Immune-Mediated Disease in Horses

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Overview
• Review components of equine immune system.
• Identify differences between primary and secondary immune-mediated disease.
• Case examples of IMM disease.
  • Presentation
  • Differential considerations
  • Diagnostic approach
  • Therapeutic options

Physical Barriers
• pH
• Skin
• Mucosal surfaces
  • Respiratory
  • Gastrointestinal
  • Genitourinary
• Surface bacteria
LAYERS OF IMMUNITY

Physical Barriers
Skin
Self-cleaning
Normal flora

Innate Immunity
Inflammation
Host-defense Peptides

Antigen Specific Immunity
Antibody production
Cell-mediated immunity

Innate Immunity
- Constituents of pathogens
- Inflammation
- Cellular
  - Neutrophils
  - Monocytes
  - NK-lymphocytes
- Chemical
  - Lysozyme
  - Host defense peptides
  - Alternate complement

Compliment Pathways
- Classical
  - Ab + C1q
  - C1r
  - C2
  - C3
- Lectin
  - MBL
  - MASP-2
  - Same as classical
- Alternate
  - P+D
  - B
  - C5
  - C6
  - C7
  - C8
  - C9
  - Terminal complement complex
Pattern Recognition Receptors (PRRs)

- Innate immunity
- Cell membrane or soluble proteins
- **PAMP** = pathogen (microbial) associated molecular patterns
- **DAMP** = damage associated molecular patterns
- Surface
  - TLRs
  - C-type lectin receptors
  - Mannose receptors
- Cytoplasmic
  - NODs

Pathogen Associated Molecular Patterns (PAMP)

- Cell wall
  - G-pos = peptidoglycans
  - G-neg = polysaccharide and lipid (lipopolysaccharide)
- Capsule (K antigen)
- Polysaccharide for protection
- Pili (fimbriae)
- Cellular attachment
- Flagella (H antigen)
- Pathogen DNA
  - CpG motifs
**Induction of Immunity**

- Innate responses result in initiation of activity
- PAMP + TLR provides a pronounced host responses
- Immediate
- Non-specific
Immune Protection

• Collectively the innate and adaptive immune responses work together to maintain health.
• Innate works immediately
  • Non-specific
• Adaptive takes time to establish
  • Specificity and memory

Acquired Immunity

• Extracellular: ANTIBODY
  • Bacteria
  • Protozoa
  • Helminth parasites
• Intracellular: CELL-MEDIATED
  • Viruses
  • Intracellular bacteria
  • Protozoa
  • Cancer cells

Source of Lymphocytes

• Yolk sac
• Fetal liver
• Bone marrow
Components of the Immune System

- **PRIMARY LYMPHOID ORGANS = sites of lymphocyte development**
  - Thymus
  - Skin
  - Bursa of Fabricius
  - Peyer's patches
  - Lymphoreticular glands
  - Bone Marrow

- **SECONDARY LYMPHOID ORGANS = sites where lymphocytes respond to antigen**
  - Lymph nodes
  - Tonsils
  - Spleen
  - Lymphoreticular trapping
  - Bone marrow

Constituents of Protection

Antibody production
Antigen Specificity

- **FC portion of antibody protein**
- **Fab portion of antibody protein**

FC receptor expression

- NK cells, monocytes, B cells, PMN, dendritic cells
- Macrophages contain many opsonin receptors
  - CD64 high affinity Ab receptor, and on PMNs
  - FCγRI, increased expression with IFN-γ
  - Hu Macs = CD32 (FCγRII) and CD16 (FCγRIII)
  - Cattle and sheep express FcyRII bind IgG1
  - Macs also bind complement components
    - CD35 (CR1)
    - CD11b/CD18 both are C3b receptors
Neutralizing Antibody Titer

Primary Immune Response

Secondary Immune Response

• Previous exposure
• Antigen specific
• Memory
  • Amnestic response
• Regulated response

Kendall et al, 2008

Secondary Response

CD Molecules

• Cluster of differentiation = CD
• CD1 – MHC-I like, presenting lipid
• CD4 – MHC-II receptor, antigen recognition
  • Helper T cells, monocytes, thymocytes
• CD5 – CD72 receptor
  • Pan T cell marker some B cells (not dogs or rats)
• CD8 – MHC-I receptor, endogenous Ag, CTL
• CD21 – complement receptor CR2
  • B cells, some T cells, dendritic cells
• CD44 – hyaluronic acid receptor
  • T cell, B cell, monocytes, granulocytes
• CD79a – alternate name for BCR
  • B cell marker
Cellular Constituents of Adaptive Immunity

