

# What's New in Neonatal Intensive Care?

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What's in a name?  
Pathogenesis of neonatal diseases  
More than you ever wanted to know about colostrum  
Is neonatal intensive care worthwhile?  
Dystocia team



# What's in a Name?





Hypoxic Ischemic Encephalopathy  
Neonatal Maladjustment Syndrome  
(HIE)

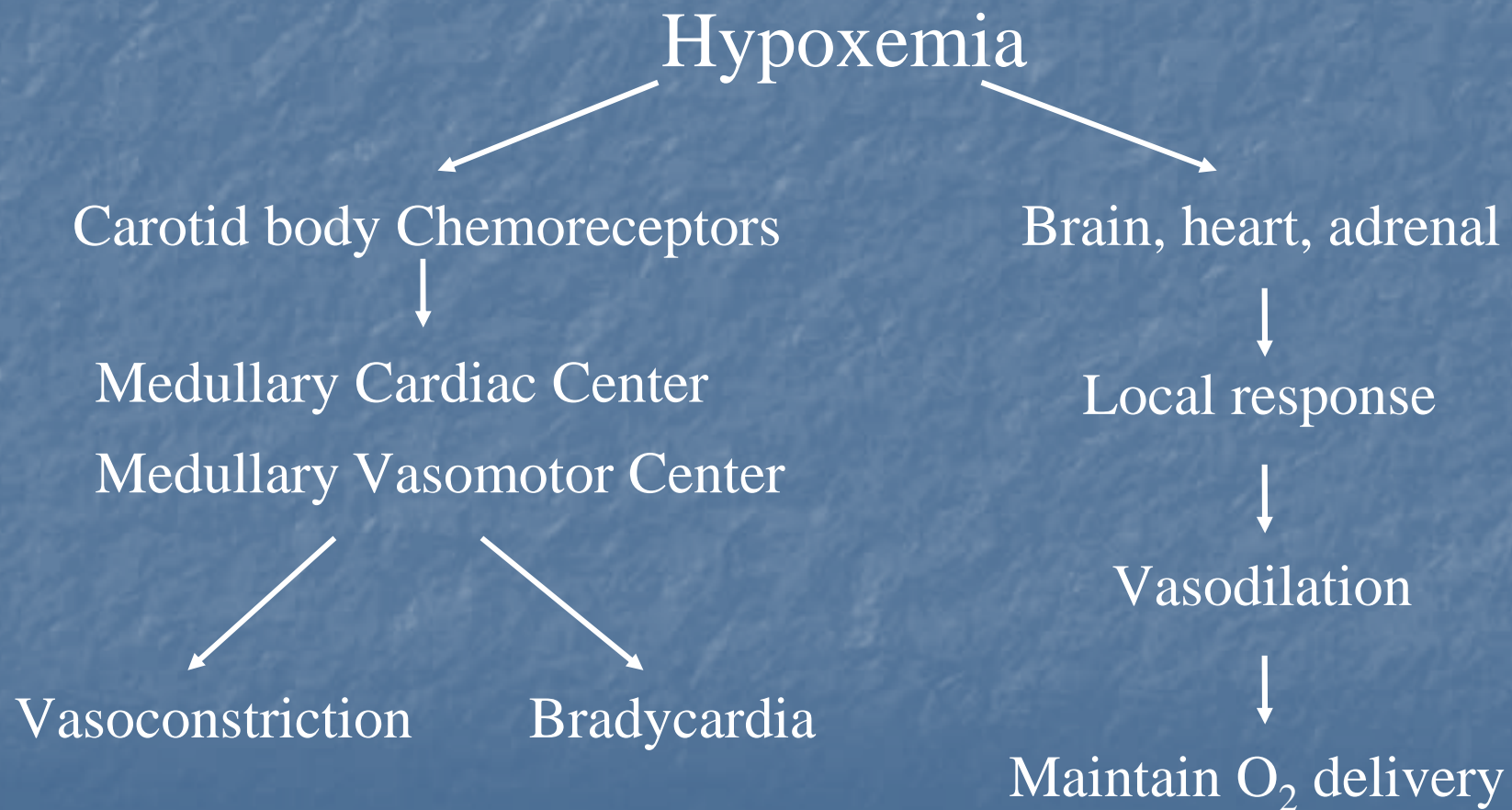
# Terminology

- NMS
  - Focuses attention on the behavioral aspects
  - Maladjustment in mental health
- Neurologic disease
  - Behavioral abnormalities
  - Other neurologic signs
    - Changes in respiratory patterns/function
    - Changes in muscle tone
    - Changes in responsiveness
    - Vestibular signs
    - Autonomic disruption
- Hypoxic ischemic encephalopathy
  - Describe the etiology
  - Generalized neurologic disruption

# Hypoxic Ischemic Insults

- Hypoxemia without ischemia
  - Compensation – no damage
    - Redirect blood supply to vital organs
    - Turn off growth – how?
    - Decrease unnecessary activity (fetal breathing)
    - Chronic hypoxia – tolerant cells
- Ischemia without hypoxemia
  - Compensation – no damage
- Hypoxemia followed by ischemia
  - Multiorgan damage
  - CNS, renal, GI
  - Endocrine disruption, metabolic disruption

