DRA. FLAMINIO JULIA

Electrolyte Balance in Horses
Management of the Foal Part I
Management of the Periparturient Mare
Muscle Diseases in Horses
4. DRA. FLAMINIO JULIA

4.1 ELECTROLYTE BALANCE IN HORSES

EXTRACELLULAR AND INTRACELLULAR FLUID SPACES

- Extracellular fluid space (ECF)
  - comprises 20-25% of body weight
  - consists of interstitial fluid space (ISF = 20% body weight) and blood plasma (5% body weight)
- Intracellular fluid space (ICF)
  - comprises 75-80% body weight

ACID-BASE BALANCE

- electroneutrality principle = sum of all cations equals the sum of all anions = neutral blood pH (7.35-7.45)
  - \([\text{Na}^+] - [\text{Cl}^-] + [\text{H}^+] - [\text{OH}^-]=0\)
  - difference between strong cations (\(\text{Na}^+\)) and the strong anions (\(\text{Cl}^-\)) = Strong Ion Difference [SID]
- water dissociates into hydrogen ions and hydroxyl ions
  - \([\text{H}^+] = [\text{OH}^-]\) = neutral pH
  - \([\text{H}^+] > [\text{OH}^-]\) = acidosis
  - \([\text{H}^+] < [\text{OH}^-]\) = alkalosis
- strong cations: \(\text{Na}^+, \text{K}^+, \text{Ca}^{++}, \text{Mg}^{++}\)
- strong anions: \(\text{Cl}^-, \text{HCO}_3^-, \text{SO}_4^{--}\)
- weak acids = plasma proteins and phosphates
• production of lactate ions under hypoxic conditions leads to lower strong ion difference (SID) and high [H+] (lower pH)

• acidosis
  o metabolic = excess acid production (anaerobic metabolism = lactic acid) or loss of bicarbonate from the blood (into intestinal tract or through kidneys)
  o respiratory = accumulation of carbon dioxide [poor lung ventilation (inadequate CO₂ excretion) or excess CO₂ production]
    ▪ PaCO₂ > 45 mmHg

• alkalosis
  o metabolic = excess loss of hydrogen ions (gastric secretions) or excess of bicarbonate in the blood (chloride losses in intestines or through kidneys)
    ▪ respiratory = low level of carbon dioxide (hyperventilation)
      ▪ PaCO₂ < 34 mmHg

• compensation to maintain blood pH neutral
  o chemical buffering (immediate response)
  o respiratory compensation: hyper or hypoventilation (fast response)
  o renal compensation: alter amount of bicarbonate absorption or excretion (delayed response)

• base excess = amount of acid required to restore 1 L of blood to its normal pH, at a PCO₂ 40mmHg
  o metabolic alkalosis = acid needs to be added to return the blood pH to normal = positive base excess
  o metabolic acidosis = acid needs to be removed to return blood pH to normal = negative base excess

ELECTROLYTES
SODIUM

• hyponatremia is often a consequence of
  o diarrhea or renal failure
  o retained in intestinal lumen (bowel obstruction)
  o vasopressin effect released during colic = free water retention
  o hyperglycemia = glucose acts as an osmotic agent, expanding the extra-cellular space
  o iatrogenic = water without electrolytes offered or administrated via nasogastric intubation

• correction of hyponatremia
  o intravenous fluid therapy
sodium chloride is the best choice, if the plasma chloride concentration is also low
sodium bicarbonate can be used when hyponatremia and hyperchloremia
rapid correction of sodium deficits = demyelination of the pontine and extra pontine neurons
- sodium should be corrected at a rate of 1 mEq/L/h in acute hyponatremia (less than 48hrs)
- less than 0.5 mEq/l/h in chronic hyponatremia (more than 48hrs)
- do not exceed 8 mEq/l during the first 24 hours in any condition
  - oral fluid therapy (free choice or via nasogastric tube)
    - electrolyte-supplemented water = isotonic or slightly hypotonic
    - hyponatremia and hypochloremia = 20 to 30ml of table salt in 4 L of water
    - hyponatremia without hypochloremia = 10ml of table salt in 4 L of water
- hypernatremia may be a consequence of
  - water deprivation or excessive sodium administration (table salt, sodium bicarbonate)
  - renal failure and diuresis
  - causes hypertonicity, hyperosmolality and cellular dehydration
- correction of hypernatremia
  - intravenous fluid therapy
    - low sodium fluids = 0.45% sodium chloride
    - sodium should be corrected at a rate of 0.5 mEq/l/h
    - do not exceed 12 mEq/l in the first 24 hours

CHLORIDE

- major anion in the extracellular fluid; hence, important in maintaining acid-base balance
- hypochloremia is observed in
  - diarrhea
  - excessive sweat
  - high volume gastric reflux
  - metabolic alkalosis
  - renal failure
  - hypomagnesaemia
- correction of hypochloremia
  - intravenous fluid therapy
    - 0.9% sodium chloride
  - oral fluid therapy
- hyponatremia and hypochloremia = 20 to 30ml of table salt in 4 L of water

- **hyperchloremia**
  - water loss (hypernatremia)
  - metabolic compensation for bicarbonate loss (respiratory alkalosis or renal tubular acidosis)
  - correction of hyperchloremia
    - intravenous fluid therapy
      - when accompanied by hypernatremia = 0.45% sodium chloride

**POTASSIUM**

- major intracellular cation
- **hypokalemia** is common in horses following
  - inappetence or dietary restrictions
  - colic surgery = enhanced mineralocorticoid and glucocorticoid release
  - infusion of large amounts of sodium-containing fluids = increase renal distal tubular potassium loss (kaliuresis)
  - potassium losses in diarrhea
  - hypomagnesemia
- consequences: muscle weakness, lethargy and inability to concentrate urine
- correction of hypokalemia
  - intravenous fluid therapy
    - infused at a maximum rate of 0.5 mEq/kg/hr (use 20 mEq/L KCl in fluid)
  - oral fluid therapy
    - dose 0.1 to 0.2g/kg
- **hyperkalemia** can be observed in
  - metabolic acidosis (diarrhea) = potassium exchange for hydrogen ions across cell membranes
  - uroperitoneum
  - kidney failure
  - muscle damage
- correction of hyperkalemia
  - mild hyperkalemia = physiologic saline
  - plasma potassium > 6 mEq/L = 5% dextrose solution or 2 ml/kg intravenously over 5 minutes; or sodium bicarbonate (1-2 mEq/L intravenously over 15 minutes)

**CALCIUM**

- participates in muscle (cardiac and skeletal) contraction, maintenance of vascular tone, neuromuscular transmission, enzyme activity
- ionized calcium better estimates plasma values
- **hypocalcemia** is observed in
  - lactic acidosis
  - excessive sweating
  - small intestine poor absorption
  - hypomagnesemia
- clinical signs of hypocalcemia = synchronous diaphragmatic flutter, tetany, muscle spasm and seizures
- correction of hypocalcemia
  - intravenous fluid therapy
    - 0.2-1.0 ml/kg of the 20 or 23% calcium borogluconate solution diluted in crystalloid fluids
    - do not be mixed with sodium bicarbonate because it promotes precipitation
- **hypercalcemia** is rare in horses
  - may occur in hyperparathyroidism and cancer
  - vitamin D intoxication
  - acidosis increases ionized calcium = displaced from protein bound sites by hydrogen ions

**MAGNESIUM**

- function in energy (ATP) production, resting membrane potential and enzymatic reaction
- **hypomagnesemia**
  - decreased intake (inappetence) or absorption = cannot be readily mobilized
  - gastrointestinal losses (prolonged nasogastric reflux)
  - renal losses, hypophosphatemia, acidemia, renal tubular acidosis
  - excessive sweating
  - can also result in refractory hypokalemia and hypocalcemia
  - causes membrane destabilization and hyperexcitability, ventricular arrhythmias, muscle tremors, ataxia, seizures
- correction of hypomagnesemia
  - intravenous fluid therapy
    - magnesium sulfate at 2 mg/kg/min (do not to exceed 50 mg/kg)
  - oral supplementation
  - magnesium-lactate-citrate or magnesium oxide (dose of 4-16 mg/kg/day); avoid magnesium sulfate = laxative
- **hypermagnesemia**
  - antagonizes the effects of calcium at the neuromuscular junction = sweating, flaccid paralysis, coma and recumbency (blockade of peripheral neuromuscular transmission)
  - iatrogenic hypermagnesemia = excessive magnesium sulfate (> 1 g/kg orally)
- correction of hypermagnesemia
  - intravenous fluid therapy
    - 250 ml of 23% calcium gluconate solution, repeated after 1 hour, followed by crystalloid fluids for diuresis

**GOALS OF FLUID THERAPY**

1. Replace lost fluids and electrolytes, and correct acid-base imbalances
   - examples are diarrhea, hyperkalemia in uroperitoneum, renal failure, metabolic acidosis associated with high lactate or hyponatremia/hyperchloremia
2. Provide maintenance daily needs to patients that cannot drink on their own
   - adult horses 60ml/kg/day
   - neonatal foals 3-5 ml/kg/h
3. Provide immediate replacement of on-going fluid and electrolyte losses
   - gastric reflux, diarrhea (200 mL/kg/day!), hyperhidrosis, and polyuria.
4. Maintain blood pressure and oncotic pressure
   - in addition to fluid losses, systemic diseases [systemic inflammatory response syndromes (SIRS) in endotoxemia and sepsis] increase vascular permeability, reduced vascular responsiveness, and cause myocardial depression, leading to hypotension, hypoperfusion and edema
   - oncotic pressure = plasma colloid osmotic pressure (COP) is the osmolarity generated by proteins unable to cross capillary membrane
     - albumin is responsible for 60-80% of plasma COP
       - reduced oncotic pressure due to albumin losses in the intestinal tract (diarrhea) or kidneys (glomerulonephritis)
     - COP can be measured by an osmometer, and should be maintained above 14 mm Hg when fluid therapy is in place
       - colloid osmotic pressure in healthy neonatal foals is between 15-23 mmHg
       - colloid osmotic pressure in normal adult horses is between 20-30 mmHg

**DEHYDRATION – HYPOVOLEMIA and HYPOTENSION**

- diagnosis of dehydration
  - physical examination
    - tachycardia, prolonged capillary refill time, slow jugular fill, reduced skin turgor, tacky mucous
membranes, poor pulse quality, cold extremities, low urine production with high specific gravity
  - low central venous pressures, hypotension
    - blood work
      - high hematocrit and total protein (careful with underlying anemia and hypoproteinemia), high lactate, metabolic acidosis (high anion gap, base deficit)

| TOTAL BODY WATER (L) = 0.6 x kg body weight |
| TOTAL BODY BLOOD (L) = 0.08 x kg body weight |
| EXTRACELLULAR FLUID VOLUME (L) = 0.20 x kg body weight |
| WATER DEFICIT (L) = 1 – Na<sub>desired</sub> / Na<sub>patient</sub> x normal total body water (L) |
| ELECTROLYTE (E) DEFICIT = (E<sub>desired</sub> – E<sub>patient</sub>) x 0.3 x kg body weight |
| SODIUM CORRECTION RATE = 0.5 mEq/hr |

**PRINCIPLES OF FLUID THERAPY**

- evaluate patient’s problems
  - degree of dehydration and electrolyte abnormalities
  - cause of fluid loss
  - hypoproteinemia (reduced oncotic pressure)
- evaluate patient’s needs
  - rapid correction due to hypovolemic shock
    - 10-20 ml/kg boluses with frequent reassessments
  - slow correction
    - calculate deficit and replace over a few to several hours
  - monitor blood parameters periodically determine changes in fluid composition and rate
- choice of fluid therapy
  - crystalloid fluids
    - replaces fluid volume
    - have a dilutional factor when plasma protein concentration is low (edema)
  - colloid
    - replaces volume and oncotic pressure
- evaluate kidney function and production of urine
  - severe dehydration can lead to renal failure, and fluid therapy is challenged when oliguria and anuria are present
CRYSTALLOID FLUIDS:

- Electrolyte solutions that distribute to all fluid compartments (intravascular, transcellular, and interstitial spaces), and only 25% of volume remains in the intravascular space.
- **Balanced crystalloids** have similar composition to extracellular fluid (ECF) = Lactate Ringer’s Solution, Plasma-Lyte 148
  - Replacement fluids are isotonic to ECF and distribute among the ECF compartments; used for rehydration.
- **Unbalanced crystalloids** have different composition from ECF = physiologic saline
  - Maintenance fluids are hypotonic (low sodium, high potassium = source of free water) relative to ECF, and distribute into both the ECF and ICF compartments; they may need electrolyte supplementation according to individual cases.
- Fluid therapy should be monitored frequently, and changes pursued based on:
  - Physical examination
    - Heart rate and respiratory rate
    - Difficulty breathing (pulmonary edema)
    - Urine production and specific gravity (renal failure)
    - Edema formation
    - Excessive weight gain
  - Blood work
    - Hematocrit and total protein (albumin)
    - Electrolytes
    - Glucose
    - Creatinine
    - Blood gas-analysis
    - Plasma lactate and PvO₂ as markers of peripheral perfusion
    - Central venous pressure and blood pressure
    - Plasma osmolarity

Sodium chloride (0.9% NaCl):

- Unbalanced isotonic fluid containing sodium (154 mEq/L) and chloride (154 mEq/L) ions
  - Sodium to chloride ratio (1:1) is different compared to that of plasma (130-140 mEq/L sodium and 90-101 mEq/L of chloride)
  - Causes relative increase in chloride and consequently mild acidosis (increase in Cl⁻, decrease in HCO₃⁻)
  - Monitor hypernatremia, hypokalemia, metabolic acidosis and hyperosmolarity (contraction of the ICF)
- Can be used in primary metabolic alkalosis (high HCO₃⁻), hyperkalemia, and for slow correction of sodium imbalances.
Hypertonic saline (7-7.5% NaCl):

- unbalanced solution promotes rapid expansion of circulatory volume in severe dehydration
  - raises plasma osmolarity, and promotes the shifting of interstitial and cellular fluids into the intravascular space
  - increases myocardial contractility
  - promotes vasodilation
- dose: 2-4 ml/kg or 1-2L IV bolus/adult horse, followed by crystalloid fluids
- preexisting hypernatremia or hyperosmolarity, hypokalemia, and uncontrolled hemorrhage.

Lactated Ringer’s Solution (LRS):

- balanced polyionic fluid containing sodium (130 mEq/L) and chloride (109 mEq/L)
  - sodium concentration is in the low end of plasma values, whereas chloride concentration is higher
  - not indicated in hyperchloremic acidosis
- also contains sodium lactate (28 mEq/L)
  - metabolized to glucose (gluconeogenesis) with a minor alkalinizing effect
  - not indicated in liver disease
  - not indicated in alkalosis
  - not indicate din hyperkalemia
- the calcium in LRS precipitates with anticoagulants in commercial plasma and bicarbonate; therefore do not mix the same fluid lines

Isotonic bicarbonate (1.25%):

- 150 mEq of sodium bicarbonate (150 mEq of sodium, 150 mEq of bicarbonate) per liter of sterile water
- indicated in metabolic acidosis (diarrhea) and hyperkalemia (uroperitoneum, muscle damage)
  - first replace fluid deficits, which may cause metabolic acidosis and retest blood bicarbonate levels
  - estimate bicarbonate deficit after hydration \[((\text{HCO}_3^{\text{desired}} - \text{HCO}_3^{\text{patient}}) \times 0.3 \times \text{kg body weight})\]
    - give half of the deficit in 2 hours, and the other half in several hours
    - monitor for hypokalemia, hypocalcemia, hypernatremia, metabolic alkalosis and during supplementation
- not indicated in severe respiratory and hypoventilation
$\text{HCO}_3^- + H^+ \Rightarrow \text{H}_2\text{CO}_3 \Rightarrow \text{CO}_2 + \text{H}_2\text{O}$ (because it further increases PaCO$_2$)

**Dextrose containing fluids (2.5%-5% solutions):**

- source of energy and free water in critically ill patients:
  - neonatal foals, gravid mares, horses at risk for hyperlipidemia/lipemia, and those with poor body condition scores
  - monitor glucose levels periodically to adjust therapy
- D5W also provides 170 kcal/L of digestible energy and it is isotonic (252 mOsm/L)
- can be combined with replacement crystalloids for maintenance fluids:
  - 2/3 as 5% dextrose in water (D5W) and 1/3 as the replacement fluid

**0.45% sodium chloride and 2.5% dextrose in water**

- isotonic (280 mOsm/L), crystalloid ½ strength saline and ½ strength dextrose
  - also source of free water
- sodium: chloride ratio 1:1
- indicated in hyperkalemia

**COLLOIDS**

- colloids are fluids that contain large molecular weight particles, which promote water retention
  - remain primarily within the intravascular space
  - recover intravascular volume rapidly and efficiently
  - they do not provide free water
- indicated in low oncotic pressure (hypoproteinemia or edema)
- good combination with crystalloid fluids
- not indicated when there is vascular permeability (pulmonary edema)
- during colloid administration, monitor
  - total protein/albumin (does not measure synthetic colloids)
  - colloid osmotic pressure (direct osmometry measures synthetic colloids)
  - clotting times and platelet counts

**Plasma Products**

- fresh or fresh frozen plasma
• rich in albumin, clotting factors, antithrombin and immunoglobulin/opsonins
  
  **ALBUMIN (ALB) DEFICIT =** \(10 \times (\text{ALB desired} - \text{ALB patient}) \times \text{kg body weight} \times 0.3\)

• expensive
  o may require combination with synthetic colloids

**Whole blood**

• indicated in hemorrhagic shock and severe anemia
• mild effect on oncotic pressure
• may induce transfusion reactions and hypocalcemia (citrate toxicity)
• collect blood in citrate (CPDA) plastic bags (do not use glassbottles for platelet-rich plasma)
• use independent transfusion line (do not mix with calcium solutions) with filter

**BLOOD TRANSFUSION VOLUME (L) =** \(\frac{\text{Hematocrit desired} - \text{Hematocrit patient} \times 0.01}{\text{Hematocrit donor}}\)

**Hydroxyethyl starch**

• available as a 6% aqueous solution in saline (Hetastarch, COP = 30 mmHg) or a lactated electrolyte solution (Hextend, Abbott Laboratories, North Chicago, IL)
• more cost-effective for colloid replacement per unit volume than plasma
  o adult horses are up to 8-10 ml/kg/day or slow continuous infusion (0.5-1 ml/kg/h, up to 10 ml/kg/day)
  o foals 3-5 ml/kg in addition to crystalloids (avoid prolonged use)
• side effects reduction in coagulation factors VIII and von Willebrand’s factor, platelet counts and function
  o not indicated in horses with coagulopathies and thrombocytopenia

**Dextrans**

• 6% solution (6% Gentran 70, COP = 60 mmHg; Baxter Healthcare Corp., Deerfield, IL)
  o glucose polymers produced by the bacterium *Leuconostoc mesenteroides*
  o comparable to hetastarch in number of larger molecules retained in the vascular compartment
• more common allergic reactions and coagulation disturbances
• interfere with crossmatching of blood products (adherence to erythrocyte membranes causes clumping)
• less indicated for use in horses

**Hemoglobin-based products**

• polymerized bovine hemoglobin product (Oxyglobin, COP = 42.6 +/- 0.9 torr, Biopure, Cambridge, MA)
• dose: 15-20 ml/kg
• potent colloid
• also increases oxygen carrying capacity (advantage in anemia, hypotension and ischemia)
• long shelf life at room temperature
• side effects
  o discoloration of mucous membranes and body fluids
  o interference with biochemical and hematocrit analyses
  o antagonizes nitric oxide (vasodilator)
  o expensive

**4.2 MANAGEMENT OF THE FOAL PART I**

**FETAL CIRCULATION and RESPIRATION**

• the fetus receives oxygenated blood (approximately 80% saturated O₂) via the **umbilical vein**

• the **ductus venosus** diverts 2/3 of this blood into the **caudal vena cava**

• the remaining 1/3 mixes with the **portal blood** of the fetus

• most of the blood entering the heart from the caudal vena cava goes to the **left atrium** through the **foramen ovale**, then to the **left ventricle**

• most of the blood from the **cranial vena cava** enters the **right atrium**, then to **right ventricle**, and progresses to the **pulmonary artery**

• because of the collapsed lungs (high pressure = high resistance), the blood follows through the **ductus arteriosus** to the **aorta**
  o the blood from the left ventricle goes to the aorta and carotida (head)
  o the blood from the right ventricle goes to the aorta and caudal body

• some of the blood is sent through the **umbilical arteries** back to the **placenta**
• during fetal life, the lungs are filled with fluid, which is expelled upon chest compressions in the birth canal; in addition, part of the fluid is reabsorbed in the alveoli

• to compensate the low O₂ saturation of the maternal blood, the fetal red cells have a greater O₂ affinity than adult red cells (different hemoglobin) and they carry O₂ more efficiently

NEWBORN CIRCULATION and RESPIRATION

• at birth, the placenta circulation is cut off when umbilicus ruptures

• ductus venosus is closed passively because of blood flow from umbilical vein ceases

• peripheral resistance rises and contributes to the increase in the pressure in aorta until it exceeds that in pulmonary artery

• the venous blood enters the right atrium, right ventricle, pulmonary artery

• the lack of maternal blood flow causes asphyxia, which induces gasping and breathing = lung expansion (facilitated by the negative intrapleural pressure created during the passage in the birth canal)

• surfactant within alveolus decreases surface tension and avoids alveoli collapse at the end of expiration

• once lungs are expanded, the vascular pulmonary resistance falls and facilitates pulmonary blood flow

• blood returns from the lungs to the left atrium and increases its pressure = closure of foramen ovale (pressure in left atrium becomes larger than right atrium)

• ductus arteriosus constricts because of the rise in arterial P0₂ after birth and because of the metabolization of the vasodilators prostacyclin and prostaglandin E in the lungs

• (OBS: prostaglandins and thromboxane are involved in pulmonary vascular regulation and maintaining ductal patency. Therefore, the use of anti-inflammatories during pregnancy inhibits prostaglandin synthesis in the fetus; the consequence is constriction of the ductus arteriosus before birth, primary hypertension, with pulmonary artery smooth muscle thickness and pulmonary artery hypertension).
GENERAL CARE AND MONITORING OF THE NEWBORN

PHYSIOLOGICAL PARAMETERS

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PREMATURITY, IMMATURITY AND DYSMATURITY

• PREMATURE NEONATE:
  • underweight, weak newborn with gestation shorter than normal
  • short, silky haircoat, doomed forehead, floppy/pliant ears, deep red tongue
  • diminished suckle reflex = risk of failure of passive transfer and septicemia
  • hypotonic muscles, flexor tendon laxity, incomplete ossification (carpi, tarsi); retention of toe caps on hooves (eponychium)
  • poor thermoregulation (hypothermia)
  • dysphagia, underdeveloped GI tract, inability to digest (diarrhea)
  • reduced collagen synthesis = weakened structure of vessels (CNS hemorrhage)
  • lung immaturity (lung atelectasia + pulmonary edema = respiratory distress)
  • ineffective reflex control of breathing
  • persistent fetal circulation, low PaO2, high PaCO2, low pH
  • anemia, neutropenia
  • azotemia, hypoglycemia, low cortisol level and poor response to ACTH