**Antigen presenting cell**
- Dendritic cell
- Macrophage
- B-lymphocyte

**T-lymphocyte**
- CD4+ = Th1, Th2, Th17
  - T(H)1 leads to abortion
  - T(H)2 leads to Th2 response
  - Th17 may occur secondary to Th17 response
- CD8+ = cytotoxic T lymphocyte (CTL)

**B-lymphocyte**
- Antibody production
- Plasma cell
- Memory B cell

**Regulatory T cells (Treg)**
- Population of CD4+ T cells that regulate the activation of other T lymphocytes and are needed to maintain peripheral tolerance to self antigens.
- Compose 5-10% of CD4+ lymphocytes
- Phenotype: CD4+ CD25+
  - α chain of the IL-2 receptor
- FoxP3 expression
  - Transcription factor
  - Correlates with suppressor activity

TLRs, Treg cells and immunity

- Treg cells exist in various species
- Depletion of CD4+ CD25+ leads to autoimmunity
- Thyroiditis
- Inflammatory bowel disease
- Spontaneous autoimmune diabetes
- TLRs may regulate the immunosuppressive effects of Treg cells

Lymphocyte Source

- T cells
  - Mature in the thymus
- B cells
  - Bursa of Fabricius in birds
  - Bone marrow in primates and rodents
  - Peyer's patches in ruminants and pigs
Sites of interaction APC and lymphocytes

- Tonsils
- Spleen
- Lymph nodes
- Peyer's patches
- Bone marrow

Antigen Presentation

- Antigen enters host
- Immune inactivation
- Respiratory
- Gastrointestinal
- Other
- Extracellular vs. intracellular
- Antibody vs. cellular response
- Enhanced efficiency with repeated exposure
T-Cell Activation

- Antigen presenting cell
- CD4+ lymphocyte
- Cellular interaction
- Co-stimulatory molecules
- Cytokine production
- Downstream cytokine-mediated effects
  - IL-2
  - IFN-gamma

T-Cell Activation

- Host cell expression of MHC-I
- CD8+ MHC I interaction
- CD8+ protein release
  - Perforin
  - Granzymes
- Host cell / altered self cell destruction
B cell Activation

- APC CD4+ interaction
- MHC II – TCR
- Costimulation
- Cytokine production
  - IL-4
  - IL-6

**B-cell activation**
- Antibody production
- Plasma cell expansion

Approximate distribution of lymphocytes based on T-cell surface markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Horse</th>
<th>Bovine</th>
<th>Sheep</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCR α/β</td>
<td>58-66</td>
<td>5-30</td>
<td>14-34</td>
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<tr>
<td>TCR γδ</td>
<td>45-50</td>
<td>31-66</td>
<td>22-68</td>
</tr>
<tr>
<td>CD2</td>
<td>41-60</td>
<td>58-72</td>
<td>10-36</td>
</tr>
<tr>
<td>CD4</td>
<td>58</td>
<td>9-28</td>
<td>8-22</td>
</tr>
<tr>
<td>WC1</td>
<td>5-44</td>
<td>40</td>
<td>15-70</td>
</tr>
</tbody>
</table>

*Tizard 10th ed. 2017*
Immune-Mediated Disease

• Bullous disease of skin and mucosa
  • Pemphigus foliaceous
  • Bullous pemphigoid and others, drug reactions
• IMM disease: anemia, thrombocytopenia and neutropenia are sporadic diseases of horses.
• Primary disease
• Idiopathic
• Secondary disease
  • Infectious disease
  • Medications
  • Neoplasia

History

• Presenting complaint (Nov. 2012)
  • Marked urticarial, wheels, crusting
  • Muzzle edema
  • Ventral abdominal swelling
  • Lower limb edema Previous treatments included
    • Prednisone
    • TMS SMZ
    • Dexamethasone (oral powder) 10 days without resolution of clinical signs

Initial Presentation
Skin biopsy

- Sedation and restraint
- Local analgesic, 2% lidocaine
- Vesicle = punch biopsy
- Bullae or ulcer = wedge biopsy with scalpel is superior

Immune mechanisms for development

- Desmoglein glycoprotein that facilitates desmosome formation
  - Mechanical integrity of epidermis
  - Linking keratin filaments, connects cytoskeleton of adjacent keratinocytes
  - Dsg-1 involved in PF in humans
  - Dsg-1 minor in dogs, desmocollin 1 in dogs
  - Exact antigen in horses, not yet determined
    - Dsg-1 has been identified in horses
    - Autoantibody then PF lesions
      - Dermatitis, sun exposure, Culicoides hypersensitivity
      - Medications, TMS-SMZ
Treatment?

