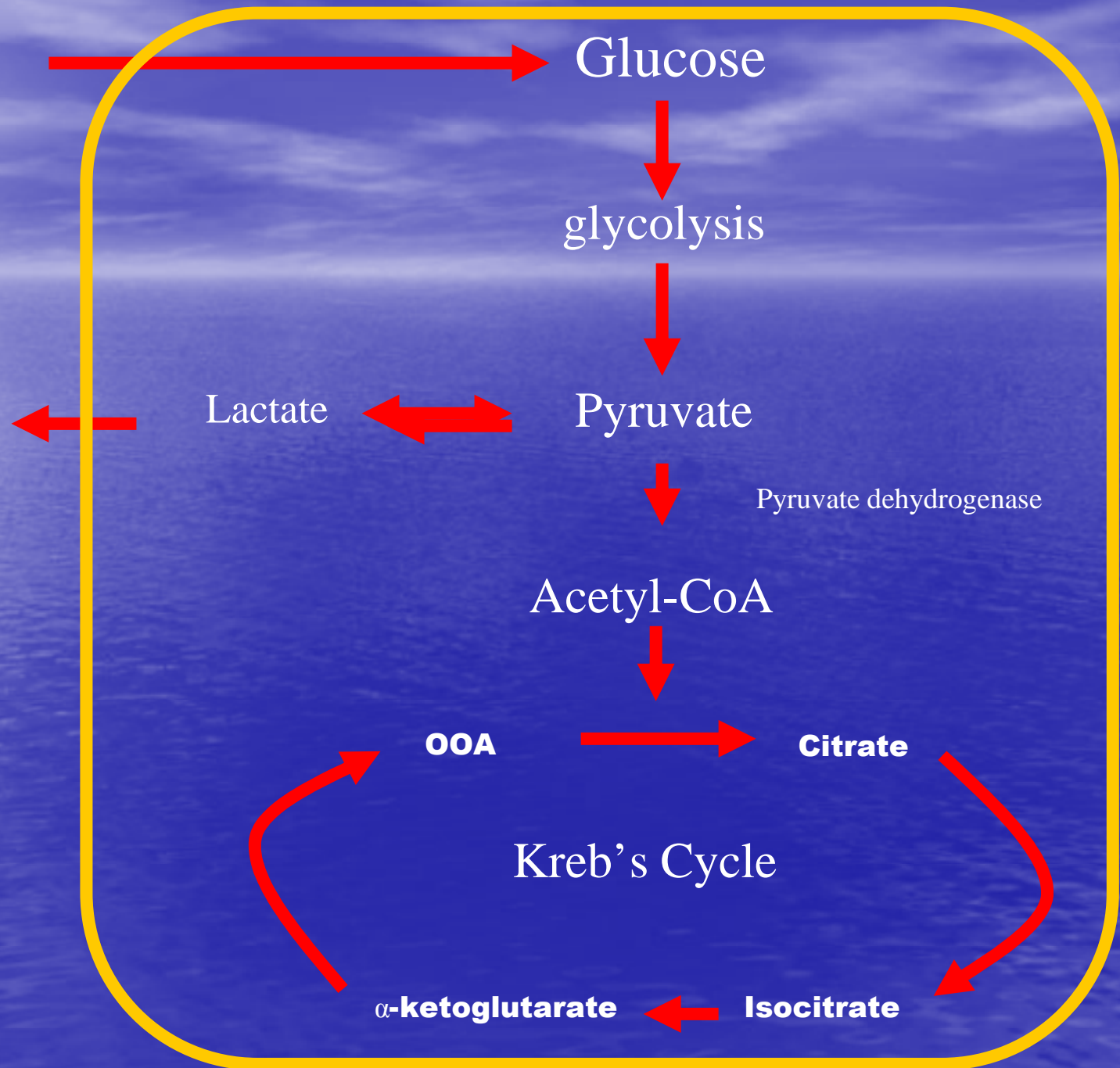
OOA

Citrate

Kreb's Cycle

α -ketoglutarate

Isocitrate



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 $\text{Na}^+:\text{K}^+$ ATPase
 - ↑↑aerobic glycolysis → ↑lactate production
 - Coupled to $\text{Na}^+:\text{K}^+$ ATPase activity in muscle
 - At rest , < 10% of its total $\text{Na}^+:\text{K}^+$ ATPase
 - Maintain Na:K gradients
- ↑activity $\text{Na}^+:\text{K}^+$ ATPase
 - ↑lactate production
 - under well-oxygenated conditions
 - One cause of ↓K
- 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 ($\text{pH} < 7.20$)
 - Liver failure

