Equine Neonatal Sepsis

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Learning Objectives

• What does a normal foal look like
• What are current definitions
• What do we commonly see
  • How do they present
• How to recognize abnormal and how to treat
Recognition of Normal

Parturition
- Should follow the 1-2-3 rule
  - Rule 1: stand in 1st hour
  - Rule 2: nurse by 2nd hour
  - Rule 3: mare pass placenta by 3rd hour

Average length of Stage II of labor is 16.7 minutes
- 2-3 or more active propulsive pushes every minute

What is normal at the time of parturition
- Initial gasping breathing pattern should breathe regularly within 30 seconds of birth
- Heart rate and rhythm
  - Averages 70 bpm immediately after birth
  - Cardiac arrhythmias during the first hour of life

Pain and sensory awareness at birth
- Develop a righting reflex with 5 minutes
- Suck reflex within 2 to 20 minutes
What does a Normal Foal Look Like

What is/was gestation length
- Normal is 315-365 average being 341

What about physical examination?
- MM pk and moist CRT<2 seconds
- Assess color: jaundice, cyanotic, injected, ulceration, petechial hemorrhage
- Pulses: strong palpable
- Thoracic auscultation
  - HR average 70-80 range 40-80 post delivery
  - Attempt to stand = tachycardic
  - Normal sinus arrhythmia first few hours
  - Holosystolic murmur first 72 hr PMI left 3 ICS
What does a Normal Foal Look Like

- Respiratory rate/effort
  - Normal 20-40 first few weeks
  - Pattern of breathing should be normal in standing foal
    - Changes with recumbency – weak IC muscles, depth of sleep
    - No paradoxical breathing pattern
So Where Are We Now in 2017?

• **Sepsis**: life threatening organ dysfunction
  - Results from dysregulated host response to infection
  - Description of a syndrome rather solely based on infection as trigger allows for other causes outside of virus/bacteria
  - No standardized diagnostic test

• **Severe Sepsis**
  - Removed thought to be redundant and hard to define

• **Organ Dysfunction**: increase in SOFA score
  - (Sequential (sepsis related) organ failure assessment) of 2 points correlated to in hospital mortality >10%

• **Septic Shock**: subset of sepsis
  - Profound circulatory, cellular and metabolic abnormalities > risk of mortality
  - Vasopressor required maintain MAP≥ 65mmHg lactate ≤ 2 mmol/L
  - Mortality approaching 40%
Risk Factors for Septicemia-History

1. Mare
   • Systemic Illness
   • Colic
   • Premature udder development
     • Streaming milk (colostral loss)
   • No udder development
   • Prolonged gestation
   • Dystocia
Risk Factors for Septicemia-History

2. Foal
   • Premature
   • Dysmature
   • Twin gestation
   • Premature placental separation
   • Meconium staining
Normal Foal-Physical Exam

• Normal foal
  • Normal size, erect ears, holds head up
  • Active; attempts to rise in 10 minutes; up within 2 hours
  • Suckle reflex within 20 minutes
  • HR: 50-70 bpm; rises to 100 bpm in 1st hour
Risk Factors for Septicemia-Physical Exam

- Small birth weight, floppy ears, ligament laxity or severe contracture
- Depression, injected mm
- Abnormal behavior (lack of mare tropism)
- Persistent bradycardia
- Poor thermal regulation
- Respiratory distress
Risk Factors for Septicemia-Physical Exam

- Abnormal mucous membranes
  - Injected or petechia
- Fever
Neonatal Septicemia
Risk Factors for Septicemia-Physical Exam

- Hypotonia, coma
- Localized infection: anterior uveitis, septic joint, diarrhea, pneumonia
Risk Factors for Septicemia-CBC

- Decreased neutrophil count
  - Degenerative left shift
- Toxic changes (neutrophils & lymphocytes)
- High fibrinogen
- High SAA

Enterococcus faecalis
Risk Factors for Septicemia-Chemistry

- Pre-existing condition
- Hypoglycemia
- Low IgG
- Low PaO$_2$
- Metabolic acidosis
Referral/Transportation

