Initial Assessment of the Critical Neonate

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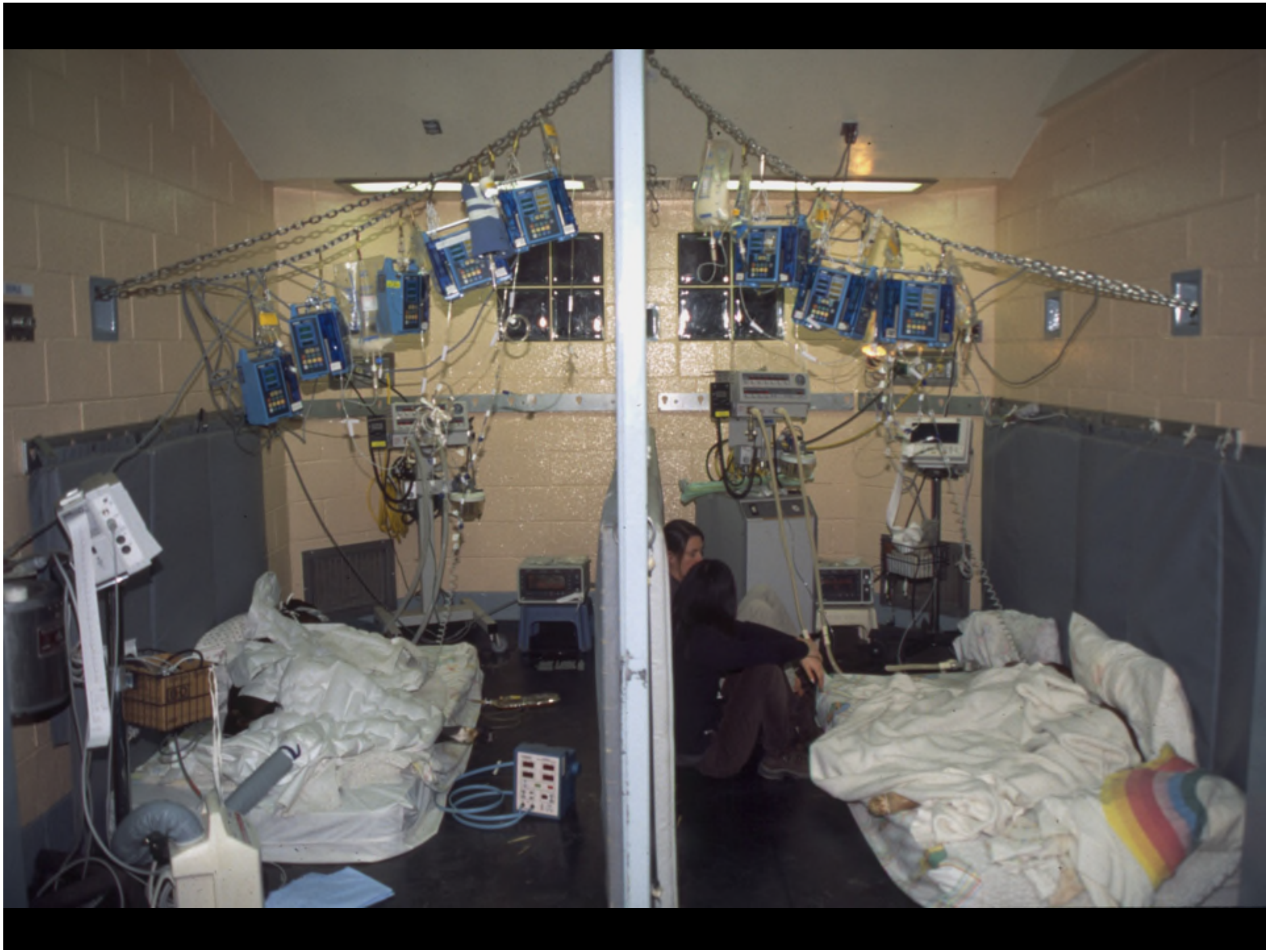



Compromised Foal

Critical 48 hours

- < 48 Hr old
  - 70-80% of admissions
- 84% survive
  - 70% fatal cases < 48 hr old

Weak or Fading Neonate

- Immediate assessment of essential organ function
- Immediate directed, supportive therapy
- Farm care
  - Practitioner's time
  - Sufficient trained
  - Adequately facilities
- Tertiary referral centers
  - Resources needed
  - Facilities
  - Coordinated care delivery team

"Scoop and Run"

"Stay and Play"

Neonatal Problems

- Fetal distress/maladaptation
- Sepsis/Infection
- Trauma/Hemorrhage

Neonatal Problems

- Rarely one problem
  - Combination of problems
  - Varying severities
- Wide array of possibilities
  - but predictable course

Goals

- Identify underlying problem
- Identify disrupted vital organ functions
- Therapeutic interventions
  - Support normal organ functions
  - Control infection