# Fetal Response to Hypoxia



# Etiology?

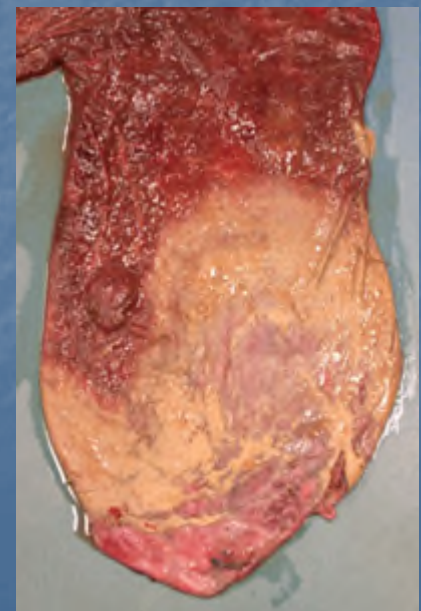
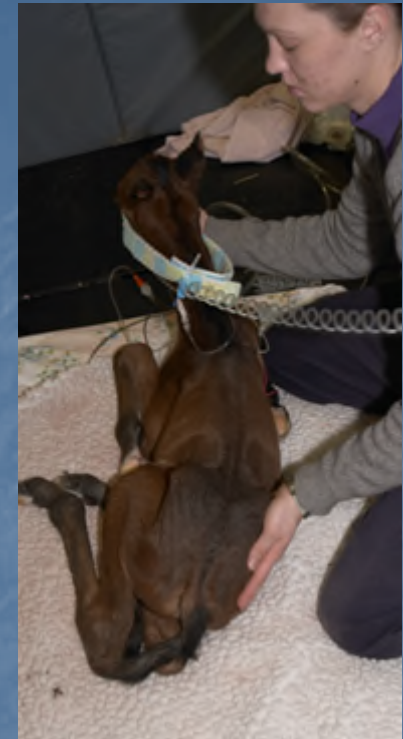
- Hypoxic ischemic insults
  - Prenatal
  - Intranatal
  - Postnatal
- 70% Prenatal
  - Many have no evidence of HI insult
  - Is this really hypoxic ischemic disease?
- Role of FIRS





# FIRS

- Fetal inflammatory response syndrome
  - Fetal version of SIRS
- Role of FIRS in preterm births
  - Human medicine
  - Equine medicine
- Role of FIRS in neonatal diseases



# New Terminology

- Independent of etiology
- Descriptive
  - Age group
  - Organ dysfunction independent of etiology
- Neonatal Encephalopathy – NE
- Neonatal Nephropathy – NN
- Neonatal Gastroenteropathy – NG

# Placentitis Associated Neonatal Problems and the Effect of Therapeutic Interventions

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# Role of Placentitis

- Many neonatal diseases
  - Multiple etiologies
  - Disruption of fetal life
    - Predispose to neonatal disease
    - Origin of the neonatal disease
- Same process - different organs
  - Neonatal Encephalopathy
  - Neonatal Nephropathy
  - Neonatal Gastroenteropathy



# Hypothesis

- The occurrence of neonatal diseases is influenced by fetal exposure to placentitis
- Treatment of placentitis will protect against the development of neonatal diseases

# Methods

- Observational retrospective study
- Population
  - Hospitalized mare/foals 2000-2005
    - Foals referred for critical care
    - High Risk Pregnancy cases
  - Fetal membranes examined
  - Foal examined
  - Data source – clinician notes
    - Placental evaluation – PLS
    - Foal evaluation – JEP



# Results

- 108 cases
- Placentitis - 44% (48/108)
  - Gross - 56%
  - Histologic 60%
  - Retention 33%
- Prepartum treatment 41% (44/108)
  - Placentitis cases treated 42% (20/48)