- Separate from mare, in car
  - Keep warm
- Continue fluids if indicated
  - Supplement with dextrose
    - 2.5-5% NO Bolus
- No evidence of colic
  - Pass tube and give 500 ml milk
- Start antimicrobials
  - Broad spectrum
- Bring placenta
- Bring any blood/cultures obtained
Neonatal Septicemia

Most common problem in neonates

Early identification and management are keys to success

Generalized vs. localized
- Naval ill / joint ill
- Diarrhea
- Pneumonia

(P)FPT (FTPI) is an important risk factor
- Lack of or poor colostrum ingestion
- Premature/dysmature foal

Route of infection
- umbilicus / GI tract / respiratory tract

E. coli most common, A. equuili
Foal Septicemia Early Identification

• The sepsis score
  • Score based on 4 categories
  • Helps understand the parameters indicative of sepsis
  • Helps predict likelihood of sepsis
• A score of 12 or more correctly predicted sepsis 93% of the time in original study
What About Illness Severity Scoring Systems

Can we accurately predict if the foal is septic or not?

Is it possible to predict outcome?
Development of a scoring system for the early diagnosis of equine neonatal sepsis

**TABLE 1: Sepsis score and individual tests in 149 hospitalised equine neonates in which the presence or absence of sepsis was confirmed**

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal tests in confirmed sepsis/Total abnormal tests</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>False positive (%)</th>
<th>False negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis score (normal &lt; 12)</td>
<td>78/87</td>
<td>93</td>
<td>86</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>White blood count (normal = 8-12 x 10^9/litre)</td>
<td>75/118</td>
<td>88</td>
<td>33</td>
<td>51</td>
<td>16</td>
</tr>
<tr>
<td>Segmental neutrophil count (normal = 4-8 x 10^9/litre)</td>
<td>65/95</td>
<td>79</td>
<td>53</td>
<td>37</td>
<td>27</td>
</tr>
<tr>
<td>Band count (normal &lt; .50 x 10^9/litre)</td>
<td>63/79</td>
<td>76</td>
<td>75</td>
<td>19</td>
<td>31</td>
</tr>
<tr>
<td>Band : neutrophil (normal &lt; .02)</td>
<td>52/126</td>
<td>60</td>
<td>86</td>
<td>11</td>
<td>34</td>
</tr>
<tr>
<td>Toxic changes (normal = 0)</td>
<td>49/61</td>
<td>58</td>
<td>81</td>
<td>14</td>
<td>55</td>
</tr>
<tr>
<td>Fibrinogen (normal ≤ 4.0 g/litre)</td>
<td>40/51</td>
<td>47</td>
<td>83</td>
<td>13</td>
<td>70</td>
</tr>
</tbody>
</table>

SS with cut off ≥ 12 was more sensitive than pure individual clinicopathologic changes.
Neonatal Case

- 8 hour old Standardbred colt “Sicky Foal 2018”
  - Covered in meconium when born
- Born premature at 310 days
- Apparently normal birth (unattended), mare passed placenta
  - Placenta thick and heavy
  - Marked areas of villous atrophy
- Mare streamed milk prefoaling
- PC: Stood, but never nursed; now very weak, can’t stand, weak suckle, diarrhea
On Presentation

- Obtunded/Depressed
- MM congested/red, CRT 3 sec
- HR 50 bpm
- R 60 bpm
- T 103.5 ºF
- No gastrointestinal sounds GI sounds
- Cold extremities and ears
What about Initial Diagnostics?

- PCV = 50%  TPP 4.0 g/dl
- Blood glucose = too low to read
- Blood lactate = 10.0 mmol/l
- Fibrinogen 600mg/dL SAA 1275 mg/dL
- Blood gas pH 7.02, PaO$_2$= 62mmHg, SaO$_2$= 80%, PaCO$_2$= 60mmHg
- Blood pressure MAP= 50mmHg
Diagnostic Aids to Quantify Dz Severity

Ultrasound
- Thoracic, abdominal and umbilical

Radiographs
- Chest, abdomen, limbs (flexural or angular limb deformities)
- Contrast studies

Joint / abdominal / CSF taps
Radiographs: What is Going On?????
Secondary Diagnostics for “Sicky Foal” 2018

- CBC/Chemistry
- IgG
- Blood Culture
- Recheck PCV/TP/Glucose/Lactate
Foal Septicemia - The Sepsis Score

