EFTBA Veterinary Newsletter 33

Field with low soil moisture & poor grass cover

R. equi

Therapy and Prevention

March 2020

. The therapy of R. equi infections is very pretentious, due to the peculiar nature of this bacterium.

. The prevention therefore plays an extraordinary great and important role.

. The key practices to fight R. equi comprise just about any aspect of managing pastures and stabling.

Welcome to EFTBA's veterinary newsletter

Dear EFTBA members,

Enclosed you will find the third and final paper from Hanspeter Meier on the dreaded disease of *Rhodococcus*, which is a scourge for the thoroughbred breeding business.

Depending on the severity of it, watching young foals waste away and struggle for breath and or scour can be a very unpleasant sight as they try to survive it.

Hanspeter is very giving and forthwith of his time and research. If you or a member of your team has any equine disease or welfare concerns, we would encourage you to email Kerry Ryan, EFTBA secretariat on kryan@itba.ie, who in turn will forward it on to Hanspeter for review.

In these very strange times for breeding horses and stock in general, the issues of welfare and biosecurity are never too far away from the media, be that newspapers or online. It seems that constant communication between stud farms and public authorities in this regard is vital.

EFTBA is your thoroughbred representative body and is here and eager to service you and your concerns.

The challenge of BREXIT continues, should a hard one come into effect.

Other challenges facing the EU breeding industry are the introduction of the new Animal Health Law, drugs, medication issues as well as "after racing" welfare for horses. Even though we may sell our horses, it would seem a collective sense of responsibility and a duty of care are being imposed on the industry as well as a series of veterinary restrictions at the point of sale. The breeder's life is a challenging one but if we just reflect on the exciting results from this year's Cheltenham, one can easily see that the joy of the victorious is simply priceless.

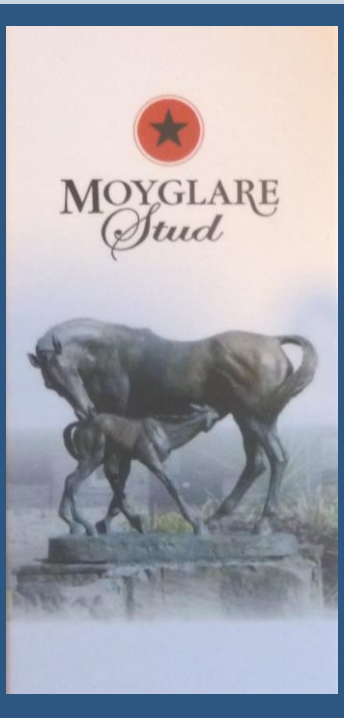
As you know the 2020 AGM takes place in Paris on 14th June. If there are any agenda items you would like tabled at this meeting, please let me know. While we are paying close attention to COVID-19, preparations for the AGM continue. Should it supersede these preparations, plans may be put in place to hold a web conference AGM. We shall keep you updated in this regard.

All the best

Joe Hernon

EFTBA Chairman

"Many thanks to Mrs. Eva-Maria Bucher-Haefner, Moyglare Stud Farm, for her valued sponsorship of this newsletter."



Editorial

The intention of our last two newsletters was to explain the exceptional and peculiar nature of the bacterium *Rhodococcus equi* - the reason for great difficulties for the therapy of affected foals. In this issue we refer to possibilities for the medical attention and above all for the prevention of our foals.

Dr Hanspeter Meier

EFTBA veterinary advisor & Newsletter editor

Introduction

Informations in the field of medicine usually contain an awful lot of technical expressions, what often can be a pretty unfavorable requirement for the understanding of important questions and answers, especially in front of a sick animal. Therefore, a glossary is attached in the annex.

In regard to the peculiarities of *R. equi*, please note as well that the following statements refer mainly to the literature in this field and always will have to be read in relation to the actual situation.

Therapy

The treatment of bacterial diseases normally occurs with the application of **antibiotics** and this method is also utilized to combat rhodococcosis – but, very sorry-to-say, not always with the hoped-for success.

