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## Foal Pneumonia (21-Jan-2002)

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### Introduction

Respiratory diseases are common in young horses, especially in foals between 1 and 6 months of age, who frequently present with lower airway infection. In a study from Texas, pneumonia was found to be the primary cause of disease and death in foals aged between 32 and 180 days [1]. In Ontario, the morbidity attributed to distal respiratory tract infection among foals was estimated to be 71% on breeding farms with endemic disease [2]. Therefore, lower respiratory tract infections in young foals continue to be a major problem for the horse industry and constitute a source of economic loss in terms of mortality, cost of treatment and prophylaxis, growth and performance retardation and loss of value [3]. Although our understanding of the etiologies and pathogenesis of foal's pneumonia has improved over the past several years, some pieces of the puzzle are lacking. The challenge of the next few years will be to understand the immunological basis of the inherent susceptibility of foal to respiratory infection with opportunistic pathogens. This text will briefly review our current understanding of pneumonia in foals aged between 1 and 6 months and because of its importance, our focus will be on bacterial pneumonia.

### Etiology and Pathogenesis

#### Bacterial Pneumonia

Pneumonia in foals is primarily caused by bacterial infection and among all isolates, *Streptococcus zooepidemicus* and *Rhodococcus equi* are the most important. These organisms can be found in pure culture or else be part of a plurimicrobial infection. Several other aerobic bacterial species may also be involved including, *Actinobacillus* spp, *Bordetella bronchiseptica*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pasteurella* spp, *Pseudomonas* spp, *Salmonella* spp and *Staphylococcus* spp [3,4]. Anaerobes appear to be uncommonly involved in primary pneumonia in foals [5]. As it is not possible to distinguish the etiologic agents involved on the basis of clinical and hematological data only, an attempt to culture the pathogen(s) should be made, at least for the first cases in an outbreak or in unusual or unresponding cases.

*Streptococcus zooepidemicus* - *Streptococcus zooepidemicus* equi subsp. *zooepidemicus* is a beta hemolytic, gram-positive coccus that belongs to the Lancefield group C. It is a commensal organism colonizing the tonsil and nasopharyngeal mucosa of healthy horses [6]. However, it is also a recognized pathogen of the horse's respiratory tract and is implicated in cases of distal airway diseases of foals [5] and young horses in training [7-9], and in pneumonia of horses following transportation [10,11]. *S. zooepidemicus* was also the most common isolate from equine bacterial cultures in our hospital [12]. In the work of Hoffman et al., *S. zooepidemicus* was isolated from 87% of uncomplicated cases of distal respiratory tract infection in foals on selected farms [5]. In 44% of these cases, it was isolated in combination with other bacterial species. In one study, *S. zooepidemicus* was also the most common etiologic agent in cases of pulmonary abscesses in foals [13].

The exact mechanisms implicated in the pathogenesis of *S. zooepidemicus* pneumonia in horses are not known. Although most horses harbor more than one strain of *S. zooepidemicus* in their pharynx, streptococcal pneumonia seems to occur following opportunistic invasion by a single endogenous clone, which may be different from one affected horse to another [14]. Opportunistic infection with *S. zooepidemicus* possibly occurs after the host defense mechanisms have been overwhelmed. Respiratory viruses, often thought to be the primary offending agents leading to secondary bacterial invasion, do not appear to be important in the pathogenesis of foal pneumonia [5,15]. In adult horses, transportation, race training and racing are thought to be predisposing factors but these are not part of the foal's routine. Overcrowding, heavy parasite burden, poor nutritional status, heat stress, congenital immunodeficiency and concurrent diseases are all plausible predisposing factors but are probably infrequently involved. Young foals sometimes experience repeated episodes of distal

airway infection indicating a persistent predisposing factor, which could possibly be an age-related immunodeficiency [16]. Further studies are needed to better understand the factors leading to *S. zooepidemicus* pneumonia in foals.

*Rhodococcus equi* - *Rhodococcus equi* is a pleomorphic gram-positive coccobacillus and a facultative intracellular pathogen of macrophages. It is a major cause of pneumonia in foals aged between 1 and 6 months with most cases occurring before 4 months [17,18]. Although the typical pathology caused by *R. equi* is a chronic pyogranulomatous pneumonia, foals may be presented as acute cases because the initial phase of the disease often goes unnoticed [19]. Affected individuals may also exhibit extrapulmonary lesions [19,20]. In a retrospective study of postmortem examinations of foals with miscellaneous *R. equi* infections, 48% of the pneumonia cases also had intestinal involvement, whereas there were only 4% of foals having intestinal involvement without pneumonia [17]. The intestinal lesions are thought to arise from repeated swallowing of infected sputum by the foals [21] and usually consist of ulcerative enterocolitis (originating in the Payer's patches) with enlarged and sometimes abscessed mesenteric lymph nodes [17,21]. Occasionally, a single large abdominal abscess is found often causing adhesions with the large or small intestine [17]. Several foals with *R. equi* pneumonia present with multiple joint distention with little or no associated discomfort, attributed to a non-septic, immune-mediated polysynovitis [22]. Hematogenous spread of the infection can also result in septic arthritis and/or osteomyelitis in some individuals [20,23,24]. Other extrapulmonary lesions that have occasionally been reported include uveitis, panophthalmitis, cellulitis, subcutaneous abscesses, ulcerative lymphangitis, nephritis, and hepatic or renal abscession [19].