- Immune suppression
  - Dexamethasone (20 mg IV)
    - Administered for 3 days with immediate and marked positive response
    - Discontinued due to increased digital pulses in all four limbs
  - Azathioprine (3 mg/kg PO SID)
- Laminitis
Treatment?

• Immune suppression
  • Dexamethasone (20mg IV)
  • Discontinued due to increased digital pulses in all four limbs
  • Azathioprine (3 mg/kg PO daily, 1500mg PO SID for 2-4wks)

• Laminitis
In summary, when AZA was administered to horses IV, the AZA molecule and the active metabolite, 6-MP, were eliminated rapidly from the plasma. Following oral administration of the drug to horses, the bioavailability of AZA and 6-MP was poor, although whether this was the result of poor absorption or a high first-pass effect could not be determined in our study. Chronic oral administration of AZA was not associated with any clinically important adverse effects. Because of the safety of the AZA doses used in our study and the successful use of the drug in a small number of previous reports, the doses used in our study, further investigation into the clinical efficacy of AZA in the treatment of autoimmune diseases in horses is warranted.

- Prednisone
- 0.2-4.4 mg/kg PO q12-24h
- 1.0 mg/kg PO q24h
- Approx. 6 weeks tapering dose

Fast forward 5 years..
Presentation

- Colic and soft feces
- Flunixin meglumine (Banamine®) and referred to KSU for further treatment.
- Spring vaccines were administered 2 wks previously and developed urticaria approx. 6 days later
- rDVM started on dexamethasone (10 mg orally daily, currently day 3/5 of therapy)

Colic Workup

- CBC/Chem
- NG tube
- Rectal
- Abdominal US
- Fecal Egg Count

CBC/Chem

- Thrombocytopenia (22,000 cells/µL)
- Causes?
  - Decreased production
  - Bone marrow dysfunction, neoplasia, myelophthisis
  - Increased consumption/destruction
    - Immune mediated thrombocytopenia - IMT
    - DIC
    - Sequestration
Diagnostics

- Equine Platelet Surface Associated Antibody Test
  - PSAIg reference interval: IgG, IgM, and IgA <4%
  - Aroco PSAIg: IgG – 1%, IgM – 22%, IgA – 26%

Treatment

- Immunosuppression
  - Prednisolone (1mg/kg PO daily) initiated on 3/24

- Monitor platelet counts
  - 3/22 – 22,000 (EDTA)
  - 3/23 – 27,000 (EDTA)
  - 3/24 – 44,000 (EDTA)
  - 3/25 – 49,000 (EDTA)
  - 3/28 – 76,000 (Heparin) 82,000 (Citrate)
  - 4/4 – 83,000 (Heparin)
    - PSAIg: IgG <1%, IgM <1%, IgA <7%

- Pemphigus fallaceus

- Immune-mediated thrombocytopenia following vaccination
• Arabian foal born to mare that suffered middle uterine artery hemorrhage pre-partum.
• 4 L whole blood transfusion 6 weeks prepartum.
• Foal delivered uneventfully.
• Profound neutropenia.

• Day 2 foal was profoundly neutropenic.
• No clinical signs of sepsis.
• Flow cytometry revealed presence of surface bound antibodies on PMNs.

• Reverse isolation implemented.
• Neupogen administered IV on day 3.
  • 300 µg dose
  • 1.5-6 µg / kg reported
• Day 6 PMNs: 5400 / µL
• Clinically healthy.
• No further neutropenia.
• Negative blood cultures.
Neupogen and neutropenia

- Persistent / severe neutropenia.
- SC or IV administration.
- Restoration of PMN in circulation.
- Low doses may be effective in full sized horses.
- Therapeutic and diagnostic
  - Bone marrow disorders may demonstrate temporary response.