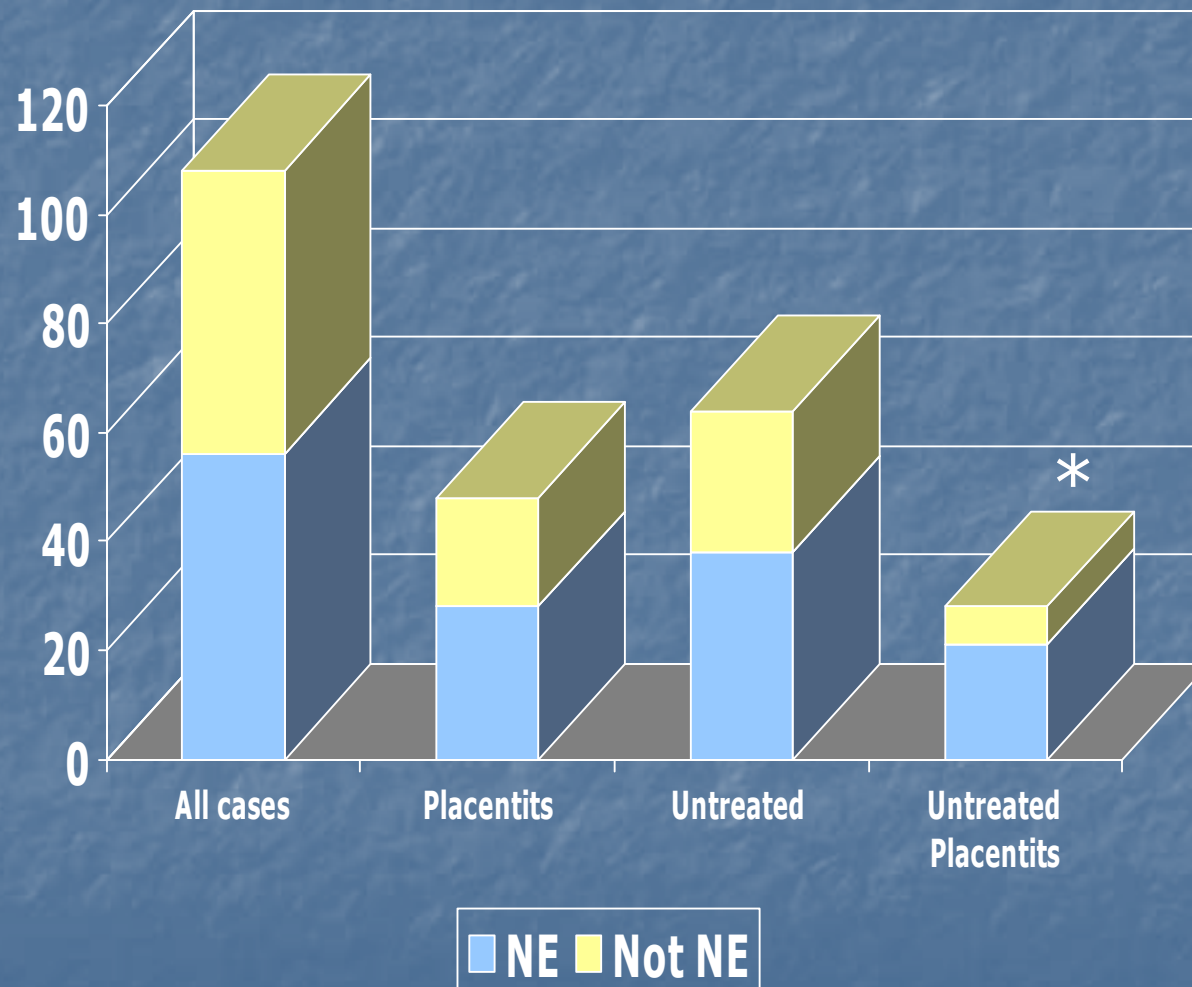
# Clinical Diagnosis

- NE 52% - 56/108
- NN 40% - 43/108
- NG 37% - 40/108
- Clinical prematurity 4.6% - 5/108
- IUGR 9% - 10/108
- Sepsis 56% - 61/108
- Bacteremia 18% - 19/108
- Normal 27% - 29/108
  - None of these problems
  - Other neonatal problems
    - Musculoskeletal problems
    - Neonatal isoerythrolysis.