According to Hines (2014), *R. equi* is sensitive to a wide variety of antimicrobial agents in vitro, but in vitro susceptibility does not always correlate with efficacy in vivo. For example, aminoglycosides appear to be highly active against *R. equi* in vitro. However, in one case series, none of the 17 foals treated with *gentamicin* and *penicillin* survived, despite all isolates being susceptible to *gentamicin* in vitro, whereas 13 foals treated with *erythromycin* and *rifampicin* survived (the combination of these drugs has the advantage, that the development of resistance to either drug is decreased when used together).

The use of the combination *erythromycin* and *rifampin* began in the late 1980s and improved the success of treatment from a survival rate of approximately 20% - 30% to 60% - 90%. This improvement showed once more the peculiarity of *R. equi* which is able to protect itself to survive and even to multiply in macrophages which normally kill bacteria; there it also is shielded from the immune system (see NL 31). The better success of *rifampin* and *erythromycin* most probably is due to the fact that these antibiotics are concentrated in granulocytes and macrophages by active mechanisms (good tissue and macrophage penetration and function in a relatively acid environment).

In some horses, especially those with mild *R. equi* pneumonia, a *trimethoprim-sulfonamide* combination also has been effective.

In the meantime, further combinations have been tried, but we don't want to go into more details of the antibiotics, as their choice is the responsibility of the attending veterinarian; he/she also has to consider the circumstances of the actual case. For instance, the chemical stability, the bioavailability after oral administration and the achievement of a higher concentration in tissues and phagocytic cells of a drug may play a role for the choice (their pharmacokinetics and susceptibility). Sometimes, there are also financial concerns.

Moreover, one may have to apply to the situation whether foals were screened and treated early, before establishment of severe lung lesions. Normally, foals with rhodococcal infection require prolonged antibiotic therapy. Treatment is frequently continued for 4 to 8 weeks, although a shorter duration may be sufficient if the disease is recognized early. In foals with well-established abscesses or osteomyelitis, a longer treatment period may be necessary.

The use of antibiotics may also be associated with side effects, e.g. diarrhea, hyperthermia and respiratory distress. Although many cases of antibiotic-associated colitis are self-limiting, occasional cases are severe and fatal. Under these circumstances, it is necessary to consider alternative antimicrobials to the *macrolide/rifampin* therapy, sometimes also because of resistance or financial concerns.

Colitis also has been observed in mares of foals being treated orally with *erythromycin-rifampin*, and in one study, *Clostridium difficile* was cultured from 5 of 11 of such mares with diarrhea.

A great concern in our times, as we all know, is **bacterial resistance**. And indeed, resistance to *erythromycin* and *rifampin* already has been encountered. It can develop rapidly, particularly when these drugs are used as monotherapy. There is significant cross-resistance between the macrolides.

R. equi isolates from foals have been documented to develop resistance to *rifampin* after monotherapy with it and to both *erythromycin* and *rifampin* during therapy.

Criteria normally used for the cessation of therapy include resolution of clinical signs, normalization of plasma *fibrinogen* concentrations, and radiographic or ultrasonographic resolution of lung lesions (Hines 2014).

Additional Therapy

The treatment of sick animals normally also includes supportive care. This refers above all to maintaining adequate nutrition and hydration, as well as maintaining foals in cool, well-ventilated environment. In cases with infection at a site other than the lungs, such as septic arthritis or osteomyelitis, local therapy may also be indicated (Hines 2014).

Passive and active immunization

Passive immunization

Immunization is a method which certainly is well known to every breeder, both in regard to the great importance for the foal to get the colostrum of its mare and all the vaccinations for different diseases (e.g. influenza, tetanus, EHV-1/4) later on.

It therefore was near at hand to try to prevent *R. equi* pneumonia by administering **hyperimmune plasma** (intravenously) to foals. Once more, in some studies this practice was effective in significantly reducing the incidence of pneumonia after experimental or natural challenge. However, other studies failed to show a significant effect. Despite these somewhat varying results, the generally beneficial effects and relative safety of administering hyperimmune plasma have made its use relatively common. So far, the optimal protocol for the administration of hyperimmune plasma has not been determined, and differences in the timing of administration may account for some of the variability between studies.