Although *R. equi* is found in the soil of most farms, pneumonia caused by this organism can be endemic, sporadic or unrecognized, depending on the farm studied [25]. Several factors may influence the incidence of the disease including the degree of contamination on the farm, density of horses, climatic conditions and virulence of the isolate. Farms that have raised horses for several years are most likely to be heavily contaminated [26] probably because the manure of horses contains simple organic acids that promote the growth of the organism [27]. Although *R. equi* does not replicate in the adult intestinal tract because of the anaerobic environment [25], it apparently proliferates in the intestinal tract of foals up to 3 months of age [28]. Therefore, the presence of foals on the farm will contribute to the infectious burden of the environment. The infection is acquired through inhalation. Environmental conditions appear to play a role in the pathogenesis of the disease with warm [27], dry and windy [29] conditions favoring multiplication and aerosolizing of the organism. The majority of cases of *R. equi* pneumonia are seen during the summer months, a time that coincide with the best environmental conditions for the bacteria's development and a population of foals in the most susceptible age [21]. Farms that have endemic problems with *R. equi* are usually contaminated with a higher proportion of virulent strains [30]. An 85-Kb plasmid, found in some strains of *R. equi* was shown to be essential for intracellular replication within macrophages and for development of bronchopneumonia in foals [31]. This plasmid contains genes that encode for several proteins that have been named virulence-associated protein (Vap) A through H [32]. VapA and VapB are not expressed by the same *R. equi* isolates with VapA being found on most foals' clinical isolates and VapB on some human or porcine isolates [33]. VapC, D and E are found on VapA-positive strains and these proteins are only expressed when the bacteria are grown at 37°C, a characteristic compatible with virulence [33]. The presence of VapA alone is not enough to restore virulence in plasmid cured isolates [31] but the simultaneous expression of several Vaps may be crucial for virulence of foal's strains.

The key to the pathogenesis of *R. equi* pneumonia is related to the ability of the organism to survive and replicate within alveolar macrophages by inhibiting phagosome-lysosome fusion after phagocytosis [34,35]. The mechanism of entry of *R. equi* into the macrophage seems to influence its fate, since opsonization with specific antibody enhances phagosome-lysosome fusion and intracellular killing [35]. Immunity to *R. equi* infection in foals, although not fully understood, probably involves both humoral and cell-mediated immunity. The role of antibodies has been shown by the protective effect of prophylactic administration of *R. equi*-specific hyperimmune plasma [36-38] or purified immunoglobulins against VapA and VapC [38]. Studies in mice have shown that CD4+ T lymphocytes are the most important cells involved in immunity against *R. equi* with a T helper-1 response allowing clearance of the infection and a T helper-2 response being detrimental [39,40]. The reasons as to why foals show marked susceptibility to *R. equi* are not fully understood, particularly considering that *R. equi* does not cause problems in adult horses or other species, except in immunosuppressed individuals [41,42]. A natural defect in cell-mediated immunity, uncovered by the fall in maternally-derived immunoglobulins (at 2 - 3 months of age), is thought to explain a foal's susceptibility to severe respiratory infections caused by *R. equi* or other opportunistic pathogens (*P. carinii* or some viruses (Equine herpes virus 2 (EHV-2)) [42]. Another possible explanation is that the plasmid-containing *R. equi* isolates modulate the cytokine response of affected foals, thereby preventing its clearance from the lung [41].

*Mycoplasma* spp - *Mycoplasma* spp have been isolated from the nasopharynx of healthy horses [43] but their role as pathogens in equine medicine remain unclear. *Mycoplasma felis* has been implicated in cases of acute pleuritis in horses [44,45] and the disease was reproduced experimentally [45,46]. A more recent report implicated the same organism as the

cause of an outbreak of lower respiratory tract disease in young horses in training [47]. However, *Mycoplasma* spp do not appear to be important pathogens in distal respiratory tract infection of foals as indicated by serologic survey [46] and culture of the lower airways of diseased foals [5].

### **Viral Pneumonia**

Outbreaks of respiratory diseases caused by viruses are common in 2 to 3 year-old horses that are kept together in enclosed space such as in race or show barns. In this group of horses, viruses are thought to be important respiratory pathogens and may predispose individuals to bacterial pneumonia. However, in suckling foals respiratory viruses do not appear to be important etiologic agents for distal respiratory tract infection [5,15] and reports of primary viral pneumonia in foals are rare [48,49].