Initial Assessment

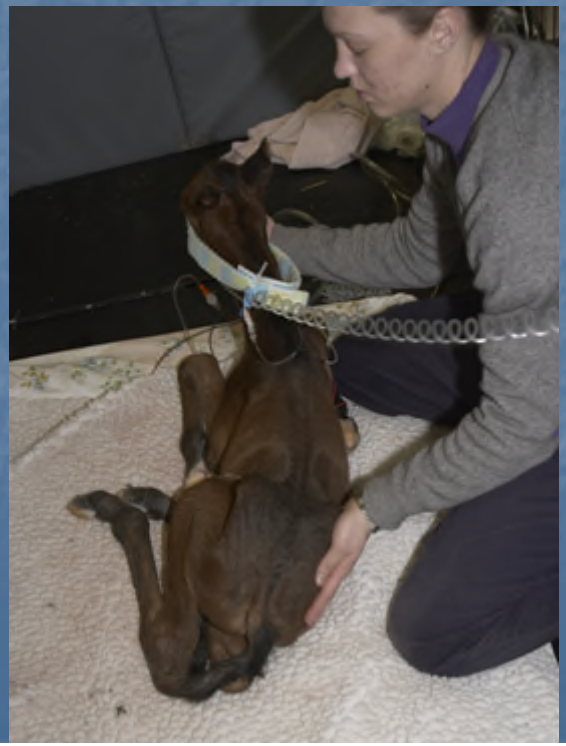
- Is there evidence of sepsis?
- Is cardiovascular support necessary?
- Is respiratory support required?
- Will enteral nutrition/fluid maintenance be possible?
  - Is intravenous fluid therapy necessary?
  - Is continuous rate dextrose infusion necessary?
  - Is parenteral nutrition necessary?
- Will assisted thermoregulation be necessary?
- Control behavioral abnormalities
- What level of metabolic support is necessary?
- Will renal support be necessary?
- Requirements for other specific supportive care

Physical Examination

- Body condition
- Musculoskeletal problems
- Mucous membrane
- Cardiovascular examination
- Abdominal palpation
- Nervous system evaluation

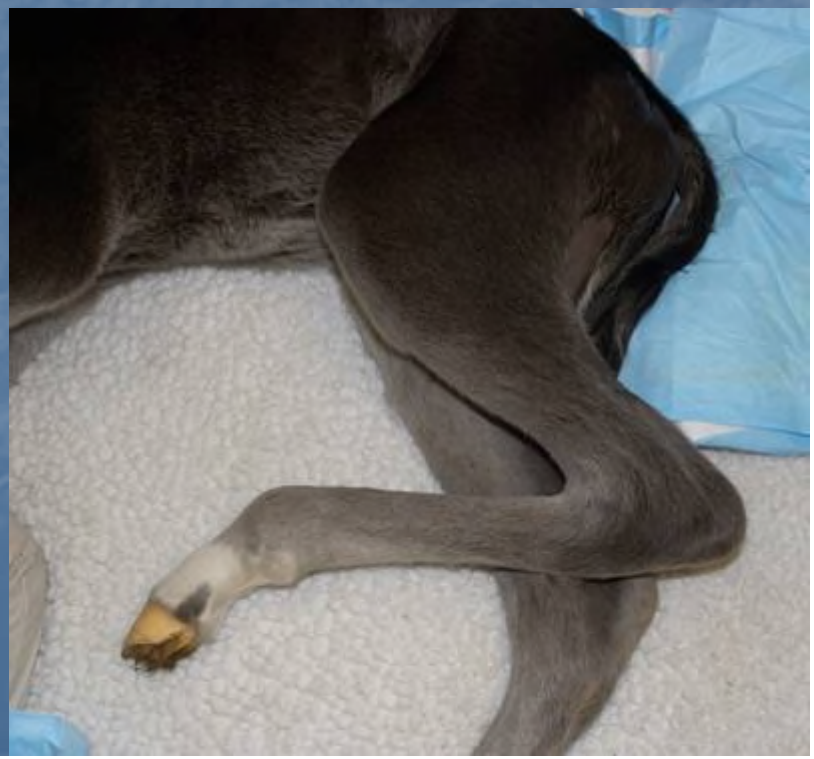
Body Condition

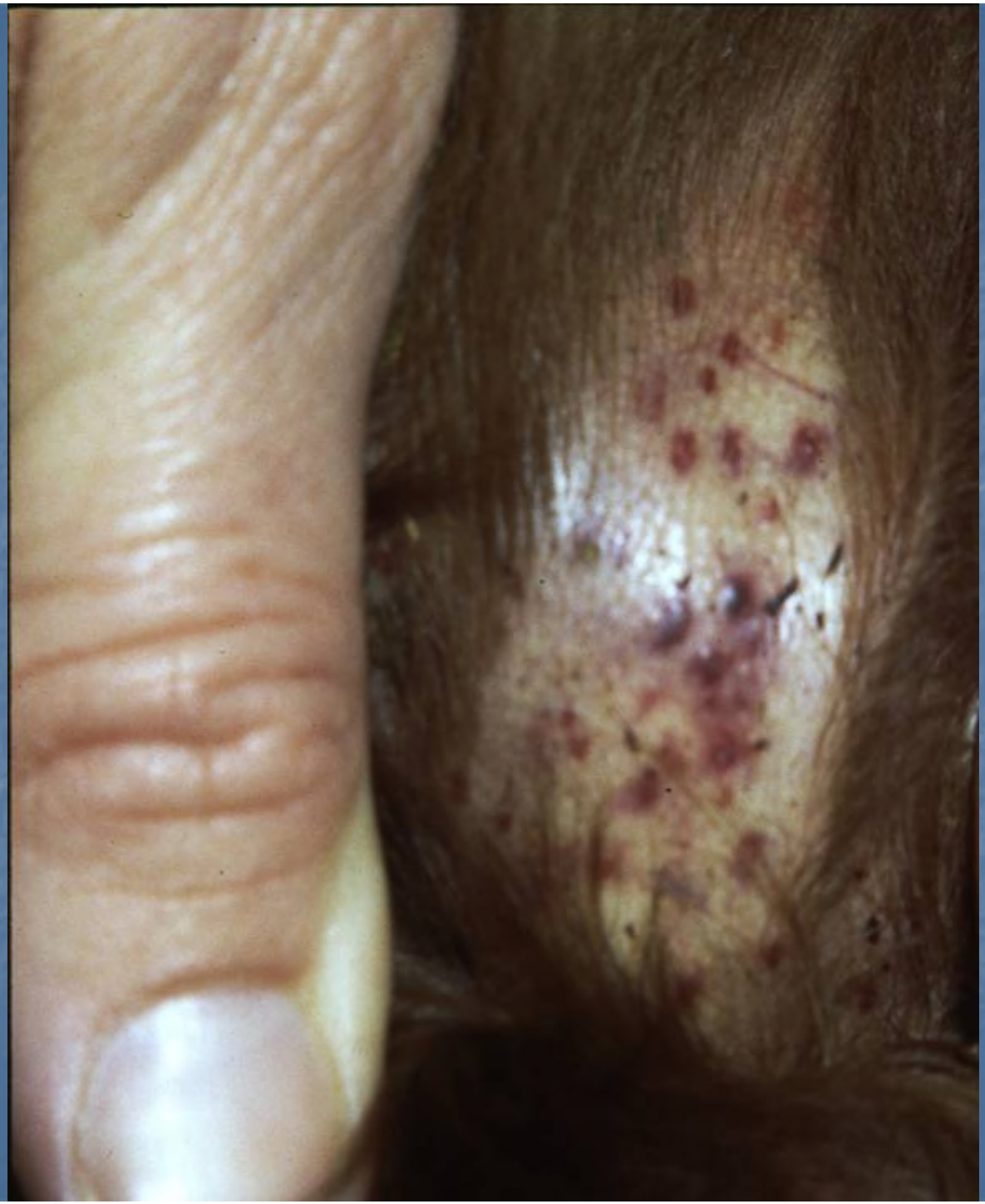
- Thin to emaciated
  - IUGR
  - Fetal SIRS
  - Prematurity
  - Post maturity