- Categories
  - CBC
    - Markers of sepsis
  - Other lab data
    - Includes IgG and glucose
  - Physical exam
    - Relates to general condition of the foal and presence of infection
  - History/Periparturient events

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**Foal Sepsis Score Sheet**

```
<table>
<thead>
<tr>
<th>Category</th>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil count</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Band neutrophil count</td>
<td>2.0-4.0</td>
<td>5</td>
<td>7</td>
<td>10</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Markers of sepsis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other lab data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Includes IgG and glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical exam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relates to general condition of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the foal and presence of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History/Periparturient events</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
```

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If a foal older than 12 h, compute the score using the IgG value you get back from the lab. If it is less than 12 h, give it a 0. If it has a history of nursing what appeared to be a good colostrum. Give the feed a 1. If it has not nursed at all in doubt.

* A score of 4 or higher predicts mortality 85% of the time. A score of 3 or more predicts non-mortality 95% of the time.
# Blood Work: Complete Blood Count

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet Eval</td>
<td>Decrease</td>
<td>/OIL FLD</td>
<td></td>
</tr>
<tr>
<td>Macros</td>
<td>None Seen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clumps</td>
<td>None Seen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Leukocytes</td>
<td>2.7</td>
<td>x10^9/L</td>
<td>4.1 - 9.7</td>
</tr>
<tr>
<td>Band Neutrophils</td>
<td>13</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Band Neutro-Absolute</td>
<td>0.4</td>
<td>x10^9/L</td>
<td>0 - 0.1</td>
</tr>
<tr>
<td>Seg. Neutrophils</td>
<td>63</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Seg Neutrophils-Absolute</td>
<td>1.7</td>
<td>x10^9/L</td>
<td>2.4 - 7.0</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>21</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes-Absolute</td>
<td>0.6</td>
<td>x10^9/L</td>
<td>1.0 - 4.9</td>
</tr>
<tr>
<td>Monocytes</td>
<td>3</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Monocytes-Absolute</td>
<td>0.1</td>
<td>x10^9/L</td>
<td>0.1 - 0.5</td>
</tr>
<tr>
<td>Eosinophils</td>
<td></td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Donle Bodies</td>
<td>Mod</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Blood Work: Serum Chemistry and IgG

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Unit</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Urea Nitrogen (BUN)</td>
<td>16</td>
<td>MG/DL</td>
<td>13 - 27</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.4</td>
<td>MG/DL</td>
<td>0.8 - 1.7</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>6.0</td>
<td>MG/DL</td>
<td>1.2 - 4.8</td>
</tr>
<tr>
<td>Total Calcium</td>
<td>11.4</td>
<td>MG/DL</td>
<td>11.1 - 13.0</td>
</tr>
<tr>
<td>Sodium</td>
<td>139</td>
<td>MEQ/L</td>
<td>132 - 142</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.33</td>
<td>MEQ/L</td>
<td>2.4 - 4.6</td>
</tr>
<tr>
<td>Chloride</td>
<td>93.5</td>
<td>MEQ/L</td>
<td>97 - 105</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>24</td>
<td>MEQ/L</td>
<td>7 - 15</td>
</tr>
<tr>
<td>Osmolality Calculated</td>
<td>274</td>
<td>MOSM/KG</td>
<td>266 - 286</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>25</td>
<td>MMOL/L</td>
<td>21 - 31</td>
</tr>
<tr>
<td>Total Protein</td>
<td>3.5</td>
<td>G/DL</td>
<td>6.4 - 7.9</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.4</td>
<td>G/DL</td>
<td>2.8 - 3.6</td>
</tr>
<tr>
<td>Globulin</td>
<td>1.1</td>
<td>G/DL</td>
<td>3.6 - 4.3</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>241</td>
<td>MG/DL</td>
<td>10 - 60</td>
</tr>
</tbody>
</table>

The values for BUN, creatinine, phosphorus, calcium, sodium, potassium, chloride, anion gap, osmolality calculated, bicarbonate, total protein, albumin, globulin, and triglycerides are provided in the table above. The normal ranges for these values are also listed.
This Foal is Septic

