High Risk Pregnancies

Perinatology

Jon Palmer, VMD, DACVIM

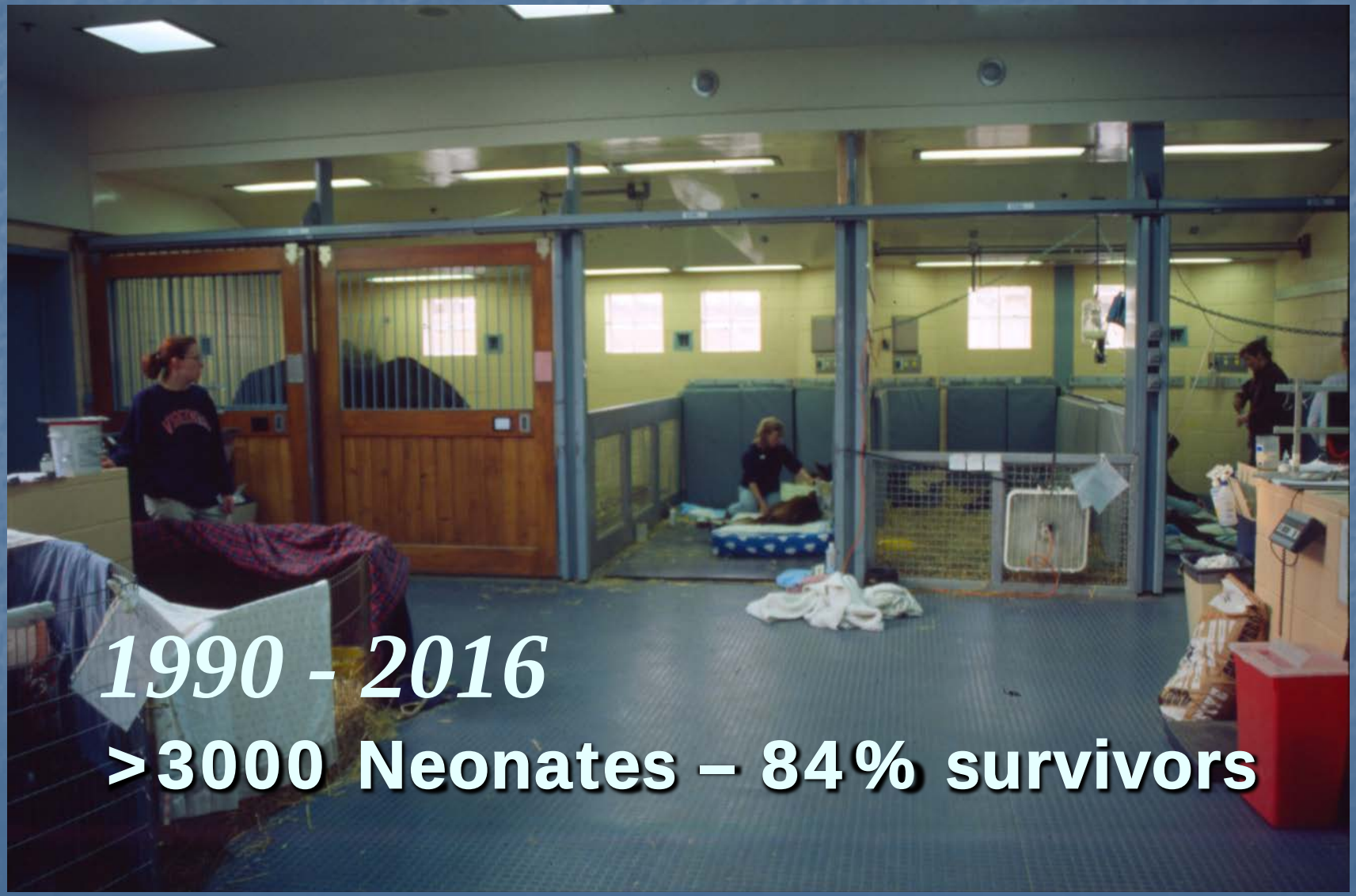
New Bolton Center, Univ Penn, USA

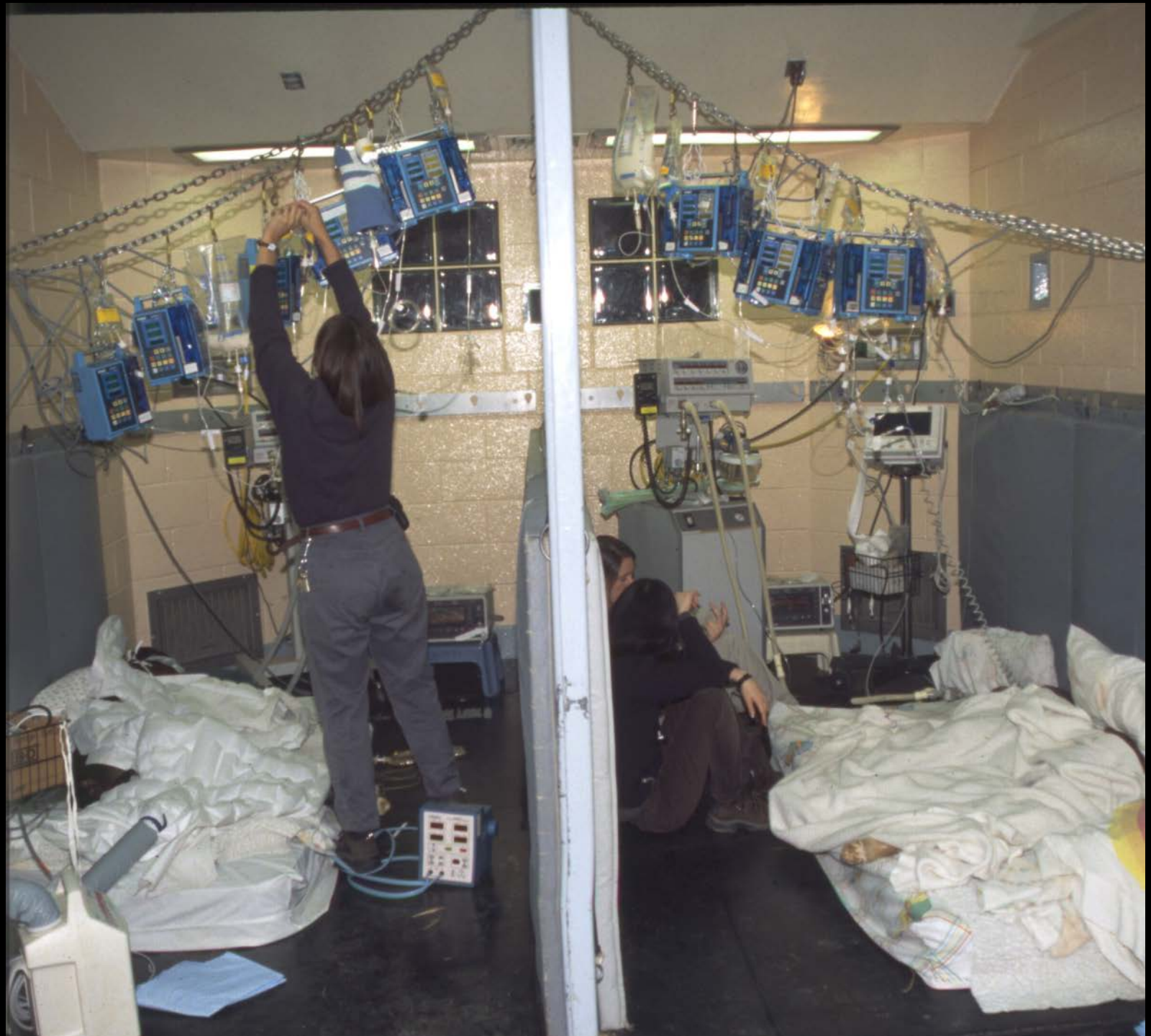
High Risk Pregnancies Perinatology

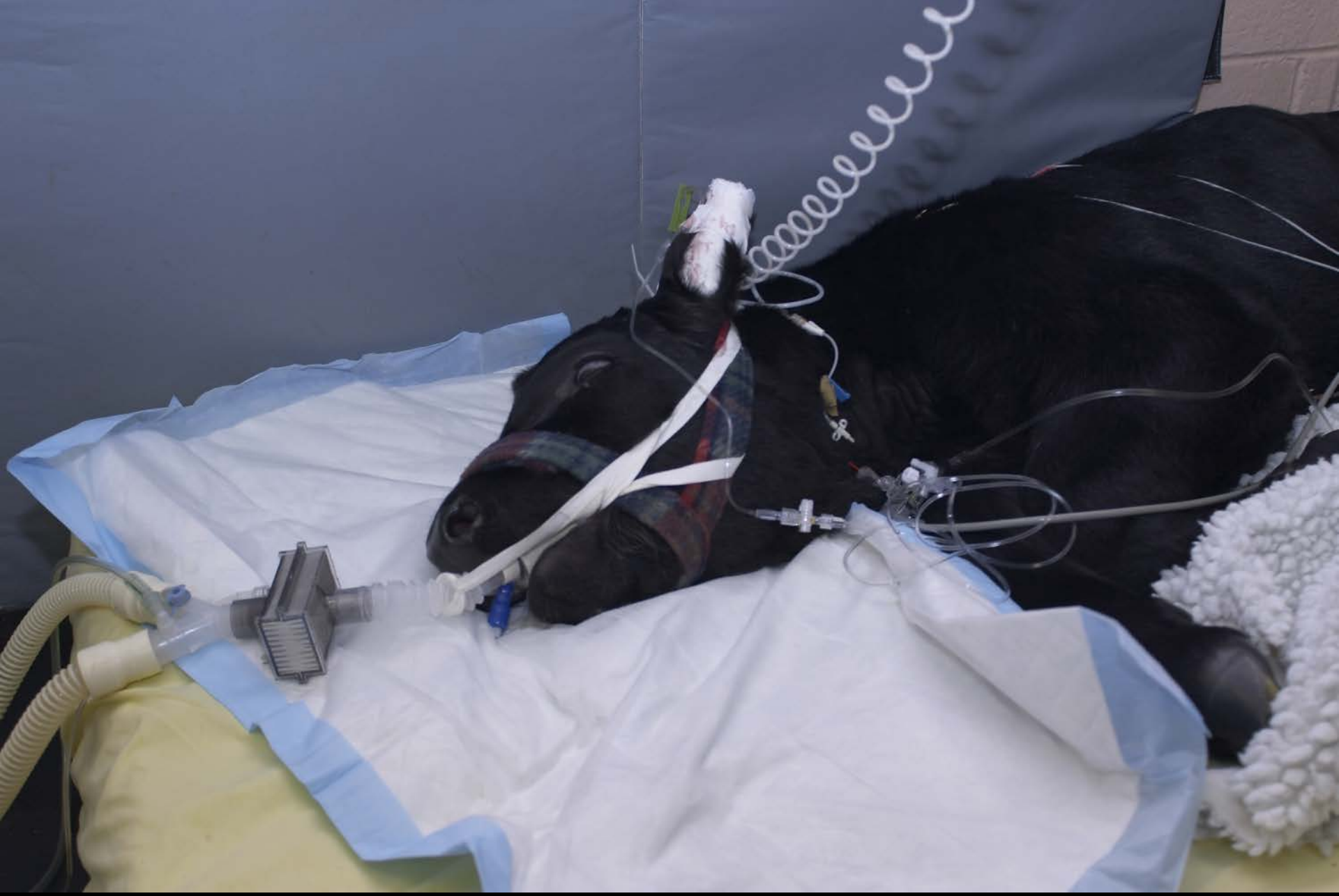
- Background, where I work
- What is a High Risk Pregnancy?
- Fetal monitoring
- Threats to fetal well-being
- Fetal resuscitation
  - Minimizing the threats

http://eceim16.nicuvet.com

Graham French Neonatal Section
Connelly Intensive Care Unit

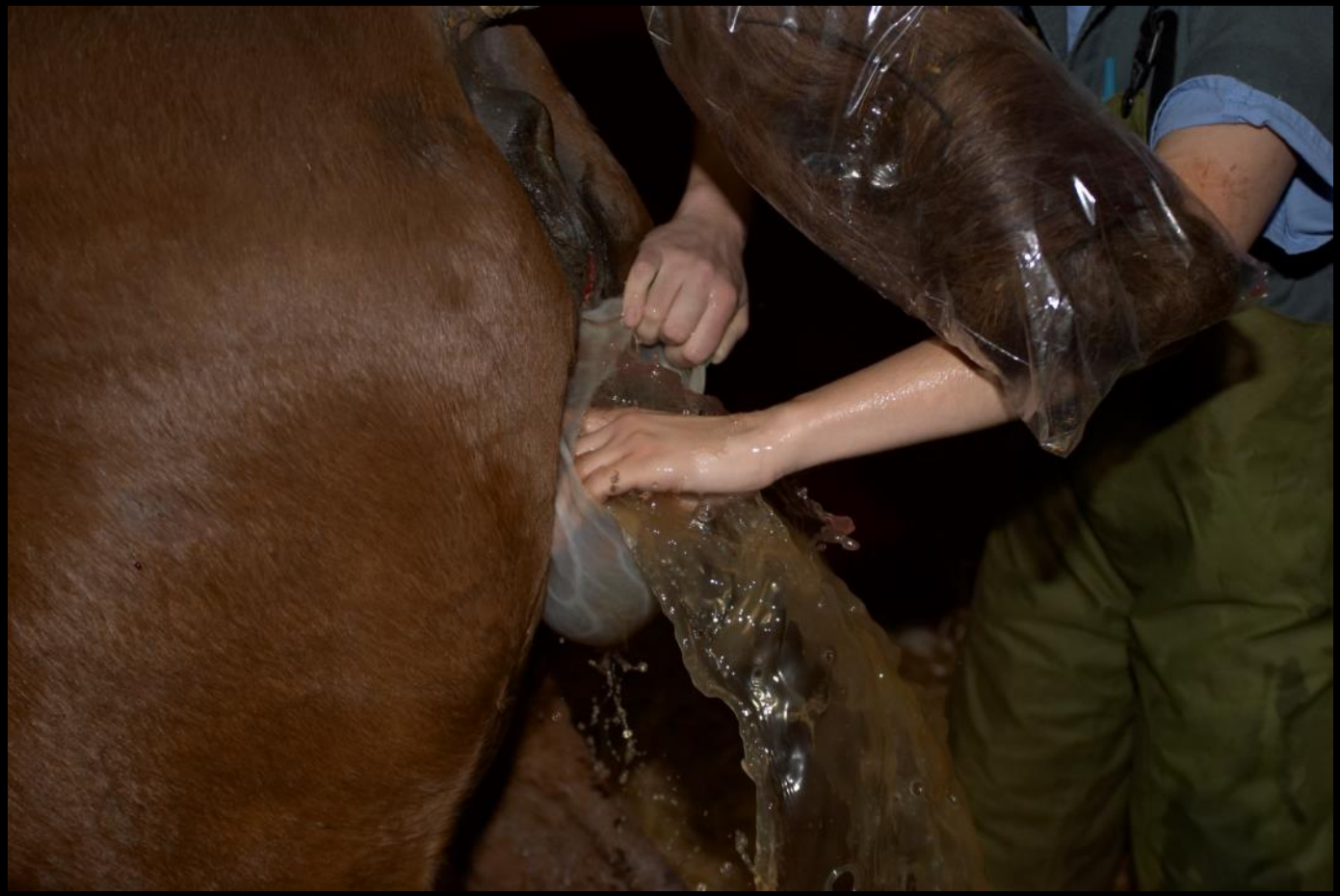







HORSE WATERER

High Risk Pregnancies Perinatology



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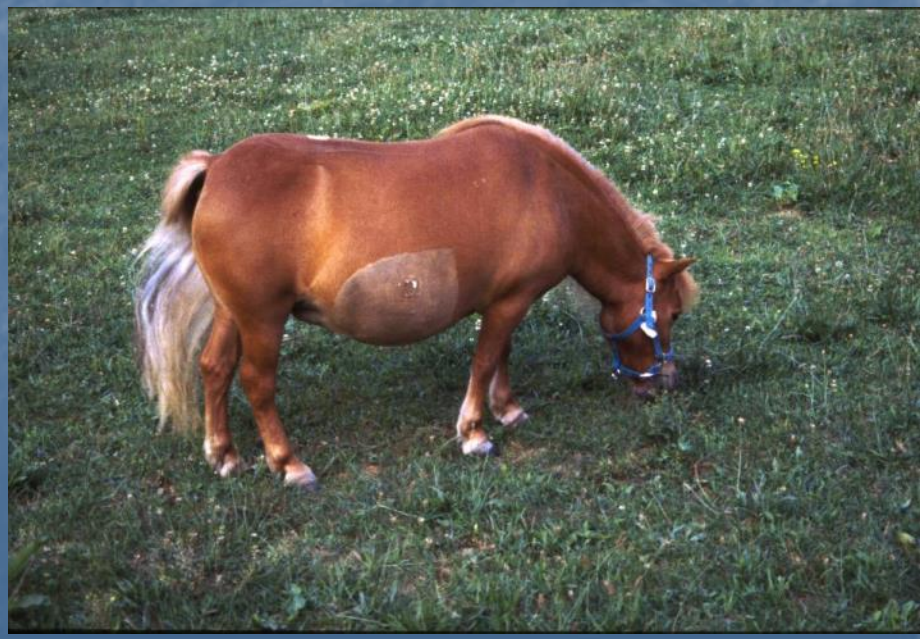
Perinatology

- Perinatology in Human Medicine
- Origins of Veterinary Perinatology

High Risk Pregnancy

- History of previous problems
- Problems during current pregnancy



Previous Problems

High Risk Pregnancy Current Problems

- Premature udder development
- Placentitis
- Twins
- Premature placental separation
- Overdue
  - Fescue toxicity

High Risk Pregnancy Current problems

- Muscular skeletal problem
- Endotoxemia
- Recent hypotension/hypoxemia
- Recent abdominal surgical incisions
- Neurologic disease
- Hydrops allantois/amnion
- Pituitary hyperplasia
- Tumors

Perinatology

- What is the threat to the fetus/neonate?
- How can the threat be eliminated?