Equine adenoviruses have received some attention in foal medicine because of their involvement in respiratory disease of Arabian foals with severe combined immunodeficiency (SCID). In this group of foals, adenoviruses are the most common respiratory pathogens [50]. Adenoviruses are widespread in the equine population and persist in the upper airways of adult horses, which act as carrier or reservoir host, but they appear to be of little significance for immunocompetent horses [51]. Equine herpes virus 2, a member of the *Gammaherpesvirinae* subfamily, is another virus of possible importance in the foal. This virus is ubiquitous in the general equine population as indicated by high seroprevalence and frequent isolation from peripheral blood mononuclear cells [52]. Foals are born free of EHV-2 infection but virtually all acquire the infection during the first months of life [53]. The role of this virus in the respiratory disease complex of foals remains unclear but it is believed to be involved based on its significantly more frequent isolation from tracheal aspirates of foals with respiratory diseases in comparison to control foals [53]. Others have implicated EHV-2 as a predisposing factor for *R. equi* pneumonia in foals and were able to prevent respiratory diseases on farms with endemic problems by active immunization of foals using immunostimulating complexes containing selected envelope components of EHV-2 [54]. However, clarification regarding the role of viruses in foal's respiratory diseases, are still needed.

### **Acute Interstitial and *Pneumocystis carinii* Pneumonia**

A syndrome of acute, severe interstitial or bronchiointerstitial pneumonia has been described in foals aged between 1 and 6 months, characterized by sudden onset of respiratory distress, tachypnea, fever, poor response to treatment and histopathologic lesions of diffuse bronchiolitis and/or alveolitis [55-57]. The cases reported were usually sporadic with only one individual affected on a particular farm [55] although cluster of cases have also been described [56]. Several etiologies have been suspected including viruses, bacteria, *Pneumocystis carinii*, heat stroke and environmental toxins [55-58]. Still, no definitive causative agent(s) or factor(s) have been identified.

*Pneumocystis carinii*, one possible etiologic agent of acute interstitial pneumonia in foals, is a fungal organism [59] that causes pneumonia in individuals with compromised immunity such as human patients with acquired immune deficiency syndrome (AIDS) [60]. In equine medicine, *P. carinii* was originally recognized as a lung pathogen in SCID Arabian foals [50]. However, since then, others have reported *P. carinii* pneumonia in apparently immunocompetent foals [58,61,62]. Most of the affected foals were 2 - 3 months old, had developed respiratory distress and showed evidence of interstitial pneumonia on necropsy. In one report, 5 cases of concurrent infection with *P. carinii* and *R. equi* were reported [58]. The authors suggested that *P. carinii* played a role in the development of respiratory distress in these foals. The pathogenesis of *P. carinii* infection is complex. The organism attaches to alveolar epithelial cells causing inhibition of epithelial growth and replication. It initiates an inflammatory response, which can either clear the organism or, if too exuberant, cause lung damage [60]. Although the CD4+ T lymphocytes play a central role in immunity to *P. carinii*, other immune effectors, such as the alveolar macrophage, are also very important [60]. Here again, the question arises as to the reason for the foals' susceptibility to an organism that is only reported to cause disease in patients with compromised immunity.

### **Parasitic Pneumonia**

Parasitic pneumonias are not common in horses, especially with today's deworming programs. The typical case involves horses pastured with donkeys infested with the lungworm, *Dictyocaulus arnfieldi* [63,64]. In foals, *Parascaris equorum* is a more common parasite and because its life cycle involves migration through the lung, which can potentially cause signs of respiratory disease. Parasite-free foals infected experimentally with *P. equorum* developed a mild to severe cough at the time of migration of the parasite through the lung [65]. Some authors have described suspected cases of lung disease due to migration of *P. equorum* in foals [66,67]. Potentially, clinical signs could result from a massive infestation causing direct lung damage and/or because of the host immune response to the parasite. However, a definitive diagnosis of parasitic pneumonia is often difficult to obtain. The infection usually does not reach patency with *D. arnfieldi* in horses [63], it may be in the prepatent period in foals with *P. equorum* [67] and it may be difficult to identify larvae in tracheal washes. For these reasons, the prevalence and importance of parasitic pneumonia are not known. On well-managed farms parasites are probably

not important etiologic agents for respiratory problems. However, parasitic pneumonia could be suspected in foals with a poor deworming history, coughing, nasal discharge and poor response to antimicrobials [66,67].

### **Clinical Presentation**

The clinical presentation of foals with pneumonia can vary substantially according to the etiology, severity and chronicity of the disease [3]. However, because of the remarkable capacity of foals to compensate for progressive loss of functional lung, extensive lesions may be present by the time clinical signs are detected [19]. For this reason, careful observation and/or regular examination of the foals are necessary, especially on farms with endemic problems, in order to rapidly identify the sick foals and reduce the mortality attributable to respiratory disease [68].

