**Outline courtesy of Macarena Sanz, DVM, DACVIM, PhD, an assistant professor in veterinary clinical sciences at Washington State University**

## What is *R. equi*?

- *R. equi* infection is a very important problem because it affects young foals worldwide and there is no vaccine available to prevent this disease
- G+ bacterium
- Everywhere in the soil
- Manure of normal adult horses
- Manure and nasal discharge of infected foals
- Aerosolization: high concentration of horses, low ventilation, dusty dry environment
- Pathogenic and non-pathogenic *R. equi*:
    - Importance of VapA surface protein for pathogenicity
    - Importance for diagnosis
    - Culture vs PCR for VapA

## Pathogenesis of *R. equi*

- Adult horses not affected by R equi unless immunosuppressed
- Immunosuppressed people (or cats/dogs) also susceptible
- Foals become infected early in life: shortly after birth to ~3 weeks age. New knowledge, will get back to this important concept
- Why foals? No definitive answer yet. Immune system not fully functional
- Oral route: Not much known about this.
    - More work is needed
    - Granulomatous enteritis – enterocolitis
    - Severe disease
    - High mortality rates
    - Caught late – affects prognosis?
    - Not as common these days
- Inhalation
    - *R. equi* infects alveolar macrophage
    - If VapA positive: macrophage can't clear it → granuloma formation
    - Typical abscesses we see: thick capsule
    - Insidious: Slow growing disease similar to TBC
    - Reason clinical signs are seen ~3m of age
    - This mislead research for years: We thought 3 months was the time of infection associated to decreased maternal antibodies
    - Models in foals: Old foals + very high doses of R equi: Severe, acute fatal pneumonia which does not replicate what is seen
    - Now have a better model: 1 week challenge with a low dose of R equi
    - Foal models are expensive and very slow (11 m pregnancies)

    - Other animal models: Not reliable
    - Mice resistant unless immunocompromised: Systemic disease vs granulomatous pneumonia
    - Ruminants get abscesses in LN, guinea pigs also failed as they appear to be resistant to infection
- In an endemic farm, >50% of the foals develop subclinical disease

**Clinical Signs**

- Vary with location of infection
- Most common lesions are pulmonary
- Of the infected foals, ~20% of the foals develop clinical signs of pneumonia. Why this 20%? million-dollar question
- 80% of them remains subclinical and will heal pulmonary lesions on their own without the need for treatment. Will get back to this
    - Fever, lethargy and anorexia
    - Increased RR  and effort, worse if hot – humid
    - Cough
    - Nasal discharge
    - Chronic: weight loss
- Extrapulmonary lesions not uncommon
- GI infection
    - Soft manure – diarrhea
    - Poor growth
    - Rough haircoat
- Bone and internal abscesses: Vary with location. We see growth plates and vertebrae infected often
- Immune mediated polysynovitis: Multiple joints, usually low-grade pain but joint effusion.
- Pulmonary forms carry low mortality but extrapulmonary lesions are more severe and prognosis is worse (based on location)

**Diagnosis**

- Definitive diagnosis is not different than any other cause of bacterial pneumonia
- Transtracheal wash (endoscopic sterile guide or percutaneous)
- Culture + PCR (for vapA) + cytology
- In endemic farms may send the first few foals but thereafter, diagnosis is done based on US + clinical signs + signalment

**Impact of Screening on *R. equi***

- There is no vaccine or other method effective for prevention of infection
- Thoracic US around 2000 for screening: All foals
- Realized >50% of foals in endemic farms had lesions on US but no clinical signs

- Resulted in all foals treated
- Search for best therapy using control, untreated groups led to the discovery that if not treated, >70% foals resolve their lesions – Dr Venner in Germany
- This shows the importance of well design studies with control individuals
- High number of treated foals for many years resulted in antimicrobial resistance AMR
    - 10% increase in resistance since US use
    - Foals are 7x more likely to die if infected with resistant strain: pneumonia >90% recovery vs 40%
    - Not many treatment alternatives
    - AMR genes inserted in mobile elements that can spread to other bacterial species
    - Similar treatment for humans
- Trying to find information that can help identify which foals should be treated vs those that can be closely monitored
- New approach
    - Treat foals with large lesions: Add diameters of lesions (15 cm or >)
    - WBC + fibrinogen
    - Parameters should be developed on each farm
    - Close monitoring of foals
    - Proportion of treated foals cut in half without changes in mortality

**Treatment**

- Treatment is based on a combination of a macrolide (azithromycin 10 mg/kg PO Q24h x 5 days and Q48h thereafter or clarithromycin 7.5 mg/kg PO Q12h) + rifampin (5mg/Kg PO q12h)
- Treatment is prolonged: 6-8 weeks depending on severity of infection and response
- Oral medication for a large number of foals + management of in and out $$$$$$
- Other macrolides under investigation
    - Tulathromycin alone is not as effective. Once a week (2.5 mg/kg) IM 1/w + rifampin Q24h (10 mg/kg) similar efficacy than azithromycin + rifampin
    - Gamithromycin IM 1/w good concentrations for 7dasy and non-inferior to azithromycin-rifampin. However, ~60% side effects (half mild to moderate pain and 35% severe pain). Self-resolution
    - More work as all work on monotherapy has been done in foals with mild-moderate lesions not severe
- Macrolides inhibit ability to sweat
    - Foals keep inside and well ventilated: out at night
    - Can’t sweat for up to 2 weeks post DC of treatment
- Antimicrobial induced diarrhea: self-resolving
- Mare’s associated severe diarrhea: Not common

- As discussed earlier, we are changing the approach to treatment
- Newer

**Prevention**

- To date no vaccine. Because foals are infected as they are born a vaccine is unlikely to protect from infection (need 2 doses 3 weeks apart). Groups working on mare's vaccination, but more studies are needed
- HIP administration
- Conflicting information: Dose, timing, volume, model, product variability, etc.
- Currently: Give 1L shortly after birth
- 2L is better
- Decreases disease severity (less clinical and subclinical foals) + shedding in manure
- More work on timing and volume
- Less clinical foals = less WBC + fibrinogen + smaller lesion + faster healing = less treated foals
- Does not prevent infection: US lesions present. Only useful if people will wait to treat
- Antibodies thought to be important
- Mechanisms of plasma protection need more work