Neonatal Isoerythrolysis

- Self proteins are expressed on RBC, platelets, lymphocytes and other cells.
- All same: monomorphic
- Variations: polymorphic
- Structural variation of proteins that can be recognized by others = alloantigens.
- Antibodies produced = alloantibodies.
- Erythrocyte and platelet antigens can be alloantigens.

- Naturally occurring incompatibilities
  - Neonatal isoerythrolysis
  - Neonatal alloimmune thrombocytopenia (NAIT)
- Iatrogenic conditions of allogenic incompatibilities
  - Organ / tissue graft rejection
  - Blood transfusion reaction
Neonatal Isoerythrolysis

- Alloantibody destruction of foal RBCs
- Alloantibody is maternal in origin
  - Transfusion
  - Exposure of foal blood to dam
  - Placental pathology
- Mare is sensitized to foreign antigens
- Incidence is low
  - TB ~ 1%
  - SB ~ 2%
  - Mules (Donkey sire, horse mare) can be 10%

• Immunogenicity of blood groups
  - Aa in the A system
  - Qa in the Q system

• Mules: a unique RBC Ag = donkey factor which has been associated with NI.
  - All horses lack donkey factor, so all donkey foals are at risk for NI.

Horses vs. humans

- Horses that lack RBC antigen(s) do not generally result in anti-RBC antibodies.
- Except Ca negative horses, they will develop low titer of anti Ca Abs.
  - Less likely to have foal with NI (protective effect).
- In humans, the lack of an RBC Ag results in Ab production due to similarly of expressed Ag in the diet.
Mare is sensitized to foreign RBC:

- Aa+ RBC
- Transfusion
- Injury
- Fetal transfer in utero (rare)

Dose-response relationship. The higher the anti-RBC titer the greater the chance for NI. Higher titers are more likely if there has been reexposure to antigen(s) prior to parturition.

Foal is Aa+ and absorbs colostrum. Maternal [colostral origin] antibodies adhere to foal RBC.

Dose-response relationship. The higher the anti-RBC titer the greater the chance for NI. Higher titers are more likely if there has been reexposure to antigen(s) prior to parturition.

Clinical Pathology

- Anemia
- PCV = 5-20%
- Hemoglobinemia
- Hemoglobinuria
- Bilirubin
- Mule foals tend to be thrombocytopenic as well.
- Antibodies in serum
  - Lytic – more reliable
  - Agglutinating
- Antibodies on foal RBC
- Coomb’s
- DIFF

Foal ingests alloantibody in colostrum. Antibody adheres to RBC which are removed via reticuloendothelial system, extravascular.

Direct lysis by complement, intravascular.

Neonatal Isoerythrolysis

- Icterus
- Foal that has nursed well!
- Multiparous mare
- Foal was normal and is depressed 12-48 hrs
- May be subclinical
- Hemoglobinemia
- Hemoglobinuria
- Peracute: death....
Table 53-7: Estimated % of mares at risk for producing foal with NI

<table>
<thead>
<tr>
<th>Breed</th>
<th>At risk for Aa</th>
<th>At risk for Qa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoroughbred</td>
<td>2%</td>
<td>16%</td>
</tr>
<tr>
<td>Standardbred, pacer</td>
<td>22% Neg</td>
<td>Stallions also neg.</td>
</tr>
<tr>
<td>Standardbred, trotter</td>
<td>3% Neg</td>
<td>Stallions also neg.</td>
</tr>
<tr>
<td>Saddlebred</td>
<td>22% 88%</td>
<td></td>
</tr>
<tr>
<td>Quarter Horse</td>
<td>25% 68%</td>
<td></td>
</tr>
<tr>
<td>Arabian</td>
<td>3% 72%</td>
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</table>

Bailey et al. AAEP Proceedings 1987

Neonatal Isoerythrolysis

- Multiparous mares (most commonly)
- Blood group incompatibility
- FPT is NOT a problem
- Icterus will vary in severity
- Remember differentials for an icteric foal
  - EHV-1 causes severe hepatopathy
  - Bacterial sepsis

Necropsy

- Pale tissues
- +/- Icterus
  - Potential for kernicterus
- Splenomegaly
- Secondary organ damage
  - Nephrosis
  - Centrilobar necrosis
Therapeutics for NI

• Make the diagnosis
• Unlikely need to withhold milk at time of dx.
• Confinement
• Fluid diuresis
• PCV < 15%
• Washed erythrocyte transfusion
• Donor: Aa‐Qa‐ / no alloantibodies
• Donor: any horse donor should be okay.
• Blood type mare and stallion
• Measure IgG last 30 days