The earlier signs of lower airway infection in foals are probably abnormal lung sounds on auscultation, nasal discharge and/or coughing [2]. The foals should have their respiratory rate and pattern monitored from a distance, during the coolest part of the day, when they are quiet. Indications for further investigation include, coughing when they get up or run, respiratory rate above 30 - 40 breaths per minute, or an increased respiratory effort. Bilateral mucopurulent nasal discharge may be detected or else, crusting may be found at the nostrils or on the dorsal canon bones where the foal may wipe its nose. Nasal discharge, however, is not a consistent finding and may be absent or undetectable if the lower airway discharge is swallowed [3]. A rectal temperature above 39°C (102°F) in a relatively quiet foal is abnormal and warrants further investigation. The thorax and trachea of the foals should be carefully auscultated at rest and while using a rebreathing bag [2,3]. Foals with lower respiratory tract infection will often cough while forced to take deep breaths, appear restless or distressed because of the rebreathing bag or show a prolonged recovery after the bag is removed. Due to their thin chest, the bronchovesicular sounds in foals are louder than in adult horses. Secretion sounds in the trachea, high or low pitch wheezes (continuous sounds) and crackles (broken sounds) are common findings in these foals. If lung consolidation is present, large airway sounds may be heard over localized or diffuse areas of the thorax [19]. Lung abscesses and pleural effusion, an infrequent finding in foals, should be suspected when decreased or absent lung sounds are detected. If thoracic percussion is performed, dull areas may indicate lung consolidation, abscesses or pleural effusion. In severe cases, abdominal breathing, nostril flaring, cyanosis and pronounced exercise intolerance will be present. While most foals with early disease continue to be bright and alert, individuals with severe lesions may be depressed or lethargic and anorexic. Some foals with pneumonia will be reluctant to lie down because of increased breathing difficulties with recumbency and may rapidly lose condition and become very weak.

Foals with *R. equi* infection have a typical pattern of clinical signs and progression [5,68]. The first indication of respiratory disease may be a cough and the presence of increased diffuse bronchial sounds on auscultation. This usually progresses into localized wheezes, cranioventrally. Fever (rectal temperature above 39°C), increased respiratory rate (over 40 breaths/min) and increased respiratory effort may develop over the next few days. If the foals are not treated, diffuse "crackles" on thoracic auscultation accompanied by marked tracheal sounds may be heard. Even at this point, foals usually remain bright and alert and nasal discharge is often absent. Signs of extrapulmonary lesions should also be looked for in possible *R. equi* foals. The intestinal form of the disease may manifest itself by fever, depression, anorexia, weight loss, colic or diarrhea [19]. Foals with immune-mediated polysynovitis will present with multiple joint distension accompanied by mild or no apparent lameness [22]. Heat, pain and severe lameness are characteristics of *R. equi* septic arthritis or osteomyelitis [19,23]. Foals with interstitial pneumonia often present with an acute to peracute onset of respiratory distress. Typical clinical signs consist of tachypnea, nostril flaring, extended head and neck position, increased intercostal or abdominal effort, cyanosis, fever, anorexia and reluctance to move [3].

### **Diagnosis**

The diagnosis of pneumonia in foals is based on clinical signs, physical examination and may involve the use of different sampling and laboratory techniques. Clinical signs, often noted late in the course of the disease in foals, include fever, lethargy, tachycardia, growth retardation, and respiratory-localizing signs such as coughing, purulent nasal discharge, polypnea, labored breathing, cyanosis, and enlarged submandibular lymph nodes. Auscultation of the thorax frequently reveals crackles, wheezes, and/or localized silent areas corresponding to large peripheral lung abscesses. A study revealed that the use of a rebreathing bag permitted the increased rate of detection of abnormal sounds at auscultation from 35% to 100% in field conditions [2]. The same study found mucoid to mucopurulent nasal discharge in 97% of the foals, cough in 56%, tachypnea in 17% and pyrexia in only 5% of cases. Clinical signs alone were accurate in the identification of foals with lower respiratory tract infection in 87% of the cases [2].

When pneumonia is suspected in a foal, confirmation of the diagnosis, evaluation of the severity of the condition and identification of the etiology of the condition can help to choose the best treatment, minimize relapse and give an accurate prognosis. Several techniques are involved in the work-up of these cases.

A complete blood count (CBC) may reveal neutrophilic leucocytosis and hyperfibrinogenemia in chronic or abscessive pneumonia [13,69]. Foals can present with a marked leukocytosis in the acute stage of the disease. Additionally, blood fibrinogen level, a good indicator of purulent inflammation, is often markedly elevated (>8g/L is not rare) when lung abscesses are present. However, these findings are not specific of pneumonia and some studies found only few hematologic abnormalities in foals with non-*Rhodococcus* respiratory infections [2]. Furthermore, in a study on *R. equi* pneumonia, clinicopathologic parameters were not good at predicting survival [69]. Although blood fibrinogen tends to be lower in cases of *S. zooepidemicus* pneumonia when compared to *R. equi*, there is considerable overlap in the values and therefore bacteriologic cultures are needed to identify the agent involved [13]. Foals infected with *R. equi* were found to be significantly younger, have higher heart rate and white blood cells (WBC), and lower packed cells volume (PCV) than foals without *R. equi* infection [13].