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• **causes:**
  - placental abnormalities (placentitis, hydroallantois)
  - twinning, congenital abnormalities
  - maternal illness (debilitation, endotoxemia, viral disease), drug therapy

• **IMMATURE NEONATE:** newborn with signs of prematurity but with normal gestation length

• **DYSMATURITY:** immature neonate with signs of placentitis or amnionitis

• **INTRAUTERINE GROWTH RETARDATION (IGR):**
  - slowed development due chronic uterine problems
    - symmetrical = all parts of the body are proportionally reduced in size
    - asymmetrical = large head, small body size = preservation of brain and bone growth

**CIRCULATORY SYSTEM:**

a) **mucous membrane color** should be pink and capillary refill time < 2 sec
   a.1) icterus could be associated with septicemia, EHV-1 infection (foal), or neonatal isoerythrolysis (foal)
   b.1) bright red – endotoxemia
   c.1) dark – shock
   d.1) purple – cyanosis (severe heart defect, severe pneumonia)

b) **cold extremities** (ears, limbs) may indicate dehydration, hypotension, hypothermia

c) physiological **sinus arrhythmias** and atrial premature contractions may be detected due to high vagal tone and asphyxia in the initial 15 min of life;

d) physiological **heart murmurs**: systolic continuous (holosystolic) murmur at the left 3rd intercostal space [patent ductus arteriosus (PDA)] with normal pulse quality, no thrill, no diastolic component;

e) **right-sided murmurs** with thrill: ventricular septum defect (VSD), Tetralogy of Fallot – confirm with echocardiogram

**RESPIRATORY SYSTEM:**

a) the **lungs** in the newborn foal are often clear; crackles and wheezes may be heard in the first few hours if C-section took place

b) observe abnormal **respiratory pattern**: flared nostrils, anxiety, excessive abdominal component (slight abdominal movement during expiration is normal), periodic apnea (abnormal neurologic stimulus), cyanosis, high PaCO$_2$, low PaO$_2$
c) check for rib fractures: shallow, frequent breathing, reluctance to move and stand up/lay down; check for hemothorax and lung laceration

URINARY SYSTEM:

a) the newborn starts to urinate within 8 to 10 hours after birth, and the frequency and amount of urination is proportional to the amount of milk nursed (normal production: foals 5-7 L/day; abnormal production if < 1ml/kg/hr)
b) the specific gravity of urine in newborns is often low [hyposthenuric to isostenuric]; therefore, it is a good indicator of milk intake and hydration status
c) serum creatinine levels may be slightly elevated soon after birth, but levels above 2.5 mg/dL may indicate placentitis, pre-renal or renal azotemia;
d) dark urine = myoglobinuria (white muscle disease) or hemoglobinuria (neonatal isoerythrolysis)
e) bladder or intra-abdominal urachus rupture that may happen during birth (bladder compression in the mare’s pelvic canal) or in septic foals (infectious/necrotic cystitis or urachitis); be careful when assisting foals to get up not to compress abdomen/bladder

- abnormal pattern of urine flow (small, frequent amounts of urine, straining to urinate, oliguria, or sometimes there are no evident urinary clinical signs until lethargy, depression, and mild colic appear
- abdominal distention = uroperitoneum, ventral edema, preputial edema, vulvar edema
- blood chemistry: hyponatremia, hypochloremia, hyperkalemia because urine is rich in K+, which is reabsorbed from peritoneal cavity; azotemia, mild metabolic acidosis; creatinine concentration in abdominal fluid is at least 2 times higher than serum
- abdominal ultrasound = excessive fluid in the abdomen
- treatment: although the treatment is surgical (cystorrhaphy), it is a metabolic emergency, not a surgical emergency
  - correction of poor effective circulating volume, electrolyte imbalances, azotemia and abdominal distention
  - fluid therapy: 5% dextrose or 1.3% bicarbonate therapy if metabolic acidosis and hyperkalemia do not correct with 5% dextrose fluid therapy
  - slow drainage of abdominal fluid (use foley catheter or teat cannula)
UMBILICUS:

a) 5-10 min after birth, there is a natural constriction of the umbilical structures about 1 inch from the abdominal wall; when the mare stands, the umbilicus ruptures at this site; if you have to intervene, never cut the umbilicus with blade or scissors; instead, hold the umbilicus tightly about 1 inch from the abdominal wall with one hand, and stretch the other end until it breaks;  
b) the umbilicus is a potential venue of entry for pathogens that cause septicemia; therefore, dip umbilicus at least 3 times in a 5% tincture iodide solution (be careful not to soak the abdominal wall with iodide) or 0.5% chlorhexidine solution in the first 18-24 hours of life;  
c) the umbilical structures in the neonate are:
- **1 urachus** = in the fetus, connects the urinary bladder with the allantois; retracts and atrophies after birth  
- **2 umbilical arteries** = carry blood from the fetus to the placenta; atrophy after birth and form the round ligaments of the bladder  
- **1 umbilical vein** = carries blood from the placenta to the fetus liver; atrophies after birth and forms the round ligament of the liver along the edge of the falciform ligament  
d) if there is excessive bleeding after the umbilical rupture, ligate the umbilical artery;  
e) patent urachus may be managed with cauterization using silver nitrate, or surgical excision of the umbilical structures;  
f) monitor umbilicus for swelling, discharge, and hernia; abscesses associated with the umbilical structures may be present in the abdominal cavity without any signs in the exterior portion of the umbilicus, including infection of umbilical arteries and umbilical vein (liver abscessation); therefore, ultrasound of the umbilical structures should be performed in foals with known septicemia, fever, neutrophilia and hyperfibrinogenemia.

GASTROINTESTINAL SYSTEM:

a) **meconium** consists of digested amniotic fluid, glandular secretions, cellular debris and bile; meconium feces are **dark colored**, tarry consistency;  
b) **meconium staining** at birth = fetal distress, possible meconium aspiration = blockage of nasal passages and pneumonia;  
c) the newborn defecates a few hours after birth (often after nursing!), and all the meconium may be passed by 18-24 hours after birth (‘milk’ feces are yellow, pasty consistency);  
d) **meconium retention/impaction** = abdominal distention, restlessness, straining to defecate (tenesmus, tail flagging), colic,
decreased nursing; dry fecal balls in small colon and/or rectum identified by digital rectum examination;
e) **abdominal radiographs and ultrasound**: intestinal distention cranially to the impaction site; barium enema demonstrates firm ingesta within the pelvic inlet

f) **nasal regurgitation of milk**: abnormal backward flow of milk from the nares with origin from the oropharynx, nasopharynx, esophagus/stomach
   - primary consequence: aspiration pneumonia
   - diagnostics: endoscopy and radiography
   - **causes (congenital or acquired)**:
     - physical obstruction or anatomical abnormality: cleft palate, subepiglottic or pharyngeal cysts, esophageal stenosis/atrophia/ulcer
     - functional abnormality: pharyngeal dysfunction (neural lesion/compression, muscle weakness due to nutrition myodegeneration)

g) **congenital diseases**:
   - **atresia coli or ani** should be considered if colic and lack of defecation (anal atresia may be associated with rectovaginal or rectourethral fistulas) = require surgical treatment
   - **Overo Lethal White Syndrome** = offsprings that have predominantly white hair, and that are the product of the mating of overo sire x overo dam may have absence of myenteric ganglia (ileocolonic aganglionosis) in the ileum, cecum and colon = no gut development = no defecation, intestinal distention, colic within 48h of life = no treatment available; **autosomal recessive trait** that can be tested for carriers at the University of Minnesota Advanced Genetic Analysis Center

**MUSCULOSKELETAL SYSTEM:**

a) neonates may have **limb deformities** that correct over time, but assistance may be necessary to avoid injury
b) **flexural deformities**: tendon laxity may require heel extensions, whereas flexor tendon contraction may require bandaging, splints, or intravenous oxytetracycline (3g in 500 ml saline IV in the absence of kidney disease), lower the heel, toe extension, desmotomy or tenotomy in severe cases
c) **angular limb deformities = valgus or varus** = may involve the carpal, intracural, intertarsal, metacarpo-or metatarso-phalangeal joints; they can be a consequence of prematurity, incomplete ossification, nutritional imbalance, abnormal loading of physis, or trauma; treatment is accomplished with walking splints, casts, corrective trimming, shoeing, periosteal stripping [by 3 weeks of age if metacarpo- metatarso-phalangeal joint is involved; by 6 weeks of
age, if the carpus or tarsocrural/intertarsal joints are involved], and growth retardation/acceleration procedures
d) **incomplete ossification** in premature foals may be confirmed by radiographs of carpi and tarsi = these foals require stall confinement to prevent angular deformities
e) **arthritis or (poly)synovitis** accompanied by lameness, joint effusion, heat and lameness = signs of infection (septicemia) = collect synovial sample for analysis (increased neutrophils and protein) and culture; take radiographs to investigate osteolysis; flush joints; local and systemic antibiotics, arthrotomy
f) **white muscle disease** or nutritional myopathy due to selenium and/or vit E deficiency:
stiff gait, weakness, swollen/firm muscles, dysphagia or nasal milk reflex, respiratory distress (poor ventilation), myoglobinuria, hyperkalemia (release of K from muscle cells), high CK and AST (when chronic) enzymes = administer vit E/Se intramuscularly prophylactically at birth; supportive treatment may include fluid therapy to avoid kidney disease and to correct electrolyte imbalances, and nasogastric administration of milk to avoid milk aspiration
g) prolonged recumbency may cause **decubital ulcers**; therefore, provide well padded area and frequent turning

**IMMUNE SYSTEM:**
a) equine, bovine and camelid **placentas** do not allow passage of **immunoglobulins** during fetal life; therefore, ingestion of **colostrum** in the first few hours of life is essential for absorption of maternally-derived immunoglobulins;
b) **colostrum**: first milk = thick, yellow-gray milk, **concentrates immunoglobulins** for systemic (IgG and IgM) and mucosal (IgA) protection; good quality colostrum has IgG > 3,000 mg/dL , which is measured in practice by its specific gravity (SG) > 1.060; IgG concentration in colostrum decreases within 4 hours post-partum; colostrum has IgG> IgM> IgA; milk has IgA>IgG >IgM = mucosal protection; in addition, provides energy requirements, **complement** and **lactoferrin**
c) absorption capacity of large proteins, such as immunoglobulins, through the intestinal mucosa decreases by 12 hours and it is abrogated by 24 hours of life!
d) **failure of passive transfer** = failure to receive and/or absorb adequate levels of immunoglobulins; serum IgG concentration **less than 800 mg/dL** after 18-24 hours of birth characterize this failure;
**factors involved**: premature lactation of the mare = dripping milk days before parturition; inadequate colostrum production or quality; delayed onset of suckling (weak foal, sick foal); immaturity of GI tract or enteritis (poor absorption of Ig); intestinal absorption of Ig peaks at 8 hrs, and decreases progressively by 24 hours
• foals: check for immunoglobulin IgG levels (enzyme immunoassay SNAP-Test®, Idexx) 8-12 hours after ingestion of colostrum
  • IgG > 800 mg/dL = adequate passive transfer
  • IgG < 800 mg/dL, less than 12 hours of life and reasonable GI function = administered 500ml-1L of colostrum by nasoesophageal tube and recheck IgG in 2 hours
  • IgG < 800 mg/dL, more than 18 hours of life and/or poor GI function = administered 20ml/kg BW hyperimmune plasma intravenously (use plasma/blood transfer sets); recheck IgG levels in 2-4 hours