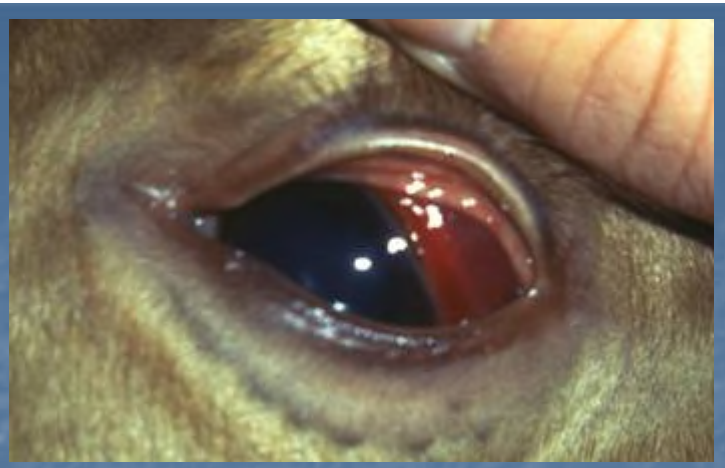


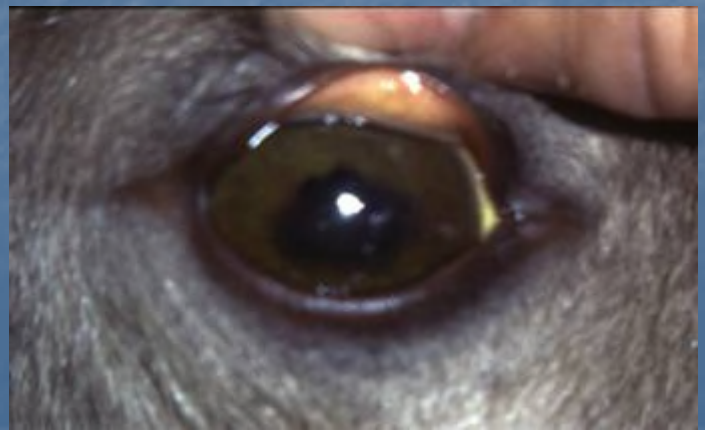
Musculoskeletal problems

- Fractured ribs
- Other musculoskeletal abnormalities
  - Fractures
  - Gastrocnemius disruption
  - Contracture
  - Laxity







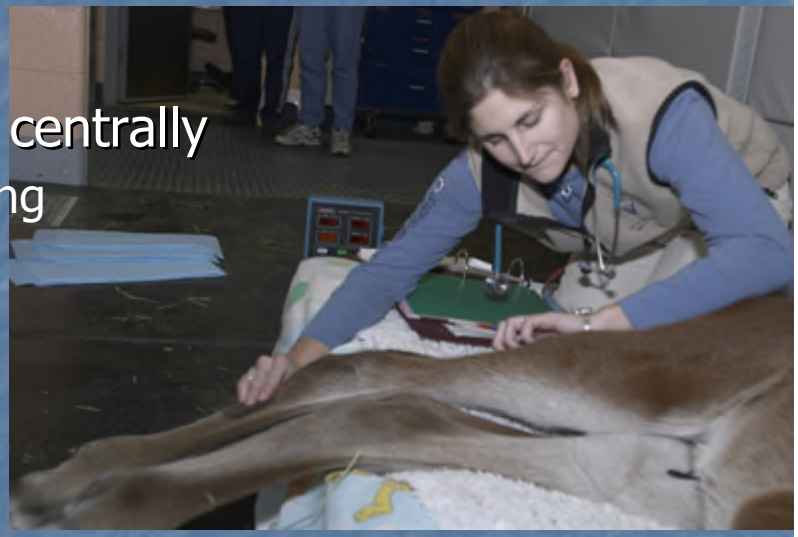


Cardiovascular Examination

- Evaluating perfusion
- Evaluating volemia
  - Volemia vs hydration
  - Dehydration rare
  - Hypovolemia common

Cardiovascular Examination

- Assess effectiveness of perfusion
  - Cold extremities as blood is shunted centrally
    - Do not be treated with active warming
  - Depressed mental status
  - Decreased borborygmi
  - Urine production
- Pulse assessment
  - Pulse quality
  - Arterial tone
  - Arterial fill
- Unreliable signs
  - Dry oral membranes
  - Capillary refill time
  - Skin turgor



