Metabolic Acid-Base Abnormalities

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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

Ammoniagenesis

• Hepatic glutaminogenesis
  Stimulated by acidosis

• Nitrogen metabolism in liver
  → Urea, glutamine, (NH$_4^+$)
  Glutamine → kidney → ↑NH$_4^+$ → ↑Cl$^-$ excretion
  ↑Glutamine → alkalosis by ↓Cl$^-$ relative to Na$^+$

• Hepatocyte
  Cells with urea production capacity
  • Closer to portal vein
  • GI tract nitrogen → urea first
  Acidosis inhibits urea formation
  • N to glutamine producing cells → ↑Glutamine →
  • Kidney → NH$_4^+$ → ↑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
Low albumin $\rightarrow$ $\downarrow$ SID
Neonate $\uparrow$ PO$_4$ $\rightarrow$ $\uparrow$ SID

Cations

Anions

Na$^+$ $\downarrow$ SID
Cl$^-$ SID
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
Decrease SID
Metabolic Acidosis
Strong Ion Acidosis
Decrease SID

Strong Cations
↓Na⁺
SID
Strong Anions
Metabolic Acidosis
Increase in Unidentified Anions
SIG < 0

Strong Cations

\[ \text{SIG} < 0 \]

\[ \text{UA}^- \]

\[ \uparrow \text{UA}^- \]
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
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 → glycolysis → Pyruvate → Pyruvate dehydrogenase → Acetyl-CoA → OOA

Kreb’s Cycle: α-ketoglutarate → Isocitrate → Citrate → Glucose

Lactate ↔ Lactate ↔ Pyruvate
Glucose → glycolysis → pyruvate → pyruvate dehydrogenase → acetyl-CoA → Kreb’s Cycle

But ...

Lactate → lactate → Kreb’s Cycle

α-ketoglutarate → isocitrate → 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
  - $\uparrow\uparrow$ aerobic glycolysis $\rightarrow$ $\uparrow$ 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
  - $\uparrow$ activity $\text{Na}^+:\text{K}^+$ ATPase
    - $\uparrow$ lactate production
      - under well-oxygenated conditions
    - One cause of $\downarrow$ 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 (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 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
Strong Ion Acidosis
Strong Ion Acidosis

Hyperchloremic acidosis

• Hyperchloremic acidosis
  $\uparrow$Cl$^-$ relative to Na$^+$
  Loss of cation relative to Cl$^-$

• Renal response Acidosis
  $\uparrow$Cl$^-$ excretion in urine
  Kidney must be source of acidosis since
  • $\uparrow$plasma Cl$^-$ rather than $\downarrow$plasma Cl$^-$

• Extrarenal $\uparrow$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 $\text{NaCl} \rightarrow \uparrow \text{Cl}^-$ $\rightarrow \downarrow \text{SID}$
      - 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) + $\text{Cl}^-$
      - If acetate $<<$ $\text{Cl}^-$ 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 $\downarrow A_{\text{TOT}}$ ($\downarrow \text{albumin}$)
- Treated 5-10X plasma volume $\rightarrow$ significant acidosis
- Unlike normal patient treated with $\text{NaCl}$
ICU Patient – no urine output

<table>
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<tr>
<th></th>
<th>SID</th>
<th>pH</th>
<th>$\text{Pa}_{CO_2}$</th>
<th>BE</th>
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<tr>
<td><strong>Baseline</strong>*</td>
<td>30</td>
<td>7.40</td>
<td>38</td>
<td>-2.0</td>
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<tr>
<td><strong>Lactic Acidosis</strong></td>
<td>20</td>
<td>7.29</td>
<td>29</td>
<td>-11.4</td>
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<tr>
<td><strong>10 liters saline</strong></td>
<td>14</td>
<td>7.13</td>
<td>25</td>
<td>-20.1</td>
</tr>
</tbody>
</table>

* 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 acidic than explained by lactate level
- **Sepsis**
  Acidosis without ↑ lactate
  May be secondary to ↑ Cl⁻
  Unmeasured 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

↓H⁺
Strong Cations

SID

↓Cl⁻
Strong Anions
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

  - Cl⁻ loss > Na

  ↑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 $\rightarrow$ ↑aldosterone $\rightarrow$ ↑Na reabsorption
  But also ↑K and Cl⁻ loss $\rightarrow$ 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
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 Cl⁻ > 20 mmol/l
  Saline therapy may temporarily correct SID

• Ongoing renal loss results in return ↑ SID
  ↑ Mineralocorticoid activity
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
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
Abnormal acid-base balance predicts the outcome of the case but often is not a direct cause of the fatality, but rather it is an epiphenomenon. Acid base homeostasis is defended as much as O₂ transport and perfusion pressure. The concentration of H⁺ in tissues is very small (only 1/1,000,000 of HCO₃⁻) 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⁻ NH₄⁺. NH₄⁺ 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 acidic (↓SID secondary to ↑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 Pco₂ because of lack
of central receptor responsiveness to Pco₂. 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 has 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 in 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 normalize 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.