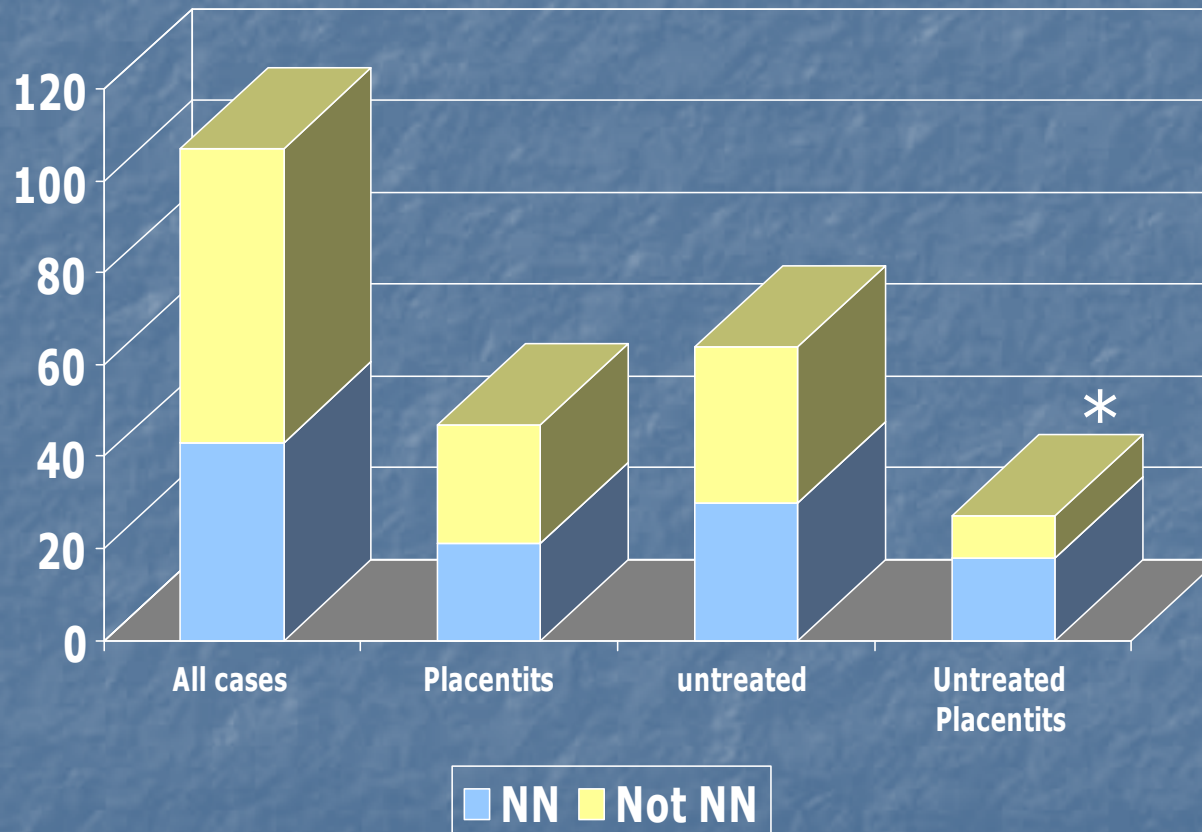


# Neonatal Encephalopathy



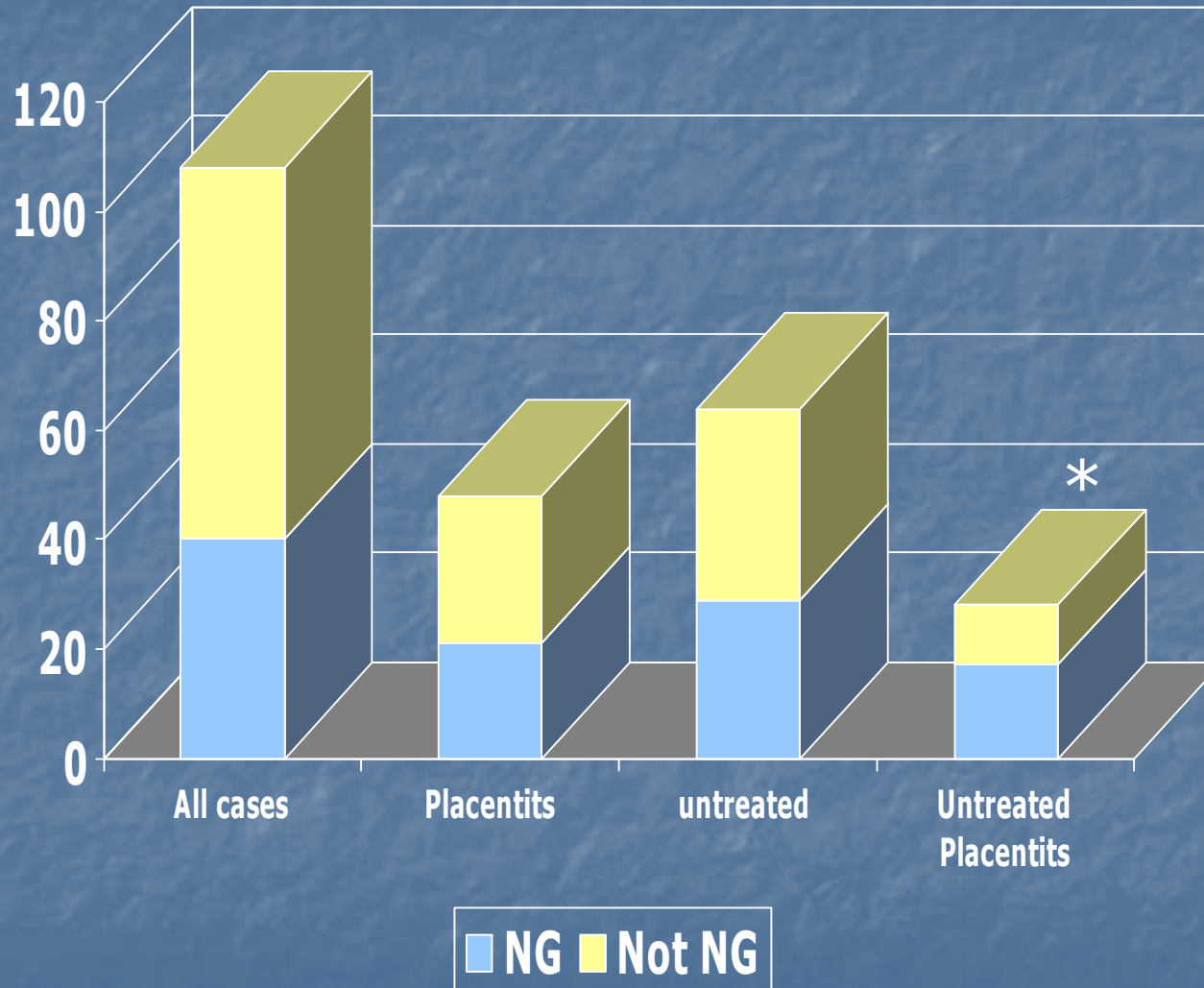
**p = 0.028, OR 3.4, 95% CI 1.1-9.8**

# Neonatal Nephropathy



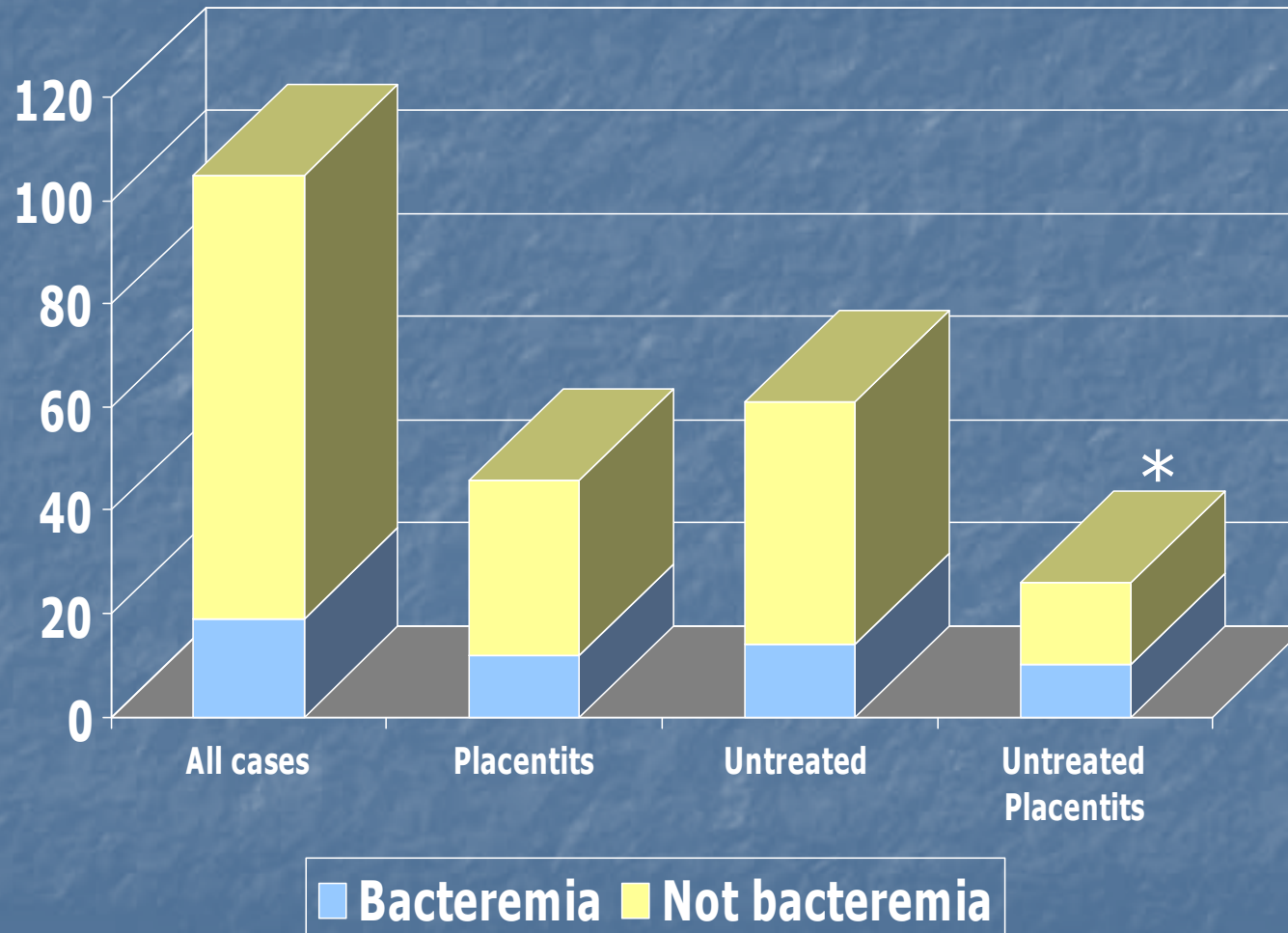
**$p = 0.011$ , OR 4, 95% CI 1.4-11.5**

# Neonatal Gastroenteropathy



**p = 0.031, OR 3.1, 95% CI 1.1-8.6**

# Bacteremia



**$p = 0.018$ , OR 4.8, 95% CI 1.3-17.9**

# Conclusions

- Strong association of untreated placentitis
  - NE, NN and NG
  - Placentitis is the etiology
- Treatment of mares with placentitis significantly increased the odds of having a foal without any of the neonatal problems studied
- Mares with suspect placentitis should be treated prepartum to prevent development of common neonatal diseases

# Colostrum

## Mother Nature's Wonder Elixir



# Sepsis

- Biggest killer in our NICU
- Complicates many of our cases
  - Increases morbidity
  - Increases mortality
- Passive transfer of colostral goodness
  - Traditional view
    - Primary role transfer IgG
  - New view
    - Primary function establishment of a healthy immune barrier
      - GI mucosa
      - Between luminal bacteria and foal

# Colostrum

- Source of IgG
- Other biologically active substances
  - Other proteins
  - Immune modulators
  - Pro and anti-inflammatory substances
  - Inflammatory cells – neutrophils, plasma cells
  - Trophic substances
- Role
  - Targeting potential pathogens
    - Before invasion
  - Insuring GI development
    - Not disrupted by inflammatory damage





# Colostrum Transfer of Protective Factors



- Paul Ehrlich in 1891
- Colostrum is tailored for the neonate
  - Incomplete compliment of immune functions
  - Initiate or augment immune functions
    - maturation of equine neutrophils
  - Immune functions absent - replaced

# Colostrum Transfer of Protective Factors

- Colostrum is tailored for the neonate
  - Defense agents in colostrum
    - Enhanced survival in the gastrointestinal tract
    - Protect without provoking inflammation
    - Inhibit inflammation
  - Targeting of pathogens
    - Without collateral damage

# Colostrum Transfer of Protective Factors

- Colostrum is tailored for the neonate
  - Agents in colostrum
    - Alter the physiologic and biochemical state of the gastrointestinal state
    - Fetal life to one appropriate to extrauterine life
  - Growth factors in colostrum
    - Favor proliferation of commensal enteric bacteria
    - Trophic factors
      - Epithelial growth and development

# Colostrum Transfer of Protective Factors

- GI is the most likely portal of pathogens