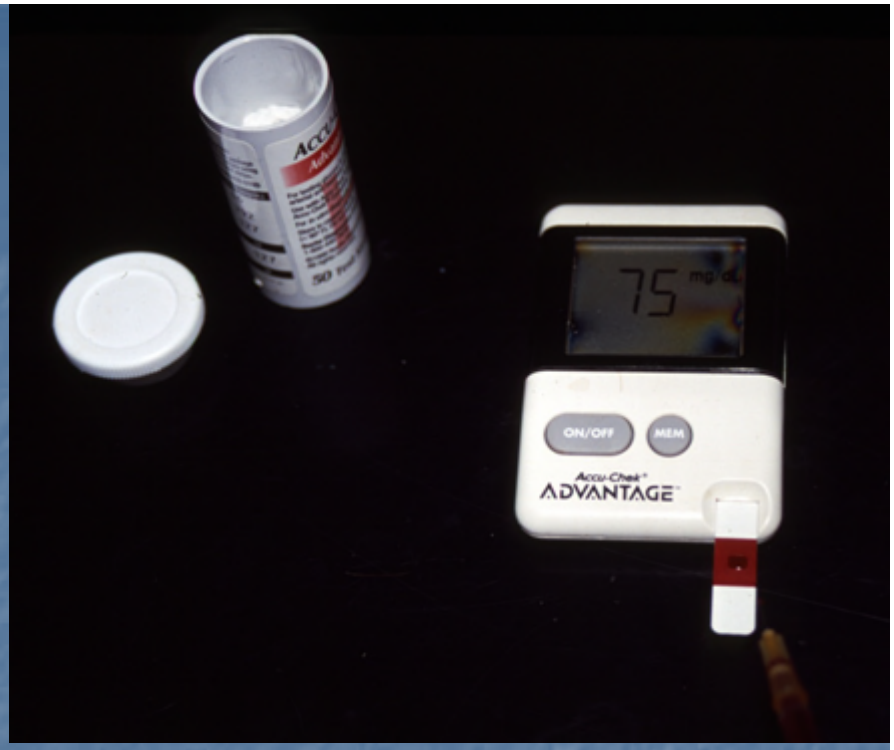
Abdominal Palpation

- Internal umbilical remnants
  - Umbilical triad (2 arteries and urachus)
  - Hemorrhage
  - Omphalitis
- Urinary bladder
  - Luminal and bladder wall hematomas
- Intestines
  - Retained meconium
  - Thickened intestinal wall
  - Pneumatosis intestinalis
  - Intussusceptions
- Kidneys
- Liver - Hepatomegaly
- Body wall defects
  - Inguinal or umbilical hernias
  - Other body wall defects

Central Nervous System

- Important parameters
  - Strength
  - Muscle tone
    - Hypertonus or hypotonus
  - Responsiveness
    - Hyperresponsive or hyporesponsive
  - Level of arousal
    - Somnolence
    - Hyperactive or hyperkinetic
  - Behavior
  - Respiratory patterns
    - Periodic apnea
    - Cluster breathing
    - Apneustic breathing
    - Ataxic breathing
  - Seizures
  - Abnormal vocalization

- Careful physical
  - Detect major dysfunction
  - Seriousness
- Dynamic monitoring
  - Serial physical evaluation
  - Laboratory analysis
    - Stall side
      - Serial blood glucose levels
    - Sophisticated
      - Arterial blood gas
      - Blood electrolyte
      - Lactate levels



Therapeutic Interventions in Neonates

Resuscitation of the Seriously Compromised Foal

- Rapid intervention
- Intensive intervention
- On Farm
- At referral center
  - Rapid transport
    - In a car
  - Short travel time
    - < 2 hours – don't treat - send
    - > 2 hours – begin treatment

Resuscitation on the Farm

- Delay in transportation
- Delay in decision making
- Lack of referral center availability
- Economic constraints
- Level of care on farm depends on
  - Environment/Facilities available
  - Experience/Energy of the help
  - Time constraints on the clinician
  - Availability of equipment

Resuscitation of the Seriously Compromised Foal

- Treat sepsis
- Stabilize blood glucose
- Respiratory support
- Insure tissue perfusion
  - Fluid therapy
- Deliver cerebral support
  - Control seizures
- Aid thermogenesis
- Correct metabolic abnormalities
- Spare renal work
- Deliver nutrition – oral/parenteral
- Give general supportive care

Treat Sepsis

- Plasma transfusion therapy
- Antimicrobial
  - Based on likely sensitivity
  - Community isolates vs. nosocomial isolates
  - Avoid
    - Commonly used antimicrobials
    - Toxic effects

Community Acquired Isolates

- 22% *E coli*
- 19% *Enterococcus*
- 19% *Pantoea agglomerans*
- 5% *Klebsiella*
- 5% *Streptococcus*
- Others
  - *Acinetobacter* , *Aeromonas,* Alpha *Strep*
  - *Burkholderia, Listeria, Mannheimia*
  - *Comamonas, Salmonella, Staphylococcus*
- 60% Gram-negative and 40% Gram-positive

Nosocomial Bacterial Isolates

- 23% *Enterococcus*
- 18% *E coli*
- 11% *Enterobacter cloacae*
- 9% *Acinetobacter baumannii , Salmonella*
- 7% *Pantoea agglomerans, Pseudomonas*
- 5% Coag neg *Staphylococcus*
- 4% *Klebsiella pneumonia, Streptococcus*
- Others
- 68% Gram-negative and 32% Gram-positive