A serum chemistry panel is not of major help in these conditions, except for identifying secondary processes such as pre-renal azotemia due to dehydration, electrolyte imbalance, or secondary foci of infection. Arterial blood gas analysis is useful to assess the respiratory function and to monitor clinical therapeutic response in critical cases. Foals usually tolerate hypoxemia better than adult horses and may not show clinical signs of respiratory insufficiency before being severely hypoxemic.

Imaging techniques such as radiography and ultrasonography allow for a better understanding of the nature and the extent of the lesions. Thoracic radiographs of young foals may be obtained in the field with portable high intensity equipment, but is often challenging when done on older foals. Attention should be paid to the choice of the plate (large size and high-speed films are preferred) and positioning of the foal. A grid, when available, can also greatly improve the quality of the radiographs. Ideally, the focal distance for thoracic radiographs should be at least fifty inches. Radiographs can be taken with foals in lateral recumbency. However, if the foal is uncooperative, has respiratory distress, or if the handler is not experienced, this can lead to injury, poor quality radiographs and damage to the equipment. Another possibility is to hang the plate on a wall and have the foal held next to it. The interpretation of field radiographs should take into account the blur due to respiratory movement. Radiographic abnormalities can be seen as the presence of large anteroventral opacities, multiple nodular opacities with sometime gas-fluid interfaces, or diffuse interstitial pattern. Opacities and bronchograms, corresponding to an alveolar pattern, are frequently noted in the area cranial and caudal to the heart, ventral to the caudal vena cava.

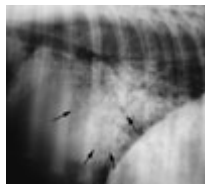


Figure 1. Thoracic radiograph of a foal with pneumonia. In the caudoventral portion of the lungs, there is the presence of a severe alveolar pattern with air bronchograms and cavitory lesions compatible with multiple abscess formations (black arrows). An interstitial pattern with peribronchial infiltration is present in the more dorsal regions of the lungs. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 2. Thoracic radiograph of a foal that presented in respiratory distress. A diffuse interstitial and peribronchial pattern is present. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Thoracic ultrasonography is probably less informative than radiography for pneumonia in foals. Nevertheless, ultrasound may allow for identifying peripheral parenchymal lesions or mediastinal abscesses. Various probes can be used for this purpose, the major restriction being the width of the tip, which should be small enough to fit between the ribs. A practical frequency that is widely used is 5.0 MHz. The ultrasound beam can not penetrate normal aerated lung parenchyma but the surface of the lung and pleura can be visualized. Consolidated lung or atelectasis generates pictures made of a combination of hypo and hyperechoic areas [70]. Abscesses appear as pockets with a thick hyperechoic wall and a content of variable echogenicity.

In foals with compromised respiratory function, endoscopic examination should preferably be performed unsedated, as  $\alpha$ -2 agonist drugs increase upper airway resistance and cause hypoxemia in horses [71]. Small diameter endoscopes (11 mm or less) are less traumatic and easier to pass through the nasal cavities of foals. The endoscope's biopsy channel should have a diameter larger than 2 mm to allow the passage of tracheal brushes or aspiration tubes. Pharyngeal lymphoid hyperplasia (graded 1 to 4) [72], mucopurulent accumulation in the pharynx, at the openings of guttural pouches, in the trachea, or the bronchi (98% of cases in a study on foals with pneumonia [2]) can be present in cases of pneumonia in foals. The endoscope

can also be used at the site of infection to take samples for cytologic examination or bacterial culture as discussed in the following paragraphs.

Identification of the infectious agents should be the next goal of the work-up. Bacteria involved in lower airway infection can be determined based on culture of tracheal samples, obtained either by transcutaneous tracheal washes [73,74] or through an endoscopic-guarded tracheal swabbing [4,75,76]. Ideally, sample material should be obtained prior to antimicrobial administration or after a sufficient period of time is allowed for tissue clearance of previously administered antimicrobial (up to 72 hours). It is important to avoid contamination during sampling that could lead to the misinterpretation of culture results. Airway sampling techniques used to retrieve fluid and/or secretions from the lower airways are primarily tracheal washes and bronchoalveolar lavages. The latter is less frequently used as a diagnosis tool of pneumonia in foals because of the frequent contamination by the upper airway bacterial flora, but may be useful for the diagnosis of conditions such as *P. carinii* pneumonia. In neonates, blood culture results may be indicative of bacterial isolate from the lungs [77], although it may be necessary to sample the respiratory tract directly when *in utero*-acquired pneumonia is suspected [78].