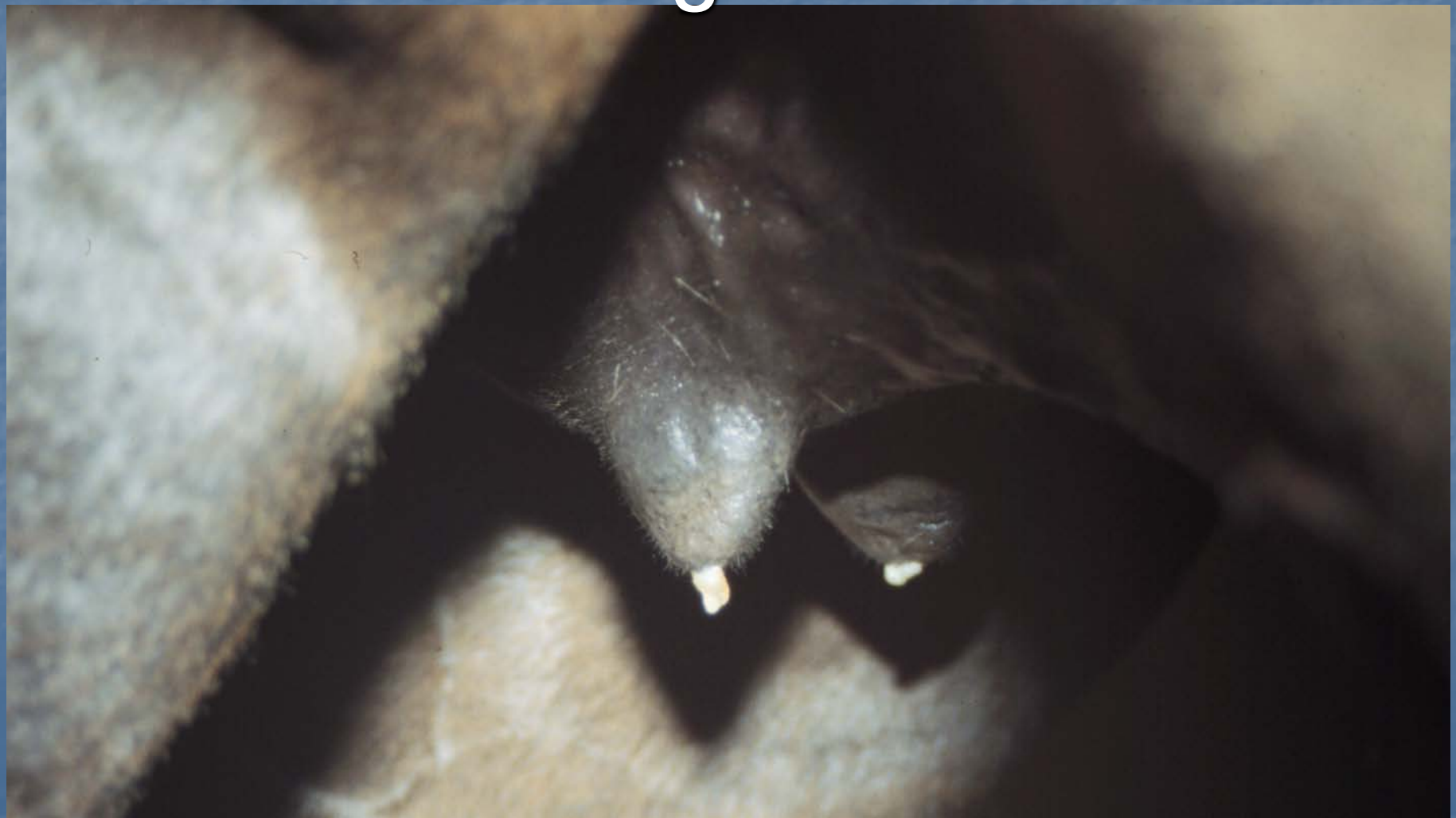
Fetal Resuscitation

- Identify the fetal problem
  - Direct therapy at the problem's source

Fetal Monitoring History

- Intrapartum fetal monitoring
  - Rational decision to hasten parturition - C-section
  - Explosive nature of parturition in the mare
- Prepartum fetal monitoring
  - Allow prediction of intrauterine distress
  - Result in effective fetal resuscitation
  - Rational decision about early delivery
- Will not predict all cases
  - Some fetal deaths no obvious cause
  - No detectable fetal, placental, maternal, or obstetrical etiology

Early Udder Development
Precocious Lactation
Most reliable sign of fetal distress



Normal Fetal Physiology

- Late term fetus
  - Level of activity is on an erratic schedule
  - 25% time - quiet sleep state
    - Infrequent breathing movements
    - Startled movements
  - 60% to 70% - active sleep state
    - REM sleep
    - Regular breathing movements
    - Intermittent abrupt movements
      - Head, limbs, and trunk

Fetal Heart Rate (FHR)

- Active (REM) sleep
  - Increased variability
  - Frequent accelerations with movement
- Quiet (non-REM) sleep
  - FHR slows
  - Heart rate variability is reduced
- Active sleep/quiet sleep periods
  - Sheep – 20 min quiet/ 40 min active
  - Late pregnancy - not predictably proportioned
  - Lack of observed active periods not useful
  - Positive observations - “reassuring”

Changes with Acute Hypoxia

- Non-vital fetal activity decreased
  - Fetal movements
  - Fetal breathing
  - Fetal swallowing
- All occur during active sleep
  - Long periods of quiet sleep
  - Is it acute hypoxemia or quite sleep?
- Fetal breathing also influenced by
  - Maternal glucose levels, other influences
- Adaptation to hypoxemia – hour or so
  - Resumption of fetal breathing/movements

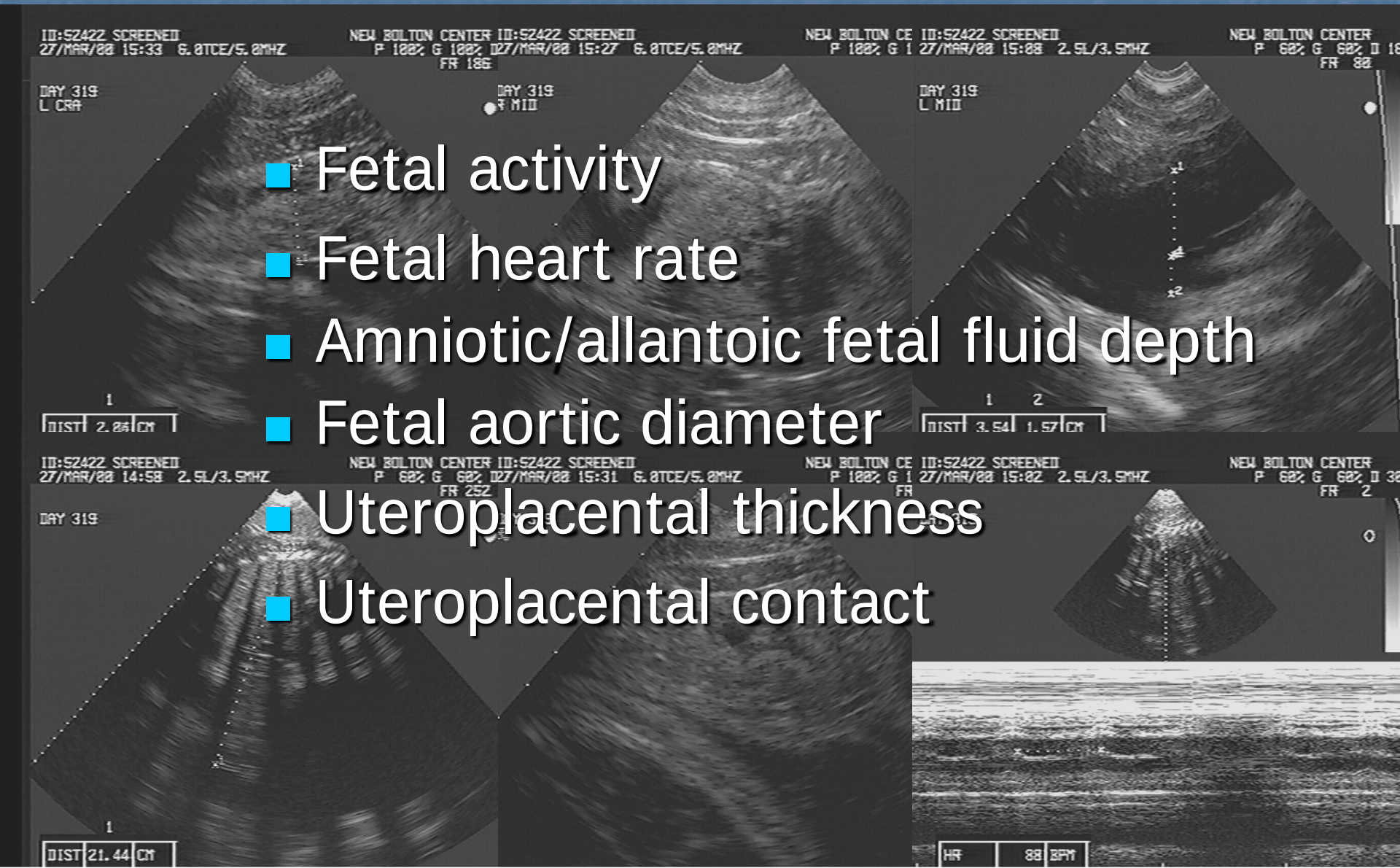
Fetal Monitoring Biophysical Profile

- Fetal Physical Examination
- Fetal Apgar Score
- A collection of observations (ultrasound)
  - Fetal CNS health
    - FHR - Doppler
    - Breathing – episode > 30 sec
    - Fetal movement, tone
  - Fetal perfusion/chronic asphyxia
    - Amnionic fluid volumes

Fetal Monitoring Biophysical Profile

- Correlate with fetal health or fetal distress
- With fetal hypoxemia - order of occurrence
  - Alterations in FHR
  - Loss of fetal breathing
  - Decreased fetal movement
  - Loss of fetal tone
- In man
  - Any single test – high rate false positive (50% to 79%)
  - Combining abnormal variables – false positive 20%
  - False-negative rate - very low

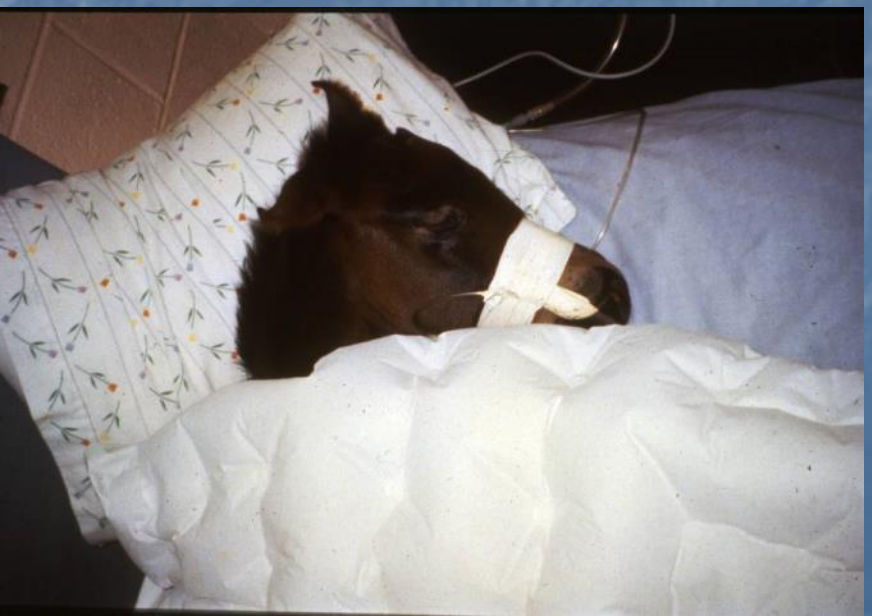
Equine Biophysical Profile



- Fetal activity
- Fetal heart rate
- Amniotic/allantoic fetal fluid depth
- Fetal aortic diameter
- Uteroplacental thickness
- Uteroplacental contact

Fetal Monitoring
Equine Biophysical Profile

- Not sensitive
  - Fetus with normal profiles may be suffering from life threatening problems



- Not specific
  - Occasionally extreme values in normal fetuses

Fetal Monitoring Ultrasound Examination

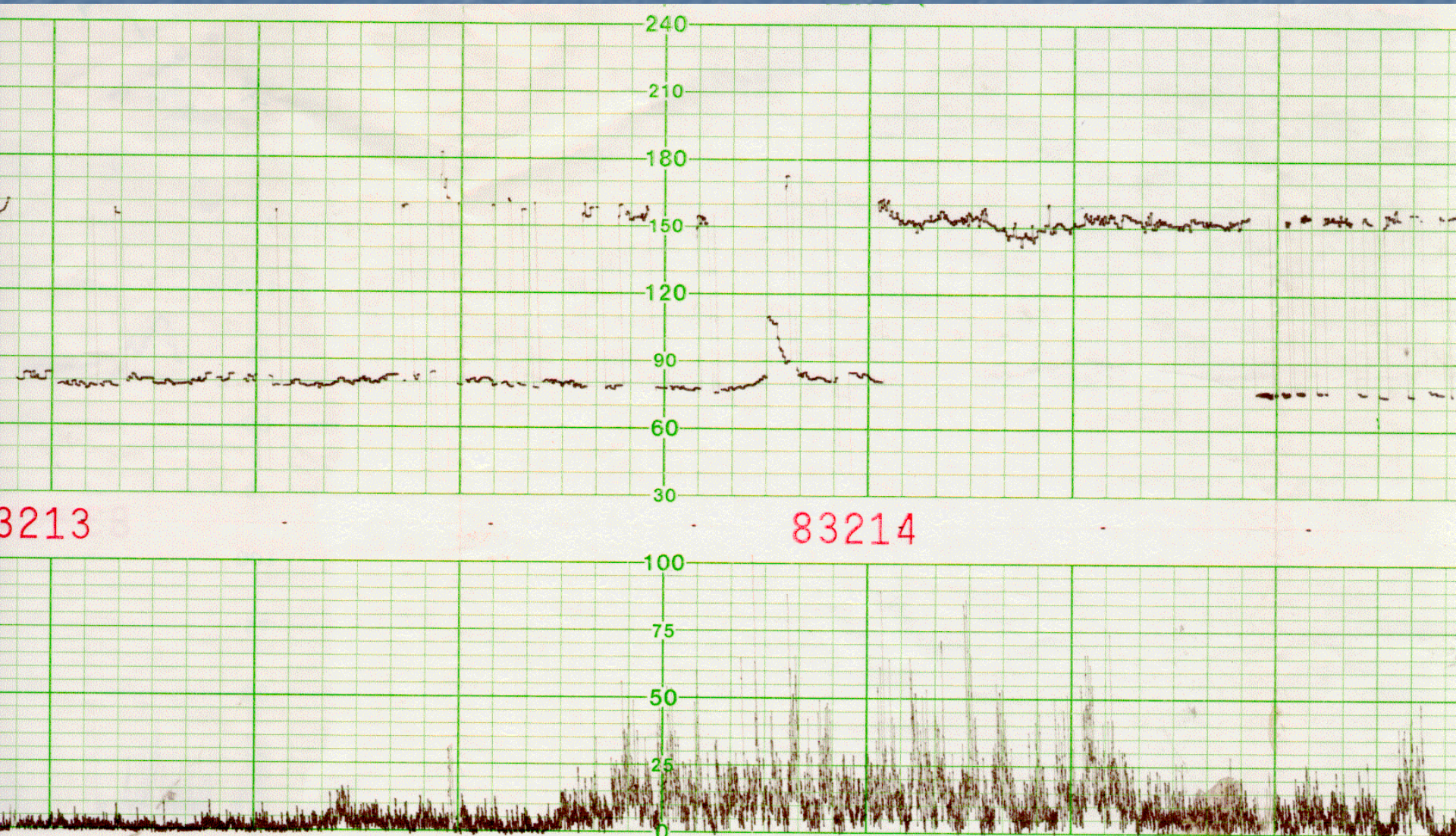
- Serial transabdominal/transrectal US
  - Detect extremes of fetal fluid volumes
  - Detect placental abnormalities
    - Sensitivity and specificity poor
  - Follow Changes
    - Sensitivity and specificity poor
- Only “see” part of placenta
- Part of assessment
  - Should not trump all other observations
  - Udder - better predicting fetal stress level