NEONATAL ISOERYTHROLYSIS

a) anemia caused by antibodies against the red cells of the foal
b) the antibodies are absorbed through the colostrum
c) the antibodies are produced by the dam during gestation
d) the foal must have inherited antigenic blood factors from the sire that are not common to that dam’s
e) if the mare gets exposed to the fetus blood during foaling, she produces antibodies against these factors;

f) antibodies are produced but peak production is only achieved about 9 days after foaling; therefore, antibodies do not reach the colostrum produced within the 12 hours after birth of that pregnancy, and the foal will not be affected
g) in the following pregnancy, the mare will transfer to the colostrum high levels of antibodies against the blood factors that she has been sensitized
h) if the foal expresses the incompatible blood factors, those maternal antibodies will lyse the foal’s red cells
i) therefore, neonatal isoerythrolysis is a risk in multiparous pregnancies but not in the first pregnancy; however, a mare that had blood transfusion in life before her reproductive phase could have been sensitized with incompatible blood factors, and she will transfer antibodies in the colostrum in her first pregnancy
j) the blood groups associated with NI are Aa and Qa (among dozens of blood groups!) because they are the most antigenic ones; Ca antibodies are not a problem but can cause false positive reactions

TESTING and PREVENTION:

blood factor assays – test for the presence or absence of factors Aa and Qa on the red cells of the dam and sire any time before breeding
• if the dam does not have factors Aa or Qa, she is at risk of producing NI-causing antibodies, and she needs to be tested for antibodies before foaling
• if the dam is positive for one of the blood groups, there is no risk for that specific blood group
• if the sire is negative for the blood groups, there is no risk
• the mare’s serum can be cross-matched with the sire’s red cells: a negative reaction indicates no risk for the foal; a positive reaction indicates a 50% risk of NI, and a cross-matching test should be done at foaling or colostrum withheld

**hemolytic assays** – test for antibodies against the blood factors in the mares serum within 30 days before foaling
- serum dilutions above 1:16 for Aa and Qa that cause hemolysis in vitro may produce NI, and withholding of the colostrum is recommended
- antibodies to Aa and Qa factors detected at 1:2 serum dilution require retest before foaling

**cross-matching** at the time of foaling – test the presence of antibodies against the blood factors in the colostrum, or the antibodies in the dam’s serum (minor crossmatch)

**jaundice foal agglutination test** – tests serial dilutions of the colostrum against the foal’s blood (red cells)

**CLINICAL SIGNS:**

* hemolytic disease that develops at 12 hours to 5 days of life
* icterus progressing to pale mucous membranes
* anemia (moderate (PCV < 25) to severe (PCV < 15))
* normal total protein (6 g/dL)
* metabolic acidosis (poor tissue oxygenation)
* depression, weakness, lethargy, tachycardia, tachypnea
* kernicterus (bilirubin deposition on neural tissues)
* mild fever
* hyperbilirubinemia (indirect bilirubin > 20 mg/dL)
* hemoglobinemia, hemoglobinuria = pigmentary nephropathy (renal failure)
* positive minor cross-matching (dam’s serum and foals red cells)
  * positive hemolytic test
  * positive Coomb’s test (although not specific for NI)

**TREATMENT:**

• milk out the colostrum from dam for 24 hours after birth (peak colostrum production is 12 hours, and immunoglobulin absorption happens up to 24 hours of life) - do not save the colostrum for other foals!!
• provide the foal with a safe source of good quality colostrum or perform plasma transfusion
• muzzle the foal for 24-48 hours after foaling, and feed milk replacer or another’s mare milk
• perform serum immunoglobulin testing in the foal’s serum at 18 hours of life to ensure adequate immunoglobulin levels
• blood transfusion (1-2 L) is packed cell volume is lower than 15% = may need more than once because donor red cells may last 2-4 days only; use washed red cells from dam, or cross-matched donors, or geldings that never received blood transfusions
• Oxyglobin (polymerized hemoglobin product) = temporary treatment until blood transfusion is possible
• minimize stress and handling

4.2.1 MANAGEMENT OF THE FOAL PART II

PERINATAL ASPHYXIA SYNDROME

• also called neonatal maladjustment syndrome or hypoxic-ischemic encephalopathy
  • foals may be called barkers, convulsive, wanderers, or dummies due to the neurological signs
• perinatal asphyxia syndrome is the name that best describes the multisystemic effects of hypoxia: nervous, cardiac, respiratory, renal, gastrointestinal, hepatic, and endocrine systems
• PROBLEMS MAY DEVELOP DURING FETAL LIFE AND COMPLICATE DURING NEONATAL LIFE
• foals may show clinical signs immediately after birth, or look normal at birth, and show progressive deterioration within 24-36 hours

• CAUSES of asphyxia:
  • decreased umbilical blood flow and/or altered utero-placental perfusion
    • placentitis = placental dysfunction (infection, endophyte-infected fescue ingestion); premature separation of the placenta
    • decreased amniotic fluid (mechanical obstruction of the umbilical cord during fetal movement and uterine contraction);
    • dystocia and difficult deliveries (cord compression, thoracic trauma, cesarean section)
    • maternal illness = endotoxemia, hemorrhage, anemia, hypoproteinemia, severe respiratory disease, malnutrition
    • use of NSAIDs during pregnancy = postnatal pulmonary hypertension
  • twinning, congenital malformations, prematurity/dysmaturity, persistent fetal circulation, meconium aspiration syndrome
• **PATHOPHYSIOLOGY**

- **asphyxia** is defined as reduction of tissue oxygenation
  - hypoxemia (decreased oxygen content in the blood)
  - ischemia (decreased blood flow)
- asphyxia results in anaerobic metabolism, lactate production, intracellular acidosis (metabolic acidemia), and sets the stage for reperfusion injury

• **NEUROLOGICAL** effects:

- hypoxic-ischemic *encephalopathy* = neurological dysfunction
- prolonged asphyxia leads to **anoxia, energy depletion**, and **ischemia**
  - energy failure leads to cellular swelling
    - failure of the Na-K-ATP pump and energy-dependent Ca pump = membrane depolarization + intracellular flow of calcium = activation of intracellular enzymes = cell death = glutamate release = neuronal death
  - ischemic-reperfusion injury of the brain = production of free radicals produced = peroxidation of membrane phospholipids = breakdown of cell membrane = cell death
  - cell death = necrosis with disruption of tight junctions in the capillary endothelium = leakage of osmotic agents into the surrounding brain interstitium = hemorrhage and edema
  - increase intracranial blood pressure = progressive brain swelling = reduced cerebral blood flow (hypoxia) and cerebellar herniation
  - seizures = emergency situation = central nervous system damage (excessive depolarization) and intermittent apnea (hypoxia)
  - clinical signs: irritability, jittery behavior, lethargy, falling asleep, hypotonia, seizures (cause additional brain injury due to hypoxia), depression, stuporous, profound flaccidity, suppressed breathing pattern (apnea), coma

• **CARDIORESPIRATORY** effects:

- cardiac insufficiency:
  - myocardium infarct = decreased contractility = decreased cardiac output = systemic hypotension = exacerbation of tissue hypoxia = metabolic acidosis
  - **RENAL** effect:
    - kidneys are very susceptible to hypoxia = tubular necrosis
• **decreased renal perfusion** and output = (oliguria (< 1ml/kg/hr), azotemia, peripheral edema

• **RESPIRATORY** effect:
  • decreased pulmonary perfusion = **decreased surfactant production** by type II pneumocytes = pulmonary **atelectasis**, hyaline membrane disease
  • suppression of respiratory center = prolonged apnea = hypoxemia, hypercarbia, respiratory acidosis

• **GASTROINTESTINAL** effects:
  • ischemic hypoxic gut injury = **necrotizing enterocolitis** = ileus, colic, abdominal distention, gastric reflux, diarrhea
  • **mesenteric hypoperfusion** = decreased mucosal cell metabolism = loss of mucosal protective layers
  • proteolytic enzymes begin **autodigestion of the mucosa** = breakage of mucosal barrier = sepsis
  • **colonization of the gut wall with bacteria** (*Clostridium*)
  • **gas accumulation in the gut wall** = development of **pneumatosis intestinalis** = intestinal perforation (pneumoperitoneum)
    • radiographs and ultrasound: linear or cystic submucosal gas accumulations within the bowel wall

• **HEPATIC** and **ENDOCRINE** effects:
  • **hepatocellular necrosis**, biliary stasis (icterus), dysfunction (coagulopathy; DIC)
  • **adrenal gland hemorrhage** = necrosis = hypocortisolemia

• **SEPTICEMIA**
  • presence of pathogenic microorganisms and their toxins in the blood
  • origin of infection and predisposing factors:
    • **respiratory** tract, **GI** tract, **umbilicus**, **hematogenous** (placentitis)
      • environmental **pathogenic organisms** (failure of passive transfer; poor ventilation and sanitation, overcrowding, inadequate umbilical disinfection)
    • **opportunistic organisms** (e.g. GI tract)

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<thead>
<tr>
<th>Gram negative</th>
<th>Gram positive</th>
<th>Fungal</th>
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<tr>
<td><em>Actinobacillus equuli</em></td>
<td><em>Streptococcus</em> spp</td>
<td><em>Candida</em></td>
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<td><em>Salmonella</em> spp</td>
<td><em>Clostridia</em> spp</td>
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<td>Pasturella spp</td>
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<td>E. coli</td>
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**SEPTICEMIC SHOCK:**

- caused by **gram negative** bacteria **endotoxin** (*Actinobacillus equuli, Salmonella spp, E. coli*) or **gram positive bacteria** **exotoxin** (*Clostridium spp*) = identified by macrophages, neutrophils = **Systemic Inflammatory Response** = inflammatory cytokine release (tumor necrosis factor, IL-6, prostaglandins, platelet-activating factor)
  - **hyperdynamic** phase: hypertension, tachycardia, bright red mucous membranes, fever
  - **hypodynamic** phase: decrease cardiac output, hypotension (cold extremities, prolonged capillary refill time, weak peripheral pulse, pale/blue/grey mucous membranes), hypothermia, dehydration (enophthalmos, entropion), renal failure (oliguria/anuria), mucosal and aural petechiations = DIC, ileus, convulsions, coma

- microthrombi = **endothelial damage** = increased pulmonary capillary permeability (**edema**) = atelectasis = ventilation/perfusion mismatch = inadequate tissue perfusion and oxygenation = **hypoxia, acidosis** = multi-organ failure
- myocardial depression and failure = decreased cardiac output = **hypotension** = oliguria, anuria = **renal failure**
- increased energy utilization and catabolism of protein, carbohydrate, fat = anaerobic glycolysis, increased lactate production, gluconeogenesis, insulin resistance, lipolysis, hyperlipemia, proteolysis

**Laboratorial data:**

- **white cells:** neutropenia (prematurity or neutrophil margination) or neutrophilia (inflammatory response) with left shift (bands); lymphopenia
- **total protein:** may be elevated due to dehydration; however, decreased absorption of immunoglobulins from colostrum may decrease total protein value; in addition, there is increased in the protein catabolism
- **fibrinogen:** normal (recent process = environmental infection) or elevated (older process = intrauterine infection)
- **variable electrolytes** (depends on hydration status, acid/base status, presence of diarrhea)
- common metabolic/respiratory **acidemia** with **hypoxemia**
• BUN and creatinine: **azotemia** (prerenal = dehydration; or indicative of placentitis)
• common **hypoglycemia**
• increased liver enzymes: unknown cause or umbilical vein infection
• hyperbilirubinemia (indirect bilirubin)
• thrombocytopenia
• hypogammaglobulinemia (< 800 mg/dL)
• culture: blood, tracheal wash, feces, CSF, joint fluid
• ultrasound of umbilical structures, thorax and abdomen
• radiographs of thorax and joints