Optimally, plasma should be given before exposure to *R. equi*, based on studies that demonstrated no benefit when hyperimmune plasma was administered after experimental challenge. The exact time of exposure of most foals is unclear but likely occurs early in life, especially on enzootic farms. Administration of hyperimmune plasma too early may result in a waning of passively transferred antibodies to nonprotective concentrations when some foals are still susceptible. Moreover, it seems that the ideal time for hyperimmune plasma administration may vary from farm to farm (Hines 2014).

Active Immunization

The development of an effective vaccine for *R. equi* would clearly be beneficial to the equine population and has been an area of active research. Most foals exposed to virulent *R. equi* mount a protective immune response and remain immune as adults, what suggests that the induction of protective immunity by active immunization should be possible. However, the development of an efficacious vaccine has proved difficult, despite the use of multiple strategies for active immunization of mares and foals.

One major challenge in developing an effective vaccine is the ability to stimulate the correct type of immune response in a neonatal foal. Because of immunologic naïveté, foals may have a diminished ability to mount a protective immune response of the required magnitude rapidly enough to prevent infection. Although specific information related to neonatal immunity in foals is limited, the immune responses of neonates appear to differ both quantitatively and qualitatively from those of adult horses (Hines 2014).

Survival rates and athletic performance

There is certainly no doubt that any breeder of sick foals wonders about the chance of survival and the ability of them to race later on.

Therefore, several studies have attempted to evaluate the long-term effects of *R. equi* pneumonia on pulmonary function and athletic performance. In a study, five horses, recovered from rhodococcal pneumonia, and five healthy controls were evaluated by endoscopy, radiography, hematology, analyses of bronchoalveolar lavage (BAL), and pulmonary function testing. There were no significant differences in these parameters between the two groups, suggesting that horses that recover from *R. equi* pneumonia do not have detectable evidence of residual lung damage. The pulmonary function of seven Standardbreds that had recovered from *R. equi* pneumonia was evaluated during intense treadmill exercise, and gas exchange was not compromised compared with reference values for normal Standardbreds.

A number of studies have evaluated racing performance. In one study of 11 horses previously affected with *R. equi* pneumonia, seven of them eventually raced, and four of the seven won races. In a subsequent study 54% of foals (45/83) surviving *R. equi* infection eventually raced at least once, compared with 65% of foals in the general popula-

tion. No physical examination, laboratory, or radiographic findings were identified that were predictive of whether foals went on to race. The racing performance of foals that went on to race was not significantly different from that of the general U.S. population of racing horses. Thus, although *R. equi* infection was associated with a decreased chance of racing as an adult, the performance of those foals that did go on to race was not impaired. Similarly, in a further study, *R. equi* in foals did not have a negative influence on racing performance, as evaluated by 2- and 3-year-old race earnings. Moreover, a clinical study of 72 foals showed that the survival rate and ability to race as 3-year-olds were similar for foals treated with *gentamicin* and *rifampin* as for those treated with *erythromycin* and *rifampin* (Bernard et al. 1991, Ainsworth et al. 1998 and 2000, Hines 2014).

Prevention

Courtesy of Camille Vercken and Romain Paillot – Many thanks!

***Rhodococcus equi*: practical everyday steps to lower the bacterial pressure on a farm!**

Sometimes breeders can feel defeatist when it comes to implement measures on their farms to reduce the pressure of *Rhodococcus equi*. Our answer usually is: "Yes, *R. equi* is a beast to fight but nothing is impossible for a breeder, it's the addition of a number of measures that will slowly decease the bacterial pressure and the risk of disease."

Very often, despite all the best efforts of the breeders, we see stud farms where all the best conditions to breed *R. equi* in a very efficient way, are present. Our aim here is to give you tools to stop this cycle.

Here are some quick wins to start to improve your dominance over these bacteria. These basic steps are complementary of all the treatment and early detection measures. They are pragmatic and can follow a handful of basic recommendations:

The disease: get a good knowledge of this sickness to understand the key practices to fight against it.

Disease transmission: dust is the main contamination factor for the young foal. Use all possible ways to keep foals out of dust between birth to 5 months, i.e.:

Premises: large farms with seasonal movement of horses are more exposed to R. equi.

Pastures & horse load: reduce the number of mares with foal per pastures.