Hyperlactatemia without acidemia

- Massive 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 $\text{Na}^+ : \text{K}^+$ ATPase activity in skeletal muscle
- Significant proportion \uparrow blood lactate
 - Unrelated to poor tissue perfusion
 - Not respond to supranormal oxygen delivery
- Increased $\text{Na}^+ : \text{K}^+$ ATPase activity
 - $\rightarrow \uparrow$ 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 assaysWill appear as unidentified anion if not assayed
- Metabolism
Will be catabolized through L-lactate pathway
Clearance is slower than D-lactate

Strong Ion Acidosis



Strong Ion Acidosis

Hyperchloremic acidosis

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

Strong Ion Acidosis

- GI tract

Diarrhea

- Diarrhea fluid $\text{Na}^+ > \text{Cl}^-$ similar to plasma
- If treat with a NaCl $\rightarrow \uparrow \text{Cl}^- \rightarrow \downarrow \text{SID}$
If treat with Plasmalyte this will not happen
- If drink water - $\downarrow \text{Cl}^-$ but $\downarrow \downarrow \text{Na}^+ \rightarrow \downarrow \text{SID}$
If drink strong ion balanced electrolyte water may avoid

- Iatrogenic

TPN/PPN

- Contains balance of weak anions (e.g. acetate) + Cl^-
If acetate $\ll \text{Cl}^-$ then plasma $\text{Cl}^- \uparrow \rightarrow \downarrow \text{SID}$

Saline - dilutional acidosis

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

ICU Patient – no urine output

	SID	pH	Pa _{CO2}	BE
Baseline*	30	7.40	38	-2.0
Lactic Acidosis**	20	7.29	29	-11.4
10 liters saline	14	7.13	25	-20.1

* Na = 130, Cl = 100

** Lactate = 10 mmol/l

Strong Ion Acidosis

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

- Renal tubular acidosis

Defect in all types of RTA

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

SIG acidosis

Unmeasured anions

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

Unexplained metabolic acidosis

- Lactic acidosis
More acidotic than explained by lactate level
- Sepsis
Acidosis without \uparrow lactate
May be secondary to \uparrow Cl^-
Unmeasured anions released from liver
 - Normally liver clears unmeasured anions
- Often $\frac{1}{3}$ 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 \downarrow SID