**affected systems** (some of them discussed in different sections):

- umbilicus (omphalophlebitis)
- respiratory system (pneumonia)
- gastrointestinal system (diarrhea)
- skeletal (arthritis)
- nervous system (meningitis)
- ocular system (hypopyon, uveitis)

**MENINGITIS:**

- progressive, multifocal or diffuse neurologic deficits
  - depression, anorexia, weakness, loss of suckling reflex, ataxia, hypermetria, proprioceptive deficits, nystagmus, anisocoria, head tilt, stiff neck, opisthotonos, blindness, intention tremor, seizures, convulsions, coma
- cerebro-spinal fluid (CSF): turbid, increased white cell count and protein; normal CSF may also be present; submit for culture

**RESPIRATORY DISORDERS**

1. Common respiratory disorders in neonates are due to failure in the respiratory system to complete the transition from the fetal, collapsed organ to perinatal air-filled organ responsible for gas exchange.
   a. **prematurity = surfactant deficiency** (hyaline membrane disease, atelectasis)
   b. **trauma** during parturition (diaphragmatic hernia, hemo/pneumothorax due to rib fracture)
   c. **meconium aspiration** (chemical inflammation)
   d. **infectious pneumonia** (*E. coli*, *Actinobacillus*, *Streptococcus*, *Pasteurella*, *Klebsiella*, *Salmonella*, EHV-1, equine adenovirus, BRSV, BVD)
2. Other conditions associated with neonatal respiratory distress are **malformations**
   a. choanal atresia
   b. laryngeal edema, collapse (anomalies, vitamin E/selenium deficiency)
   c. epiglottic cysts
   d. tracheal collapse
   e. pulmonary hypoplasia

3. Respiratory disorders may also be **secondary to other systemic processes**
   a. respiratory depression due to ischemic-hypoxic encephalopathy and seizures
   b. heart disease (insufficiency, anomalies), pulmonary hypertension
   c. thoracic or cardiac muscle insufficiency (vit E/Se deficiency)
   d. anemia, hypovolemia (gas transport insufficiency)
   e. pain, fever, excitement (increased respiratory rate)
   f. abdominal distention (thoracic compression)

4. **Surfactant deficiency**
   a) surfactant = mixture of phospholipids and proteins is produced and stored in type II alveolar pneumocytes; increases lung compliance and stabilize alveoli; produced in late gestation
   b) primary surfactant deficiency = prematurity of pneumocytes type II, asphyxia = respiratory distress syndrome (RDS)
   c) increased alveolar permeability leads to hyaline membrane formation (accumulation of protein and cellular debris in the alveoli) = alveoli disruption, pulmonary edema and further surfactant inactivation
   d) clinical signs are progressive in the first 24 to 48 hours after birth
   e) thoracic radiographs: diffuse alveolar pattern

5. **Physical examination**
   a. respiratory rate and effort:
      • tachypnea
      • alternating apnea and tachypnea (decreased central respiratory stimulus = hypoventilation = hypercapnia and hypoxemia
   b. lung sounds: easy to auscultate in neonates: **crackles** and **wheezes**; harsh
      sounds with fever (increased respiratory rate), pneumonia, recumbency
(tendency of immature lung to collapse); careful because lung auscultation may not correlate with severity of disease; **tracheal rattle** may indicate aspiration (placental fluids, colostrum/milk)

c. **mucous membrane color**:
   - **cyanosis** may not be detected even when hypoxemia (< 40 mmHg) is present, more common in cardiac anomalies and persistent fetal circulation;
   - **pale** mucosas = anemia, hypotension

6. **Diagnostics**:

- **arterial blood gas analysis**
  - sampling from the great metatarsal artery or brachial artery are commonly used, facial and femoral arteries are also possible
  - PaO\textsubscript{2} values are expected to be lower in lateral recumbency
  - **pulse oximetry** do not replace arterial blood samples but decrease samplings; careful with hypotension because it decreases peripheral perfusion
  - normal values: pH = 7.37, PaCO\textsubscript{2} = 45 mmHg, PaO\textsubscript{2} > 85 mmHg
  - **hypoxemia with normal PaCO\textsubscript{2}**
    - hypoxia drives to hyperventilation, therefore lowering PaCO\textsubscript{2}
    - ventilation-perfusion mismatching
    - right-to-left shunting (O\textsubscript{2} supplementation does not improve PaO\textsubscript{2})
  - **hypoxemia with high PaCO\textsubscript{2} (hypercapnia)**
    - hypoventilation = high PaCO\textsubscript{2} = respiratory acidosis
    - incompetence of respiratory muscles, neurologic dysfunction
- **thoracic radiographs and ultrasound**:
  - increased interstitial pattern, alveolar pattern, aspiration (cranioventral alveolar pattern), fracture ribs, hemothorax, pneumothorax, lung consolidation (atelectasis)
  - **endoscopy** indicated when noisy breathing = suggestive of laryngeal obstruction; milk reflux may be present (milk coming out from narines)
  - **transtracheal wash** culture (if patient is stable and not in severe respiratory distress), cytology, Gram stain

**GASTRO-INTESTINAL DISORDERS**
See meconium impaction above

**GASTROINTESTINAL ULCERATIONS**
- neonates are very susceptible to GI ulcerations (1-6 months of age)
- **gastric ulcers**:
  - squamous mucosa adjacent to the margo plicatus
• may cause poor growth, diarrhea, rough haircoat
• often heals spontaneously
• glandular mucosa
• clinical signs: bruxism, ptyalism, interrupted nursing, colic (dorsal recumbency, limbs in the air), gastric distention, delayed gastric emptying, diarrhea
• secondary to concurrent diseases (infectious (diarrhea, pneumonia), pain (orthopedic problems) and nonsteroidal anti-inflammatory therapy

• **duodenal ulcers:**
  • solitary or multiple lesions

• **right-dorsal colon ulcers:**
  • associated with the use of nonsteroidal anti-inflammatory drugs
  • occult blood in feces and significant loss of protein (hypoproteinemia)

• endoscopy is not always necessary
  • stressful procedure, and clinical signs are very reliable
  • may be necessary for perforating ulcers (toxic shock, fever, peritonitis)

• **therapy:**
  • anti-ulcer medication: H2 blockers (famotidine, ranitidine, cimetidine); proton pump inhibitor (omeprazole), mucosal protectant (sucralfate), prostaglandin analog
  • gastric ulcers heal much faster than right dorsal colon ulcers
  • esophageal and duodenal constrictions can be produced by healing ulcers = gastroesophageal reflux

**DIARRHEA**

• can cause rapid life threatening dehydration and electrolyte/acid-base imbalances = metabolic acidosis (loss of bicarbonate), hyperkalemia, hyponatremia, hypochloremia
• clinical signs include watery feces, ileus, abdominal distention, colic, gastric reflux, fever; absence of diarrhea in enteritis may happen if patient is severely dehydrated

• **pathophysiology:**
  • hypersecretion = bacterial enterotoxins alter the activity of membrane pumps of intestinal cells for Cl, Na and K
  • destruction of crypt cells = maldigestion (lactase deficiency) of milk in small intestine = passes to large intestine = osmotic diarrhea and bacterial fermentation
  • destruction of absorptive villous epithelial cells + hyperplasia of crypt cells = increased secretion, decreased absorption
  • destruction of mucosal integrity = absorption of bacteria and toxins
  • necrotizing enterocolitis: intestinal ischemia/hypoxemia during fetal life, parturition or cardiopulmonary insufficiency may lead to
bacterial colonization of intestinal wall; the bacteria rely on nutrition provided by feeding (in special, milk replacer); abdominal ultrasound/radiographs reveal pneumatosis intestinalis (intramural gas in the intestine); clinical signs include colic, ileus, abdominal distention

- **nutritional**: excessive milk intake, poor quality milk replacer, lactose intolerance
- **physiological = foal heat diarrhea**: foals from 6-14 days of age may present watery diarrhea with no fever, electrolyte imbalances or depression; they are bright, alert, and nurse normally; the etiology is unclear but may be associate with the development of the gastrointestinal tract after birth; often, no treatment is necessary, but monitoring of nursing and attitude.
- **antibiotic induced**: use of antibiotics, even parenterally, may cause normal intestinal flora imbalance and, consequently, diarrhea
- **diagnosis**: fecal culture, testing for bacterium toxins (*Clostridium*), and testing for parasites
- **infectious agents**: *E coli*, *Clostridium perfringens* type A, B and C (acute necrotizing hemorrhagic enteritis with or without septicemia), *Clostridium difficile* (watery diarrhea or necrotizing hemorrhagic enteritis), *Salmonella* (often associated with septicemia); *Cryptosporidium* (diarrhea of hypersecretion; associated with immunodeficiency in foals)
- **treatment**: fluid therapy, electrolyte correction, dietary adjustment (reduce milk intake, parenteral nutrition), oral lactase, flora replacement (yogurt), use of metronidazole in case of *Clostridium*, deworming

**SURGICAL INTESTINAL CONDITIONS**

- volvulus, intussusception

**GENERAL DIAGNOSTICS AND TREATMENT**

Neonatal patients often have a combination of problems: a foal that presents hypoxic-ischemic encephalopathy or prematurity may develop septicemia because it may not have nursed colostrum properly. Likewise, a foal with limb flexural deformities may have difficulty to nurse and becomes dehydrated, hypoglycemic and hypothermic.

In addition, neonatal patients often present multi-systemic conditions: a foal may present a primary diarrhea that develops severe dehydration, hypotension, and kidney failure! A foal with painful tendon contraction may develop severe gastritis!

Therefore, evaluate system by system, and look for problems that might not be so obvious. If you find a problem, treat it – do not wait and see!
DIAGNOSTICS

- **Basic tests and monitoring:**
  - CBC/serum chemistry/electrolytes analysis
  - periodic arterial blood gas analysis
  - blood culture
  - urinalysis/urine output quantitation
  - serum IgG quantitation
  - thoracic and abdominal ultrasound (including umbilical structures)
  - blood pressure (sphygmomanometer applied to tail or greater metatarsal artery = 50-95 mmHg)

- **If respiratory clinical signs are present**
  - thoracic radiographs
  - transtracheal wash culture
  - pleuritis: thoracentesis and fluid cytology, culture and Gram stain
  - milk reflux or noise breathing: endoscopy of airways

- **If gastrointestinal clinical signs are present**
  - abdominal ultrasound and radiographs
  - diarrhea: fecal culture, toxin identification, virus isolation

- **If lameness and/or joint effusion are present**
  - arthrocentesis, joint fluid cytology, culture and Gram stain
  - physiography
  - prematurity: tarsal and carpal radiographs

- **If meningitis is suspected:**
  - CSF cytology and culture

- **If heart murmur with a palpable thrill is present:**
  - echocardiography and electrocardiography

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Because of the development of multi-systemic diseases in neonates, many of the treatments for one system will overlap with another. For instance, gastric protectants are used in any condition that causes stress to the neonate. A certain antibiotic may be chosen for its spectrum and permeability for the treatment of both meningitis and pneumonia in cases of septicemia. Fluid therapy is used to correct dehydration and electrolyte imbalances due to diarrhea, to correct hypotension and to maintain renal function.

Use medications cautiously because some drugs can be nephrotoxic or gastrointestinal toxic.