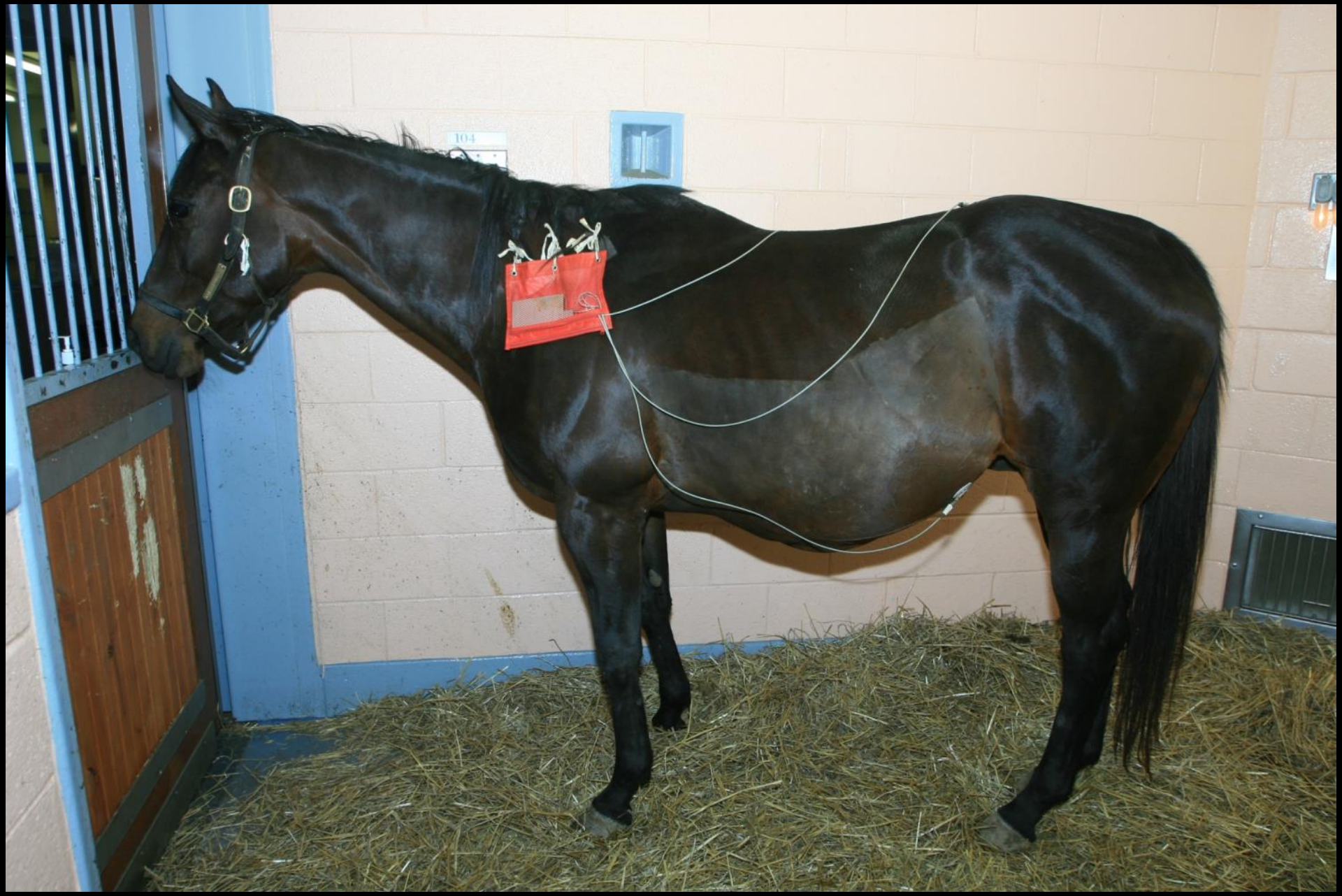

Fetal Heart
Rate Response

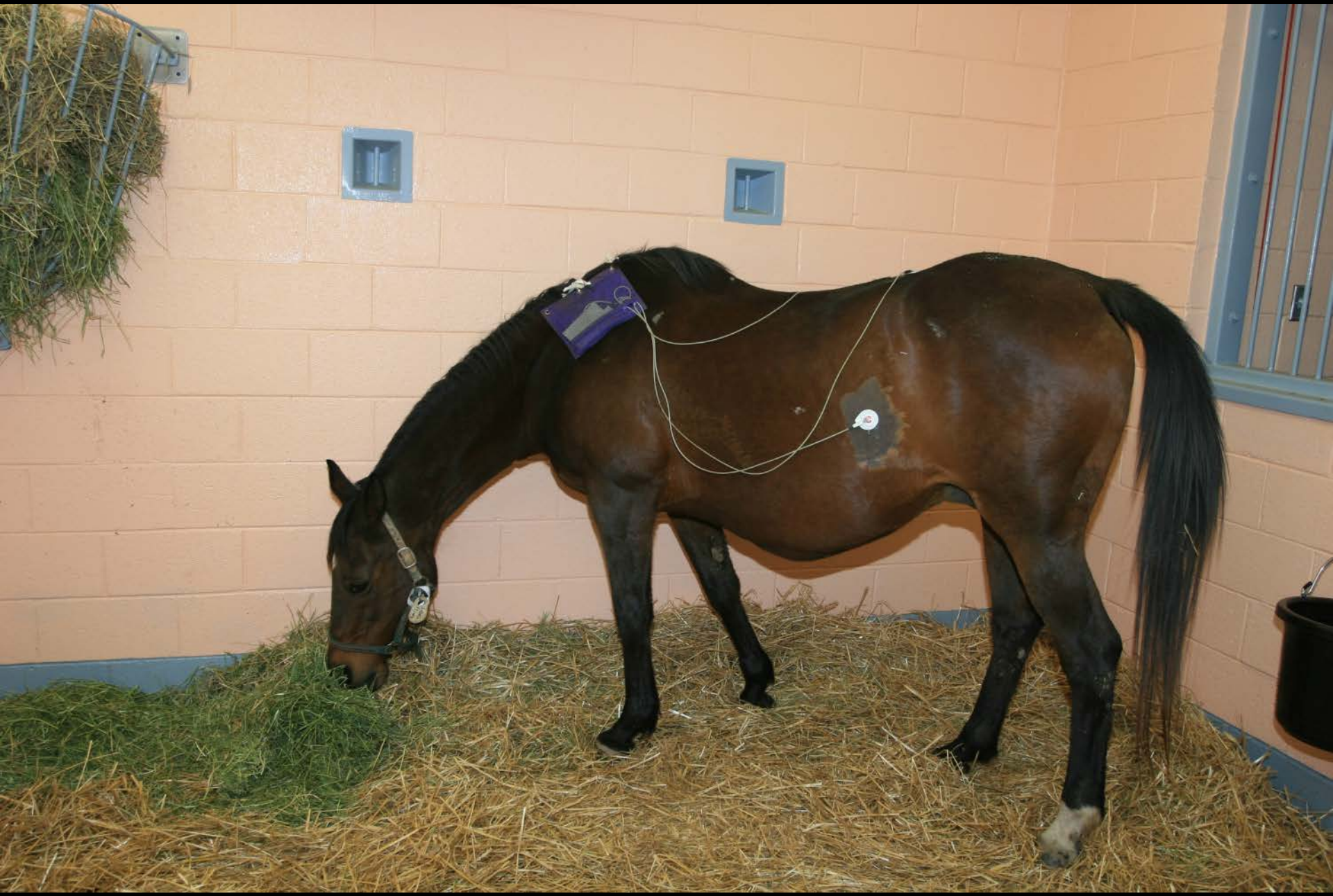
Fetal Monitoring
Fetal Heart Rate

- Methods of measurement
  - Transabdominal fetal ultrasound
  - Fetal Doppler
  - Fetal ECG
- Fetal ECG
  - Any ECG with recording capabilities
  - Telemetry
  - 6-8 observations during the night

Toitu Doppler
Fetal Heart Rate/Activity Tracing







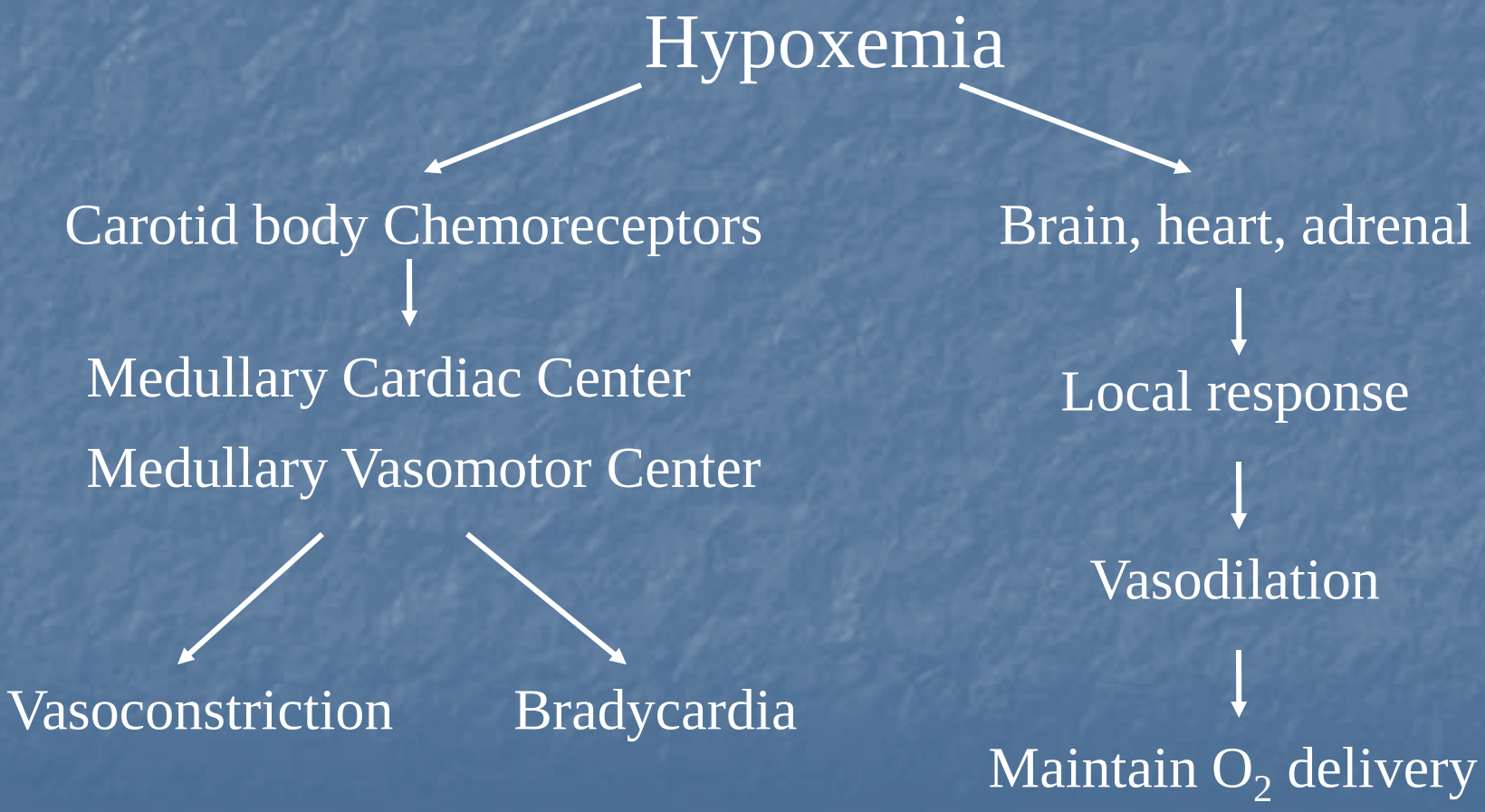
FHR Patterns

- Observations
  - Heart rate
  - Occurrence of accelerations/decelerations
  - Beat to beat variability
  - Changes in the complex
  - Arrhythmias
  - Presence of 2 distinct patterns - twins

FHR Patterns
What's Normal?

- Average FHR decreases with gestational age
  - 170 – 240 days about 115 bpm
  - Term decreases to 60 - 80 bpm
- Accelerations - reassuring sign
  - During active sleep 22-25/hr
  - Intact neurologic coupling CNS and heart
  - 85% accelerations associated movement
  - 90% movement associated acceleration
  - Quiet sleep – no accelerations (human 40-80 min)
  - Maternal sedation

FHR Response to Hypoxia



FHR Patterns
Adaptation to Hypoxemia

- Initial protective response
  - Bradycardia
  - Redistribution of cardiac output
  - Acidosis required for decreased CO
- Sudden hypoxemia
  - Increased vagal tone
  - Bradycardia & increased variability
- Hypoxemia > 30-60 min
  - Increasing circulating adrenergics
  - Modulation of vagal activity
    - Endogenous opiates
  - FHR return to baseline or higher
- Late decelerations

FHR Patterns Normal Fetus

- Baseline HR
  - 60 - 75 bpm
  - Can be in the 50s
- Low HR
  - 40 - 75 bpm
  - 80% < 70 bpm
  - 55% < 60 bpm
  - 14% < 50 bpm

FHR Patterns
Normal Fetus

- Transient low heart rates
  - Common
  - Not ominous
  - High vagal tone - uterine contraction
  - Highest beat to beat variation
  - During Stage II can drop to 25-35 bpm

FHR Patterns
Normal Fetus

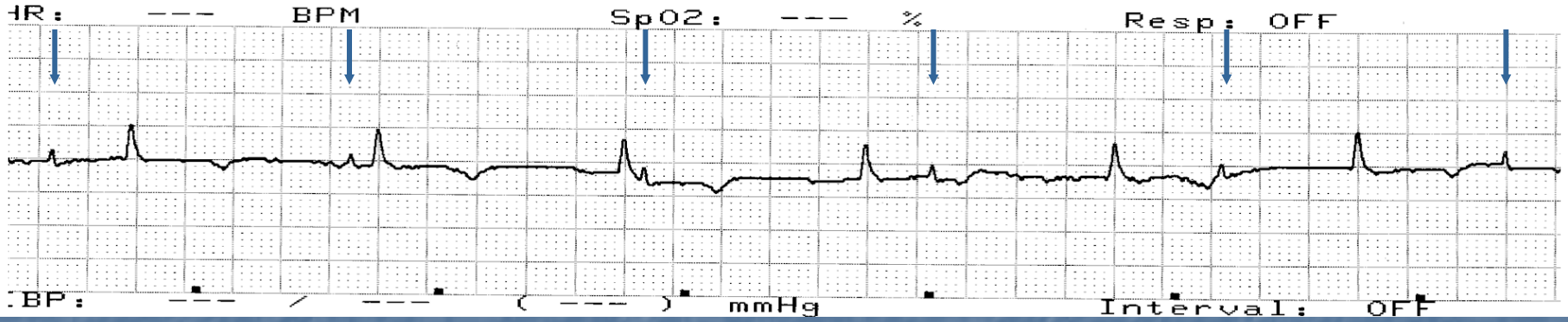
- High FHR
  - 80 - 250 bpm
  - 86% > 100 bpm
  - 50% > 120 bpm
  - 20% > 200 bpm
- Transient high heart rates
  - Common – reassuring
  - Fetal activity
  - Not ominous unless consistent