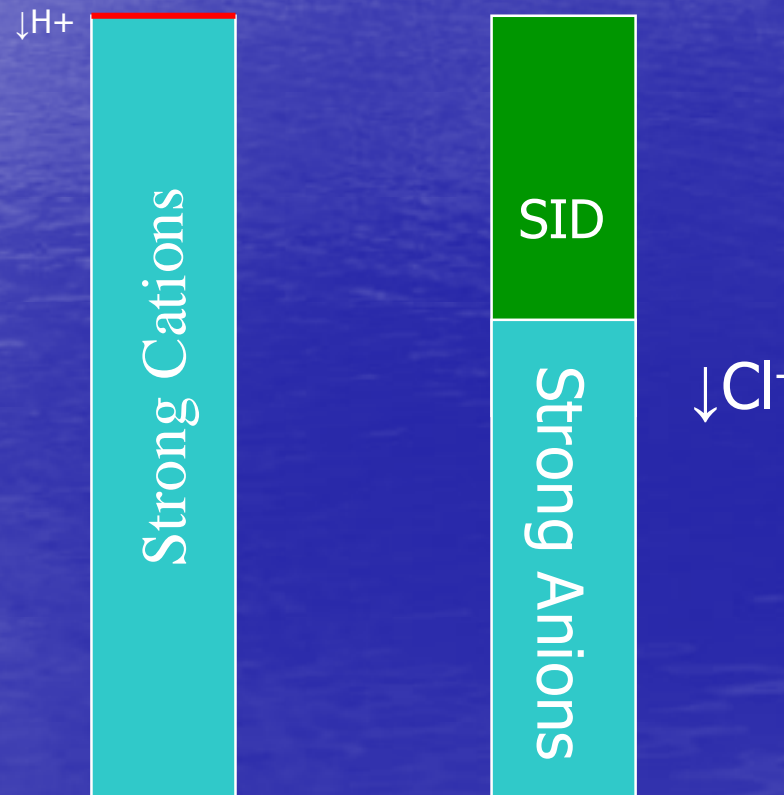
Metabolic Alkalosis



Metabolic Alkalosis

Strong Ion Alkalosis

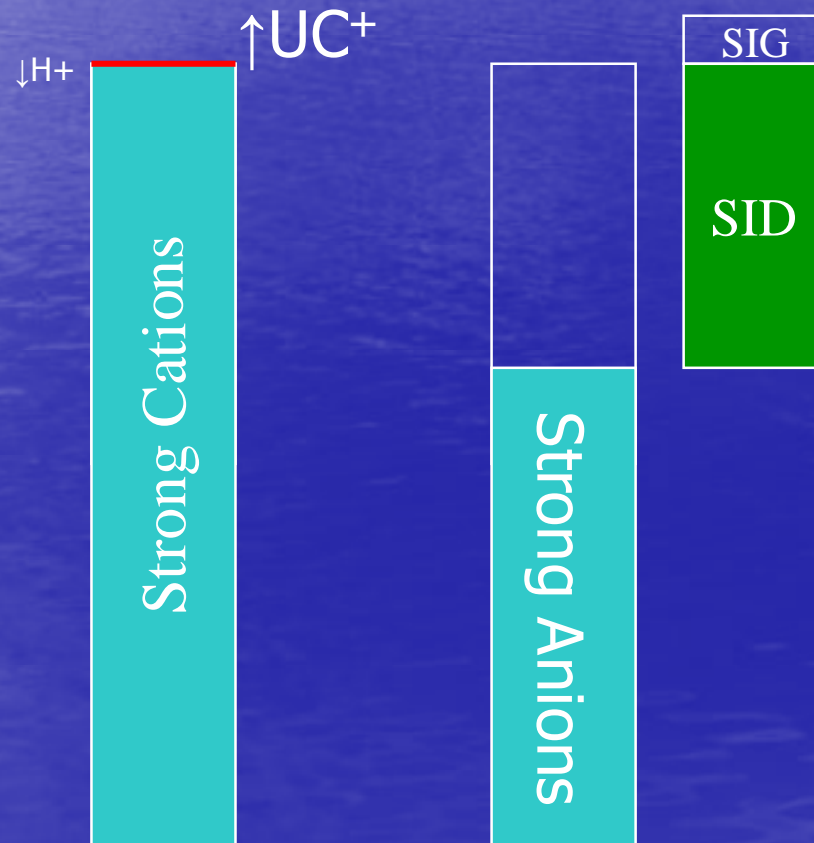
Increased SID



Metabolic Alkalosis

Unidentified Cation Alkalosis

$SIG > 0$



Metabolic Alkalosis

- Metabolic alkalosis

$\uparrow \text{SID} \rightarrow \text{Results in } \downarrow \text{ free H}^+ \rightarrow \text{alkalosis}$

- $\uparrow \text{SID}$

Loss of anions > cations

Diuretics

Renal disease

Metabolic alkalosis

- \uparrow SID

Loss of Cl^- -- \downarrow anions

- Cl^- loss $>$ Na

\uparrow Cations (rare?)