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GENERAL TREATMENT

- **SUPPORTIVE GENERAL CARE:**
  - soft, clean, dry bedding
  - heating lamp and heating pads to help with hypothermia
  - keep sternal position to facilitate lung ventilation/perfusion
  - turn sides every 2 hours to avoid skin sores
• dip umbilicus 2X to 3X in 0.25% chlorhexidine solution or 5% iodide solution
• clean perineal area and change ‘dippers’ as needed
• change urine collecting bag as needed and record urine production
• entropion: place supporting lid sutures and apply lubricate eye ointment
• gastric protectants are used whenever neonates are stressed (foals)
• intramuscular selenium/vitE injection is given soon after birth in the areas where selenium is deficient in the soil

**CARDIOVASCULAR SUPPORT:**
• **resuscitation:** thoracic compression (90/min), epinephrine
• **fluid therapy** = correct dehydration (maintain blood pressure and organ perfusion) and provide maintenance,
  • maintenance 100 ml/kg/day
  • careful with overhydration: cerebral hemorrhage/edema; pulmonary edema
• electrolyte and acid-base correction:
• crystalloid solutions containing Na, Cl, Ca, Mg, K
  • attention to severe hypo or hypernatremia = correct slowly!
  • do not use hypertonic solution (hypertonic saline) = neurological damage due to osmolar shifts
• correction of acidosis
  • use isotonic 1.3 % bicarbonate solution
    • careful with severe respiratory compromise in which there is accumulation of CO₂ because bicarbonate administration can worsens acidosis

\[
\text{HCO}_3^- \text{ deficit} = \text{BW (kg)} \times 0.4 \times (\text{normal HCO}_3^- - \text{actual plasma HCO}_3^-)
\]

• low oncotic pressure (low total protein): colloidal solutions (Hatastarch) or plasma transfusions
• monitor peripheral pulse, blood pressure, oncotic pressure, urine production, cardiac murmur, arrhythmias
• **persistent hypotension** (despite fluid therapy): dobutamine
• prevent disseminated intravascular coagulation (**DIC**): heparin

**RESPIRATORY SUPPORT:**
• **resuscitation:** endotracheal tube and assisted ventilation (Ambu bag)
• oxygen therapy = nasal insufflation 5-10 L/min
  • hypoxemia (PaO₂ < 60 mmHg)
• mechanical ventilation (assisted or controlled)
• hypercapnia (PaCO₂ > 60 mmHg)
• prematurity: intratracheal surfactant administration
• sternal recumbency and stand periodically
• bronchodilators – nebulization with beta-2 agonists (albuterol, terbutaline)
• respiratory center stimulant – caffeine
• anemia (hemolytic): blood transfusion
• antibiotics:
  • foals: amikacin + potassium penicillin (if no signs of renal disease and severe dehydration), ceftiofur (safer in case of kidney disease and dehydration), trimetoprim-sulfonamide (the distribution in the tissues is very good but many organisms are resistant); chloramphenicol and imipenem are used when the initial antibiotic therapy is not effective or when organism sensitivity is tested; quinolones may cause arthropathies in neonates
  • aminoglycosides are very nephrotoxic and ototoxic = use only when euhydration and normal renal function (normal creatinine)
• hemotherax: slow chest drain, pain relief (butorphanol)

• RENAL SUPPORT:
  • closed urinary collection system (catheterization
  • normal urine production: 150ml/kg/day (6-7ml/kg.hr)
  • monitoring of urine output = early detection of oliguria/anuria (< 2ml/kg/hr)
  • ultrasound kidneys
  • oliguria: furosemide; anuria: dopamine, dobutamine

• NERVOUS SYSTEM SUPPORT:
  • diuretics: mannitol is used in hypoxic-ischemic encephalopathy
  • antibiotic therapy = ideally, the antibiotic should have broad spectrum, bactericidal activity, and cross the blood-brain barrier (BBB)
  • third generation cephalosporins (cefotaxime sodium, ceftazidime), TMS, chloramphenicol, rifampin, metronidazole cross the BBB
  • ceftiofur, amikacin, tetracycline, penicillin, and quinolones do not cross BBB
  • extensive use of antibiotics may predispose to Candida albicans infection = white film over the tongue/oral mucous membranes
• anti-inflammatory therapy:
  • corticosteroid – meningitis is the exclusive indication for the use of corticosteroids in a infectious process = reduce inflammatory mediators and severity of sequelae; used 20 minutes before antibiotic therapy
• DMSO – reduces reperfusion injury in cerebral ischemia
• **seizure control** = diazepam, phenobarbital, magnesium sulfate
• **anti-oxidant and protective therapy**: vitamin E, vitamin C, thiamine

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**GASTROINTESTINAL SUPPORT:**

• **meconium retention**:  
  - warm, soapy enemas using flexible tubes (100 ml)  
  - 4% acetylcysteine solution retention enema under sedation (severe cases!)  
  - oral laxatives: mineral oil (by nasogastric tube only!)  
  - intravenous fluids  
  - analgesics (butorphanol)  
  - unresponsive cases: surgical enterotomy

• **gastric ulcers**:  
  - histamine H2-receptor antagonists (cimetidine, ranitidine, famotidine)  
  - cytoprotective agent: sucralfate  
  - H+ - K+ ATP pump blocker: omeprazole  
  - prostaglandin analogue: misoprostol

• **diarrhea**:  
  - fluid and electrolytes therapy; plasma therapy (in protein loss)  
  - bismuth subsalicylate orally, charcoal by nasogastric tube  
  - metronidazole therapy if *Clostridium* is involved  
  - vaseline or Densitin on perineal area

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**IMMUNE SYSTEM SUPPORT:**

• within 18-24 hrs after birth: colostrum supplementation  
• beyond 24 hrs after birth: plasma [foals (1L)] or whole blood (1L) intravenous transfusion slowly (use blood transfusion set);  
• repeat serum IgG concentration 4-12 hours after transfusion and in 7 days if septicemia persists

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**NUTRITIONAL SUPPORT:**

• **enteral feeding** – nasoesophageal/gastric tube or bottle feeding  
  - healthy neonate foals consume 20% BW daily in milk; sick foals may have their diet adjusted because of their decreased ability to digest (start with 10% BW and increase from that)  
  - foals: feed every 2 hours (dam’s milk is reach in mucosal protective IgA), or goat’s milk, or milk replacer (healthy foals may nurse every 30-45min); esophageal tube or pan; feeding with bottle often induces aspiration pneumonia  
  - monitor for diarrhea, lack of defecation (impaction caused by milk replacer), tympany
• control the amount of feeding, and consider alternate
  with balanced oral electrolyte solution if diarrhea is
  present, or switch to parenteral nutrition
• add lactase to the milk in case of diarrhea
• neonate foals should gain 1-2 lbs/day body weight
• **parenteral feeding:**
  • PPN = partial parenteral nutrition PPN) = may be used
    when there is gastrointestinal dysfunction
  • monitor lipemia, hyperglycemia, glucosuria to help
    regulate PPN rate
  • **dextrose therapy:** use isotonic dextrose 5% and aim for
    normoglycemia
• **MUSCULOSKELETAL SUPPORT:**
  • **contracted tendons:** supportive wraps, splints (careful
    creating soreness), physiotherapy, controlled exercise
  • single dose oxytetracycline (only in well hydrate foal and not
    azotemic)
  • use NSAIDs cautiously for pain
  • **tendon laxity:** controlled exercise, monitor for angular
    deformity, heel extensors
  • **septic arthritis:** joint lavage (10% DMSO in LRS), systemic
    and intraarticular antibiotic injection (amikacin), arthrotomy,
    bandage
**muscular integrity and function:** monitor vitamin E and selenium
  levels; administer intramuscular selenium and oral vitamin E in the
  first day of life and when necessary (be careful with selenium
  toxicity!)

4.3 MANAGEMENT OF THE PERIPARTURIENT MARE

**Maternal illness**

• maternal disease may affect the fetus with hypoxemia and
  ischemia (poor perfusion), leading to abnormal fetal
  development and premature delivery
  o colitis results in dehydration and electrolyte imbalances,
    endotoxemia, hypotension, and hypoproteinemia;
  o pneumonia results in toxemia and hypoxia
• mares should be treated with broad spectrum antibiotics, fluid
  therapy, anti-endotoxic therapy, plasma transfusion for
  replacement of protein, and progesterone supplementation
• prolonged use of non-steroidal anti-inflammatory drugs may
  cause persistent fetal circulation
• fetuses from sick mares should be evaluated frequently by
  transabdominal ultrasound for heart rate, activity and placental
  thickness.
Fetoplacental examination
• equine placenta comprises the allantochorion, allantoamnion, and umbilical cord
• the chorionic portion attaches to endometrium by diffusely distributed microcotyledons, except at the cervical star
• the umbilicus contains 2 umbilical arteries, 1 vein and 1 urachus
• 150 days of gestation:
  o fetal electrocardiography
  o transabdominal ultrasonography (ventral abdominal wall)
• fetal heart rate (80-120 bpm) and activity, placental thickness, determine fetal fluid quality (meconium defecation, hemorrhage, fibrin tags) and volume (small volume, hydrops), detect twins, estimate fetal size (aortic diameter)
  ▪ persistent bradycardia or tachycardia, and arrhythmias are associated with fetal stress
  ▪ normal placental thickness 8-15mm; inflammation (edema, hemorrhage) and separation show greater thickness
• 270 days of gestation: fetus should be more active
  o pericervical allantochorion may be evaluated by transrectal ultrasound for thickness and signs of impeding abortion
• 300 days of gestation: fetal heart rate between 70-130 bpm with transient bouts of tachycardia after activity
• post-partum placenta examination
  o normal placenta should weigh approximately 10% of the foal’s body weight
  o placentitis: heavier placenta and discoloration of the chorion

Placentitis
• placental insufficiency may be due to a non-infectious condition (twin pregnancy) or infectious
• ascending (more common) or hematogenous infection of placenta is responsible for 25% of abortions, stillbirths and premature deliveries
  o bacterial (Streptococcus zooepidemicus, Escherichia coli, Enterobacter agglomerans, Klebsiella pneumoniae, Leptospira, Pseudomonas aeruginosa, Nocardioform actinomycete), fungal (Aspergillus, Candida) or viral (equine herpesvirus-1)
• IMPORTANT clinical signs that suggest placentitis: premature udder development and lactation, cervical softening, vaginal discharge may or not be present; often no systemic signs of infection
• **ultrasonography** (5 MHz sector scanner) may detect areas of placental separation or thickness (changes can be subtle and not detectable by ultrasound)
  o transrectal ultrasound = ascending infection
    ▪ maximal combined thickness of uterus and placenta (CTUP) close to the cervical star, measured in the ventral part of the uterine body, between the middle branch of the uterine artery and the allantoic fluid (note that CTUP is normally thick on the dorsal part of the uterus)
      • 151-270 days gestation < 5 mm
      • 271-300 days gestation < 7 mm
      • 301-330 days gestation < 9 mm
      • > 331 days gestation < 12 mm
  o ventral transabdominal ultrasound = hematogenous infection
    ▪ minimal and maximal CTUP: 7 and 11 mm, respectively
• culture and sensitivity of cervical swabs (careful not to contaminate with feces)
• **endocrine tests**
  o progesterone and prostagens
    ▪ serial blood samples should be tested to clinically assess progesterone concentration, and fetal-placental progesterone is rapidly metabolized into 5-pregnanes
    ▪ progesterone is initially produced by the primary and secondary corpora lutea (CL), then by the placenta between 150 and 200 days
    ▪ progestagens (5 alpha-pregnanes) are produced by the fetoplacental unit starting after 60 days, followed by a rapid increase in maternal progestins 30 - 60 days prepartum
    ▪ a rise in progestins before 60 days before foaling has been associated with abnormal pregnancies, placental pathology, and premature lactation
    ▪ a drop in progestin levels have been observed in mares delivering dead or compromised foals (EHV-1), surgical or medical colic and uterine torsion, and endophyte-infected fescue (prolonged gestation, agalactia, hypoprolactinemia)
  o estrogens (estradiol and estrone sulfate)
    ▪ maternal levels increase during the 7th and 8th month, followed by a gradual decline
    ▪ normal maternal estrogen concentrations require both fetus and placenta for biosynthesis, and can be a marker for viability of the fetoplacental unit
relaxin
  - produced by the placenta, and maternal levels increase after day 75 of gestation
  - no test available commercially