Transtracheal wash (TTW) is widely done in field practice (Fig. 3). The skin should be clipped and aseptically prepared on an area over the middle to upper third of the trachea. Local subcutaneous anesthesia can be done using 1 to 2 ml of lidocaine 2% injected where the trachea is palpated under the skin. With a blade (Surgical blade #11, Becton Dickinson AcuteCare, NJ, USA), a 1 cm long cutaneous incision, over the corresponding anesthetized area, may be made into the middle of the trachea. This leaves the skin open, which may decrease the risk of local abscesses and cellulitis due to contamination with bacteria brought up with the catheter from the trachea. The trachea is stabilized using one hand and an intravenous catheter (Catheter, 12 G- 3 in., Becton Dickinson Infusion Therapy Systems Inc., UT, USA) is then inserted between two tracheal rings. Care should be taken to tilt the catheter 45 degrees downside during the insertion. Failure to do so can lead to positioning of the tube into the upper part of the trachea and larynx. When the external catheter is positioned and the stylet removed, a piece of tubing (Polypropylene Catheter, Sovereign-Sherwood Medical, MD, USA) is inserted and 10 - 30 ml of sterile isotonic saline, free of antibacterial or conservative products, is injected and immediately aspirated. If no resistance is felt and only air comes out, the tube should be inserted further or withdrawn slowly with continued suction. At the end of the procedure, the tube is pulled out of the trachea and the catheter is removed followed by the application of a gauze with iodine paste over the wound. Caution should be taken when transtracheal aspiration is performed in a foal with severe respiratory distress because of the risk of transient worsening of the hypoxaemia. Other complications observed with TTW include, subcutaneous emphysema and bacterial cellulitis at the catheter entry site that can spread to the whole neck and to the mediastinum.

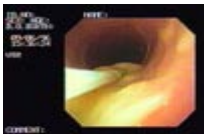


Figure 3. Transtracheal wash performed using a large bore catheter inserted into the trachea percutaneously. Inside the catheter a small tube is inserted for administration of saline and collection tracheal material. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Endoscopic guarded tracheal swabbing can be performed using double sheathed brush catheters to avoid upper airway contamination [4,75,76] (Fig. 4).

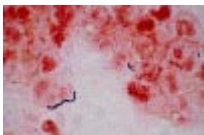


Figure 4. Tracheal wash or aspiration performed using an indwelling catheter inserted into the biopsy channel of an endoscope. This technique allows for the collection of secretions under visual guidance (Figure 3). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Also of interest is the endoscopic guarded aspiration catheter, which allows for a greater volume of secretions and number of bacteria isolates than transendoscopic brushes [4] (Fig. 5).

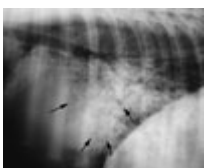


Figure 5. Sampling of tracheal purulent secretions with a tracheal brush passed through the accessory channel of an endoscope. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Processing of the sample should be done rapidly following the procedure. We suggest to transfer the first part of the tracheal fluid recovered into a commercial transport media for laboratory analysis and to prepare slides for cytology. Gram staining

can be done on-site before shipping the sample and can be very helpful in choosing the initial antibiotic therapy until culture and sensitivity results are reported. Centrifugation of the lavage fluid will improve the quality of the cytologic preparation, particularly if the sample has low cellularity and bacteria numbers. One study found Gram stain cytology to have a good specificity for the prediction of bacteriological culture results [79], while another found a good sensitivity for detection of isolates [5]. Gram-negative bacteria will stain red orange and Gram-positive bacteria will stain blue purple (Fig. 6).



Figure 6. Gram stain of a tracheal aspirate. Chain of Gram positive (blue) bacteria suggestive of *Streptococcus* spp. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Geographical differences are expected in the bacterial species recovered from the pneumonic lungs but *S. zooepidemicus*, a gram-positive bacteria, is the most frequent isolate [5,12,13,16,79,80]. Other bacteria often implicated are *Bordetella bronchiseptica*, *Actinobacillus*-like spp, *Pseudomonas* spp, and *R. equi*. One study found indirect fluorescent antibody technique and PCR targeted on the VapA antigens and structural gene respectively, to be less sensitive than bacterial isolation for the diagnosis of *R. equi* pneumonia [81], while a more recent study found the PCR technique to be more sensitive and specific [82].

The information gathered from the cytologic examination of tracheal samples may be difficult to use as an indicator of bacterial infection in foals. Total cell count and the percentage of neutrophils tend to increase in cases of airway infection [16,73]. However, the results can be significantly affected by the sampling technique [83,84]. Also, normal values seem to be different in foals as they tend to have a higher percentage of neutrophils than in adult horses [2].

Nasopharyngeal and pharyngeal swabs can be done easily without any sedation on foals using a guarded culturette (Culturette, Becton Dickinson Microbiology Systems Inc., MD, USA) or a guarded uterine swab (Culture swab 25 in., Continental Plastics, WI, USA), respectively. Samples should be processed rapidly and using a commercial transport media (Port-A-Cult, Becton Dickinson Microbiology Systems Inc., MD, USA), although adding costs to the procedure, it can greatly improve the results of the culture. Complete bacteriologic examination of a nasal or pharyngeal swab is often not warranted because of the presence of normal bacterial flora, but it can be used to detect the presence of specific pathogens such as *Streptococcus equi*.