- Cl^- Responsive
- Cl^- Resistant

Metabolic alkalosis

Cl Responsive

- Cl^- loss easily treated

Cl^- loss $>$ Na^+

Temporary loss

Not ongoing (Ucl low)

Metabolic alkalosis

Cl Responsive

- Gastrointestinal
 - Reflux, Cl wasting diarrhea
- Post diuretic
 - Volume contraction \rightarrow \uparrow aldosterone \rightarrow \uparrow Na reabsorption
 - But also \uparrow K and Cl^- loss \rightarrow alkalosis
- Post chronic lactic acidosis
 - \downarrow 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

Metabolic Alkalosis

Cl Resistant

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 $\text{Cl}^- > 20 \text{ mmol/l}$
Saline therapy may temporarily correct SID
- Ongoing renal loss results in return \uparrow SID
 \uparrow Mineralocorticoid activity





Case 1

Case 2

Hyperchloremic acidosis 61119

- Diarrhea noted day 3
- Referred day 4
 - WBC 10.9
 - 77% Segs
 - 3% bands
 - 20% Lymphs
 - Fibr 824mg/dl
 - IgG > 800 mg/dl

Hugsie 60237



- History
 - Term foal
 - 10 minute stage II
 - Placenta 25 lbs (foal 122 lb)
 - Accompanied sick mare 3 hrs old
- Problems
 - Neonatal encephalopathy
 - Somnolence, hypertonus, seizures
 - SIRS
 - Neonatal gastroenteropathy

66943

Thelma's Beauty

- 3 yr old TB race horse
- Day of presentation
 - Raced
 - "Collapsed"?
 - Colic
 - Rx Banamine 2X
- Admission PE
 - Quiet/depressed
 - General muscle fasciculations
 - Slightly dehydrated
 - Reflux – 10 l
 - Very thirsty (despite fluid therapy)

66943

Thelma's Beauty

- 1/9 8 pm - venous
- pH – 7.570, 7.542
- Pco₂ – 59.9, 64.9
- BE - +29.4
- HCO₃ – 55.3
- Na – 154.2
- K – 2.96
- Cl – 88 (85)
- Ca⁺⁺ - 3.70
- Mg ⁺⁺ - 0.81
- Glu – 366
- Lac 5.3
- Cr – 2.3

66943

Thelma's Beauty

- $SIDa = Na + K + Ca + Mg - Cl - Lac$
- $SIDa = 69$
 $BE = +29$
- $SIDe = 70$ (assuming $PO4 = 4.0$)
- $Osm = 335$ mOsm
- Low Ca^{++} , Mg^{++} , K

66943

Thelma's Beauty

- Rx

IV Norm R

MgSO₄ – 25 gm

Ca

K

- 0 hrs - 12 hrs – 36 hrs

pH - 7.570 => 7.492 => 7.432

Pco₂ - 59.9 => 56.9 => 40.2

BE - +28 => 18 => 3.1

Na - 154 => 158 => 137

K - 2.96 => 3.08 => 4.43

Cl - 85 => 106 => 99

Ca - 3.70 => 4.08 => 5.14

Mg - 0.81 => 0.79 => 1.00

SID - 69 => 56 => 45

mOsm - 334 => 328 => 267

Metabolic Acid/Base Abnormalities

Jon Palmer, VMD, DACVIM

Director of Neonatal/Perinatal Programs

Graham French Neonatal Section, Connelly Intensive Care Unit

New Bolton Center, University of Pennsylvania

Abnormal acid-base balance predicts the outcome of the case but often is not a direct cause the fatality, but rather it is an epiphenomenon. Acid base homeostasis is defended as much as O_2 transport and perfusion pressure. The concentration of H^+ in tissues is very small (only 1/1,000,000 of HCO_3^-) but very important because of its effect on H^+ bonds, protein configuration and binding and receptor activity.

Disorders of acid-base balance result from disorders of primary regulating organs (kidney or GI tract), exogenous drugs or fluids that alter the body's ability to maintain normal acid-base balance or abnormal metabolism that overwhelms the ability of the normal defense mechanisms to work.