Neonatal Alloimmune Thrombocytopenia

• Maternal alloantibodies targeted at foal platelets.
• Self limiting, TP until alloantibody is metabolized.
• Profound thrombocytopenia in the face of adequate passive transfer.
• Similar pathogenesis as NI.
• Screening should be performed on subsequent foals.
KJ

- 7yr old QH mare
- 48 hour non-resolving suspect cellulitis
- rDVM: Ceftiofur(Excede) and phenylbutazone
- Up to date on vaccines(core)/de-worming
- No reported history of any herd illness in recent past (respiratory, etc)

Presentation:

- BAR
- HR: 42 bpm
- RR: 32 rpm
- T: 101.4F (on phenylbutazone)
Treatment

• Presumptive septic cellulitis

• Sweat wrap and hydrotherapy
• Phenylbutazone 2.2mg/kg IV BID
• Oxytetracycline 6.6mg/kg IV BID
Progression

- QAR
- Icterus
- Persistent tachycardia (60-80bpm)
- Pigmenturia
- Elevated AST (3695U/L; 186-412)
- Elevated Creatine Kinase (131,760U/L; 97-355)

PCV/TP in the 1st 48 hrs

<table>
<thead>
<tr>
<th>Time</th>
<th>PCV (%)</th>
<th>TP (g/dL)</th>
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<tbody>
<tr>
<td>Admission</td>
<td>27</td>
<td>6.3</td>
</tr>
<tr>
<td>7/10: 3pm</td>
<td>13</td>
<td>6.3</td>
</tr>
<tr>
<td>7/10: 7pm</td>
<td>15</td>
<td>6.5</td>
</tr>
<tr>
<td>7/11: 1am</td>
<td>13</td>
<td>6.3</td>
</tr>
<tr>
<td>7/11: 7am</td>
<td>12</td>
<td>6.4</td>
</tr>
<tr>
<td>7/11: 2pm</td>
<td>18</td>
<td>6.4</td>
</tr>
<tr>
<td>7/11: 7pm</td>
<td>17</td>
<td>6.4</td>
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</table>

*Received blood transfusion
Problem List

- Marked and progressive limb and ventral edema
- Grade 3/5 LH lameness
- Acute and marked anemia
- Icterus
- Pigmenturia
- Elevated muscle enzymes
- Tachycardia
Differential Considerations

- Purpura hemorrhagica
- Streptococcal (S. equi var equi)
- Staphylococcal
- Viral
- Toxic/Drug Associated
- Immune-mediated hemolytic anemia
- Pigment associated nephropathy (ARI)
- Myocarditis

Further diagnostics

- SeM ELISA
- Surface-associated RBC Ig Antibody
- Crossmatching and blood transfusion
- Culture and sensitivity (FNA aspirate LH edema)
- ECG and Cardiac Troponin I
- Blood chemistry testing
- Endoscopy

CK and ARI

- Concern of myoglobinuria or hemoglobinuria
- Non azotemic
- USG 1.023

<table>
<thead>
<tr>
<th>Date</th>
<th>CK (U/L)</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
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<tr>
<td>7/9</td>
<td>351,768</td>
<td>16,095</td>
<td>676</td>
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<td>7/11</td>
<td>61,839</td>
<td>6766</td>
<td>1921</td>
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<td>7/12</td>
<td>85,162</td>
<td>9621</td>
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<td>7/13</td>
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<tr>
<td>7/15</td>
<td>26,724</td>
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RBC Surface Antibody

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<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
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<tbody>
<tr>
<td>Patient</td>
<td>7%</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Reference Range</td>
<td>&lt;3%</td>
<td>&lt;3%</td>
<td>&lt;3%</td>
</tr>
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</table>

- IMHA
- Does not differentiate primary vs. secondary IMHA

Crossmatching

<table>
<thead>
<tr>
<th>Horse</th>
<th>Horse 1</th>
<th>Horse 2</th>
<th>Horse 3</th>
<th>Horse 4</th>
</tr>
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<tbody>
<tr>
<td>Major</td>
<td>3+</td>
<td>3+</td>
<td>3+</td>
<td>2+</td>
</tr>
<tr>
<td>Minor</td>
<td>3+</td>
<td>3+</td>
<td>4+</td>
<td>1+</td>
</tr>
<tr>
<td>Auto Control</td>
<td>None</td>
<td>None</td>
<td>2+</td>
<td>None</td>
</tr>
</tbody>
</table>