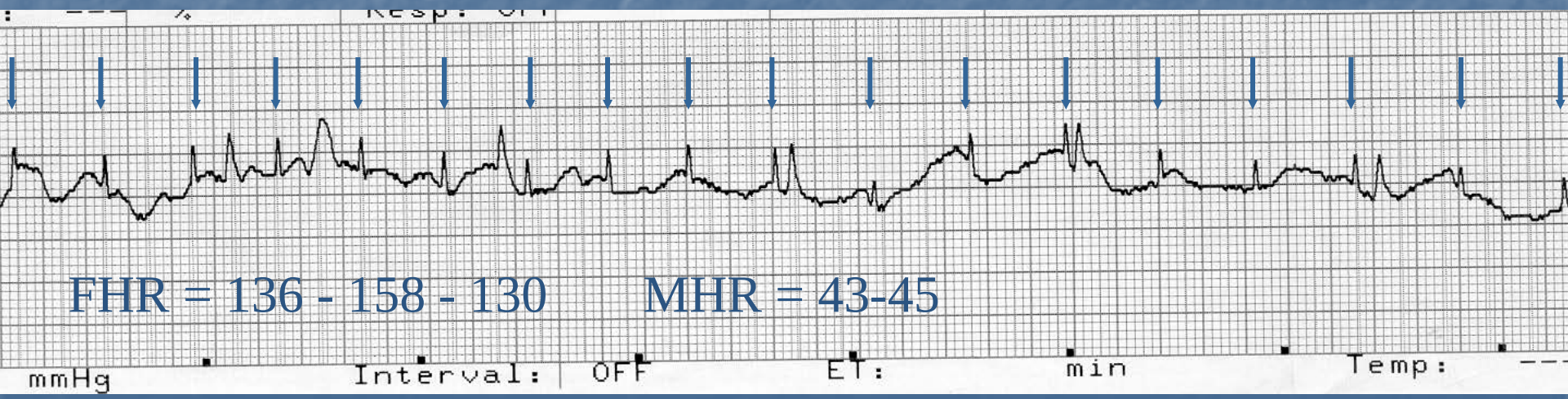
FHR Patterns Abnormal Fetus

- Consistent low HR – usually normal
  - Unless no beat-to-beat variation
  - IUGR
- Consistent tachycardia
  - Often 160 – 180
- Atrial fibrillation-like pattern
- Sudden changes in QRS complex
  - Size, orientation, timing
  - Premature ventricular contractions
  - Runs of V-tach

Fetal heart rate measurements
Fetal ECG

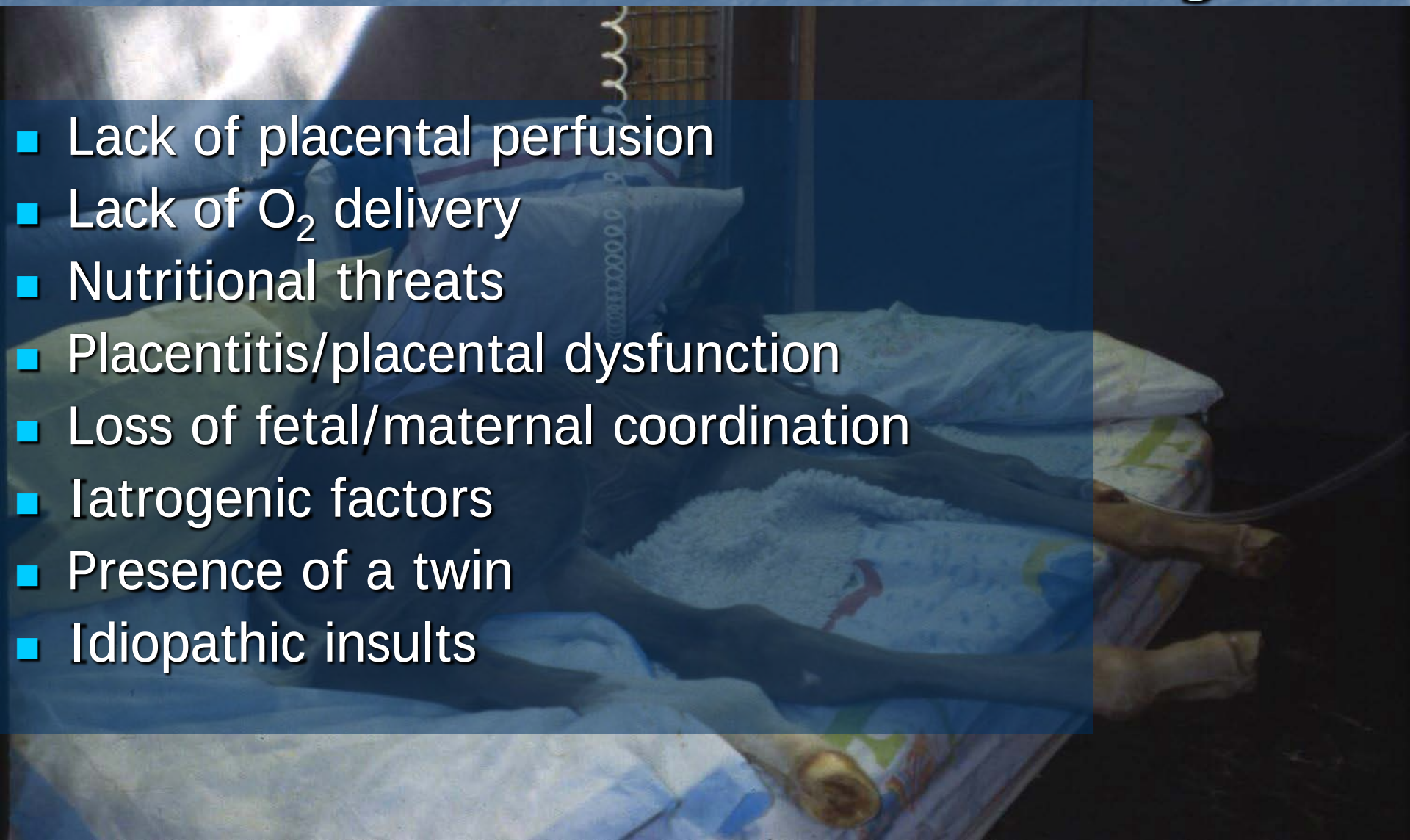
FHR = 48-52 MHR = 60





FHR = 136 - 158 - 130 MHR = 43-45

High Risk Pregnancy
Threats to Fetal Well-being



- Lack of placental perfusion
- Lack of O_2 delivery
- Nutritional threats
- Placentitis/placental dysfunction
- Loss of fetal/maternal coordination
- Iatrogenic factors
- Presence of a twin
- Idiopathic insults

Threats to Fetal Well-being Lack of Placental Perfusion

- Normal physiology – late term
  - Maternal Blood volume increases 30-50%
  - Maternal cardiac output increases 30-50%
    - Uterus
    - Git
    - Kidneys
    - Skin
- At term
  - Maternal placenta 15% mare's CO
  - Fetal placenta 40% fetal foal's CO

Threats to Fetal Well-being Lack of Placental Perfusion

- Late term fetus
  - High oxygen demand
  - Must receive constant perfusion
  - Margin of safety in late pregnancy small
- Maternal compromise
  - Dehydration/Shock
  - Decreased perfusion for any reason
- Placental response limited
- Compromised placental circulation
  - Hypoxic ischemic insult

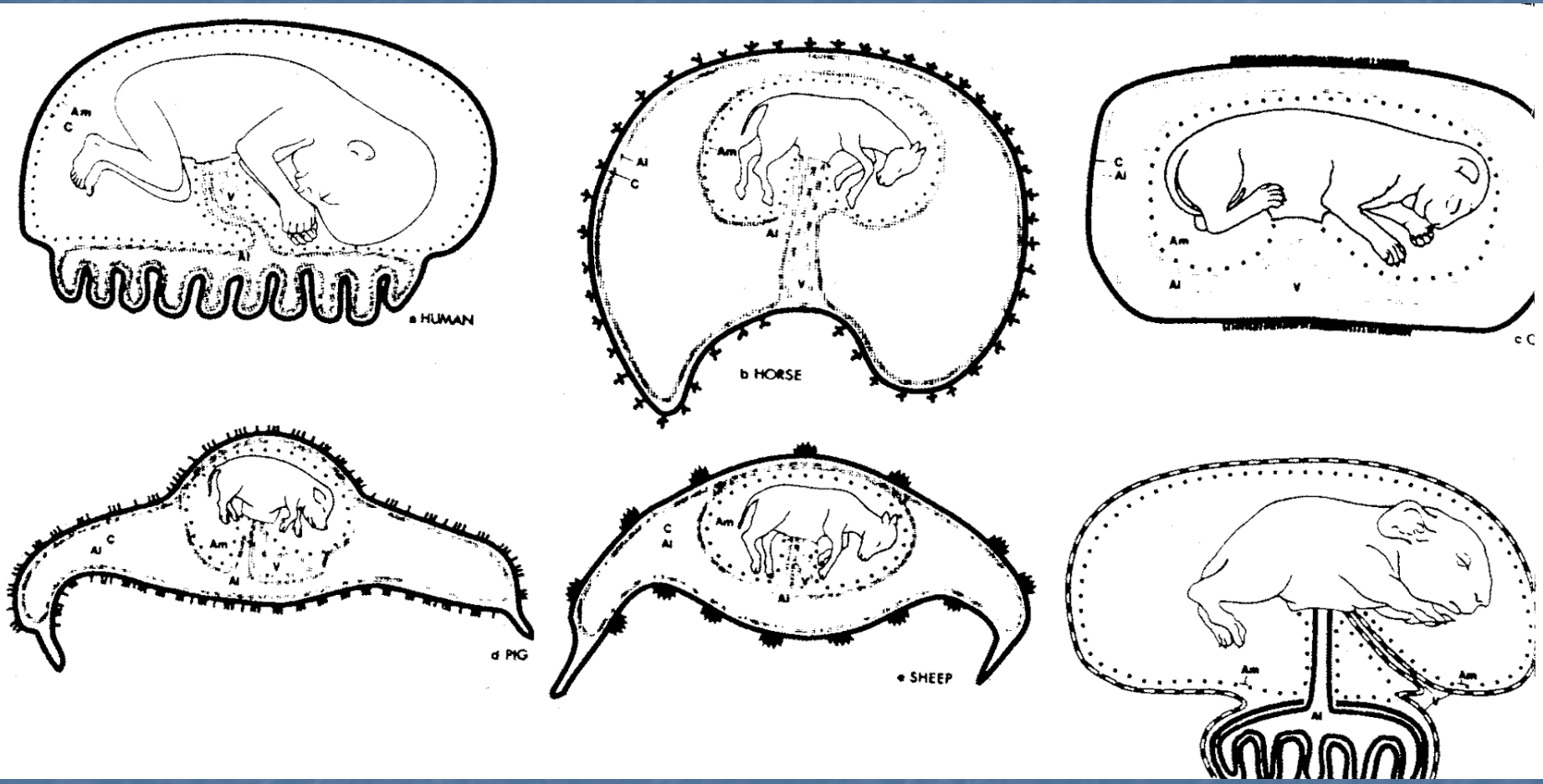
Fetal Resuscitation
Maintenance of Placental Perfusion

- Aggressively treat hypovolemia
- Avoid adrenergics in pregnancy
  - No central control placental circulation
  - Sensitivity and response changes – complex
  - Uterine blood flow in pregnancy
    - Decrease – dobutamine, epinephrine and norepinephrine
    - Variable – dopamine
    - Increase – ephedrine
  - Maintaining blood pressure with adrenergics ≠ uterine perfusion
- Avoid anesthesia in late term mares

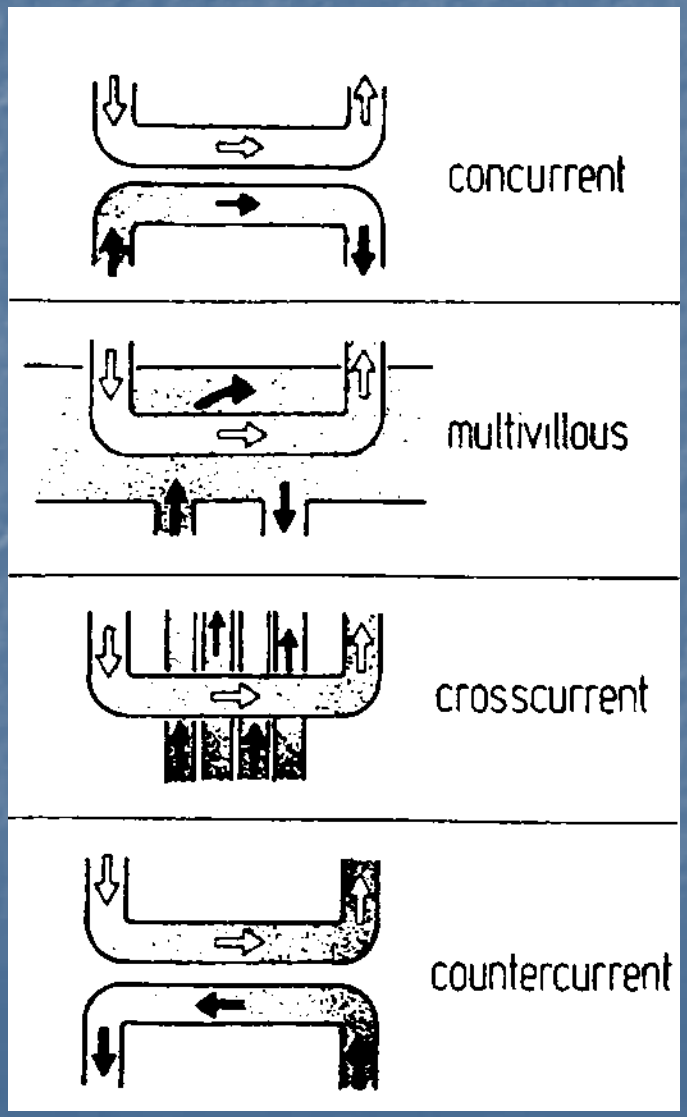
Threats to Fetal Well-being Lack of O_2 Delivery

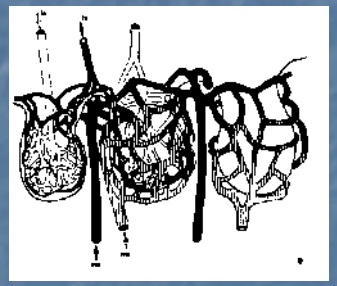
- Maternal threats
  - Maternal anemia
  - Maternal hypoxemia
  - Decreased perfusion
- Fetal response
  - Unique aspect of placentation
  - Placental oxygen transport mechanisms