Pastures: reduce soil erosion and deterioration of the grass cover, especially areas near paddock entrances, water troughs, etc. Move regularly water troughs and feeders when it is possible (Fig. 1 & 3).

Pastures: when the weather is dry, water hose paddocks, their entrances, and water troughs areas.

Pastures / round pens: avoid long exposures of susceptible foals in areas without grass cover. Remove droppings and feces in paddocks housing young foals (Fig. 2).

Pastures: turn up the soil in autumn paddocks at risk and, if the acid level of the pasture allows it: spread lime (get a soil expert advice for this).

Stablings: keep away young foals from the manure storage and pile.

Barns: minimize the generation of dust when cleaning the barn, especially if foals are housed in the barn at the time (e.g. avoid blowers or sweepers).

Barns: in foaling and young foals barns, review the air flow circulation in order to reduce the amount of dust, and to provide proper movement of air from bottom to top.

Floors in stable: avoid having young susceptible population on dusty flooring (Fig 5 & 6).

Disinfection: clean floors and walls before the breeding season and in between foalings.

Horses venues: avoid mixing resident and seasonal mares (a good biosecurity principle to have in any case).

Stabling: Do not forget to isolate sick foal at the suspicious stage.

Quarantine: test potential carriers for *R. equi* prior to them enter your farm, if possible.

Staff: train your staff to observe foals in order to improve early detection of cases, provide basic information on how the bacteria spread around the farm.

Of course, all the treatment aspects continue to apply to sick animals and all the early detection methods as well as immunity reinforcement methods recommended by your veterinarian.

Fig. 1 Avoid pastures with low grass cover for mares and foals in the sensible period
(coll privée equiways)

Fig. 3 Move regularly water troughs when it is possible or reseed or water regularly
(coll privée equiways)

Fig. 2 Remove regulary droppings from paddocks with mares and foals at foot
(coll privée equiways)

Fig. 4 Reseeding is always a good solution
(coll privée equiways)

Fig. 5 Do not use dust ground for young foals - muck out regularly (coll privée equiways)

Fig. 6 This is a suitable floor for sensible foals (coll privée equiways)

One take home message

Adding up all the measures that are feasible on your farm will get you started on the prevention side of the sickness and will slowly reduce the bacterial pressure on your stud farm.

Camille Vercken (equiways) & **Romain Paillot** are currently undertaking a research project on *R. equi* dedicated to combining biosecurity measure to severity of the bacterial presence given by soil analysis. This project is funded by IFCE (French national studs).

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Summary

(newsletters 31-33)

R. equi

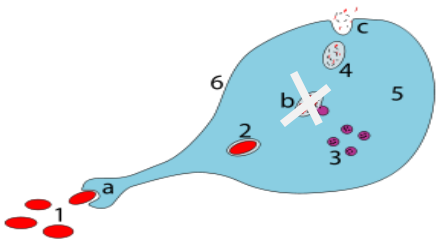
is present in soil, manure and feces of herbivores (saprophyte).

How do foals get it?
By inhaling the bacterium *R. equi*,
whose prevalence is associated with the airborne burden.

The airborne concentration of *R. equi* is elevated with low soil moisture concentration, low pasture heights, pens and lanes devoid of pasture cover.

Etiology

Most infectious germs are ingested by macrophages (white blood cells) and broken down. Contrary to this (due to plasmid-genes), *R. equi* is not only able to survive but even to replicate in macrophages.



(see newsletter 31)

Which foals get sick?

Mainly those with immature/naïve immune systems, and
those on farms with unfavorable environmental factors.

Exposed foals either:

Remain healthy (the majority)
Develop abscesses but recover without treatment; or develop abscesses and progress to clinical disease.
Rarely, *R. equi* can also infect:
pigs, goats, sheep, cattle, dogs, cats, and humans

Clinical Signs

Fever, lethargy and decreased appetite
Nasal discharge and sporadic cough
Respiratory distress and abdominal lift at the end of exhalation.

Infection

Abscesses form in the lungs, but *R. equi* can also cause joint infection, osteomyelitis, diarrhea, inflammation of the abdominal lymph nodes, abdominal abscesses and immune-mediated diseases.