  - Preventing luminal establishment of pathogens
  - Prevent proliferation of pathogens
  - Prevent invasion of pathogens
  - Protecting the neonate from sepsis



# Antimicrobial Factors in Colostrum

- Proteins
  - Lactoferrin - bacteriostasis by Fe chelation
  - Lactoferricin - causing bacterial killing
  - Lysozymes – bacteriolysis
- MUCI - inhibits the binding of fimbriated *E coli*
- Lactadherin - binds viruses
- Oligosaccharides and glycoconjugates
  - Receptor analogues
  - Enteric pathogens and toxins
- Monoglycerides
- Fatty acids
  - Disrupt envelope viruses
  - Inactivate certain bacteria
  - Defend against *Giardia*

# Antimicrobial Factors in Colostrum

- PAF-degrading enzyme
  - PAF is an important proinflammatory mediator
  - High levels in neonate
  - Protects mucosal cells from damage
- Erythropoietin
  - Protects against epithelium apoptosis
  - Trophic substance
- Epidermal Growth Factor (EGF)
  - Role in mucosal barrier function
  - Down-regulates apoptosis

# Colostrum Substitutes

- Why measure IgG levels?
  - Only measurement available
  - Surrogate for of the establishment of this immune barrier
  - Surrogate for transfer of immune competence
  - Quantity vs. quality

# Colostrum Substitutes

- IgG concentrate colostrum substitutes
  - Poor trade off
  - Only thing available
  - Not a true colostrum replacement





# Colostrum Substitutes

- IgG quantity
  - Is not the aim of passive transfer
  - Misconception
    - Market of IgG based colostrum substitutes
  - Hyperimmune plasma is not a true substitute
    - Donor is stimulated – variety IgG (quality)
    - Contains many helpful factors other than IgG

# Mother Nature's Wonder Elixir

- May not be appropriate for all foals
  - Critically ill foals
    - Poor perfusion
    - Hypoglycemia
    - Hypoxia
    - Other challenges
  - Feeding colostrum
    - More of a risk than a benefit
    - Considering referral – talk to us
    - Significant NG and secondary sepsis
    - On farm critical care - moderate volumes

# Mother Nature's Wonder Elixir

- Foals not fed first few days of life
  - "Trophic" feeding
  - Small volumes of colostrum
    - 0.5-1% or 0.5 – 2 oz q4-6h
    - Fresh colostrum
    - Frozen colostrum
    - Fresh mare's milk



A brown horse is captured in the middle of rearing up on its hind legs in a dirt and grass paddock. The horse is facing left. In the background, there is a wooden fence, a blue metal gate, and a yellow house with a brown roof. The sky is overcast. A semi-transparent blue box with white text is overlaid on the upper part of the image.