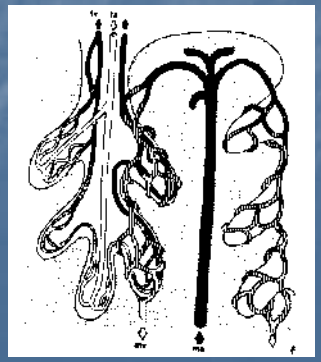
Placentation

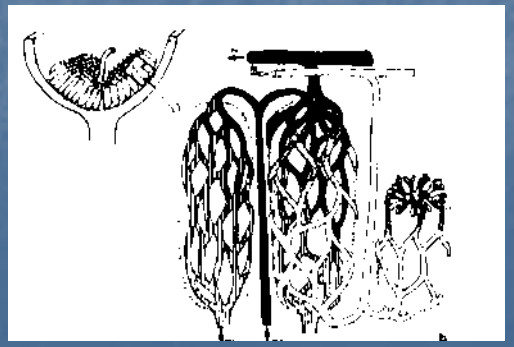


Placental Circulation

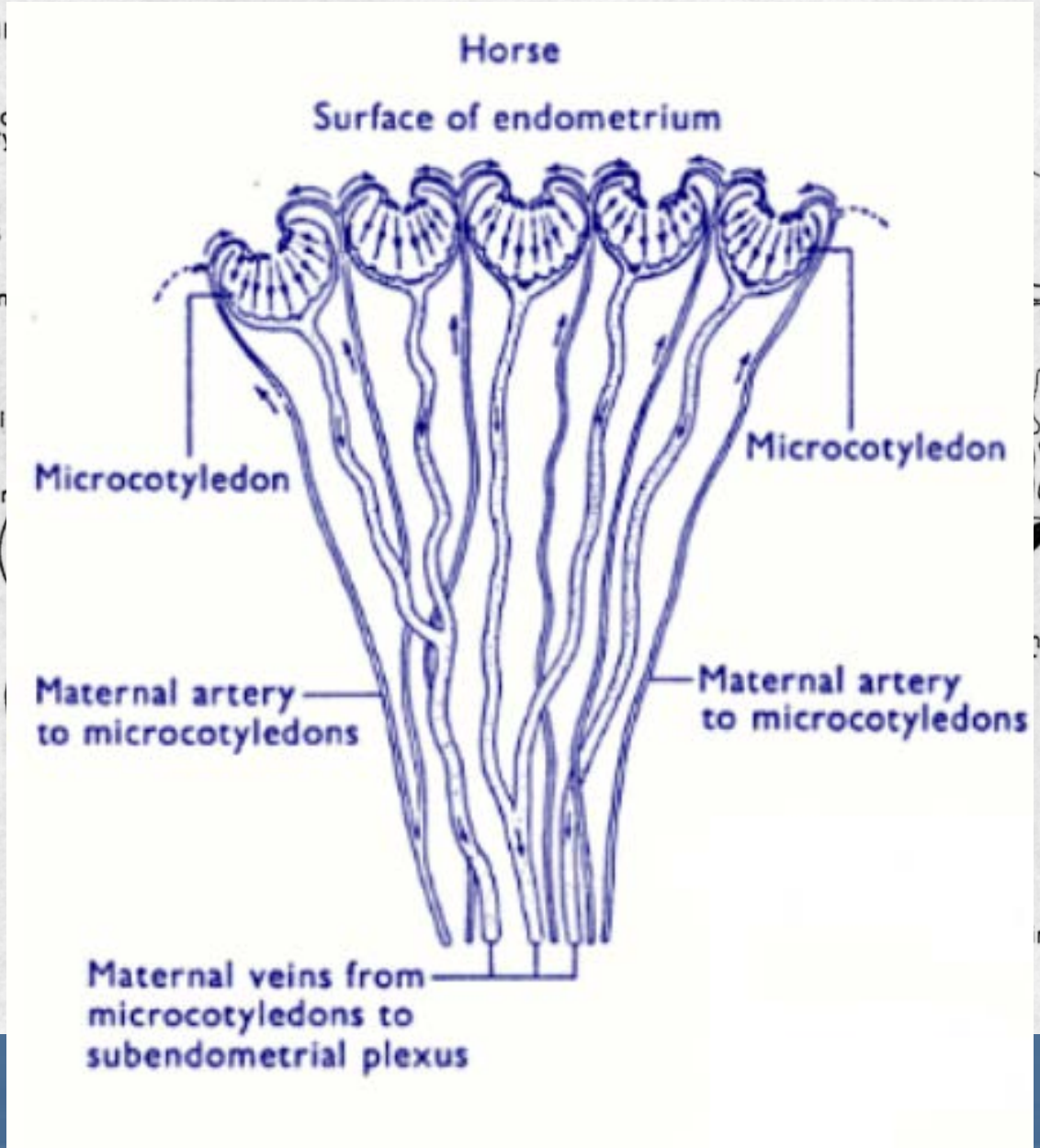








Equine Placentation



Effect of Maternal Oxygen Therapy

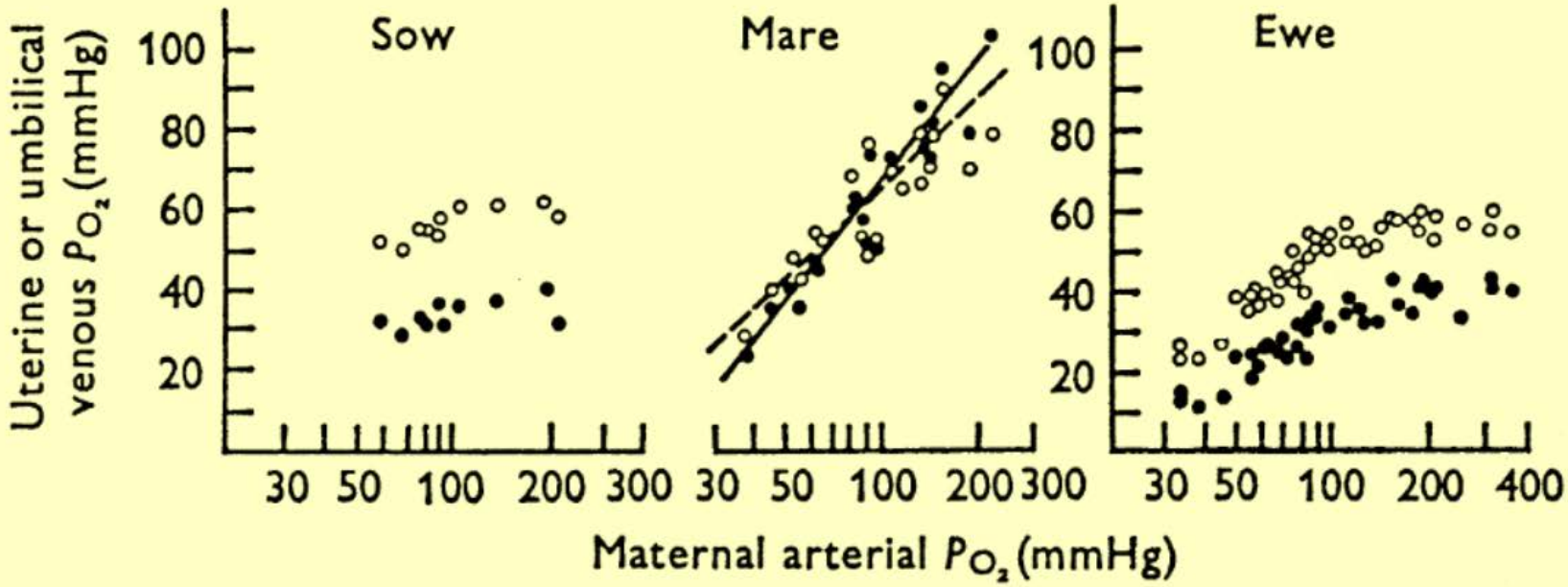
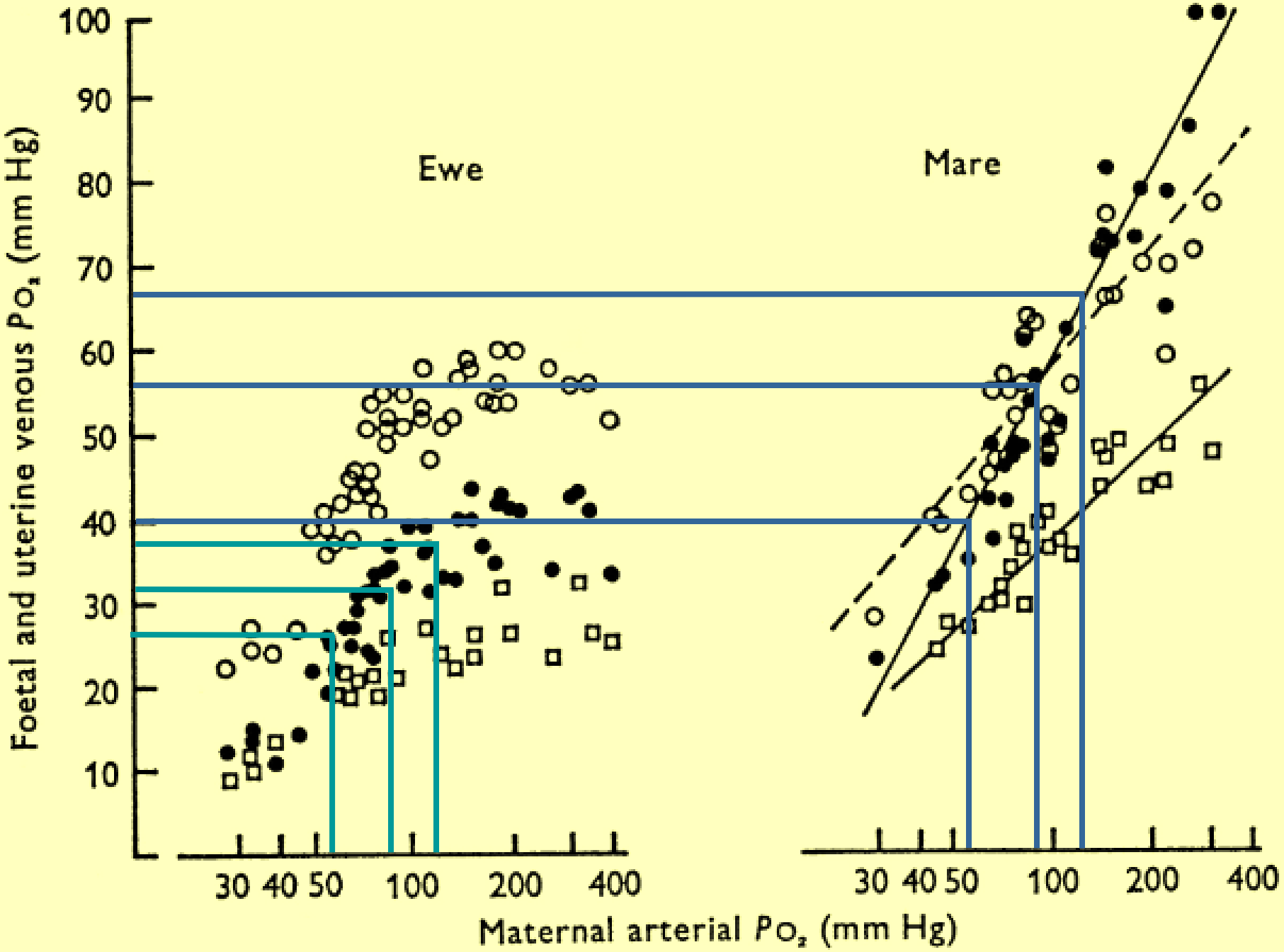


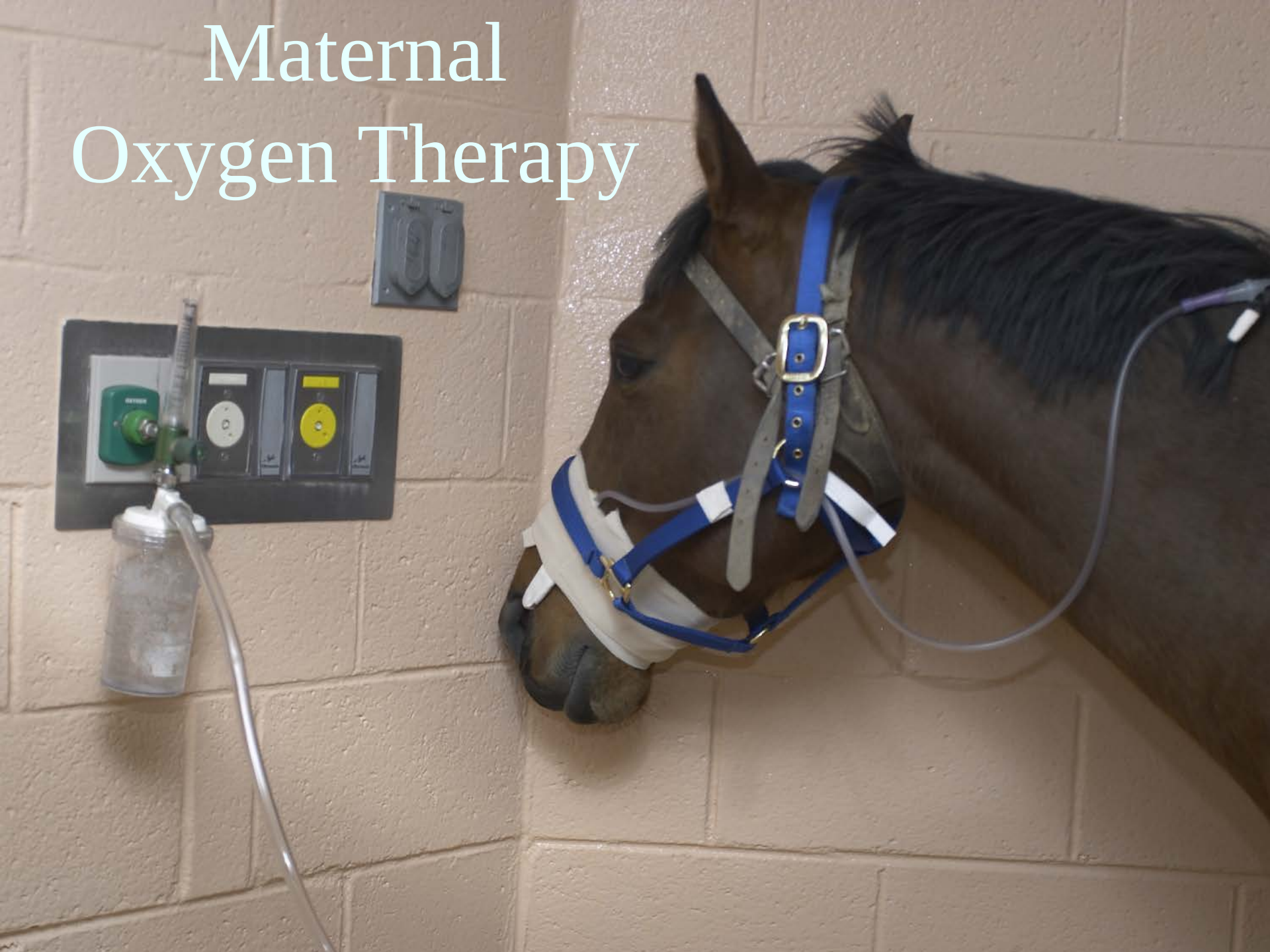
Fig. 4. The relationship between P_{O_2} in maternal arterial blood (log scale) and that in the uterine vein (○) and umbilical vein (●) in seven ewes and seven mares (data from Comline & Silver 1970*b*), and in five sows.


Ewe
Mare
Foetal and uterine venous P_{O_2} (mm Hg)
Maternal arterial P_{O_2} (mm Hg)
100
90
80
70
60
50
40
30
20
10
30 40 50 100 200 400
30 40 50 100 200 400

Fetal Resuscitation Lack of O_2 Delivery

- Fetal hypoxemia - supplement with INO_2
  - Take advantage of the countercurrent system
  - Even if normal Pao_2 in mare, foal may benefit
  - Important with generalized placental disease?
  - May see improved FHR parameters

Maternal Oxygen Therapy



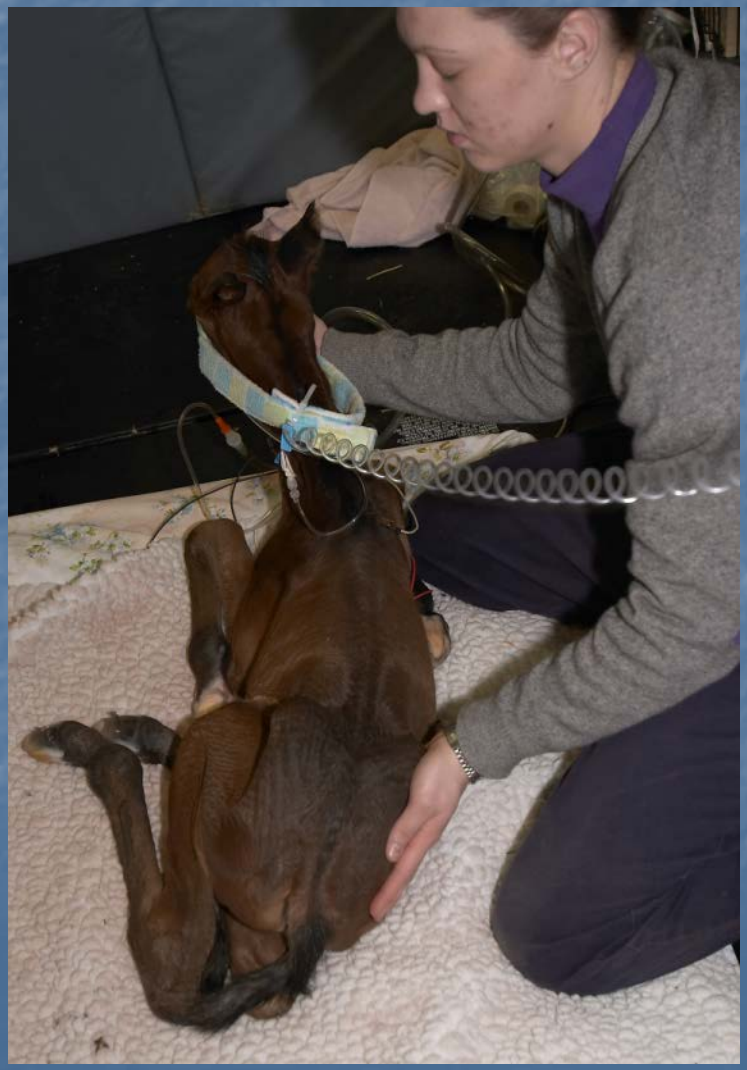
Placental Functions Glucose Transport

- Predominant source of energy for fetus
- Glucose transport
  - Carrier mediated passive transport
- Low or high maternal glucose levels
  - Fetus is protected

Nutritional Threats Glucose Utilization

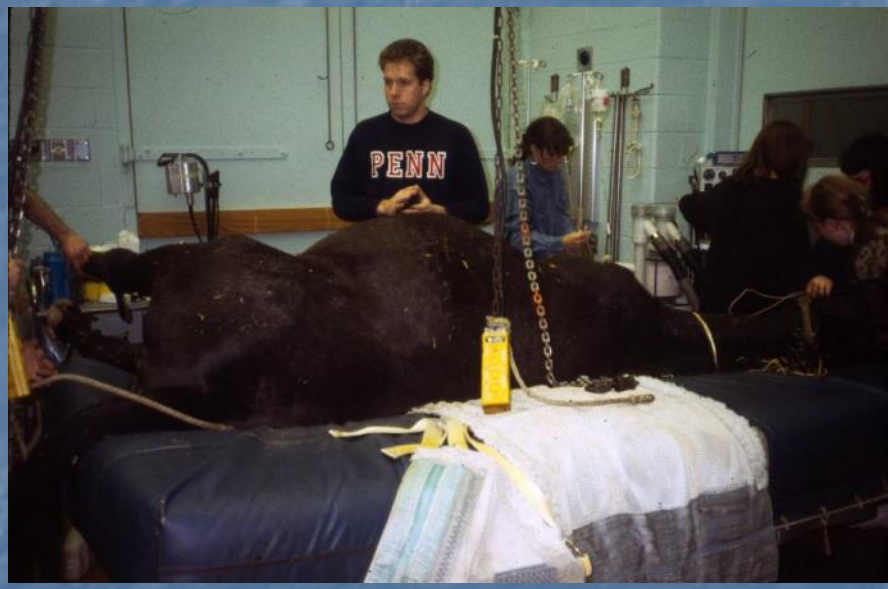
- The placenta
  - Actively metabolic tissue
  - High glucose utilized by placenta in horse
  - Glucose for placenta can also come from fetus
- Maternal distress – less glucose
  - More glucose delivered from fetus
  - Negative net glucose transport to fetus