Antimicrobial Choices

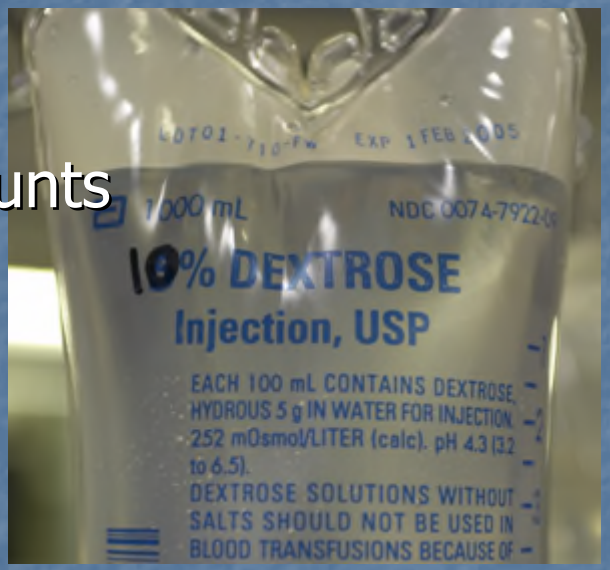
- Community acquired infection
  - Ambulatory patient, controlled sepsis
    - Cefuroxime
    - TMS - IV
  - Critically ill neonate, uncontrolled sepsis
    - Ceftiofur Na - IV
      - 10 mg/kg IV QID
      - Continuous rate infusion (CRI)
- Nosocomial infection
  - Penicillin and amikacin – IV
  - Ticarcillin with clavulancic acid - IV

Glucose Therapy

- Bedside monitoring – Glucometers
- Levels reflect homeostasis
  - Not availability
- Normal values
  - Birth – ½ maternal glucose
    - 30-50 mg/dl,
  - Drop - low point 2 hrs after birth
  - Increase with time/nursing
- High glucose levels at birth (>70 mg/dl)
- Low glucose levels at birth (< 20 mg/dl)

Glucose Therapy

- All compromised neonates
  - Will benefit from glucose therapy
- Placental glucose transport
  - Equine delivers 6.8 mg/kg/min
  - Range between 4 – 8 mg/kg/min
- Neonatal liver produces similar amounts
- Glucose therapy
  - Begin 4 mg/kg/min
  - Goal of 8 mg/kg/min
- Hyperglycemia - insulin therapy
- Hypoglycemia – hypermetabolism
- Glucose boluses
  - Metabolic anarchy
  - Often more harmful than continued hypoglycemia

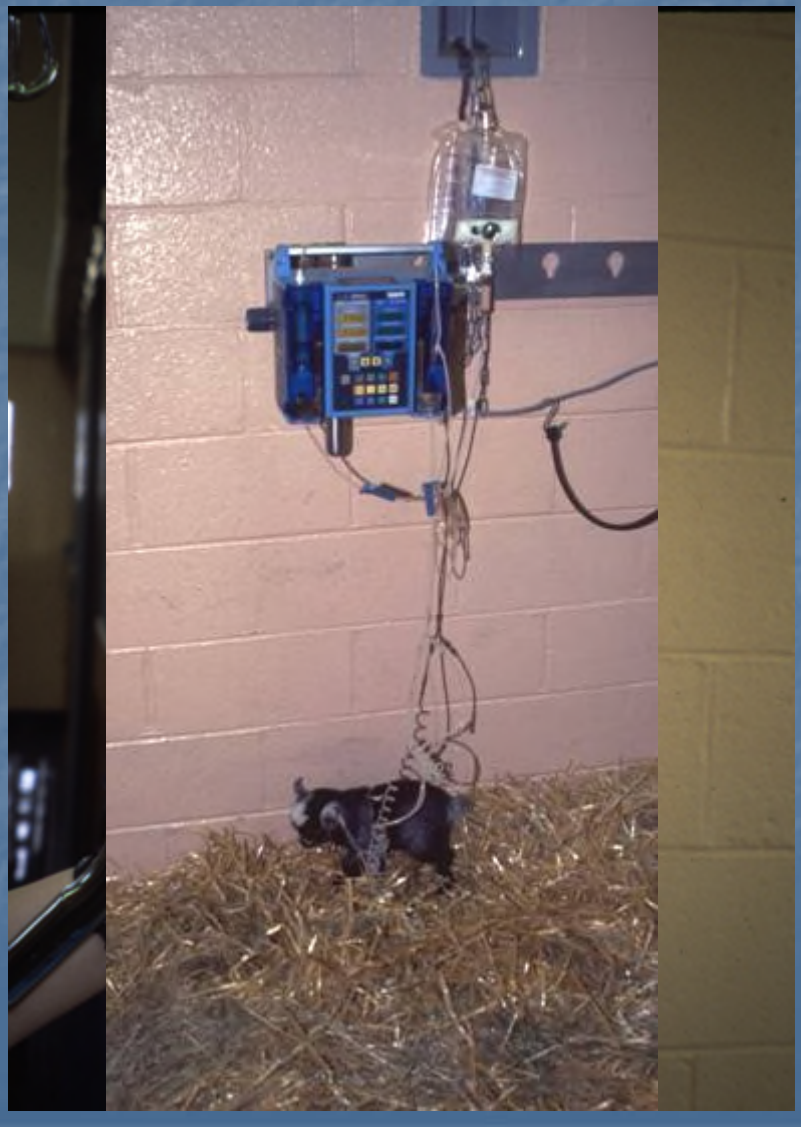


Respiratory Support

- Frequently hypoxemic
  - Ventilation perfusion mismatching
- Intranasal oxygen insufflation
  - Pa_{O2} < 60 torr
  - SaO_2 < 90%
  - Goal
    - Pa_{O2} 80 - 110 torr
    - SaO_2 > 92%
  - Nasal cannula
    - Flow rate of 6-10 lpm (2 to 15 lpm)
    - Preconditioned - water filled humidifier
- Central respiratory depression
  - Caffeine (10 mg/kg PO or PR)
  - Positive pressure ventilation.