Is treatment at a  
tertiary care facility  
worth while?

Outcome

# Graham French Neonatal Section Connelly Intensive Care Unit



*1990 - 2005*

*2053 Neonates – 84% survivors*

# How successful have we been?



- Racing graduates (TB & STD)
- Control population - siblings
- Racing
  - NICU survivors 60%
  - Siblings 75%
- Racing results
  - Standardbreds No difference
    - Places per start
    - Earnings per start
    - Earnings
  - Thoroughbreds No difference after 1<sup>st</sup> year
    - Places per start
    - Earnings per start
    - Earnings

# Dystocia Team



# Dystocia Team





# Dystocia Team



# Dystocia Team



# Dystocia Team





## WHAT'S NEW IN NEONATAL INTENSIVE CARE?

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Neonatology is a constantly evolving specialty. As our understanding of fetal and neonatal physiology and pathophysiology increase, our approach to therapy is modified and constantly refined. Approaches to therapy based on new ideas are introduced as those found to be based on incorrect assumptions are abandoned. I will describe some of our changing ideas which are perhaps most perplexing to the referring practitioner.

First, let me describe changes in terminology. Over the years neonatal foals with neurologic signs have been referred to using various descriptive terms such as “barkers,” “wanderers,” “dummies,” and most persistently as having Neonatal Maladjustment Syndrome (NMS). More recently NMS has been abandoned in favor of Hypoxic Ischemic Encephalopathy (HIE) because the former focuses attention on the behavioral aspects colored by the use of the term maladjustment in mental health. The neurologic disease of neonatal foals not only involves behavioral abnormalities but also other neurologic signs including changes in respiratory patterns/function, changes in muscle tone, changes in responsiveness, vestibular signs and autonomic disruption (loss of vascular control, loss of thermoregulation, inappropriate bradycardia, etc.). HIE not only was felt to describe the etiology, it implied a more generalized neurologic disruption. As it turns out, HIE is also not an ideal term. Although a hypoxic ischemic insult may be responsible for some cases, in most the underlying etiology is uncertain. We have followed the lead of MD neonatologists in simplifying the terminology to describe the organ system involved and the age group and not implying an etiology. Thus the term we use to describe neonatal foals with neurologic signs is Neonatal Encephalopathy (NE). We use the same conventions for disorders of other organ systems: Neonatal Nephropathy (NN), Neonatal Gastroenteropathy (NG), etc. Hopefully this terminology will survive further expansion of our understanding of the underlying pathophysiology and will not need to be changed in the future.

Foals with Neonatal Encephalopathy (NE) may show changes in responsiveness, muscle tone, behavior or evidence of brain stem damage or seizure-like behavior. Changes in responsiveness include hyperesthesia, hyperresponsiveness, hyperexcitability, hyporesponsiveness, periods of somnolence or unresponsiveness. Often foals go through a period of increased responsiveness followed by a period of decreased responsiveness. Changes in muscle tone include increased extensor tonus, hypotonia and other less common changes such as neurogenic myotonia or failure to protract front legs. Changes in behavior are very common and include loss of suckle response, loss of tongue curl, loss of tongue coordination, disorientation especially relative to the udder, aimless

wandering, loss of affinity for the dam and abnormal vocalization. Foal with NE commonly have changes in respiratory patterns with central tachypnea, apneusis, apnea, cluster breathing, ataxic breathing, Cheyne-Stokes breathing or central hypercapnia. Other signs of brain stem damage include loss of thermoregulatory control, generalized weakness, anisocoria, pupillary dilation, pinpoint pupils, central hypotension, decreased responsiveness, difficult to arouse, loss of consciousness, vestibular signs (circling, head tilt), facial nerve paresis and a variety of other signs. Foals with NE have a wide variety of signs and degrees of severity. More than 90% of affected foals are normal within 10 days.

Foals may also develop Neonatal Nephropathy (NN). There is a wide spectrum of disease seen in cases of NN including incomplete transition from fetal renal physiology, water/sodium retention, mild tubular dysfunction (sodium wasting), abnormal excretion of drugs (e.g. high amikacin trough levels), acute tubular necrosis or decreased GFR. Often the signs of dysfunction are subtle and easily overlooked unless anticipated. Although almost always transient, on occasion significant acute damage may lead to chronic renal disease. These foals often have a decreased GFR as reflected by a slow decrease birth Creatinine or decreased creatinine clearance, delayed water excretion with edema formation and weight gain and slow response to fluid challenges.

Neonatal Gastroenteropathy (NG) can be manifested by a wide spectrum of signs ranging from mild indigestion with dysmotility and enema dependence to moderate disease with ileus, diapedesis of blood into the lumen and mucosal edema to severe disease with epithelial necrosis, intussusceptions, structures, hemorrhagic gastritis/enteritis/colitis, and pneumatosis intestinalis. Even mild forms predispose to sepsis and SIRS with increased likelihood of translocation of bacteria. Like NN, often the signs of dysfunction are subtle and easily overlooked unless anticipated. The most common manifestation is dysmotility with meconium retention and lack of fecal passage for days (range 2-30 days). Despite fecal retention, an important aspect is lack of discomfort. Classically, foals with classic motility will not return enema fluid or strain associated with rectal distension.

Often, affected foals have the triad of Neonatal Encephalopathy, Neonatal Nephropathy and Neonatal Gastroenteropathy. Other problems seen include metabolic maladaptation, autonomic failure and other systemic problems. Most of these foals have no clear history of an intrauterine hypoxic ischemic insult but certainly have had some intrauterine challenge.