<table>
<thead>
<tr>
<th>Number of points to assign:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sepsis score:</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>CBC</td>
</tr>
<tr>
<td>record Exact #</td>
</tr>
<tr>
<td>Neutrophil count (NOT TOTAL WBC)</td>
</tr>
<tr>
<td>&lt;2.0 × 10^9</td>
</tr>
<tr>
<td>or &gt;12.0</td>
</tr>
<tr>
<td>Band neutrophil count</td>
</tr>
<tr>
<td>&gt;0.2 × 10^9</td>
</tr>
<tr>
<td>3.</td>
</tr>
<tr>
<td>Toxic, granulation, Or vacuolization In neutrophils</td>
</tr>
<tr>
<td>marked</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
</tr>
<tr>
<td>&gt;600</td>
</tr>
<tr>
<td>Other Laboratory Data</td>
</tr>
<tr>
<td>1. Hypoglycemia (mg/dl)</td>
</tr>
<tr>
<td>&lt;49</td>
</tr>
<tr>
<td>2. IgG (mg/dl)</td>
</tr>
<tr>
<td>&lt;200</td>
</tr>
<tr>
<td>3. Atrial oxygen</td>
</tr>
<tr>
<td>&lt;40 Torr</td>
</tr>
<tr>
<td>4. Metabolic acidosis</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>5. Clinic Examination</td>
</tr>
<tr>
<td>1.</td>
</tr>
<tr>
<td>No secondary to eye</td>
</tr>
<tr>
<td>Disease or trauma</td>
</tr>
<tr>
<td>Marked</td>
</tr>
<tr>
<td>2. Fever (°F)</td>
</tr>
<tr>
<td>&gt;100°F</td>
</tr>
<tr>
<td>3. Hypotonia, coma</td>
</tr>
<tr>
<td>depression, convulsions</td>
</tr>
<tr>
<td>Marked</td>
</tr>
<tr>
<td>4. Anterior uveitis</td>
</tr>
<tr>
<td>Diarrhea, respiratory distress</td>
</tr>
<tr>
<td>Swollen joints, open wounds</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>6. Historical data</td>
</tr>
<tr>
<td>1. Placenta, vulvar</td>
</tr>
<tr>
<td>Discharge prior to delivery,</td>
</tr>
<tr>
<td>Dystocia, long transport of mare,</td>
</tr>
<tr>
<td>Mare sick, foal induced</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>2. Prematurity</td>
</tr>
<tr>
<td>&lt;300 days</td>
</tr>
</tbody>
</table>

Total Points 27

If a foal older than 12 h, compute the score using the IgG value you get back from the lab.
If it is less than 12 h, give it a +2 for IgG if it has a history of nursing what appeared to be a good colostrum. Give the foal a +4 if it has not nurse or if in doubt.
A score of 12 or higher correctly predicts sepsis 93% of the time. A score of 11 or less predicts non-sepsis correctly 88% of the time.
Initial Treatment Plan

- IV catheter: central venous
- Volume resuscitation
  - Polyionic crystalloids
  - Plasma therapy
- Keep warm?
- Broad-spectrum antibiotics
  - Empiric therapy
- Nasal oxygen?
- Frequent reassessment!
Cardiovascular Support: General

- **BP = CO x SVR**
- **CO = HR x SV**
- **DO₂ = CO x CaCO₂**

**Preload**
- Hemoglobin
- SaO₂

**Afterload**
- PaO₂

**Contractility**

**Pressors**
- Crystalloid
- Colloid

**Commonly used medications for cardiovascular support**
- Transfusion
- Oxygen
- Vasodilators
- Inotropes

\[ \text{Hemoglobin} \quad \text{SaO₂} \quad \text{PaO₂} \]
Fluid Resuscitation

- Initial resuscitation with a SHOCK dose
  - Equivalent to one (1) blood volume within the first hour
  - 80ml/kg (50 kg foal = 4L)
    - Divide into ¼ or 1/3 boluses and reassess BP/physical parameters after each bolus (e.g. 1L every 15-20 minutes)
  - Isotonic, polyionic crystalloid if electrolytes are unknown
    - (P-148, LRS, Norm-R)
Fluids