Fluid Therapy

- Hypoperfusion
  - Hypovolemia due to poor vascular tone
  - Almost never dehydrated
    - Hyperhydrated but hypovolemic
- Correct the hypovolemia
  - 20 ml/kg blouses over 10 to 20 minutes
- Maintenance fluids
  - 100 ml/kg/day for the 1st 10 kg weight
  - 50 ml/kg/day for the 2nd 10 kg weight
  - 25 mg/kg/day for each kg above 20 kg



Thermogenesis

- Thermogenesis
  - Successful resuscitation
- Active warming
  - Contraindicated early treatment
  - Hot air blanket

Seizure Control

- Phenobarbital
  - Hypothermia
  - Hypercapnia
  - Hypotension
  - Infused over 15-20 min
  - Half-life of >200 hrs
- Phenytoin
- Others
  - Diazepam
  - Midazolam

Cerebral Support

- Maintaining cerebral perfusion
  - Fluid replacement
  - Maintaining adequate BP
- Thiamine
- $MgSO_4$
- Not used
  - DMSO
  - Mannitol

Renal Function

- Neonatal diseases target
- Normal neonatal kidney
  - Fluid handling
  - Sodium regulation
- Goal - minimize renal work
  - Regulating fluid balance
  - Regulating sodium balance
- Fluid and Na overload
  - Inappropriate weight gains
  - Development of edema
- Drugs to avoid
  - Flunixin meglumine
  - Aminoglycoside antimicrobials
    - Unless blood levels are measured

Oral Nutrition

- Colostrum
  - Large volumes
- Critical neonate
  - Hypoxemia, hypoperfusion
  - Hypoglycemia, hypothermia
  - Can't support enterocytes
- Criteria for feeding
  - Pao_2
  - Blood glucose
  - Perfusion
  - Core temperature is > 100 F
  - Borborygmi present
  - Meconium is being passed

Oral Nutrition

Oral Nutrition
What should be fed?

Indwelling Enteral Feeding Tube

Ulcer Prophylaxis
Reasons not to suppress acid

- Sick neonates produced little acid
- Acid blockers have a decreased efficacy
- Gastric ulcer pathogenesis
  - Acid plays a minor role
- Acid is protective against nosocomials
  - Should not be suppressed or neutralized
- Ulcer prophylaxis not affect incidence of ulcers
- Occurrence decreasing
  - More effective supportive therapy for neonates

Summary

- Treat sepsis
- Maintain blood glucose homeostasis
- Maintain fluid balance
- Keep the patient warm
- Give respiratory support
- Maintain tissue perfusion
- Control seizures and support cerebral perfusion
- Maintain renal function
- Conservatively approach oral nutrition
- Deliver general supportive nursing care.

Avoid

- Excessive fluid
- Excessive sodium
- Aggressive warming
- Large volumes oral feeding
- NSAIDs (flunixin meglumine)
- DMSO
- Gastric acid blocking therapy

INITIAL ASSESSMENT OF THE CRITICAL NEONATE

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Neonates with inconsistent or complete lack of nursing behavior, who are weak or develop progressive weakness and become recumbent during the first 48 hours after birth, are critically ill and require immediate intervention with supportive therapy. In our tertiary care practice, 70-80% of neonatal admissions are within the first 48 hours after birth. Of the neonates that we can't save, 70% die within this initial 48 hour period. Neonates who become weak and recumbent during this critical period require immediate attention with assessment of essential organ function and immediate directed, supportive therapy. Although, in some cases, the level of care needed can be delivered on the farm, the ability of the busy practitioner to dedicate the time needed without compromising the rest of his practice, the availability of sufficient trained help on the farm with the energy and dedication to deliver care and the lack of adequately equipped facilities on the farm significantly limits this possibility.

The initial step in delivering life saving care, whether treatment is to be dispensed on the farm or at a referral center, is recognizing the seriousness of the problem. The foal that is weak from birth or initially seems normal and then fades during the first 48 hours of life may have a number of different underlying problems. These problems can be generally classified as those secondary to fetal distress/maladaptation, those secondary to sepsis/infection and those secondary to trauma/hemorrhage. Problems associated with fetal distress/maladaptation include the complex of neonatal encephalopathy (maladjustment syndrome), neonatal nephropathy, neonatal enteropathy (NEC), neonatal metabolic/endocrine maladjustment (hypo/hyperglycemia, hypo/hypercalemia, poor insulin response, autonomic failure, vasopressin deficiency, cortisol deficiency, etc.), neonatal cardiovascular failure (hypoperfusion secondary to lack of adrenergic sensitivity, vasoplegia, central failure; myocardial dysfunction), prematurity/dysmaturity, IUGR, sick cell syndrome, etc. Problems associated with sepsis/infection include SIRS, generalized sepsis, localized or systemic infection (bacteremia, aspiration pneumonia, umbilical infections, etc.), infectious enteritis (clostridiosis, salmonellosis), coagulopathies, immune dissonance, MODS (ARDS, NEC, etc.), severe sepsis, septic shock, etc. Finally those problems associated with trauma/hemorrhage include birth trauma (fractured ribs with associated damage, gastrocnemius rupture), anemia (umbilical hemorrhage, fractured rib associated hemorrhage, gastrocnemius associated hemorrhage, femoral fractures), etc. In reality, there is rarely one problem but a combination of problems with varying severities. In fact there is a seemly endless array of possibilities.