IUGR
Intrauterine Growth Restriction



Threats to Fetal Well-being Nutritional Threats

- Chronic malnutrition of the dam
  - Lack of intake
  - Malabsorption
  - Tumor cachexia
- Acute fasting of the dam
  - Forced fasting
  - Capricious appetite - late gestation



Threats to Fetal Well-being Nutritional Threat of Acute Fasting

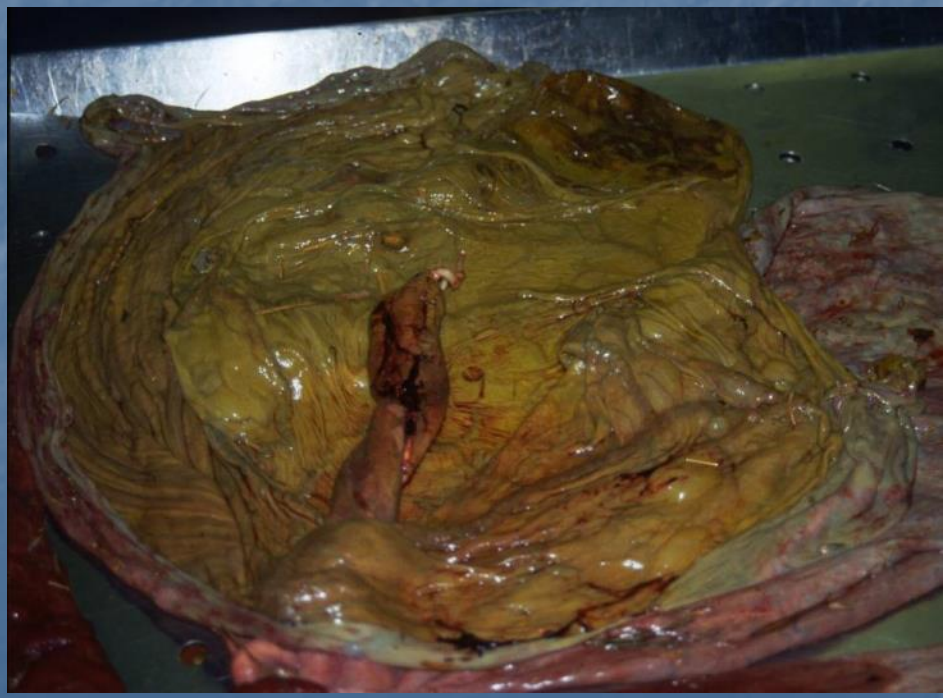
- Fasting the mare for 30-48 hr
  - Must be complete fasting
  - Decreased glucose delivery
  - Rise in plasma FFA
  - Increased PG's in uterine and fetal tissues
- Increased risk of preterm delivery
  - Within one week of ending the fast
    - Myometrial sensitivity to hormones

Fetal Resuscitation Nutritional Threats

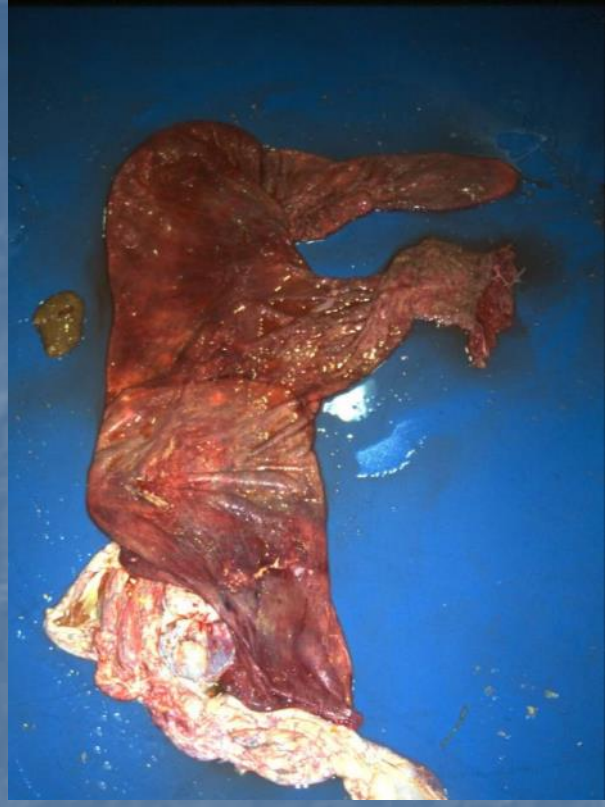
- Support the mare's nutritional needs
  - Enteral supplementation
  - Parenteral supplementation
  - Encourage a high plain of nutrition
- Avoid acute fasting
  - Avoid elective procedures requiring fasting
  - Encourage anorexic late term mares to eat
- If acute fasting is unavoidable – colic, anorexia
  - Supplement with intravenous glucose therapy
  - Consider flunixin meglumine therapy

Threats to Fetal Well-being Placentitis/Placental Dysfunction

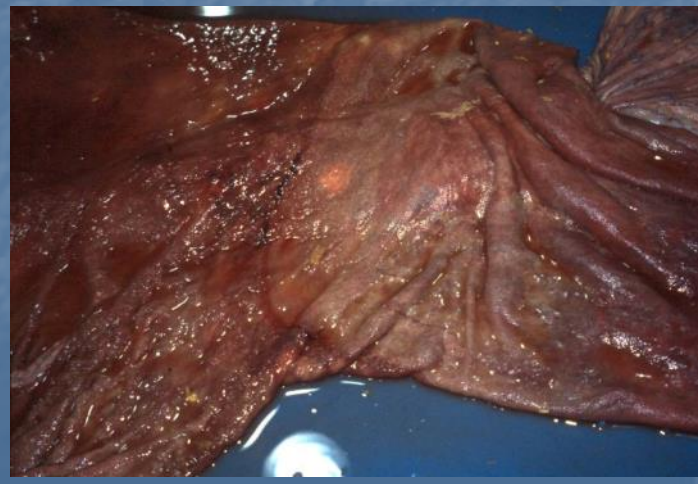
- Premature placental separation
- Infection
- Inflammation
  - Tent Caterpillar
- Degeneration
- Edema
- Hydrops

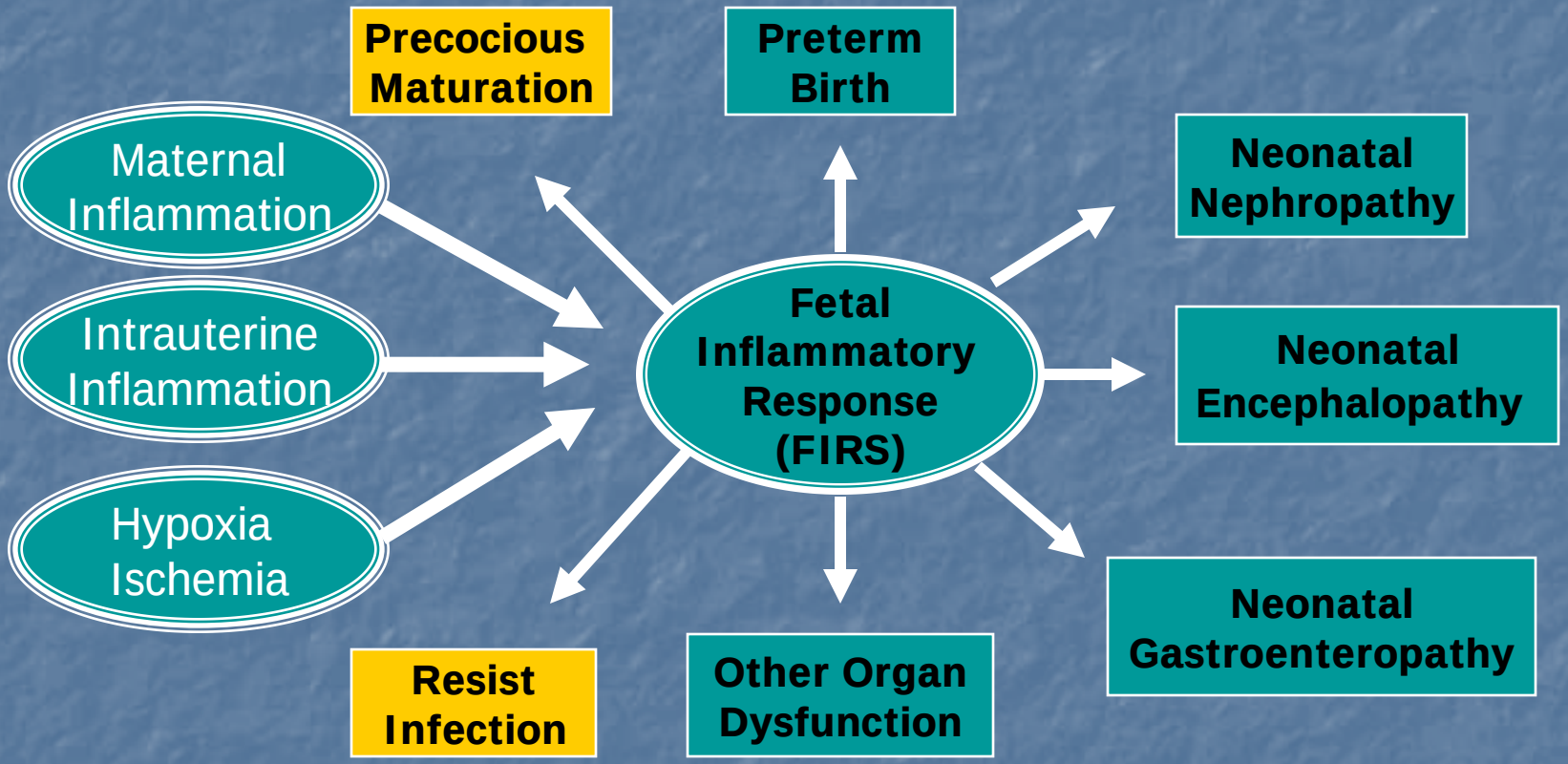


Threats to Fetal Well-being Placentitis



- Percentage of abnormal placenta
  - Not a predictor of fetal outcome
- Presence of abnormal placental tissue
  - Is enough to cause serious problems
  - Production of inflammatory mediators
- Fetal foals born with placentitis
  - More likely to have neonatal diseases




Precocious Maturation
Preterm Birth
Maternal Inflammation
Intrauterine Inflammation
Hypoxia Ischemia
Fetal Inflammatory Response (FIRS)
Neonatal Nephropathy
Neonatal Encephalopathy
Neonatal Gastroenteropathy
Resist Infection
Other Organ Dysfunction

Placentitis Therapy?

- Anecdotal clinical experience
- Evidence from experimental models
- Lessons from sepsis therapy in man
- No large prospective clinical trials
- No solid evidence to direct therapy

Therapy?

Evidence Based

Traditions

Beliefs

Experience Based

Placentitis Therapy

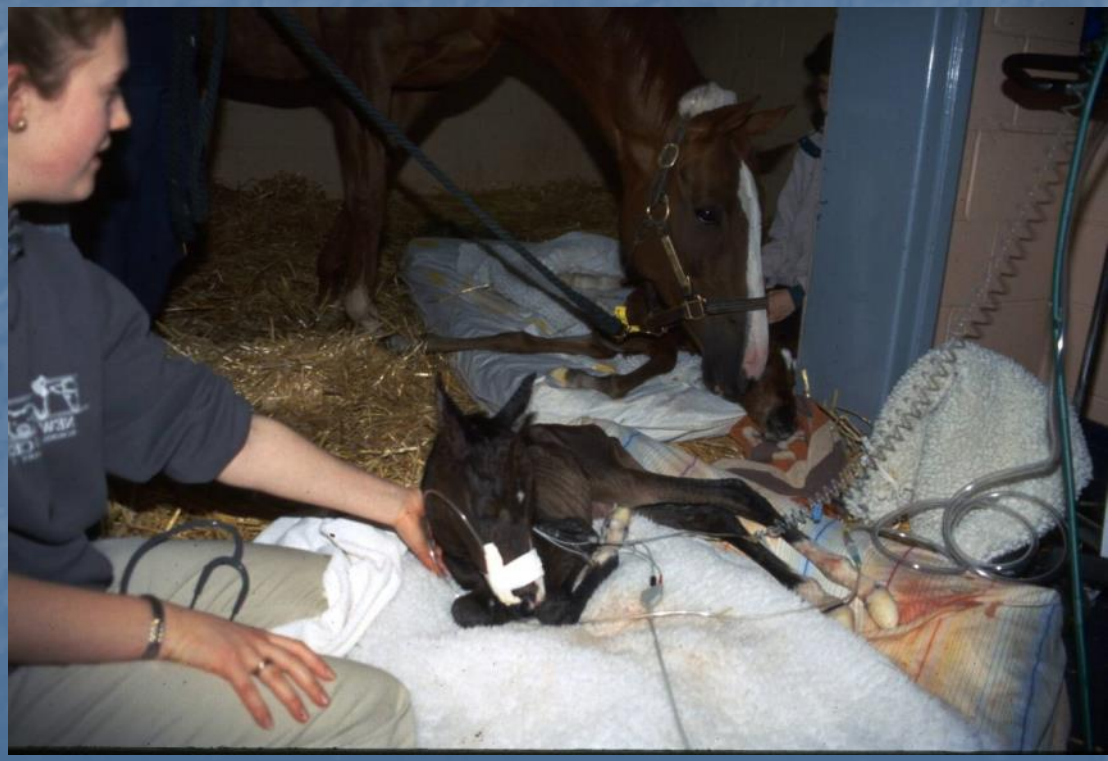
- Treat as infectious
  - Trimethoprim potentiated sulfa drugs
- Try to minimize PG formation
  - NSAIDs - flunixin meglumine
- Hormone supplementation therapy
  - Altrenogest (ReguMate)

Treatment of Placentitis

- Increases odds of a normal foal
  - Retrospective
  - 108 pregnant mares
  - 48 with placentitis
- For normal foals from placentitis
  - Any treatment
    - p=0.032, OR 7.9, CI 1.2 - 53
  - Antimicrobials - TMS
    - p=0.013, OR 11.2, CI 1.7 - 75
  - NSAIDS - flunixin
    - p= 0.014, OR 14.2, CI 1.7 - 119
  - Progestins - altrenogest
    - p= 0.043 OR 7.1 CI 1.1 - 47

Threats to Fetal Well-being

- Iatrogenic Factors
  - Early delivery
  - Drugs
- Presence on a Twin
- Other peripartum events

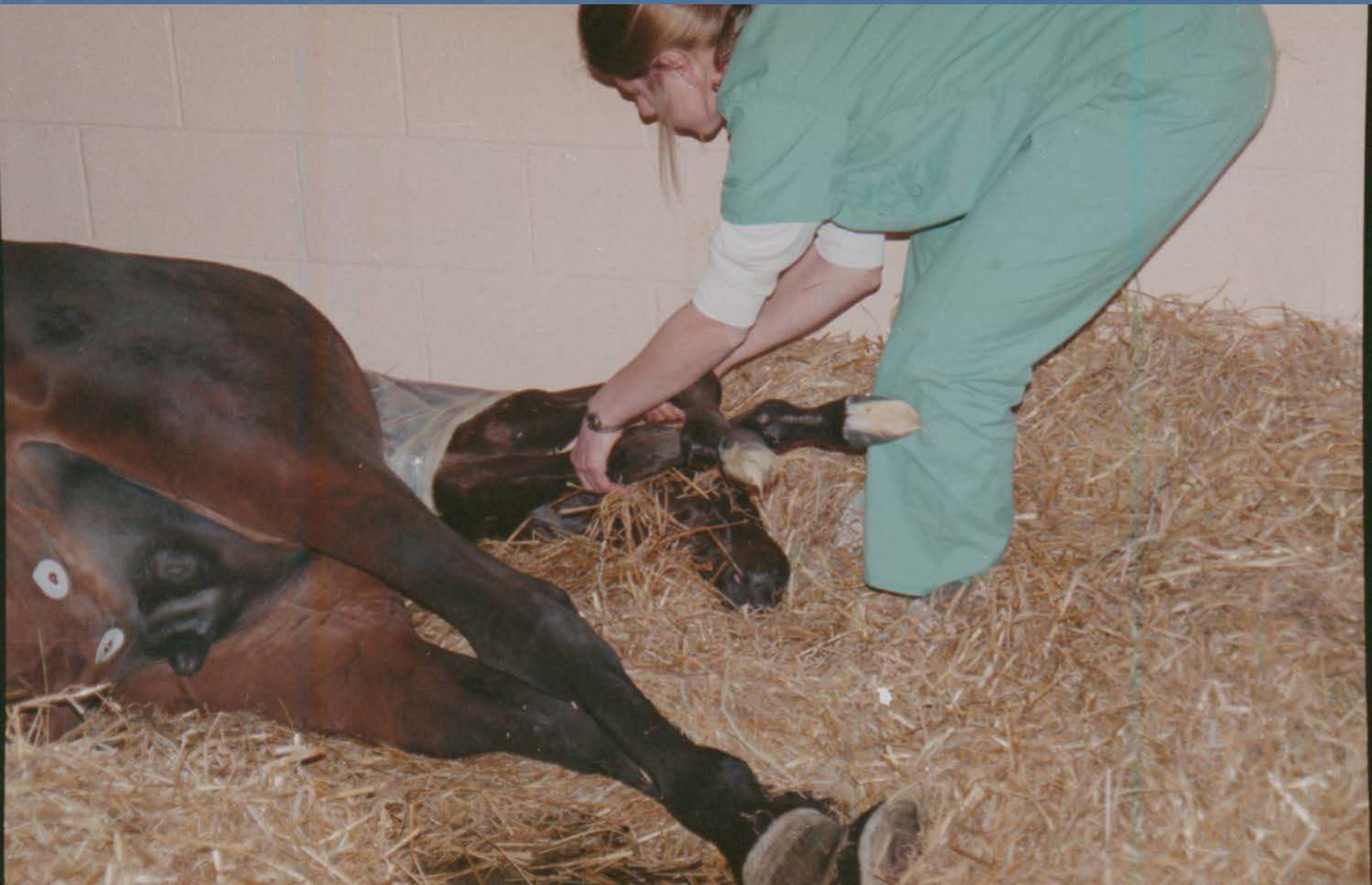


Fetal Resuscitation
If Fetus Clearly in Distress

- Consider early induction, early delivery
  - Oxytocin induction
  - C-section

- **These should be considered high risk procedures for the fetus and mare**

No way back



High-Risk Pregnancies

Jon Palmer, VMD, DACVIM
Neonatal Intensive Care Service
New Bolton Center, University of Pennsylvania
Kennett Square, PA, USA

Perinatology is the clinical specialty which focuses on the fetus during the end of gestation, birth, and the initial neonatal period. In our clinic perinatology encompasses the care of high-risk pregnancy patients, high-risk births, and initial therapy for the neonate through the transition of birth and adaptation to neonatal life. Although our original efforts were primarily directed towards the equine, over the years we have adapted similar techniques in the other farm animal species depending on their economic and emotional value.