Other specific pathologies such as *Pneumocystis carinii* and *Mycoplasma* spp lung infections require particular techniques to obtain a diagnosis . In particular, diagnosing *P. carinii* infection antemortem is difficult because the clinical, radiographic and cytological findings in affected foals are not specific for this condition. Affected foals may show increased opacities of interstitial pattern over the entire lung field and miliary reticulonodular pattern on chest radiographs [58,61]. In human medicine, transbronchial biopsies are used to diagnose a lung infection by *P. carinii*. In equine veterinary medicine, bronchoalveolar lavage or tracheal aspiration, after 3% hypertonic saline nebulisation, may be possibly increase the chances to isolate *P. carinii* in affected foals [58,85-88]. Samples need to be stained with a Gomori's methenamine silver staining. Postmortem confirmation of the diagnosis can be done using immunohistochemistry, immunostaining or Gomori's methenamine silver staining.

Although not reported as a significant pathogen for foals, when *Mycoplasma* spp infection is suspected, one must remember that specific culture techniques may be required for its isolation . Lastly, prevalence of EHV-1 and EHV-2 in foals seems to be high, but their role as pathogens in these animals is uncertain [52-54,89]. Viral isolation and serologic examinations can be performed to confirm viral infection in suspected cases.

## Treatment

Foals of 1 to 6 months of age will commonly experience respiratory tract infections, which may not necessarily require therapy. However, the presence of labored breathing, fever, depression or appetite, or in the presence of leukocytosis and hyperfibrinogenemia, antimicrobial therapy should be initiated without delay. The antimicrobial selection should be based on the pathogens isolated or suspected and on host factors which may influence the disposition and toxicity of the drug [90]. The most frequent pathogen of the respiratory tract is *S. zooepidemicus*, which are susceptible to  $\beta$ -lactams antimicrobial, including penicillins [12,90]. Orally administered  $\beta$ -lactam antibacterials are poorly absorbed and therefore parenteral administration is preferred [91]. Procaine penicillin G (25000 ui/kg q 12h), trimethoprim-sulfadiazine (TMS) (30 mg/kg q 8h to 12h) and ceftiofur (2.2 to 4.4 mg/kg q 12h) are usually effective against most pulmonary bacterial isolates of foals. Procaine penicillin should not be used in combination with TMS, as procaine may antagonize the antimicrobial effects of TMS [92]. Duration of therapy should be based on clinical response and up to 30% of foals will relapse after 7 - 14 days of therapy [16]. A combination of erythromycin (25 mg/kg q 6 - 8h) and rifampin (5 to 10 mg/kg q 12 - 24h), administered orally, is usually an effective therapy for *R. equi* infection. Erythromycin administration can be associated with side effects

such as severe diarrhea in foals and in their accompanying mares [93,94], hyperthermia and respiratory distress [56,95,96]. A retrospective study found 35.6% of foals treated with erythromycin developed diarrhea and 24.7% and 15.1% had hyperthermia or respiratory distress, respectively [96]. Other drugs under investigation for the treatment of *Rhodococcus equi* include azithromycin (10 mg/kg q 24h) and clarithromycin (7.5 mg/kg q 12h)[97,98].

The treatment of *P. carni* infection in foals is not well documented. In human medicine, treatment of *P. carni* is based on the use of pentamidine or trimetoprim-sulfamethoxazole. However, studies are necessary to assess the efficacy and dosage of these drugs against this infection in foals [99]. In the veterinary literature to date, only one foal treated with trimetoprim-sulfamethoxazole combination survived the infection [88,99].

Foals with pneumonia should be kept in a controlled environment, avoiding extreme conditions of temperature and humidity. Supportive therapy, including bronchodilators and antipyretic agents (Table 1), may be necessary in foals with impaired pulmonary function. Commonly used bronchodilators are methylxantine derivatives, such as theophylline and aminophylline, and the  $\beta$ 2-adrenergic agonists, clenbuterol and terbutaline. Clinical response to aminophylline (3 to 5 mg/kg q 12h, serum level <15  $\mu$ g/ml) is variable and toxic side effects including tachycardia, excitement and sweating are frequently observed. In addition to its bronchodilating effect, aminophylline may also induce a dose-related increase in respiratory muscle contractility.