Fortunately, it is not necessary to identify the exact nature of the underlying problem to successfully treat the neonate. Instead, the clinician should identify which vital organ functions have been disrupted and institute therapeutic interventions which support normal function while

simultaneously attempting to control any infection which is present. With these 2 goals met, the foal has the opportunity to heal and recover. So the object of the initial assessment of the critically ill foal is to identify organ dysfunction and then to tailor therapy toward supporting vital organ function. The questions which need to be answered by the initial assessment of the neonate include: is there evidence of sepsis; is cardiovascular support necessary to insure tissue perfusion and if so to what degree; is respiratory support required; will enteral nutrition and fluid maintenance be possible or is parenteral nutrition necessary; will assisted thermoregulation be necessary; what type of intervention will be necessary to control behavioral abnormalities; what level of metabolic support is to be expected; will renal support be necessary; and are there requirements for other specific supportive care (assisting to stand, musculoskeletal physical therapy, special restraint, etc.). With a careful, complete physical examination and with simple laboratory analysis (e.g. patient side glucose determination), the practitioner can rapidly make an assessment of what level of supportive therapy is necessary and whether or not this level will require local hospitalization or referral to a tertiary support facility.

BODY CONDITION

A thin to emaciated foal at birth suggests intrauterine growth restriction (IUGR). In this condition, abnormal placental metabolism, such as may occur with placentitis, results in an energy drain from the fetus producing fetal weight loss and emaciation. Alternately, fetal SIRS may result in the same outcome. Finding a small body frame with fine bones along with a fine, short hair coat, domed forehead and poor ear cartilage development suggests prematurity. A foal with a large body frame (large bones and large joints), with long hair coat suggests post maturity. A careful search for fractured ribs and other musculoskeletal abnormalities (fractures, gastrocnemius disruption, contracture, laxity, etc.) should be made.

MUCOUS MEMBRANE EVALUATION

Mucous membranes should be carefully evaluated for signs of icterus, injection (including large vessel injection where individual vessels are easily identifiable and small vessel injection caused by generalized capillary filling), petechia (oral, aural, scleral), erythema (lingual, periocular, nasal, nasal septum, aural, segmental oral) and coronitis. The presence of icterus suggests sepsis/SIRS, retained meconium, hemolytic disease (isoerythrolysis) or hemorrhage (internal umbilical remnant, fractured ribs, thrombocytopathies, intestinal bleeding associated with NEC, etc.). Large vessel injection is associated with excitement, hypoxic ischemic disease, local irritation, drying injury and occasionally sepsis/SIRS. Small vessel injection is associated primarily with sepsis/SIRS but also equally with hypoxic ischemic disease with loss of vascular control. Oral, aural and scleral petechia may all be induced by birth trauma but are more commonly associated with sepsis/SIRS. When examining the foal for petechia, care must be taken not to mistake the end-on vessels in the oral mucous membranes for petechia. These vessels, when engorged, resemble petechia (I refer to them as “pseudopetechia”), but can easily be differentiated since they blanch when pressure is applied. Also, although Culicoides may occasionally cause bleeding aural petechia, similar bleeding petechia can be caused by sepsis/SIRS. Palpable petechia are not common and when identified should direct attention towards coagulopathies. Erythema is most often identified around the head affecting the lingual, aural, periocular, nasal skin, nasal septum and oral membranes. Lingual erythema is most commonly associative with hypoxic ischemic syndrome but occasionally is striking even in normal foals when they initially begin to suckle. Aural, periocular and nasal skin erythema are

primarily associated with uncontrolled SIRS. Nasal septum erythema may be associated with sepsis/SIRS or with hypoxic ischemic syndrome. Regional erythema of the oral membranes may be striking because of the sudden transition from normal to erythematous membranes. Although on casual inspection, these areas may look like submucosal hemorrhage, the fact that they will disappear within hours rules out this possibility. It is more likely the result of regional loss of vascular control associated with hypoxic ischemic syndrome. Finally, coronitis is also a sign associated with sepsis/SIRS and occasionally severe hypoxic ischemic syndrome. Initially, coronitis is more noticeable on non-pigmented hooves, especially beginning at the heels. The hemorrhagic line will become more noticeable as the foal's disease progresses and over and several days it makes a transition to a purple, bruised appearance.

AUSCULTATION

Careful attention to heart rate and rhythm is important noting whether inappropriate bradycardia is present (heart rate inappropriately low in the face of marginal perfusion) and noting the occurrence of any premature contractions or other arrhythmias. Flow murmurs are very common in foals and should not be over interpreted. They may be identified as flow murmurs if there are significant changes in a quality and volume with changes in the foal's body position or heart rate. Most foals with retained fetal circulation do not have unusual murmurs. Careful auscultation of the lungs is important. Moist bronchovesicular sounds should be heard for the first few hours after birth as resorption of fetal fluids may take some time. Because of the stiff nature of neonatal lungs, find crackles associated with collapsing and reinflation of alveoli should be expected. Recumbent foals, because of the compliant nature of their chest wall and the stiffness of the lungs, will consistently have rales in the recumbent lung. Sick, recumbent foals are particularly susceptible to aspiration resulting in pneumonia. Careful auscultation of non-recumbent lung with deep breaths is important in identifying pneumonia. Auscultation of the GI tract should reveal frequent but not constant borborygmi if the foal is receiving oral nutrition. Sometimes the GI tract will remain quiet when milk is being withheld. Identification of a good variety and frequency as well as quality of borborygmi is important in assuring gastrointestinal health. Foals with hypoxic ischemic intestinal disease, such as necrotizing enterocolitis, frequently have quiet and distant borborygmi with occasional loud gas sounds.

ABDOMINAL PALPATION

Just as a careful rectal examination can be revealing in adults, careful and thorough abdominal palpation can be an important adjunct to the physical examination of the neonate. In order to be successful, the foal should be quiet and have a relaxed abdominal wall as occurs in depressed, septic foals, foals with hypoxic ischemic syndrome or normal foals in the somnolent postprandial state. Although the technique is usually practiced on the quite, recumbent foal, it can be adapted to the standing foal. With practice, many structures can be readily identified and abnormalities recognized. The internal umbilical remnants, especially the umbilical triad (2 arteries and urachus) should be palpated to identify recent hemorrhage or inflammatory disease (omphalitis). Also, palpation of the umbilical arteries may reveal retained pulses and their juxtaposition will indicate whether or not the urinary bladder contains urine. The urinary bladder can often be identified and both luminal and bladder wall hematomas recognized. The intestines should be palpated to detect retained meconium (most often felt in the right colons just under the rib cage or in the caudal abdomen near the bladder). In cases of necrotizing enterocolitis, thickened intestinal wall, pneumatosis intestinalis and intussusceptions may all be palpated. The kidneys

and the liver can be evaluated. Hepatomegaly is not an unusual finding in the critically ill neonatal foal. Identification of inguinal or umbilical hernias and other body wall defects can also be important.