Gravid dams are considered at high-risk when they have a history of problems during past pregnancies or have developed a new problem during the current pregnancy. There are many different problems that place a pregnancy at risk such as placentitis, premature placental separation. body wall tears, uterine artery hemorrhage, hydrops, laminitis, major fractures, colic, recent colic surgery, pneumonia, pleuritis, liver disease, cardiac disease, enteritis, lymphosacroma, anemia, pelvic obstruction, pelvic fracture callus, renal disease, liver disease, neurologic disease, any maternal inflammatory disease, etc. There is almost an endless list of possibilities of maternal problems which may place the fetal foal at risk for a poor outcome. Certainly the maternal problems need attention but when the goal is saving the fetal foal thinking in terms of the maternal problem falls short of being helpful. Rather than focusing on the mare's problem I find it more useful to think of the mare's problem in terms of how it threatens fetal or neonatal well-being. That is how the fetus perceives the maternal problem. After understanding the threat to the fetus, then a plan to try to minimize or eliminate the threat can be made and carried out.

FETAL MONITORING

Fetal monitoring has a long history in human medicine. Although initially introduced for intrapartum use, prepartum fetal monitoring has been used successfully for any years and is currently standard of care in high-risk pregnancies in man. We have used similar techniques on fetal foals since the mid-1980s. The aim of fetal monitoring is to detect fetal distress so that intervention can be directed at eliminating the cause of the distress before it results in fetal death or premature delivery. However, at least in man 20% of fetal deaths have no obvious fetal, placental, maternal, or obstetrical etiology, and this percentage increases with advancing gestational age.[1] In the mare the percent of unexplained deaths is likely greater than this. Late-gestation stillbirths are more likely to have no identifiable etiology.[1] This makes identifying the fetus in distress problematic.

Normal Fetal Physiology and Response to Hypoxia

The basis of fetal monitoring is the detection of normal behavioral patterns and normal physiologic responses by ultrasound observations or fetal heart rate (FHR) monitoring that when present are reassuring but when absent indicate the possibility of fetal distress. It should be appreciated that, during the third trimester, the normal fetus may exhibit marked variations in its neurologic state and thus its level of activity is on an erratic schedule. In other species the near-term fetus spends about 25% of its time in a quiet sleep state and 60% to 70% in an active sleep state. Active sleep is associated with rapid eye movement (REM). In fetal lambs, REM sleep is marked by regular breathing movements and intermittent abrupt movements of its head, limbs, and trunk. The fetal heart rate in active sleep near term exhibits increased variability and frequent accelerations with movement. During quiet, or non-REM, sleep, the fetal heart rate slows and heart rate variability is reduced. The fetus may make infrequent breathing movements and startle movements. In near term lambs, periods of quiet sleep may last 20 minutes, and those of active sleep about 40 minutes.[2] However clinical observations show that the periods are not predictably proportioned, especially late in pregnancy. Quiet sleep may last for periods of well over an hour and active sleep may be very brief.[3] As a result, basing conclusions about fetal health from lack of observed active periods or not detecting associated fetal heart rate accelerations is tenuous at best. On the other hand positive observations are much more likely to indicate fetal health and are often termed “reassuring” in recognition that fetal health is likely although not guaranteed. The mechanisms that control these periods of rest and activity in the fetus which may confound observations are not known.

Changes in fetal behavioral patterns have been observed with acute hypoxia. Non-vital fetal activity is decreased or becomes absent. This is thought to be an adaptive change in an effort to decrease non-vital oxygen utilization with the direction of perfusion and oxygen delivery to the vital organs (heart, brain and adrenals). In response to experimental hypoxemia there is a decrease in fetal movements of limbs, head/neck and trunk, a decrease in fetal breathing efforts and a decrease in fetal swallowing. However, as all of these activities occur during periods of active sleep and as gestation progresses periods of quite sleep become more prolonged in normal fetuses the question arises whether the absence of these movements are an indication of fetal distress secondary to hypoxia or merely an indication of the presence of the quite sleep state. Several factors other than fetal state and hypoxia can influence the presence of fetal breathing movements. As maternal glucose levels rise, fetal breathing movements becomes more frequent, and during periods of maternal hypoglycemia, fetal breathing movements decrease.[2] To further confound the value of the observations fetal activity levels have been seen in animal studies to adapt to hypoxemia with resumption of fetal breathing and body movements after a period of hypoxemia, especially if induced gradually. Therefore, observation of these fetal states during antenatal testing does not guarantee a normoxic fetus.

External factors such as maternal activity, ingestion of cold water, and maternal nutrition may also play a role in fetal activity patterns. Other factors that may decrease fetal movement in the third trimester include fetal CNS anomalies, maternal exposure to corticosteroids or sedatives, low amniotic fluid volume; and decreased placental blood flow due to placental insufficiency.[4]

FHR Patterns

In general FHR of the normal fetal foal decreases from an average of 115 bpm at day 170 to 240 of gestation to approximately 80 bpm by day 320 of gestation.[5] While our clinical observation of large number of high risk pregnancy cases producing normal foals show a similar average, there is a wide variation of individual observations (see below). This slowing of the average FHR with gestational maturity probably reflects increase in functional vagal tone as the autonomic nervous system matures. So it reflects a normal increase of autonomic influence over heart rate.

In healthy fetal foals 22 to 25 accelerations 2 SD above the baseline FHR have been reported per hour during active sleep.[5] These accelerations average for a period of 30 to 40 beats. The presence of these accelerations require intact neurologic coupling between the fetal CNS and the fetal heart and thus are a reassuring sign. In the term human fetus these accelerations are associated with fetal movement more than 85% of the time, and more than 90% of gross movements are accompanied by accelerations (the connection between fetal movement and accelerations first occurs at the beginning of the 3rd trimester). But FHR accelerations may be absent during periods of quiet fetal sleep. Studies on human fetuses demonstrated that the longest time between successive accelerations in the healthy term fetus is usually about 40 minutes. However, the fetus may fail to exhibit heart rate accelerations for up to 80 minutes and still be normal.[3] No such information is available for the fetal foal. Although an absence of fetal heart rate accelerations is most often attributable to a quiet fetal sleep state, commonly used sedative/analgesics such as α2-adrenergic agonist and butorphanol may also result in an immediate and profound fetal bradycardia with no accelerations.[7] This will confound the use of FHR monitoring as an indication of fetal distress during a colic case workup in a pregnant mare or other situations where the mare is sedated.

Fetal adaptation to hypoxemia is mediated through changes in heart rate and redistribution of cardiac output but decreases in fetal cardiac output (with disastrous consequences) only occur when there is coexisting acidemia. In response to sudden hypoxemia, the fetal heart rate will slow with increased variability mediated through chemoreceptor responses influencing vagal tone. In a number of experimental models in other species the fetus has been shown to display this vagal response to hypoxemia. But if the hypoxia lasts longer than 30 to 60 minutes, increasing levels of circulating adrenergic agonists and modulation of vagal activity by endogenous opiates lead to a fetal heart rate return to or rise from the previous baseline.[7] Thus the fetal bradycardia caused by hypoxemia is unlikely to be detected by routine FHR monitoring unless it is performed at the onset of hypoxemia. Development of acidemia on top of hypoxemia can accelerate the rate of fetal deterioration and amplify the hypoxemia by a shift of the oxyhemoglobin dissociation curve to the right, further reducing oxygen carrying capacity of fetal blood and eventually lead to a redistribution of cardiac output that will maintain circulation to the brain, heart and adrenal glands.[7]

The fetal bradycardiac response to acute hypoxemia is the bases for the detection of fetal distress by finding “late decelerations” in the human fetus. Uterine contractions produced a reduction in blood flow to the maternal and fetal placenta and at the same time produce a fetal bradycardia (a vagal or trigeminal response). In the normal fetus the heart rate returns to baseline immediately as the uterus relaxes. But in the fetus with inadequate placental respiratory reserve (placental insufficiency) the uterine contraction will produce an acute hypoxemia resulting in

increased vagal tone which will prolong the bradycardia for a few seconds after the uterus relaxes. This delay in return to a normal baseline heart rate is termed a "late deceleration" and is a reliable sign of fetal distress. Decelerations have been noted in normal fetal foals to occur about 30 times an hour for a period of about 30 heart beats and we frequently see decelerations in fetal foals in high risk pregnancy monitoring but without the ability of knowing the juxtaposition of these decelerations with uterine contractions their identification is not useful in identifying fetal distress in the fetal foal.[5,8]

Equine FHR Monitoring

Fetal heart rate can be measured via ultrasound or ECG. Although the ultrasound technique has been commonly utilized, since it only measures the rate by measuring the difference between two beats the result can be inaccurate. Also since measurements are made over a very short period, it may be misleading. When using an ECG to obtain fetal heart rate, any ECG machine with recording capabilities will work, although a unit specifically designed to monitor fetal foal ECG has been developed. The electrical signal from the fetal heart is low amplitude necessitating placing the electrodes as close to the fetus as possible. Electrodes are basically placed in a pattern that produces the best amplitude in fetal complexes. The ideal pattern varies from mare to mare. In general, one electrode is placed in the lumbosacral area of the mare and the other 2 in the mid flank region. Initially the 2 flank electrodes are placed just below the lumbosacral electrode. However if the tracing is not adequate, one of the flank electrodes may be moved cranially and the other caudally and ventrally. Usually the best location for the flank electrodes is with one mid-abdomen placed a little cranial to the lumbar electrode and the other placed somewhat lower (stifle level) and a little caudal. Generally the best tracing is obtained with the ground at the lumbar electrode so the axis travels through the abdomen. At times it works better to have the axis run from the lumbar to one side or the other. Again trial and error is used to find the best position on the mare and during recordings as the fetus move the complex size and polarity often changes.

As stated earlier the fetus has unpredictable quiet sleep and active sleep cycles. Quite sleep which will not result in a reassuring heart rate pattern can last in other species longer than 80 minutes at times.[3] As a result, although a 10 minute recording may be sufficient if a reassuring FHR pattern is found, if it's not the recording may need to be done for 90 minutes or longer before deciding the FHR pattern may be ominous. For this reason for the past 25 years I have recorded FHR for short periods multiple times a day in order to increase the chance of recording a reassuring reading. I have also found that fetal foals seem to have more active periods at night (although there are some exceptions to this general rule) so I concentrate my exams at night. I use very old telemetry units made for man and place them on the mare at 6 pm and remove them at 6 am and take 40 sec recordings at least 7 times (every 2 hr) overnight or more often when appropriate. Important fetal heart rate parameters to measure are the heart rate itself, the occurrence of accelerations, decelerations, the beat to beat variability, changes in the complex, presence of arrhythmias and the presence of more than 1 distinct pattern (in addition to the mare's) suggestive of a twin.

When I measure heart rates and beat-to-beat variability, I generally measure the distance between each complex noting rate, accelerations, decelerations, complex polarity changes, rhythm and beat-to-beat variation. During the last weeks of pregnancy fetal foals that are normal at birth usually have a baseline heart rate between 75-60 bpm with a low heart rate in the range of 75-40 bpm (80% will have a low fetal heart rate < 70 bpm, 55% low FHR < 60 bpm, 14% low FHR < 50 bpm) and the high FHR in the range of 83-250 bpm (86% will have a high fetal heart rate > 100 bpm, 50% high FHR > 120 bpm, 20% high FHR > 200 bpm).[14] As indicated, transient low heart rates <60 bpm occur in over half of normal foals and even FHR < 50 are not uncommon and should not be considered ominous unless they are consistent with no accelerations. These decelerations probably represent periods of high vagal tone perhaps during a uterine contraction as discussed above. It is also interesting that these low heart rates often have the highest beat to beat variation, perhaps also a vagal response. Although it is very difficult to record readable tracings during stage II labor I have occasionally found some FHR to drop as low as 25-35 bpm in foals which are normal at birth. Whether this is the result of high vagal tone or trigeminal pressure simulating the diving response of mammals is unclear; perhaps it is a combination of both. In any case the FHR is usually about 6o bpm as the head emerges from the birth canal.

FHR may also show accelerations which transiently rise above 200 bpm. Transient FHR > 120 bpm are not ominous unless they are consistently increased and never drop to baseline levels. In either case, when FHR are <60 or >120 throughout an observation period (over a night), repeat assessment within 24 hours or less is indicated. Beat-to-beat variability generally ranges from 0.5-4 mm with most in the range of 1 mm. When measuring the variation, periods when the heart rate is not accelerating or decelerating should be used for an accurate observation. The finding of no beat-to-beat variation in the absence of maternal drugs that may sedate the fetus may be an ominous sign (especially if the FHR is slow) and repeat observations are indicated.

Fetal arrhythmias may be noted during FHR monitoring. It is most common to see occasional VPCs as noted usually by an early complex which is wider than the other fetal complexes and may have different polarity. Infrequent occurrence is not clinically important but a regular occurrence may be a sign of fetal distress. An irregularly irregular rhythm which is likely atrial fibrillation may be seen (as fetal P waves are often difficult or impossible to see definitive diagnosis is usually lacking). This too may be quite transient but if consistent suggests significant fetal distress and even if it spontaneously resolves before birth the foals often have lactatemia (10-15 mmol/L or more) at birth confirming the fetal distress. Occasionally what appears to be runs of fetal ventricular tachycardia may be seen and the more unusual sinusoidal pattern which is defined as a pattern of fixed, uniform fluxuations of the FHR that creates a pattern on Doppler monitors resembling successive sine waves. Occasionally a severe, consistent bradycardia with FHR < 40 bpm often associated with IUGR will be seen. Finally sometimes persistent tachycardia with HR ranging from 120-240 bpm (usually fairly consistent rates of 160-180 bpm) may be seen. Profound fetal acidosis may be present in these foals at birth. In general a fetal arrhythmia which is not transient is an ominous sign.

Fetal Biophysical Profile

A collection of ultrasound and FHR derived observations called a biophysical profile was first proposed by Manning in 1980 and has been successfully used in man to assess fetal health or distress.[9,10] It has been seen as an *in utero* physical examination and evaluates dynamic functions reflecting the integrity of the fetal CNS. It combines FHR observations with ultrasound observations of the presence of fetal breathing movements (as defined as at least one episode of more than 30 seconds of stained breathing), normal fetal movement, normal fetal tone, and normal amnionic fluid volumes.[9] Fetal breathing, fetal movement, and fetal tone are mediated by complex neurologic pathways and should reflect the function of the fetal CNS at the time of the examination. On the other hand, amnionic fluid volume should provide information about the presence of chronic fetal asphyxia as it depends on renal perfusion and urine output.[9]

The fetal biophysical activities that are present earliest in fetal development are the last to disappear with fetal hypoxia. So, in theory, alterations in FHR are the first sign to disappear followed by disappearance of fetal breathing, decreased fetal movement and finally loss of fetal tone. The biophysical profile score in man has been developed to be similar to the Apgar score used to assess the condition of the newborn.[9] The presence of a normal parameter was awarded 2 points, whereas the absence of that parameter was scored as 0. The highest score a fetus can receive is 10, and the lowest score is 0. Any single test has been associated with a significant false-positive rate ranging from 50% to 79%. However, combining abnormal variables significantly decreased the false-positive rate to as low as 20%. The false-negative rate, that is, the incidence of neonates who were compromised but who had normal testing, was very low.