- treatment:
  - broad-spectrum antibiotic therapy: trimethoprim-sulfadiazine (20 mg/kg PO BID)
  - low doses flunixin meglumine (1 mg/kg IV BID) as an anti-inflammatory
  - altrenogest (Regumate 0.088 mg/kg PO SID)
  - pentoxifylline (7.5 – 10 mg/kg PO BID or TID) has been used to optimize placental perfusion.
  - oral vitamin E (10 IU/kg PO SID) is administered as an antioxidant

- after abortion or delivery, the placenta must be examined thoroughly
  - information helps predict fetal developmental problems and neonatal septicemia

Uterine torsions, dystocias, cesarean sections and premature placental separation

- risk of fetal and perinatal hypoxia
  - dystocia: cord compression and thoracic trauma (fractured ribs)
  - cesarean: maternal hypotension due to anesthetic depression and dorsal recumbency = placental hypoxia
  - premature placental separation ('red bag delivery') = fetal/neonatal asphyxia

- fetal hypoxia = intrauterine passage of meconium that results in aspiration, chemical pneumonitis, airway obstruction/atelectasis, surfactant dysfunction, pulmonary hypertension

- the foal can be intubated and ventilated using a hand held resuscitator (Ambu bag) during cesarian section or dystocia

Induction of parturition

- criteria
  - pregnancy risk for the mare or fetus
  - stage of gestation and chances of fetus survival after birth (risk of dysmaturity/prematurity)
  - gestational length > 330 days
  - mammary development and electrolyte concentration in secretion (calcium rises within 24-40 hours before labor; stall-side tests (Predict-A-Foal, Animal Care Products, Vernon, CA)
    - maiden mares produce colostrum very close to parturition, and placentitis/twin pregnancies may develop udder much sooner; therefore, test may not be helpful in predicting stage of gestation
cervical relaxation allows fast delivery, and can be induced with prostaglandin E₂ (PGE₂)
check fetal position before and periodically after induction of parturition
oxytocin: 15-20 IU IV every 30 minutes until foaling

**Hydrops**
- excessive accumulation of fetal fluids in the last trimester due to increased fluid production or decreased absorption
  - differential diagnosis: twin pregnancy
- rectal palpation reveals uterine distension occupying the dorsal abdominal cavity, and it is difficult to feel the fetus
- **hydramnios** = mild abdominal distention over a period of weeks to months associated with umbilical cord problems or abnormal fetal development; poor prognosis
- **hydrallantois** = rapid onset and progress, with significant increase in abdominal size, poses more risks to the mare; the fetus is often normal
  - maternal clinical signs: depression, tachycardia, tachypnea or dyspnea, difficulty to walk, ventral edema
  - grave consequences: uterine rupture, abdominal hernia (increase in serum creatine kinase levels), prepubic tendon rupture (accompanied by lordosis and hemorrhagic secretion from udder), intra-abdominal hemorrhage
  - risk at delivery: hypotensive shock in the mare due to the fast release of third-space occupying volume
- support therapy: intravenous fluids (careful with dose), laxative diet, diuretics, flunixin meglumine, progesterone, supportive belly band, stall confinement
- induced and assisted parturition
  - allantoic fluid may be drained slowly before parturition with a long trocar through the vagina and cervix into the chorioallantois, while the mare receives intravenous fluid (to prevent hypovolemic shock)
  - **oxytocin** (20 IU IV given repeatedly every 30 minutes) to induce parturition or **cloprostenol** (500 mcg IM every 30 minutes; laboring often starts after second dose)

**Uterine artery rupture (intraabdominal hemorrhage)**
- occurs more often in older mares due to arterial degeneration (parasitism with *Strongyulus vulgaris* or equine arterial arteritis), uterine torsion, uterine rupture, and trauma during parturition
  - more frequently on the right side (cecal displacement)
  - involves middle uterine artery, uterine-ovarian artery or external iliac artery
  - can still happen within 12 hours post foaling
hemorrhage into the peritoneal cavity (often fatal, observed by transabdominal ultrasound – intraabdominal swirling hypoechoic fluid) or broad ligament between myometrium and uterine serosa (felt on rectal palpation; no excessive blood in the peritoneal cavity)
  o abdominocentesis is indicated to rule out intestinal rupture

clinical signs are colic, tachycardia, pale mucous membranes, hypotension, depression or acute death
  o differential diagnosis: large colon volvulus (a very common disorder following parturition, which tends to be more painful)

confine mare to small stall

careful with sedation because most drugs are hypotensive

start fluid therapy controlled fluid therapy immediately
  o if mare is hypotensive, use aggressive fluid therapy for resuscitation (catheterize both jugulars) starting with 2 L of 7.5% hypertonic saline bolus;
  o follow with crystalloid solutions such as Plasmalyte or Normosol-R enough to maintain blood pressure and oxygenation compatible to life but not too high
  o add 4-6 L of plasma IV

cross-match blood transfusion is often necessary based on vital parameters and blood analysis (hematocrit, lactate, acidosis)
  o make sure to use intravenous blood transfusion sets with filter, and change as often as necessary
  o autologous blood transfusion can be used if intraabdominal hemorrhage is intense

after the mare is stabilized, aminocaproic acid (70 mg/kg in fluids as loading dose, followed by 15 mg/kg every 6 hours)

flunixin meglumine (1 mg/kg IV BID) as anti-inflammatory

furosemide (1-2 mg/kg IV once) to promote renal perfusion after fluid therapy

broad-spectrum antibiotic therapy (trimethoprim-sulfa 20 mg/kg PO BID)

Retained fetal membranes and intrauterine hemorrhage

the placenta is normally passed within 1 hour after foaling; after 3 hours, it is considered retained
  o predisposing factors: abortion, dystocia, twinning
  o more often attached at the non-gravid horn

acute infectious metritis leads to serious risk of endotexemia, laminitis, septicemia, disseminated intravascular coagulation, and death
  o fever, tachycardia, tachypnea, injected mucous membranes, depression
  o emergency treatment to prevent bacterial replication
• do not pull placenta = major risk of uterine rupture and damage
  o exposed placenta should be tied in a knot to prevent uterine tension (do not add extra weight)
• use repeated doses of oxytocin (10-20 units IV or IM) every 3-4 hours
• encourage nursing
• uterine lavages with 5-10 L 1% povidone warm solution (using nasogastic tube), once or twice a day to remove necrotic tissues and excessive bacteria; followed by infusion with 1L Lactate Ringers with 6 grams Ampicillin
  o in case of uterine hemorrhage, do not perform uterine lavages and do not remove blood clot for 3-4 days
• treat endotoxemia with intravenous fluid therapy (if necessary, calcium supplementation)
• antibiotic therapy with potassium penicillin (22,000 units/kg IV QID) plus gentamicin (6.6 mg/kg IV SID)
• anti-inflammatory therapy with flunixin meglumine (0.25 mg/kg IV TID or QID)
• ice on feet for laminitis
• check blood work and biochemistry to treat systemic effects of endotoxemia
• check tetanus toxoid vaccination status

Uterine prolapse
• secondary to dystocia or retained placenta
  o may present uterine arterial hemorrhage and shock = emergency!
• use epidural anesthesia with 3-4 ml lidocaine (careful with sedation due to hypotensive effects)
• fluid therapy and blood transfusion of necessary
• flunixin meglumine anti-inflammatory dose 1 mg/kg IV BID
• clean uterine tissue carefully and replace
• antibiotic therapy (potassium penicillin 22,000 units/kg IV QID plus gentamicin 6.6 mg/kg IV SID)
• pseudo Caslick’s after uterine treatment is completed

Mycotoxin-infected fescue grass
• mycotoxins are ergopeptine alkaloids that interact with D2-dopamine receptors
• cause of abortion, placentitis, premature placental separation, prolonged gestation length, dystocias, agalactia and weak/hypoxic foals
• remove mare from the infected pasture at least 30 days prior to her due date
• daily administration of dopamine antagonist (domperidone 1.1 mg/kg PO SID) at least 2 weeks prior to the mare’s due date
for agalactia, other drugs are perphenazine (0.3 – 0.5 mg/kg OP BID) or acepromazine (20 mg per horse IM QID)

**Induction of milk production for adoption of orphan foal**
- **lactation** can be induced in non-pregnant mares that have foaled in previous years with a 2-week hormonal treatment including progesterone, estrogen, and a dopamine D2 antagonist (sulpiride or domperidone = same efficiency)
  - milk quality is the same as normal pregnant mares, but colostrum is rarely produced
- chose a mare in good body condition and known to be a good mother
- **hormonal treatment:** estradiol-benzoate (single injection 50 mg/500 kg mare IM) plus altrenogest (Regumate 22 mg/day PO for 7 days) and sulpiride (1 mg/kg IM BID) or domperidone (1.1 mg/kg PO SID)
  - the mare will start milk production in 4-7 days after the start of sulpiride treatment = keep milking 6-7 times/day
  - after 3-4 days of milking, production should reach 3-5 L/day, and adoption may be pursued
  - continue sulpiride or domperidone 10-15 days after adoption
  - milk production will persist even after sulpiride is discontinued
- **adoption protocol**
  - vigorous vaginal stimulation with massage of the external portion of the cervix, and attempt to dilate the cervix
  - hold the foal close to the mare’s head at safety during the procedure, but allow mare to sniff the foal
  - apply stimulation 2 times (2 min each, at 10 min interval)
  - slowly test the mare with the foal to check for nursing tolerance at this time, the mare should demonstrate adoption behavior.

**4.4 MUSCLE DISEASES IN HORSES**

**Exertional rhabdomyolysis** is a syndrome of muscle pain and cramping associated with exercise.

**CLINICAL SIGNS**
- stiff, short gait, lameness or reluctance to move shortly after the onset of exercise
- firm and painful lumbar and gluteal muscles
- anxiousness, sometimes confused with colic signs (posturing to urinate, stretching-out, pawing)
- sweating and muscle fasciculations
- increased creatine kinase (CK) and aspartate transaminase (AST) serum levels
- tachypnea and tachycardia
- discolored urine (dark from tea to coffee color) = myoglobinuria due to muscle damage or necrosis
- renal failure
- recumbency

**PATHOPHYSIOLOGY**

**Acute, sporadic and chronic exertional rhabdomyolysis**
- **Acute** ER occurs when a horse is exercised in excess of its level of conditioning or excessively.
- **Sporadic** ER occurs *infrequently* when horses are not exercised routinely, and/or receive diets with higher energy content that is utilized by exercise ('Monday morning muscle disease').
- **Chronic** ER is a heritable myopathy [Polysaccharide Storage Myopathy (PSSM) or Recurrent Exertional Rhabdomyolysis (RER)] that occurs *repeatedly* with minimal exercise.

Therefore, not all horses with muscle stiffness have the same type of muscle disease
Lactic acidosis is part of the pathophysiology of acute and sporadic ER, but not chronic ER.

Nevertheless, decreasing or dosing the amount of grain or non-structural carbohydrate in the diet helps all forms of rhabdomyolysis. The horse should receive the amount of energy that is spent during exercise to prevent building up storage in the muscles.