CARDIOVASCULAR SYSTEM

Evaluating perfusion and volemia is essential in managing sick neonates. The distinction should be made between volemia and hydration. Hydration refers to the adequacy of cellular fluid volume and to a lesser extent, adequacy of the cellular reserves, which is the interstitial volume. Volemia refers to adequacy of circulating volume. Almost universally, neonates are born with excessive hydration, having a higher percent total body water than adults. With fetal distress, often the neonate is born with even more body water secondary to greater fluid shifts from the fetal fluids to the interstitium. So rehydration is almost never required except in rare circumstances such as after extensive external hemorrhage. However, hypovolemia is common in ill neonates resulting in hypoperfusion. In such cases, hypovolemia needs to be addressed aggressively.

The object of the cardiovascular examination is to assess effectiveness of perfusion. Physical examination signs of hypoperfusion include cold extremities as blood is shunted centrally. The cold limbs should not be treated with active warming as this will defeat the circulatory compensation. The ears and nose may also be cool to cold and hypoperfusion can result in a depressed mental status and decreased borborygmi. Urine production is a very reassuring sign indicating perfusion of the kidneys. However, it should be remembered that unlike other neonates, foals usually don't urinate for the first 12 hours after birth. Lack of urine production in the foal that is only hours old, even in the face of fluid therapy can not be taken as evidence of poor kidney perfusion. Other physical findings that relate to perfusion are pulse quality, arterial tone and arterial fill. Careful assessment of pulse quality can help determine pulse pressure (difference between systolic and diastolic pressure). Arterial wall tone is assessed by the amount of finger pressure required to feel the pulse and the amount required to eliminate the pulse. If the pulse can only be felt by a very light touch, there's little tone to the arterial wall. On the other hand if even with firm pressure the pulse still can be felt there may be increased arterial wall tone. This quality roughly corresponds to blood pressure and responsiveness to adrenergic tone. Arterial fill is assessed by feeling the size of the artery's lumen as finger pressure is applied. Arterial fill relates to the blood volume on the arterial side of the circulation. These clues can relate much information about blood pressure and perfusion. Dry oral membranes are an unreliable aid in determining hydration status since many ill foals keep their mouths open allowing the mucous membranes to dry. Likewise, capillary refill time is not particularly helpful since it may be determined more by the state of mucous membrane injection and venous pressure/return than by volemia. Skin turgor is an unreliable sign in the neonate.

The heart rate should be appropriate for the state of perfusion. When perfusion is poor and blood pressures low, a high heart rate is appropriate. When perfusion is good and blood pressures adequate, a low heart rate is appropriate. If the heart rate is not appropriate, the cause of the disparity (e.g. level of discomfort, abnormal central control, excitement or primary myocardial disease) should be identified. Inappropriate bradycardia is a frequent finding in critically ill neonates and may relate to retention of fetal physiology in which bradycardia is an important part of the response to distress. The rhythm should be carefully evaluated since it is common to

have arrhythmias in the neonatal period secondary to primary myocardial disease, trauma from fractured ribs and metabolic abnormalities. Transient cardiac arrhythmias which spontaneously resolve are not unusual during the first hours after birth. Cardiac murmurs are almost universally present during the neonatal period (first 30 days of life). It is a widely held misconception that these are from a patent ductus arteriosus. Most neonatal murmurs, even during the first 24 hours of life, are in fact flow murmurs which often change character as the foal's body position or heart rate changes. Murmurs associated with significant cardiac anomalies are often course whereas flow murmurs are generally soft. The presents of a persistently loud, coarse murmur should raise the suspicion of a significant congenital defect which will require further investigation.

CENTRAL NERVOUS SYSTEM

When evaluating the nervous system of neonatal foals, it is important to evaluate strength, muscle tone, responsiveness and ability to arouse the foal. Clinicians commonly think about behavioral changes such as loss of suckle and search behaviors as well as loss of tongue control and coordination (hypertonic lingual dissociation). Other neurologic signs may be equally as important including the development of facial nerve and vestibular signs, becoming hyperresponsive or hyporesponsive, developing hypertonus or hypotonus, becoming hyperactive or hyperkinetic or developing somnolence. Careful observation of respiratory patterns may show periodic apnea (>20 seconds without breathing), cluster breathing (several rapid breaths followed by a respiratory pause or apnea), apneustic breathing (breath holding) or ataxic (irregular) breathing. Severely affected foals will have seizures. Most of these are generalized clonic tonic activity centered on the front of the body (head, neck and front legs) or more generalized animated seizures with clonic tonic paddling motion (galloping). A dramatic sign sometimes present is abnormal vocalization which may mimic a barking dog but more often mimics a squealing pig.

A careful physical examination will help the clinician detect major organ dysfunction indicating the seriousness of the condition. Further important information can be gained by dynamic monitoring of organ function and by laboratory analysis of blood samples. Simple monitoring, such as serial blood glucose levels can be easily achieved using inexpensive patient side monitors. But vital information, such as arterial blood gas, blood electrolyte and lactate levels require more sophisticated equipment which is better suited to be used in a hospital. Many therapeutic modalities, although possible on a farm, are much more manageable in a referral hospital practice. The most advanced therapeutic modalities, such as mechanical ventilation, are only possible in a tertiary referral center.