The kidney excretes only small amounts of strong ions in the urine per minute (because most is reabsorbed) so the renal compensation for acid-base abnormalities takes hours. In the diet there are similar ratios of strong cations and anions. There's sufficient Cl^- available to filter. If it is not reabsorbed then there is an increase in SID. Cl^- excretion is the primary regulating mechanism of acid base balance by the kidney. Renal Na and K handling is influenced by priorities other than acid-base balance. The reason for kidney ammoniagenesis is to excrete Cl^- without Na^+ or K^+ as $Cl^- NH_4^+$. NH_4^+ is important not because the H^+ (< 0.01 mEq/liter) but because of its role in allowing Cl^- excretion.

The gastrointestinal tract is an important site for development of acid-base imbalance and may play a role in acid base regulation. Chloride transported from the gastric mucosa to the lumen results in a decrease in SID in the gastric juices making them acidic and simultaneously an increase in SID in the plasma resulting in the "alkaline tide" at the beginning of the meal. Reabsorption of chloride and the duodenum returns the SID in the plasma to its normal level. If gastric fluid is refluxed there's a loss of Cl^- resulting in alkalosis (increased SID). Pancreatic secretions have a increased SID because the low concentration of Cl^- resulting in a decrease in plasma SID during its formation which helps counter act alkaline tide. If pancreatic fluid is lost through reflux, the plasma remains acidotic (\downarrow SID secondary to $\uparrow Cl^-$). The small intestine is very efficient in absorbing Cl^- . This results in the colonic fluid having an increased SID because of the Na^+/K^+ left in lumen. Usually, Na^+ is absorbed primarily through the transport with VFAs with water following but if diarrhea occurs there will be loss of Na^+/K^+ relative to Cl^- resulting in a decreased plasma SID (acidosis). During SIRS, the GI tract may compensate for systemic acidosis by removal of anions resulting in an increased SID.

Critical neonates appear to have a tendency to develop acidosis in situations that would not result in acidosis in normal patients. This can be explained by the observation that they often have a low SID (30 rather than the usual 40 but without acidosis). This results in less reserved so that a smaller increase in acid or a smaller treatment with NaCl will have more effect and more easily result in a significant acidosis by further decreasing SID. This low resting SID is primarily secondary to a low resting albumin resulting in a decrease in A^- and the tendency not to decrease P_{CO_2} because of lack

of central receptor responsiveness to P_{CO_2} . The small effect of this decrease on pH has to do with the fact that decreases in SID does not result in linear decreases in plasma pH. As the SID < 20 there is a greater decrease in pH so that as SID approaches 20, a small insult may result in a dramatic decrease in pH.

Brief exposure to acidosis is tolerated well as with exercise, but chronic mild acidosis (pH < 7.33) can result in metabolic bone disease and protein catabolism. Critically ill patients do not tolerate acidosis well. The underlying cause of the acidosis is much more important than the degree of acidosis in determining the overall negative effect on the condition of the patient. In general, metabolic acidosis can cause decreased inotropy, conduction defects, arterial vasodilation, venous vasoconstriction, decreased oxyhemoglobin binding, decreased 2,3-DPG levels, respiratory depression, decreased sensorium, protein wasting, bone demineralization, insulin resistance, catecholamine stimulation, PTH stimulation, aldosterone stimulation, increased K, increased Ca and hyperuricemia. In general, metabolic alkalosis may cause increased inotropy (Ca⁺⁺ entry), altered coronary blood flow, increased oxyhemoglobin affinity, increased 2,3-DPG, neuromuscular excitability, encephalopathy, seizures, decreased K, decreased Ca, decreased PO₄⁻ and impaired enzyme function.

Lactic acidosis: In many critical patients, production of the strong ion lactate is an important to cause of acidosis. The origin of lactic acid has been often misinterpreted in the past. The availability of the ability to easily and repeatedly measure lactic acid levels has helped us understand its significance. Traditionally the amount of lactate produced has been linked to total O₂ debt, magnitude of hypoperfusion and severity of shock. However, it is now clear that there are a number of other underlying causes of increased lactate production and when these are ignored and attempts are made to treat increased lactate as hypoperfusion, to the exclusion of the other possible causes, poor outcomes can result.