- Marked autoagglutination (4+)
- Horse 3 is universal donor
- Transfused 8L from Horse 4

ECG and Cardiac Troponin I

- Ventricular Premature Complexes
- Marked tachycardia (60-80bpm)
- 41.83ng/mL (Reference range: 0-0.07)
- Myocarditis

- Ventricular Premature Complexes
- Marked tachycardia (60-80bpm)
- 41.83ng/mL (Reference range: 0-0.07)
- Myocarditis
Strep. equi

S. equi: Complications

- ~20%
- Metastatic and Immune Mediated
- Increase fatality rate to 40% (c.f. 8.1%)
- Organism spread by:
  - Hematogenous
  - Lymphatic migration
  - Close association with a septic focus
- Common sites: Lung, mesentery, liver, spleen, kidneys, and brain
- Guttural pouches

Purpura Hemorrhagica

- Aseptic necrotizing vasculitis
- Type 3 hypersensitivity
  - Deposition of immune complexes in blood vessel walls
  - Most commonly associated with S equi
  - IgA and IgG others
  - Histology: leukocytoclastic vasculitis
**S. equi** assoc. Immune Mediated Myopathies

1. Infarctive purpura hemorrhagica
2. Rhabdomyolysis with progressive atrophy
   • Cross-reactivity between SeM and myosin

**Infarctive PH**

• Immune mediated vasculitis
• Infarction of:
  • Skeletal muscle
  • Skin
  • GI
  • Lungs
• Guarded prognosis
Purpura haemorrhagica in 53 horses

- 17: Exposed to or infected with S. equi
- 9: Corynebacterium pseudotuberculosis
- 5: Vaccinated with S. equi M protein
- 5: Respiratory infection of unknown aetiology
- 2: Open wounds
- 15: No history of recent viral or bacterial infection

Serology: SeM Titer

- S equi: 15 + surface or secretory proteins
- SeM is the most common protein used
- Does NOT distinguish between vaccine and infection response
- Titers peak ~ 5 weeks after exposure
SeM ELISA Titer Results

- **Negative:** No previous exposure to S equi or vaccine or recent exposure (<7 days)
- **Weak Positive (1 : 200–1 : 400):** Very recent or residual antibody from exposure to S equi or vaccine. Repeat testing in 7 to 14 days
- **Moderate Positive (1 : 800–1 : 1,600):** 2 to 3 weeks after exposure or the infection occurred 6 mos -2 yrs previously
- **High Positive (1 : 3,200–1 : 6,400):** 4 to 12 weeks after infection or following vaccination (1 to 2 weeks IM or 2 to 4 weeks IN)
- **Very High Positive (>1 : 12,800):** Metastatic abscess or purpura hemorrhagica (immune-mediated vasculitis)
- Vaccination is **contraindicated** in horses with existing high levels of antibody (>1 : 1,600)

KJ

- SeM titer: <1:200
- Negative

KJ Culture and Sensitivity

- **Staphylococcus aureus**
  - Sensitive to:
    - Amikacin
    - Azithromycin
    - Cefazolin
    - Ceftriaxone
    - Chloramphenicol
    - Clarithromycin
    - Doxycycline
  - Resistant to:
    - Gentamicin
    - Orcein
    - Trimethoprim
    - TMS

Henoch-Schonlein

- Sequela to streptococcal or other bacterial infection, viral infection, or a drug reaction in humans
- Circulating IgA immune complexes and high serum concentrations of C3d
- Most common in children (90% of patients are <10 years old)
- More severe recurrent form seen occasionally in adults

Clinical signs: Rash on the legs and buttocks
- 75% of patients developing arthritis of the knees and ankles
- 40% of patients developing nephritis
- 50% to 75% of patients developing abdominal pain, gastrointestinal tract bleeding, and, rarely, intussusception.
- Muscle involvement is rarely documented in these cases
- Treated with high doses of methylprednisolone IV, cyclophosphamide and azathioprine

Pillebout et al. 2002
Blanco et al. 1997

Henoch-Schonlein purpura assoc. with MRSA infection
Eftychiou, C. et al. 2006

- MRSA associated purpura has been reported
- Staph. superantigens - massive stimulation of T-cells and production of cytokines that cause tissue damage
- Link specific variable parts of the β chain (Vβ) of T-cell receptor with class II MHC molecules
- (IL)-1β, IL-2, IL-6, IL-8, TNF-α
- Polyclonal production of IgA and IgG-9 Immune Complex formation
Treatment of PH