- If MAP still < 65 mmHg
  - Consider additional crystalloid challenges (10 ml/kg) OR colloid (Hetastarch®^; 3 ml/kg)
- If MAP still < 65 mmHg
  - Decisions?
    - The system is volume loaded, so is the problem pump failure or underfunction?, poor vascular resistance or both?
- Colloids: many foals will receive hyperimmune plasma as therapy for FTPI, but on a ml for ml basis, synthetics give you more “BANG for you BUCK!”
  - COP plasma = 20 mmHg
  - COP Hetastarch® = 33 mmHg
Immunoglobulin status

- Colostrum
  - Need adequate IgG levels in mare’s colostrum
  - Functional GI tract in foal
- Plasma
  - Hyperimmune
Immune therapy

- Increased non-selective IgG
- Improved oxidative burst activity in septic foals receiving plasma
  - McTaggart et al, *Aust Vet J* 2005
- Improved opsonization activity in septic foals receiving plasma
- Increased survival in foals receiving hyperimmune anti-LPS plasma (OR 6.7)

**Plasma Dosing**

- 0-400mg/dL = 40ml/kg
- 400-800mg/dL = 20ml/kg

Recheck IgG especially in septic foals
Antibiotics: How to choose?

- Antibiosis and infection control is essential
- Choice of drugs is geographic, disease and case specific
- Changes in culprit organisms and their sensitivity patterns needs to be considered
- Common approach
- Broad spectrum antibiotics with changes made depending on isolates obtained by MC&S
Ampillicin + Amikacin remains the most appropriate initial antibiotic therapy until MC&S results are known.

- Penicillin + Amikacin would also be comparable
- Emerging ceftiofur resistance is concerning and perhaps warrants either high dose [10mg/kg IV q6hr] dosing or minimizing its use entirely
Neonatal Septicemia

Treatment = broad spectrum antibiotics
  • Farm/area variations
Supportive care
  • Nutrition - enteral to parenteral
  • Address localized infections (source identification and control)
  • Control seizure activity (midazolam)
Should improve within 72 hr
Septic arthritis is major complication
  • $$$
  • Guarded prognosis – life/use
Provide Stabilization for Success

- Heat: prevent hypothermia
- Respiratory support: nasal $O_2$, caffeine
- Eye care: correct entropion
- Fluid therapy: long (over-the–wire) catheter
  - Crystalloid/plasma
  - Give glucose
    - Glycemic control
- Control seizures:
  - benzodiazepines
Lethargic/Recumbent Septic Foal

**problem = 48-72 hr for culture results**

**solution = sepsis score**

Hx = presence of risk factors

PE findings, localizing signs?

Initial lab data = CBC, IgG, glucose

*Be aggressive with prophylactic antibiotics!*
Complications

Corneal ulceration

- Trauma
- Entropion (turned in eyelid)
- May lose vision/eye
- Significant uveitis
Complications

Bed sores

- Foal skin very easily injured
- Source of sepsis
  - Joint, tendon, etc
- +/- bandage
Diagnosis? Hopefully + Outcome

**DIRECT METHODS**

- Culture
- PCR
- Serology
  - Less useful except lentiviruses
- Cytology
- + evidence of SIRS
  - Species specific SIRS criteria

**INDIRECT METHODS**

- Presumed infection
  - Clinical findings
- + evidence of SIRS
- Predictive Scoring systems
  - Less accurate
  - Geographic/institution specific variables
  - Various models of disease severity etc exist in the literature, notably critically ill foals
Conclusions

1. Start resuscitation early
2. Source control remove the inciting cause
3. Intravenous fluids (resuscitative, maintenance, ongoing loss oncotic support, correction of ↓↓ IgG, nutritional support)
   - Frequent reassessment of volume status
   - Aim for
     - a) CVP 8–12 mm Hg
     - b) MAP ≥ 65 mm Hg
     - c) Urine output ≥ 0.5 mL/kg/hr
     - d) Scvo2 ≥ 70%
   - Normalization of lactate
   - Normalization of glucose
4. Empirical antibiotic administration
   - Obtain cultures (all pertinent areas: blood, jnt, TTA, csf, etc.)
5. Perform a sepsis score
6. Frequent patient evaluation
Thank You!