This brings me to the second “new” idea in equine neonatology. That is the connection between placentitis and many neonatal diseases and the protective effect of treatment. For many years we have suspected that the occurrence of placentitis is important in predisposing to neonatal diseases. In human medicine, intrauterine sepsis has been connected to early termination of pregnancy (prematurity) and experimental models have recently reinforced this connection. But the connection between placentitis and neonatal problems goes far beyond prematurity based on preliminary data from an ongoing study. Disruption of the intrauterine environment may be the initiator of many serious neonatal diseases. The inflammatory response may directly affect placental sufficiency or the

inflammatory cascade accompanying the placentitis may have secondary adverse consequences for the fetus. On the other hand, the up-regulation of the fetal inflammatory response may help to hasten maturation and prepare of the fetus not only for neonatal life but modify its response to septic challenges.

In a preliminary analysis of an observational retrospective study of the relationship between occurrence of placentitis and neonatal diseases and the effect of therapy we have found a significant connection between neonatal diseases and untreated placentitis. There is a strong association of placentitis and NE, NN and NG. This strong association supports the hypothesis that placentitis is the cause of these diseases. In addition prepartum treat of the mare for placentitis appears to strongly protect against development of these diseases. The commonly utilized therapy of antimicrobials, NSAIDs and progestins all seemed to contribute to this protective affect. Surprisingly, treatment, independent of the presence of placentitis, showed a trend to protect against sepsis suggesting that something other than placentitis which responded to treatment could predispose the foal to sepsis. Alternately, treatment of the mare might decrease the exposure of the neonatal foal to factors that predispose to sepsis. This trend will be explored further as more cases are added to this data set. Although bacteremia was more likely in foals from mares with untreated placentitis, prepartum treatment of the mares did not protect from sepsis. Treatment of mares with placentitis significantly increased the odds of having a foal without any of the neonatal problems.

So the bad news is placentitis, a prevalent, recurring problem in many of our mares, is a major cause of some of the most serious neonatal diseases we treat. It may not be the only cause of these diseases but it significantly contributes to morbidity in our foals. The good news is that the commonly utilized therapy of placentitis in mares will protect foals from these diseases. So the take home message is that mares with suspect placentitis should be treated prepartum with the traditional therapy of TMS, ReguMate<sup>®</sup> and flunixin to prevent development of common neonatal diseases in their foals. It is nice to have clinical impressions reinforced by clinical studies.

The development of sepsis in our neonates is not as closely associated with placentitis in the mare as the other neonatal diseases, even though bacteremia is more likely to occur in foals born from placentitis. Sepsis is still the biggest killer in our NICU and complicates many of our cases. This leads to the next topic: a better understanding of passive transfer. Rather than following the traditional view that the primary role of colostrum is to transfer IgG, I feel that colostrum's primary function is the establishment of a healthy immune barrier between the luminal bacteria and the foal at the GI mucosa. Although colostrum is an important source of IgG, it contains many other biologically active proteins, immune modulators and pro and anti-inflammatory substances. All of these substances are important in insuring the development of an effective protective barrier targeting potential pathogens before their invasion and insuring that the fragile development of the gastrointestinal tract is not disrupted by inflammatory damage.

It was Paul Ehrlich in 1891 who first recognized the importance of colostral transfer of protective factors. Colostrum is tailored for the neonate who has yet to develop a

complete complement of immune functions. Certain agents in colostrum initiate or augment functions which are otherwise poorly expressed in the neonates. In fact, without some agents in colostrum, immune development will be delayed (e.g. maturation of equine neutrophils). Certain immune functions that are initially absent in neonates are replaced by factors in colostrum. In addition, defense agents in colostrum have enhanced survival in the gastrointestinal tract of the recipient compared to their plasma derived counterpart. Also, defense factors in colostrum protect without provoking inflammation and some agents inhibit inflammation both allowing targeting of pathogens without allowing the inflammatory reaction to disrupt the development of the neonate's gastrointestinal tract. There are also agents in colostrum that alter the physiologic and biochemical state of the gastrointestinal state from one suited to fetal life to one appropriate to extrauterine life. Finally and perhaps most importantly, growth factors in colostrum augment the proliferation of the commensal enteric bacteria. Since the gastrointestinal tract is the most likely portal of entry of pathogens, the action of colostrum in preventing luminal establishment, proliferation and invasion of pathogens is vital in protecting the neonate from sepsis.

Antimicrobial factors in colostrum include proteins such as lactoferrin (bacteriostasis by Fe chelation), lactoferricin (causing bacterial killing), lysozymes (bacteriolysis by degrading peptidoglycans), MUCI (inhibits the binding of S-fimbriated *E coli* to epithelial cells), lactadherin (binds viruses so prevents epithelial attachment), oligosaccharides and glycoconjugates (receptor analogues which inhibit binding of enteric pathogens and toxins to epithelial cells) and monoglycerides and fatty acids (disrupt envelope viruses, inactivate certain bacteria, defend against *Giardia*). Other important factors in colostrum include PAF acetylhydrolase (PAF-degrading enzyme; PAF is an important proinflammatory mediator in the GI tract with high levels in the neonate; this enzyme protects mucosal cells from damage caused by PAF by degrading it), erythropoietin which protects against apoptosis of intestinal epithelium, epidermal growth factor which has been shown to play an important role in mucosal barrier function in developing intestine, and down-regulates apoptosis of intestinal epithelium.