- Dexamethasone at 0.1–0.2 mg/kg followed by a tapering dose regime is used
- KJ received between 40–60mg BID
- Prolonged treatment (>7 days)
- Laminitis: ice boots
- NSAIDs
- Antibiotics
- Vitamin E
- Omegavascul
- Supportive Care

Anti-penicillin antibodies

- 23 YO Belgian draft mare
- 7 day hx cough
- rDVM dx pneumonia
- Ceftiofur sodium x 4 doses
- Phenylbutazone 2g PO q24h

- Swelling in neck, suspected cellulitis
- Placement of IV catheter
- Potassium penicillin G (22,000 IU/Kg IV)
- 17 mL administered
- Pectoral fasciculations
- Administration stopped
• HR = 120 bpm
• RR 82 brpm
• Art. Blood gas
  • PaO2 = 95 mmHg
  • PaCO2 = 17.5 mmHg
  • Lactate = 7.5
  • PCV = 22%
• Hematuria

• UA = rare RBC
• Persistent tachycardia
• PCV + 6 hrs = 18%
• Placed on nasal insufflation of oxygen
• IV fluids 60 mL/kg/d
• Furosemide 250 mg IV
• Dexamethasone 40 mg
• Diphenhydramine 600 mg

Surface associated RBC IgG
• Flow cytometer and class specific Ab
• Patient serum with healthy horse RBC
• Healthy horse serum with healthy horse RBC

• RBC surface antibodies – 23% IgG, <1% IgA, IgM
• APA antibody – IgG 98%, IgM 4%, IgA 24%
• Corticosteroids
• Antibiotics
• Colic management
  • Reflux x 3 days
  • Total patient charges = $25K

Polysynovitis
• Foals
• Lame?
  • Septic arthritis
  • Medication history
  • Enrofloxacin
• Infectious disease
  • R. equi
  • Secondary to primary disease
History: Two month old TB filly with swollen joints. Swelled in IL farm history of Rhodococcus equi and was given R. equi hyperimmunized plasma at 5 days of age. The filly was transported to Kentucky where she was screened for Rhodococcus infection. A lung abscess was noted in the right lung field. Blood was then taken for a CBC which indicated an elevated fibrinogen of 600 mg/dL. The filly was treated with azithromycin and rifampin for approximately 10 days.

Approximately one month later, the filly was transported to Kansas City where swollen joints were noticed by the owner. The DVM referred the filly to KSU CVM for further workup.

Physical Exam: Upon presentation, the physical exam findings were within normal limits, however joint effusion was noticed and palpated in both carpi and tarsi, with the right sides worse than the left. Physical exam parameters remained within normal limits during the filly's hospitalization until 6/24 when a fever of 102.4°F was noted at 7 am. The fever responded to Banamine.
R. equi and polysynovitis

- Polysynovitis may occur secondary to R. equi infection.
- Lameness may be present.
- Arthrocentesis reveals high protein, possible increase in leukocytes, non-degenerate PMNs may be identified.
- Culture negative.
- Resolution with clearance of primary infection.

Polysynovitis in adult horses

Two year old Georgian Grand filly
- Severe tibiotarsal effusion
- Lameness
• Synovial fluid cytology
  • No organisms
  • Non-degenerate neutrophils
• Lyme disease (Borrelia burgdorferi) titer negative.
• S. equi
  • 1:200 EDS, Lexington, KY

• Prednisone
  • 0.2-4.4 mg/kg PO q12-24h
  • 1.0 mg/kg PO q24h
  • Approx. 6 weeks tapering dose
Immune-mediated disease

- Skin lesions are best investigated with skin biopsy.
- Cell line involvement (RBC, platelets, PMN) may be primary or secondary.
- Primary determined by ruling out associated conditions.
- Secondary, eliminate inciting cause when possible.
- Medication
  - Disease resolution
  - Surface Ig testing for appropriate cell populations can be diagnostic.
- Immune suppression
  - Corticosteroids
    - Dexamethasone: 0.05-0.1 mg/kg IV / PO
    - Prednisolone: 0.2-1 mg/kg PO 2 12-24 hrs
  - Antimicrobial concurrent when indicated.