Equine Biophysical Profile

An equine biophysical profile consisting of a collection of ultrasound derived observations of fetal heart rate, fetal aortic diameter, maximum fetal fluid depths, uteroplacental contact, uteroplacental thickness and fetal activity has been proposed.[11-13] Unlike Manning's profile the equine profile is a mix of morphogenic and physiologic measurements with less precise definitions. The FHR determination is based a limited number of ultrasound measurements of single contraction intervals instead of the 20 to 40 min standard Doppler ultrasound observation watching for FHR accelerations used by Manning. The recording of the fetal activity is subjective assessment made over the entire observation period with no clear objective criteria. These 2 parameters plus fetal fluid depths reflect the state of the fetus at the time of the examination. The other 3 parameters are morphometric measurements with the aortic diameter reflecting chronic growth restriction and the placental contact and thickness reflecting a possible underlying source of fetal distress. As a profile, in my hands it lacks sensitivity (a fetus with a normal profile may be suffering from a life-threatening problem) and specificity (occasional extreme values are found in normal fetuses e.g. bradycardia, placental separation). Its overall utility is unproven in prospective studies. However anecdotal experience shows the information gathered about the placenta and fetal fluids in conjunction with other critical information can be quite valuable in selected cases. The use of both transrectal and transabdominal ultrasound in conjunction will give the best information about placental health. Serial examinations are also important to follow progress of the changes. However caution in interpretation should be used. No matter how good the ultrasound image or how experienced the operator at times the ultrasound appearance does not correlate with the placental pathology. As with all aspects of medicine, no one clinical finding should trump all others and ultrasound findings need to be interpreted in conjunction with all other clinical findings. In fact, in my experience, when the udder development conflicts with the ultrasound findings the udder more often accurately reflects the fetal stress level.

THREATS TO FETAL WELL-BEING

It is important to remember that the fetus must get everything from the mother. The mother has almost total control of the fetal environment. There are no known means for the fetus to directly communicate its changing needs to the dam. Despite this, the fetus does have some ability to compensate for changes brought about because of disturbances in maternal homeostasis. Threats to fetal well-being can be considered in the following categories: lack of placental perfusion, lack of oxygen delivery, nutritional threats, inflammatory threats (placentitis/placental dysfunction/maternal inflammation), loss of fetal/maternal coordination of maturation, interaction with other fetuses (multiple pregnancy) and iatrogenic factors (drugs or other substances given to the mother, early termination of pregnancy e.g. induction). Many fetal problems may go undetected, so a gestation which appears to be normal may result in an abnormal neonate.

Lack of Placental Perfusion

Both blood volume (plasma and red cells) and cardiac output of the mother increases 30 to 50% during pregnancy.[15] About half of the increase in cardiac output goes to the uterus and the rest to other areas such as the GIt, kidneys and skin with each of these areas increasing their blood flow by approximately 50% to compensate for the increased demands of pregnancy.[16-18] During the last trimester there's a dramatic increase in blood flow to the placenta in parallel with fetal growth. The maternal placenta receives about 15% of the mare's cardiac output whereas the fetal placenta receives about 40% of the fetal cardiac output.[19] The late term fetus has a very high oxygen demand and must have a high rate of placental perfusion from the mother to receive a constant flow of enough oxygen. Unfortunately oxygen cannot be stored so there can be only short term compensation (through redistribution of fetal blood flow) for poor placental perfusion resulting in decreased oxygen transfer.[20] The margin of safety in late pregnancy is small. There are many maternal problems which occur in late pregnancy that may decrease maternal systemic perfusion. Thus whenever maternal perfusion is compromised and there is an insufficient maternal systemic compensatory response, placental circulation and oxygen delivery to the fetus may be compromised resulting in a significant threat to the fetus. Because of this, maternal hypovolemia must be treated aggressively.

If pressors are used, they should be used with care. The blood vessels of the maternal placenta are largely new growth and as such have no accompanying nerves so there is no central control of placental perfusion. Although there is fairly complex local control scheme (PG mediated and local renin/angiotensin systems) maternal placenta circulation is subject to circulating adrenergic influences. Pregnancy alters the sensitivity and response of different vascular beds to adrenergic agents in a complex and poorly understood way. Whereas dobutamine, epinephrine and norepinephrine decrease uterine blood flow in pregnancy and dopamine has a variable effect, only ephedrine consistently increases uterine blood flow.[21] It is best to avoid adrenergic support in the pregnant mare where possible and when it's not possible to keep in mind that maintaining systemic blood pressure with adrenergic drugs does not mean that maternal placental blood flow is being maintained.

Lack of oxygen delivery to the fetus

Although the major reason for the lack of oxygen delivery to the fetus is decreased placental perfusion, maternal anemia and maternal hypoxemia may also be involved. Survival of the fetus depends on efficient oxygen transport which is determined by unique aspects of placentation or placental oxygen transport mechanisms. Placental gas transport is thought to be independent of diffusion and completely flow dependent. That is, there is no significant loss of transport in the face of a diffusion barrier. Rather, the pattern of flow of maternal and fetal blood determines the efficacy of gas transport.

Although the basic function of all placentas are the same, physically there's almost as many different placental designs has there are species. This is especially true in the alignment of maternal and fetal circulation. When looked at histologically, the blood vessels in the equine are primarily aligned so the fetal and maternal blood flow follows a countercurrent flow pattern (the vessels are parallel to each other and the flows are opposite). This is the most efficient pattern for transfer of oxygen and nutrients and getting rid of waste products. With this pattern the venous side of the fetal capillary bed is aligned with the arterial side of the maternal capillary bed so that the gradient of oxygen and other nutrients is the highest possible. This pattern is almost ideally realized in the equine placenta. This efficient arrangement of blood flow patterns in the horse has important implications in transport mechanisms and adaptive processes.

Because of the countercurrent circulatory pattern, the gradient between maternal and fetal blood O_2 and CO_2 are different in the fetal foal compared to other farm animals. In most species (sheep, cows, pigs) the difference between uterine vein and umbilical vein P_{o2} is 20 mmHg resulting in an umbilical venous P_{o2} of 30-34

mmHg in the fetal sheep. However in the horse, this gradient is near 0 mmHg resulting in an umbilical venous P_{o2} of 48-54 mmHg.[22] Likewise, in most farm animal species the difference between uterine vein and umbilical vein P_{co2} is 4-5 mmHg. In the horse, this gradient is again near 0 mmHg.[22,23] In most species, changes in maternal P_{ao2} do not significantly change fetal values since the gradient is heavily influenced by the venous side of the maternal circulation which is relatively stable under these circumstances until extreme changes occr.[24] However, the fetal foal is heavily influenced by changes in maternal P_{ao2}. For reasons that are not completely clear, in the face of maternal hypoxia, the fetal foal's umbilical P_{o2} is 5-10 mmHg < uterine vein P_{vo2}. Thus, maternal hypoxemia may have a profound effect on the fetal foal, perhaps another reason for the frequent finding of signs of hypoxic ischemic asphyxial disease in the foal. On the other hand, when maternal P_{ao2} is increased with inhaled oxygen, the umbilical P_{o2} rises higher than the uterine vein P_{vo2}. This is probably a matter of an increased driving force allowing more efficient transport.

We have used this physiologic phenomenon to therapeutic advantage by supplementing pregnant mares with intranasal oxygen when we have the clinical impression that the foal is suffering from significant hypoxemia. Placing the mare on intranasal oxygen insufflation at a rate of 10-15 lpm even when the mare's arterial oxygen level is normal may increase the mare's Pao_2 to 115 - 125 mmHg which may effectively increase placental oxygen transport. Although I have used this treatment on a number of high risk pregnancy mares I have never been certain of its benefit. I have at times seen FHR patterns become reassuring after initiating oxygen therapy in some mare's but have never done any type of critical assessment. This therapeutic approach is a holdover from the time when we thought that if we found an abnormal value in a patient, if we applied therapy that would return that value to normal we would be making the patient normal. We all now know that is far from the truth. I rarely use this therapeutic approach currently but if maternal oxygen therapy is used I feel it should be reserved for the last 4-6 weeks of gestation when the rapidly growing fetal foal is pushing the limits of the placental to deliver adequate oxygen. Unlike in man, the equine placenta continues to develop throughout gestation. The continued ingrowth of fetal microcotyledons and decreasing distance between fetal and maternal vessels seems to be stimulated in part in other species by relative local hypoxia. Maternal oxygen therapy may produce a placental environment which may interfere with local development. So I don't think this type of supportive therapy should be utilized to support a fetal foal before the last month of gestation.

Serious consideration should be given to blood transfusion therapy in severely anemic dams to prevent fetal hypoxia. It should be understood, however, that giving blood transfusions to a brood mare may predispose her to produce antibodies against blood groups resulting in neonatal isoerythrolysis in future foals.

Nutritional

The mare's nutritional state may directly affect the fetal foal's well-being. Chronic malnutrition such as occurs with lack of intake (because of lack of opportunity), malabsorption, tumor cachexia and other conditions and acute fasting such as occurs when elective surgical procedures are performed, when the mare has colic during late term or merely because of a capricious appetite of the late gestational mare can have a negative effect on fetal well-being. After 30-48 hr. of complete fasting in the late term mare there is a decrease in glucose delivery and a rise in plasma free fatty acids.[25] These changes are associated with an increase in prostaglandin production in both maternal and fetal placenta (maternal and fetal placenta and fetal fluids contained a complex mix of prostaglandins which seems to be important in maintaining pregnancy and may have a role in initiation of parturition).[25] In fact when the late term mare is being fed concentrate feed there will be a very small fluctuation in prostaglandin production such that there will be peak production just before the mare is fed and a drop associated with feeding.[25] For unknown reasons, there is an increased risk of preterm delivery within one week of ending a complete fast (no hay and concentrate intake) whereas in other species the early delivery occurs within 48 hr of starting the fast. This is believed to be associated with the change in prostaglandin levels however the levels will have been normal for some time before delivery is initiated. The delivered foal often appears premature and not ready for birth. The likelihood of survival in these foals is small. Current theories suggest that the changes in prostaglandin production may lead to an increase in myometrial sensitivity to hormones leading to the increased risk of delivery.

For these reasons it is important to support the mare's nutritional needs as she reaches the end of gestation. The mare may need supplementation and may need to be encouraged to stay on a high plane of nutrition. Acute total fasting should be avoided whenever possible by avoiding elective procedures requiring fasting. If the mare has to be fasted or becomes completely anorexic, intravenous glucose supplementation should be used. Studies indicate that providing intravenous glucose in such cases will negate the changes in prostaglandins and probably greatly decrease the risk of early delivery. The glucose infusion does not need to meet the mare's caloric deficit, just suppress fat mobilization.[25] When mares are periodically anorexic and encouraging them to continue to eat is difficult, placing them on flunixin meglumine in an attempt to prevent prostaglandin changes may also be rational.

Since stressed late term mares are glucose intolerant, placing them on glucose therapy to suppress fat mobilization without resulting in hyperglycemia is a balancing act. Maternal hyperglycemia may result in fluid and electrolyte diuresis complicating fluid therapy and as the fetal glucose level is approximately half the maternal level, if the mare is hyperglycemic so is the foal to a certain extent (the ratio of maternal to fetal glucose levels is not linear at high levels). The fetal hyperglycemia will increase fetal insulin levels and if maintained for a prolonged period result in β-cell hypertrophy resulting in severe birth hypoglycemia. The mare should not be placed on a given percent glucose infusion as the amount delivered depends on the fluid rate. I usually begin at a rate of 0.5 to 1 mg/kg/min and if the mare does not become hyperglycemic and spill glucose in her urine I will gradually increase the amount to 2 mg/kg/min if possible. It is important to keep the glucose infusion rate constant despite changes in total fluid rate.

Inflammatory threats (placentitis/placental dysfunction/maternal inflammation)

There are a number of placental diseases seen in the late term mare including: premature placental separation, placental infection, non-infectious inflammation, placental degeneration, placental edema and hydrops allantois/amnion. Infectious placentitis is most commonly caused by ascending bacterial or fungal pathogens. It may also be caused by hematogenous spread of viral, bacterial, ehrlichial or fungal pathogens. On rare occasions we see what appears to be a non-infectious placentitis. Recently the hirsute (hairy) cuticle of the Eastern Tent Caterpillar has been implicated in causing physical injury to placental vessels resulting in significant placentitis and fetal distress.[26] It should be noted that the percentage of placenta affected is not a predictor of the outcome of the pregnancy. That is, a foal born with widespread placental lesions may be no worse off than a foal with a focal placental lesion. It appears to the presence of placentitis, even if very limited, is enough to predict a serious problem. There are much higher odds of the occurrence of Neonatal Syndrome (Neonatal Encephalopathy, Neonatal Nephropathy and/or Neonatal Gastroenteropathy) in foals born to mares with untreated placentitis.

In other species there is evidence that inflammatory foci anywhere in the mother may result in the same outcome to the fetus as placentitis. The suggestion is that exposure to systemic inflammatory mediators such as cytokines may result in the same threat to the fetus.[27-29] This explains the connection between inflammatory lesions such as laminitis or lymphangitis and neonatal disease.

Since most mares with placentitis have bacterial placentitis, all suspect cases should be treated as such until proven otherwise. Although there have been a few reports of treatment of experimentally induced bacterial placentitis in the mare there are no prospective clinical trials to direct evidence based treatment.[30-32] We all probably have our own favorite approach to these cases based on our individual clinical experience and beliefs. The treatment I have found anecdotally to work best over the years when a specific etiology has not yet been identified is the combination of an antimicrobial (specifically trimethoprim potentiated sulfa drugs), a NSAID (flunixin meglumine) and hormone supplementation (altrenogest – which is also an anti-inflammatory). In a recent retrospective study we found that all 3 of these treatment modalities are important in preventing Neonatal Encephalopathy, Neonatal Nephropathy and/or Neonatal Gastroenteropathy in foals born to these mares.[33]

Loss of Fetal/Maternal Coordination of Readiness for Birth

The normal timing of parturition is decided cooperatively by maternal, fetal and placental events. There is a dynamic interaction between these three distinct forces which coordinates the readiness for birth. The loss of coordination will result in premature, dysmature or postmature foals. Factors determining which occurs are beyond the scope of this talk.

Iatrogenic Factors

There are a large number of possible iatrogenic factors that may threaten the well-being of the fetus. A major one is poor timing of induction of delivery. When the timing of induction is solely based on the calendar and convenience of the owner or veterinarian, the result is often disastrous. When delivery is timed based on emergency considerations for the mare, equally unfortunate outcomes often occur. Many of the drugs mares receive affect the fetus in a variety of ways. Some such as tranquilizers and analgesics (detomidine, butorphanol) can have immediate and profound effects on the fetal cardiovascular system.

Presence of a Twin

The mare is somewhat unique in her inability to support multiple fetuses. At least to me, the reason for this is not entirely clear. Certainly the presence of a co-twin competes for uteroplacental attachment area, competes for nutrients and oxygen, competes for space and significantly increases the risk of dystocia. Most species deal with

multiple births without problems sharing resources between each fetus resulting in smaller offspring but the mare appears to be preprogramed to insure the failure of multiple births.

Idiopathic Factors

Many foals born with Neonatal Syndrome have no history of abnormalities occurring during gestation or parturition. Certainly many events occur without our knowledge. Although it is attractive to blame problems during parturition, most these problems occur during the antepartum period. Although many veterinarians are satisfied with placing the blame on occult hypoxic ischemic disease my observations agree with those in man where it is thought that most hypoxic ischemic episodes are overt and as a sole cause likely account for less than 10% of foals with neonatal encephalopathy.[27] My clinical experience suggests that most foals born with Neonatal Syndrome have had exposure to inflammatory mediators either secondary to placentitis or other maternal inflammatory foci. Neonatal Syndrome is primarily secondary to inflammatory disease.

Other Conditions

There are a number of other conditions I have not been able to mention but may be recognized in the late term mare which places the pregnancy at high risk and should be carefully monitored and managed. These include a wide range of problems such as prepartum uterine artery hemorrhage especially when the hematoma is present in or dissects through the uterine wall resulting in placental detachment, development of hydrops and/or maternal body wall tears, fetal malposition (caudal, breech or transverse presentation), pelvic obstruction and recognition of fetal anomalies such as fetal megacystis, umbilical cord abnormalities or gross fetal malformations. In many of these situations once the problem is recognized therapeutic interventions will not change their course but careful monitoring and management may help in avoiding serious secondary complications.

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