<b>Table 1. Drug dosages for the treatment of foal pneumonia</b>				
<b>Drug Name</b>	<b>Dose</b>	<b>Route of Administration</b>	<b>Frequency</b>	<b>Precautions</b>
<b>Antimicrobials</b>				
Azithromycin	10 mg/kg	PO	SID	
Ceftiofur	2.2 mg/kg	IM or IV slow	BID	
Erythromycin estolate	25 mg/kg	PO	QID	May induce diarrhea, hyperthermia or respiratory distress
Erythromycin phosphate or stearate	37.5 mg/kg	PO	BID	Idem
Gentamicin sulfate	6.6 mg/kg 2.2 mg/kg	IV or IM IV or IM	SID TID	Nephrotoxic
Metronidazole	20 mg/kg	PO	QID	May induce anorexia
Penicillin G sodium or potassium	22 000 IU/kg	IV (slow if potassium salt is used)	QID	
Penicillin G procaine	22 000 IU/kg	IM	BID	
Rifampin	5 - 10 mg/kg	PO	SID to BID	
Trimethoprim-sulfas	30 mg/kg	PO	BID	
<b>Anti-inflammatory drugs</b>				
Flunixin meglumine	0.5 - 1.1 mg/kg	IV or PO	SID to BID	May induce renal papillary necrosis or colonic ulceration
Phenylbutazone	1.1 - 2.2 mg/kg	IV or PO	SID to BID	Idem
<b>Bronchodilators</b>				
Clenbuterol	0.8 - 3.2 $\mu$ g/kg 0.8 $\mu$ g/kg	PO IV	BID	Tachycardia, sweating
Aminophylline	3 - 5 mg/kg	PO	BID	Tachycardia, excitement, sweating

Clenbuterol, administered at 0.8 µg/kg PO, is generally well tolerated by horses. Side effects (tachycardia, excitement and sweating) are more common when it is administered IV or when higher dosages (up to 3.2 µg/kg) are required to improve airway function. Beta 2-adrenergic agonist drugs and parasympatholytic bronchodilators may also be administered to foals, by inhalation, when practical.

The use of nonsteroidal anti-inflammatory (NSAIDs) drugs (Table 1), may be beneficial in controlling hyperthermia and improving the well-being of foals with severe pneumonia. When using NSAIDs, clinicians should always keep in mind possible side effects such as gastrointestinal ulcers and acute renal failure.

In foals with severe hypoxaemia (< 65 mmHg), oxygen delivered intranasally or using a transtracheal catheter may be indicated [77,100-102]. Maintaining hypoxaemic foals in sternal recumbency can help to improve the VA/Q (Alveolar ventilation/perfusion) ratio and decrease the need for oxygen supplementation. Intranasal oxygen delivery can be done using a small diameter tube introduced into the pharynx and fixed to a nostril. Significant oxygen enrichment necessitates flow rates as high as 10 liters/minute of pure oxygen, whereas, the use of a small transtracheal catheter for oxygen delivery is more efficient allowing for a decreased flow rate [102]. Oxygen therapy requires close monitoring of foals as a rapid correction of arterial hypoxemia may attenuate the respiratory drive and thus worsening hypercapnia. Also, if foals are ambulatory and accompanied by the mare, oxygen delivery is difficult to maintain because delivery tubes are frequently twisted or stretched.

Bronchointerstitial pneumonia in foals may be seen as a distinct syndrome [55-57,61,103]. While no definitive causative agent has been identified, toxic, allergic, and viral insults have been suggested [55-57,103]. The diagnosis of bronchointerstitial pneumonia is usually done post-mortem, although lung biopsy have been done successfully in a few cases [56]. Treatment with antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs, antihistamines and bronchodilators are often unrewarding [55,57], although, one study did have a better survival rate of foals and found an improvement of the condition after treatment with corticosteroids [56]. It is important to rule out bacterial infection first before using corticosteroids because of their immunosuppressive effects in foals.

Once therapy has been established, its effects are best assessed by monitoring clinical signs, respiratory rate, nasal discharge, wheezing and coughing. Fever and hematologic abnormalities (mainly neutrophilia and hyperfibrinogenemia) are often not present at the beginning of the treatment in non-*R. equi* pneumonia in foals. Therefore, these are not always reliable parameters for monitoring the effects of therapy [16].

### Prognosis

A favorable outcome is expected in most cases of foal pneumonia when an appropriate antimicrobial therapy is initiated early in the course of the disease. However, a high reinfection rate is common, suggesting that persisting predisposing factors may contribute to the illness [16]. Severe parenchyma lung lesions, the presence of severe inciting (ie SCID, dysphagia...) or concurrent infections in extra-pulmonary sites, such as bacterial osteomyelitis, will lead to a poor prognosis [24].

In a retrospective multicenter study of 115 cases with *R. equi* infection, 72% of the foals survived the infection [69]. Heart rates > 100 beats/min, respiratory distress and severe radiographic abnormalities were associated with a poor prognosis. In another study of *R. equi* infection, foals that died had significantly higher respiratory rate, rectal temperature, blood neutrophil count and plasma fibrinogen values than surviving foals [18]. Survival rate may also be lower when lung abscesses or *Pneumocystis carinii* infections are present [13,18,58].

The future athletic performance of horses that have a history of pneumonia as foals has not been thoroughly investigated. However, current evidence suggests that these horses may race successfully or perform the task for which they were intended [13,69,104]. One study found that foals with *R. equi* infection may have a small decreased chance of racing as an adult but those that eventually raced performed comparably to the overall racing population [69]. Similarly, a history of *R. equi* infection did not affect the racing performance of horses as assessed by the earnings of these horses as 2 and 3 year olds [104]. However, in the same study a history of β-*Streptococcus* infection resulted in a decrease in the monetary earning of horses as 3 year olds.

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