Besides tissue hypoxia, hypodynamic shock and organ ischemia, high lactate levels will result from hypermetabolism as with increased aerobic glycolysis (from epinephrine), increased protein catabolism and increased muscle activity, decreased lactate clearance as with liver failure or shock, inhibition of pyruvate dehydrogenase as can occur in thiamine deficiency or SIRS and activation of inflammatory cells as with ARDS. So when lactic acidosis develops, the underlying cause must be identified, so that the underlying pathology can be addressed, since the cause of the lactate elevation is more important than the resulting acidosis. In most cases it appears that elevated aerobic metabolism is more important than metabolic defects (pyruvate dehydrogenase inhibition) or anaerobic metabolism in increasing lactate. Epinephrine, whether given exogenously or if stimulation results in endogenous increases, stimulates an increase in lactate levels by stimulating cellular metabolism (e.g. ↑hepatic glycolysis). This effect does not occur with dobutamine or norepinephrine and is not related to tissue perfusion.

Lactate is a strong ion because at physiologic pH it is completely disassociated. Since the body can produce and dispose of lactate rapidly, pH will quickly and sometimes drastically change as lactate levels increase and decrease changing SID. Hyperlactatemia can exist without acidosis. This will occur when lactate is administered as Na lactate. It will also occur when as lactate increases, another strong anion decreases. The corresponding strong ion is usually chloride. With sustained lactate production Cl⁻ moves out of plasma space maintaining a normalized pH.

The increase in lactate in sepsis is probably not a sign of tissue dysoxia, but rather a combination of factors. Metabolic dysfunction from mitochondrial/enzymatic dysfunction in sepsis will result in an increase in lactate levels (decreased pyruvate dehydrogenase activity). This results of an increased lactate production in sepsis secondary to increased aerobic metabolism (hypermetabolism). Epinephrine induced increase lactate production may so occur in sepsis and finally release of lactate during the development of ARDS may be an important source.

Hyperchloremic acidosis: Hyperchloremic acidosis occurs when there is an increased chloride relative to Na or a loss of cation relative to chloride. In response to acidosis from any cause, the kidneys will excrete chloride ion in the urine and take compensatory measure to increase the SID. When hyperchloremic acidosis occurs, even when the kidneys are not the source, the implication is that the kidneys are not responding appropriately and thus are somehow compromised. Hyperchloremic acidosis may arise from renal disease (renal tubular acidosis), treatment with chloride containing fluids (saline) or excessive GI loss of cations.

Unexplained (hyperchloremic) acidosis: Often as much as one-third of the acidosis is unexplained by lactic acidosis or hyperchloremia. This may occur because of partial loss of Donnan equilibrium of plasma. With severe capillary leak (or in the neonates with normal high capillary permeability and development of high capillary pressure) there will be a loss of albumin from the vascular space. To maintain charge balance Cl^- moves into the vascular space from the interstitium resulting in a hyperchloremic acidosis. Alternately, other cations may be present secondary to sepsis.

Metabolic alkalosis: Metabolic alkalosis occurs when there is an increase in SID from a loss of Cl^- , a decrease in unidentified anions or from an increase in cations (rare). Hypochloremic alkalosis is a common finding at birth in neonatal foals. The hyperchloremia is likely a compensatory change mediated through the placenta in the face of a more chronic intrauterine lactic acidosis. The lactic acidosis is probably cleared just before birth leaving the hypochloremic metabolic alkalosis. The hypochloremia may persist since renal regulation will not occur until the kidney has completed its transition from fetal physiology to neonatal physiology. After the birth transition, when alkalosis is from chloride loss in excess of Na, it may be chloride responsive or chloride resistant. Chloride responsive alkalosis frequently is from transient GI loss, post diuretic loss or post hypercapnia. In these cases treatment with chloride in the form of sodium chloride or potassium chloride and/or rehydration usually results in rapid correction of the alkalosis. Chloride resistant hypochloremic alkalosis is usually a result of ongoing loss from hormonal mechanisms and will only temporarily be corrected with chloride therapy.