High carbohydrate diets have been developed for the horse to meet demands of intense exercise.
Recurrent Exertional Rhabdomyolysis (RER)

- affects Thoroughbreds (young females?) and likely Standardbred and Arabian horses
- heritable (autosomal dominant inheritance) defect in intracellular calcium regulation leading to excessive muscular contraction and necrosis with exercise
- increase in frequency proportionally with the degree of fitness
- often stress-induced, in horses with nervous temperament
- subclinical elevations of serum CK and AST
- may also occur with halothane anesthesia; therefore, similar to malignant hyperthermia, but with distinct biochemical basis

Polysaccharide Storage Myopathy (PSSM)

- affects Quarter Horses, and less frequently Paints, Appaloosas, and Morgans
- glycogen storage disorder characterized by the accumulation of glycogen and abnormal polysaccharide complexes in 1-40% of skeletal muscle fibers = muscle glycogen concentrations are 1.5 to 4 times greater than normal horses, and [G-6-P] is up to 10x normal
- glycogen accumulation in PSSM is not due to the inability to metabolize glycogen (as observed in human patients), but it is associated with enhanced insulin sensitivity (increased rate of clearance of blood glucose in normal to low insulin response) and glycogen synthesis
  - therefore, PSSM horses enhanced insulin sensitivity, glucose clearance and synthesis of glycogen
  - periodic exercise helps utilization of stored glycogen and reduction of insulin sensitivity
- the gene GYS1, encoding skeletal muscle glycogen synthase (GS), was identified as a candidate for PSSM
  - DNA sequence analysis revealed a missense mutation resulting in an arginine-to-histidine substitution in a highly conserved region of GS
  - functional analysis demonstrated an elevated GS activity in PSSM horses
    - haplotype analysis and allele age estimation demonstrated that this mutation is identical by descent among horse breeds
    - the mutation was identified in horses from 17 different breeds
    - the prevalence of the GYS1 mutation in PSSM horses was high in Draft- (87%) and Quarter Horse-related breeds (72%) and lower in Warmbloods (18%) and other light horse breeds (24%), when diagnosis histopathologic was based on grade 2 diagnostic criteria
there is a possibility of a second glycogenosis in horses with neuromuscular disease (type 2 PSSM) because there has been absence of the GYS1 mutation in horses diagnosed with excessive glycogen accumulation in muscle.

- histology of muscle biopsy: subsarcolemmal vacuoles, high density of stains for glycogen; muscle necrosis, macrophage infiltration of myofibers, regenerative fibers, and occasionally atrophied type 2 fibers, and periodic acid Schiff’s (PAS) positive inclusions in fast twitch fibers
  - pre-incubation of muscle sections with amylase should result in complete digestion of glycogen in normal horses; the PAS positive inclusions in horses with PSSM are very slow to digest leaving distinctive residues that indicate an abnormal polysaccharide is present.
  - the structure of polysaccharide in PSSM muscle by is less branched than normal muscle glycogen.

- clinical signs are observed immediately (5-10min) after mild exercise, more commonly after a week or more of rest, or changes in the exercise routine.
- serum CK is persistently elevated even when there is no exercise activity.
- the severity of the disease varies according to heterozygosity or homozygosity for the disease trait.

**Equine Polysaccharide Storage Myopathy (EPSM)**
- affects Draft horses
- similar glycogen storage disorder but with more vacuolization of muscle fibers and atrophy on muscle biopsy
- often have normal CK or mild elevations in serum CK and AST
- clinical signs include difficulty backing, difficulty holding up limbs for the farrier, shivers-like gait, loss of muscle mass, weakness, and recumbency.
- responsive to dietary fat supplementation.

**Electrolyte imbalances that may predispose to myopathies**
- electrolyte deficiency is more significant in hot humid weather where significant losses of electrolytes occur in sweat, or horses performing long distances (endurance horses), leading to electrolyte imbalances; the most significant loss is chloride, which promotes metabolic alkalosis (due to increase in bicarbonate to compensate for the loss of negative charges).
- urinary fractional excretion ratios of electrolytes have mixed results revealing the importance of supplementation or actual deficits.

\[
\% \text{ urinary fractional excretion} = \frac{\text{urine electrolyte} \times \text{plasma creatinine}}{\text{plasma electrolyte} \times \text{urine creatinine}} \times 100\%
\]
**Electrolytes:**
- Electrolyte deficiency is more significant in hot humid weather where significant losses of electrolytes occur in sweat, or horses performing long distances (endurance horses), leading to electrolyte imbalances; the most significant loss is chloride, which promotes metabolic alkalosis (due to increase in bicarbonate to compensate for the loss of negative charges).
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\]

**Potassium**
- Potassium may play a role in regulation of blood flow in exercising muscle, from which its intracellular content is released during exercise, resulting in dilatation of local arterioles and increasing in blood flow.
  - Depletion of body potassium has been associated with chronic intermittent exercise-associated rhabdomyolysis in horses:
    - Contraction of the precapillary sphincter limits the supply of oxygen and nutrients to the muscle, and limit lactate removal from the cell.
    - Altered membrane potential and muscle excitability.

- Serum or plasma concentrations of potassium, which is mainly an intracellular ion, do not adequately reflect total body potassium.
  - Because 60% of potassium is found in the muscle, measurement of total muscle potassium should estimate total body potassium; yet it requires a biopsy.
  - Determination of erythrocyte potassium concentration as a reflection of intracellular or total body potassium levels has been suggested as a non-invasive test.

- Urinary fractional excretion of electrolytes may be helpful in assessing electrolyte status in horses with rhabdomyolysis, although it does not reflect the muscle potassium concentration.
  - Can indicate dietary imbalances and suggest corrections.
  - Normal horses usually excrete large amounts of potassium, and abnormally low excretion suggests attempted conservation and/or inadequate intake.

**Calcium**
- Calcium is required for its role in muscular contraction and relaxation, and also to maintain the sodium concentration in nerve cells.
- An excess of intracellular calcium causes mitochondrial damage, protein release and cell death.
• lack of calcium allows spontaneous diffusion of sodium into nerves, resulting in fasciculations and involuntary contractions of the muscles
  o hypocalcemia is also implicated in producing exertional rhabdomyolysis and less severe myopathies
• if the diet is reach in calcium, parathyroid function is suppressed, and the process to mobilize ionized calcium rapidly from the gut bone is not fast enough to supply demand
  o lowered levels occur through sweating to meet thermoregulatory obligations
• calcium-induced calcium release in the muscle
  o in vitro halothane contracture responses, typical of individuals with malignant hyperthermia, have been reported in skeletal muscle from several horses with chronic intermittent rhabdomyolysis
  o horses with chronic intermittent rhabdomyolysis have shorter caffeine contractures and lower threshold for calcium-induced calcium release in heavy sarcoplasmic reticulum fractions, suggesting that calcium regulation at the sarcoplasmic reticulum is abnormal
    ▪ the pathogenesis of the abnormal caffeine contractures is unclear as it could be non-specific or associated with altered calcium regulation in the myoplasm
    ▪ there is no relationship between fiber types and caffeine contractures

Muscle enzymes
• exercise can normally induce small leakage of skeletal muscle proteins into the blood stream
• muscle damage (myodegeneration or necrosis) = leakage of cellular enzymes into the surrounding tissues and circulation
• elevated creatine kinase (CK) and aspartate aminotransferase (AST)
  o not always the rise in activity reflects the severity of clinical signs
  o elevation in CK and AST = recent active myonecrosis;
  o CK persists elevated = persistent necrosis;
  o elevated AST and declining CK = myodegeneration is not continuing; or previous episodes of injury
• CK = specific indicator of myonecrosis
  o rises rapidly to a peak within 6 hours, and declines within 2-3 days (half-life = 2 hrs)
• AST = can be also elevated in response to hepatocellular or red blood cell damage
  o rises more slowly, peaking within 24 hrs, and declines between 14-30 days (half-life = 7 days)
• Lactate dehydrogenase (LDH) = is found in many tissues and must be electrophoretically separated into isoenzyme fractions before definitive evidence of myodegeneration
  o LDH 1 and 2 are predominant in cardiac muscle
  o LDH 4 and 5 are predominant in skeletal muscle
  o it tends to peak in 12-24 hrs of cellular breakdown, and remains elevated for up 5-10 days

**MANAGEMENT of MYOPATHIES**

**DIET and DIETARY SUPPLEMENTATION**

**Grain**

• **high fat low starch diet** = decrease the amount of starch in the ration and substitute with dietary fat to meet daily caloric requirements
  o **for RER**
    ▪ feed no greater than 20% of daily digestible energy (DE) as nonstructural carbohydrate, and supply 20-25% of daily DE from fat
    ▪ effective in reducing ER episodes and post-exercise serum CK
  o **for EPSM**
    ▪ horses exercised regularly do well on low-calorie, low-starch diets
      • eliminate grain or keep nonstructural carbohydrate content < 10% of the daily DE
      • add fat to achieve caloric requirement (often 10-15%); more than that may lead to excessive weight gain
        o either rice bran (1-5 lbs) or oil (300-600 mls) on alfalfa pellets added to the diet
      • grass hay or mixed hay, and a balanced vitamin and mineral supplement
  • **low to moderate exercise intensities** = 1-5 lbs of grain combined with 600 ml of vegetable oil or up to five pounds of rice bran per day with a balanced vitamin and mineral mix
    o change diet gradually by increasing the amount of oil and decreasing high carbohydrate-based diet
    o vegetable oils are highly digestible (90-100%) = corn, soy, peanut, coconut, safflower, linseed, flaxseed, and canola
      ▪ when feeding vegetable oil, add vitamin E to the diet
    o rice bran (pellets) = 20% digestible fat plus contain vitamin E;
    o when feeding rice bran, add mineral supplement designed to correct its naturally high phosphorus content.
• **intense exercise** = more difficult to reach required energy
  o Re-Leve ([www.Re-Leve.com](http://www.Re-Leve.com)) is a special high-fat, low-starch pelleted diet
    ▪ contains 15-20% DE as fat (rice bran and corn oil) and only 9% DE as starch
    ▪ other options to add energy: highly fermentable fiber sources (soy hulls, beet pulp)
• do not forget FORAGE at 1.5-2% of body weight!
  o feed forage two hours before fat supplement
• feed small meals to reduce postprandial glycemic response

**Selenium and vitamin E:**
• selenium deficiency unlikely is the primary cause for ER, although muscle work generates free radicals; therefore, supplementation may decrease severity of clinical signs
• careful with overdosing selenium
  o side effects: excitement, mane/tail hair loss, wrinkled, dry/flaky hooves
  o adequate selenium supplementation: 0.2-0.3 mg/kg/diet dry matter of selenium
  o adequate vitamin E supplementation: 500-1000 mg of vitamin E per day
  o make sure ration does not already provide adequate daily needs before supplementation
• **sodium chloride**
  o formulated diets are low in sodium
  o sodium supplementation: 1-2 ounces of dietary salt – make sure fresh water is available at all times!
  o electrolyte mixtures 2:1:4 ratio of sodium:potassium:chloride are often used
• **sodium bicarbonate**
  o although believed to improve the lactic acidosis effect of rhabdomyolysis, there is no proof for a positive effect in the use of bicarbonate cocktails
  o not indicated in endurance because of the potential metabolic alkalosis

**Thiamine, branched chain amino acids, dimethylglycine and lactinase**
• may reduce lactic acid accumulation in muscle or increase lactic acid degradation = no scientific proof
• may help with sporadic ER but not chronic ER

**Methylosulfonylmethane (MSM)**
• natural anti-inflammatory effects?

**TRAINING AND MANAGEMENT**
• no prolonged stall rest or stall confinement
- turn-out keeps the muscles moving and reduce stress and excitability
  - feed excitable horses first to minimize stress
  - provide compatible equine company avoid nervousness induced by high doses of selenium supplementation