Screening Tests

Taking temperature daily
checking complete blood counts
ultrasound of lungs and/or chest radiographs
confirmation on bacterial DNA culture.

Treatment

Antibiotics and supportive care
(if necessary anti-inflammatory meds,
iv fluids, O_2 supplementation).
Only treat symptomatic foals and avoid antibiotic resistance by not mass-treating foals on endemic farms.

Prevention

A knowledge as good as possible of the peculiar nature of *R.equi.*
A very careful herd and pasture management in any respect (limit stocking densities, group foals by age, soil erosion, grass cover, soil moisture).
Remove droppings regularly, keep stables dustfree.

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If there is any aera you would like covered in these very informative newsletters you should contact Kerry on kryan@itba.ie and she will forward your request on.

Joe Hernon, Chairman EFTBA

European Federation of Thoroughbred Breeders' Associations EFTBA
c/o Irish Thoroughbred Breeders' Association
ITBA HQ, Greenhills, Kill, Co. Kildare, IRELAND
Tel: +353 45 877 543
Fax: + 353 45 877 429
E-Mail: info@eftba.eu Web Site www.eftba.eu

Glossary	
AGID	Agar gel immunodiffusion (test)
aminoglycosides	Aminoglycosides are a medicinal and bacteriologic category of traditional Gram-negative antibacterial medications. They inhibit the synthesis of protein and contain an amino-modified glycoside (sugar). Aminoglycoside antibiotics display bactericidal activity against Gram-negative and some anaerobic bacilli where resistance has not yet arisen. Streptomycine is the first-in-class aminoglycoside antibiotic. It is derived from *Streptomyces griseus* and is the earliest modern agent used against tuberculosis. Other examples of aminoglycosides include kanamycin, tobramycin, tobramycin, gentamicin and neomycin (Wikipedia).
BAL	Bronchoalveolar lavage (tracheal wash) (not to mix up with 'blood alcohol level', please)
fibrinogen	Fibrinogen is a glycoprotein complex that circulates in the blood of vertebrates. During tissue and vascular injury, it is converted enzymaticylly by thrombin to fibrin and then to a fibrin-based blood-clot.
granulocyte	Granulocytes are a category of white blood cells in the innate immune system characterized by the presence of granules in their cytoplasm. They are also called polymorphonuclear leukocytes or polymorphonuclear neutrophils.
hyperimmune plasma	Hyperimmune plasma is prepared from the plasma of donors with high titers of antibody against a specific organism or antigen. Administration of hyperimmune plasma provides passive immunity against an agent. This is in contrast to vaccines that provide active immunity. However, vaccines take much longer to achieve that purpose while hyperimmune globulin provides instant passive short-lived immunity. Hyperimmune globulin may have serious side effects, thus usage is taken very seriously.
in vitro	In an artificial environment outside the living organism
in vivo	Within a living organism
macrolide antibiotic	Generally speaking, the macrolides are bacteriostatic antibiotics with a broad spectrum of activity against many Gram-positive bacteria. Their mechanism of action is also inhibition of bacterial protein biosynthesis. In human medicine, currently available macrolides are well tolerated, orally available and used to treat mild-to-moderate infections, e. g. some respiratory and soft-tissue infections. However, **macrolides are *not* to be used on non-ruminant herbivores, such as horses and rabbits**. They rapidly produce a reaction causing fatal digestive disturbance. **It can be used in horses less than one year old, but care must be taken that other horses (such as a foal's mother) do not come in contact with the macrolide treatment** (Wikipedia).
macrophage	Macrophages (Greek: 'big eaters') are a type of white blood cell, of the immune system, that engulfs and digests microbes, cellular debris, foreign substances, cancer cells, and anything else that does not have the type of proteins specific to healthy body cells on its surface in a process called phagocytosis.
saprophyte	A saprophyte or *saprotroph* is an organism which lives on and gets its energy from dead or decomposing organic matter or waste.
US	Ultrasound / ultrasonography
virulence	A pathogen's or microbe's ability to infect or damage a host.
WBC	White blood-cell count. White blood cells, also called leukocytes, are the cells of the immune system that are involved in protecting the body against both infectious disease and foreign invaders.