Using IgG concentrates as a substitute for colostrum is a poor trade off. If it is the only thing available, it should be used but not with the expectation that it is a true colostrum replacement. When we measure IgG plasma levels as a reflection of passive transfer, what we are doing in essence is making the only measurement of the establishment of this immune barrier and transfer of immune competence available to us. There is no way to test to see if the enteric protective barrier has been established, to insure that protective and modulating substances are present and in place at the mucosal level resulting in an effective immune barrier. There are no simple techniques to see if the colostrum substances have had their stimulating effect on the neonate's immune function or have stimulated the healthy maturation of the neonate's mucosal barrier. So we use the measurement of plasma IgG levels as a surrogate for these things. Transfer of a quantity of IgG is important but not the most important part of passive transfer. It's not the quantity but the quality of IgG that's important. Having a large quantity of IgG targeted against influenza virus is not helpful in protecting the neonate against bacterial pathogens. But since we have no method to measure the quality of IgG transferred, we



rely on quantity as a surrogate. It is unfortunate that we have largely lost sight of this and frequently teach that the surrogate, IgG quantity, is the aim of passive transfer. In fact a whole industry has grown out of this misconception and IgG concentrates are frequently marketed as colostrum substitutes. Even when hyperimmune plasma transfusion is used as a colostrum substitute, a significant quantity of IgG transferred will be to pathogens that aren't a threat to the neonate. But when the donor is stimulated to produce this unhelpful IgG, other, more useful antibodies will also be produced as well as immune modulating substances which may be important in the neonate who has not benefit from colostrum.

I hope you will widen your view of passive transfer and think of it in broader terms than just transfer of IgG. When we have a foal who can't tolerate oral feeding during the first few days of life, I will frequently give him what we call "trophic" feeding. That is very small volumes of colostrum (0.5 – 2 oz up to 0.5-1% of the foal's body weight in several small feedings) for its trophic effect (fortunately many of the trophic substances don't need to be present in large quantities to be effective). When foals with GI disease such as necrotizing enterocolitis (NEC) are able to begin oral feeding I often will use the combination of frozen colostrum (often the poor quality/old colostrum) and milk right out of the mare (some of the substances are destroyed by freezing but still may be present in mammary secretions even after colostrum is gone).

I would like to make it very clear that even if colostrum is Mother Nature's wonder elixir, it may not be appropriate for all foals. Giving large volumes of colostrum to critically ill foals with poor perfusion, hypoglycemia, hypoxia and other challenges is more of a risk of sepsis than a benefit in protecting against sepsis. If you are considering referral, we would like you to talk to us before feeding the critical foal. It is likely that we will suggest not feeding colostrum or only feeding an ounce or two of fresh colostrum right out of the mare. Critical foals fed large volumes of colostrum before referral are more likely to suffer from significant NG and secondary sepsis resulting in a longer and more expensive hospital stay and more likely fatal outcome. If referral or on the farm critical care is not in the foal's future, then moderate volumes of fresh colostrum may be the best course, giving the foal the best chance despite the possible drawbacks.

Is treatment at a tertiary care facility worth while? This is another question which we studied a few years ago. While there are no studies comparing outcome of therapy on farms compared to referral centers, our experience has been very positive. Although we treated critical neonates for many years before it opened, our current Neonatal Intensive Care Unit is 16 years old. As of the end of 2005, we have treated 2053 neonates. Of these, 84% have gone home. Foals with complicated conditions such as neonatal encephalopathy (maladjustment syndrome) with renal and GI involvement (neonatal nephropathy, neonatal enteropathy) have a survival rate of 87%. The foals with the poorest outcome are those presenting in septic shock where less than 50% survive.

What about long term outcome? We performed a long term outcome study on our graduates who were bred for racing (both Thoroughbreds and Standardbreds) a few years ago. We used the siblings of our patients as controls to insure that we were gauging

outcome based on the potential of our NICU patients. We found that 60% of our NICU survivors raced compared to 75% of their siblings. The 15% dropout from the NICU survivors included foals with significant musculoskeletal abnormalities, premature foals and twins. The dropouts primarily had conditions that intuitively have poor prognosis for racing. Of those Standardbred graduates who raced, during the first 2 years of racing there was no difference between the places per start, earnings per start or total earnings. With the Thoroughbreds, there was less earnings per start and less total earnings during the first year of racing but these differences disappeared during the second year or if the first and second year results were combined. During both years there were no differences in the places per start, suggesting that during the first year of racing, the thoroughbred NICU survivors were entered in races with smaller purses.

Both the short term and long term outcomes are very encouraging. Neonatal intensive care can make a significant difference in the recovery of patients with critical conditions during the first days of life. Most survivors will perform up to their expectations. The viability of equine neonatal intensive care depends on whether the owner feels that the investment in care is worth the likelihood of a positive outcome. In our practice many of our owners are repeat customers.

Another change in our practice in the past decade is the development of a dystocia team. Many of you are aware that this exists but perhaps not what it entails. The dystocia team consists of a staff emergency surgeon and 1 or 2 surgery house officers, a senior reproduction clinician and reproduction resident, a senior neonatologist and neonatology house officer, an anesthetist, an OR nurse, 1 or 2 critical care nurses, 1 or 2 nursing assistants and a laboratory technician. These dozen staff members are joined by students in emergency/critical care, reproduction, neonatology, anesthesiology and various nursing students. This team can be mobilized within 20 minutes 24 hours a day. Neonatology's role in this is to begin assessment and resuscitation of the fetal foal while it is still in the birth canal using a technique we call EXIT (ex-utero intrapartum treatment) consisting of intubation and ventilation of the foal before complete delivery and then of course performing intensive resuscitation once the foal is born. If successful, EXIT procedures provide the luxury of time to correct the dystocia, a means to assess fetal viability, a means to rescue fetal foals during dystocia and potentially a means to increase the successful referral radius.

There are many other new approaches we have developed in the past decade. We use small diameter indwelling nasogastric tubes for feeding foals. We have always used CRIs (continuous rate infusions) but are much more commonly using this technique to deliver beta-lactam antimicrobials. Our approach to fluid therapy is different from many other neonatologists and continues to evolve. We are continuing to adapt new therapies such as nitric oxide delivery techniques, the use of sildenafil in PPHN, the use of vasopressin in CPR and as a vasopressor and the use of many other approaches. For more information about our current approaches to therapy feel free to visit our web site (<http://nicuvet.com>).