THE ROLE OF *Histophilus somni* IN BOVINE RESPIRATORY DISEASE: AN UPDATE

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SUMMARY

*Histophilus somni* is described as an ethiological agent of a variety of diseases in cattle that include respiratory, nervous, septicemic, myocardial and polyarthritis presentations. The bacteria can be isolated from the nasal mucosa of apparently healthy cattle, but in situations of immunesupression it takes a role as ethiologic agent of acute fibrinous or fibrin-hemorrhagic bronchopneumonia in calves. Some case control studies have found incidences of *H. somni* of 28 to 43% in pneumonic lungs. Different well known factors make of *H. somni* a bacteria that has been traditionally misdiagnosed in Europe. Humoral immunity has been shown to be a necessary protection mechanism against *H. somni* infections. Amongst other measures to control environment, vaccination is now feasible in EU with a vaccine that proves reduction of clinical signs, lung lesions and use of medical treatments.

KEYWORDS

*Histophilus somni*, TEMA, myocarditis, pleuropneumonia, septicaemia, diagnosis, prophilaxis.

INTRODUCTION

Bovine respiratory disease (BRD) is an important cause of disease in the cattle industry in many countries (10). The BRD complex is multifactorial in nature and involves two main types of predisposing factors:

- **Infectious:** Bacteria: *Mannheimia haemolytica, Histophilus somni, Pasteurella multocida, A. pyogenes.*
  Mycoplasma: *M. bovis, M. dispar, Ureaplasma spp.*
  Virus: IBRV, BRSV, PI-3, BVDV, Adenovirus

- **And management and environmental conditions:** Such as shipping, weaning, mixing different origins, overcrowding, castration, starving, bad weather, dusty environments, …

Within the family *Pasteurellaceae* six genera with interest in veterinary medicine are found: *Pasteurella, Mannheimia, Histophilus, Haemophilus, Actinobacillus and Phocoenobacter*. The first 3 genera are of particular interest in BRD of cattle. *Histophilus somni* (*H. somni*) is generating increasing interest and is described as an ethiological agent of a variety of diseases in cattle that include respiratory, nervous, septicemic and myocardial presentations (5). In Denmark, *H. somni* is one of the most common bacteria isolated from severe cases of calf pneumonia (8).

This paper reviews different aspects related with the presence and importance of *H. somni* in BRD, amongst other ethiological agents. Therefore basic knowledge of its epidemiology, clinical symptoms and lesions, diagnosis and control are reviewed, which wants to be a base for a practitioner in its daily field work against pneumonia.

EPIDEMIOLOGY

Phylogenetic studies based on the polymerase chain reaction (PCR) have concluded that the genera *Histophilus* includes the following species:

<table>
<thead>
<tr>
<th>Species</th>
<th>Host</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Histophilus somni</em></td>
<td>Cattle</td>
<td>Septicemia, thromboembolic meningoencefalitis, broncopneumonia, sporadic infections of reproductive tract</td>
</tr>
<tr>
<td><em>Haemophilus somnus</em></td>
<td>Ovine</td>
<td>Epididimitis, vulvitis, mastitis and reduced fertility, septicemia, arthritis, meningitis and lamb pneumonia</td>
</tr>
<tr>
<td><em>Haemmophilus parasuis</em></td>
<td>Swine</td>
<td>Glässer disease, secondary invasor in respiratory infections</td>
</tr>
</tbody>
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**Histophilus sp.** present a small size (less than 1 μm diameter x 1 to 3 μm length) and are bacilum – cocobacilum Gram negative. These bacteria require of one or both growth factors: X (hemina) and V (nicotinamide adenine dinucleotide, NAD), not growing then in McConkey agar like the majority of bacteria belonging to the family Pasteurellaceae. These microorganisms are facultative anaerobic, and for this reason its optimal growth occurs in a 10% CO₂ enriched atmosphere, in chocolate agar supplemented with both growth factors X and V.

**H. somni** can be isolated from the nasal mucosa of apparently healthy cattle, although its prevalence and number are increased in animals that have been stressed or that have an underlying infection; the prevalence of **H. somni** in the upper respiratory tract has been reported to range from 0 to 50% (9). Isolation of **H. somni** from the nasal cavities of calves was considered as evidence of an early infection, which might originate from the mother at birth (persistence of at least nine weeks) or from other pen mates. Horizontal transmission from carrier to non-carrier calves has been reported (4). **Histophilosis** occurs shortly after calves enter the feedlot, although, deaths from **H. somni** infection may continue for up to two to three months post-arrival (9).

In situations of immune suppression it can cause pneumonia, and its role as a cause of BRD is actually being increasingly recognized. This role as ethiologic agent of acute fibrinous or fibrin-hemorrhagic bronchopneumonia in calves has been described worldwide, with reports of the disease from North America, Europe and Australia; in some countries, it is the first cause of death in fattening units (4). In case control studies, **H. somni** has been found in pure culture in as many as 28% of the cases of pneumonic lungs examined microbiologically (4). We have confirmed these findings in our diagnostic laboratory since 1999 by the isolation and identification of **H. somni** from pneumonic lungs of beef calves in Spain with 43% incidence of positive results to **H. somni** and 24% to **M. haemolytica** (non-published data). These results agree with other studies from countries with a different environment and production system like Denmark, where the reported incidence was 41% to **H. somni** and 29% to **M. haemolytica** (Dr. Oystein Angen, National Veterinary Institute, Tech. Univ. Denmark, personal communication).

As well as participating in the cause of BRD, **H. somni** causes also meningoencephalitis, septicemia, myocarditis and polyarthritis. It is the most important pathogen associated with myocarditis in fattening calves.

Exposure to **H. somni** is widespread and up to 25% of the cattle population may have serum antibodies to this bacterium, and in some premises it may be higher than 50%. Many of these animals experience subclinical infections or develop an asymptomatic carrier state, so seroconversion and the presence of serological titers would mean that animals have experienced a subclinical infection but not always necessarily a clinical disease (4, 6, 9).

The pathogenic mechanisms of **H. somni** have not been well defined yet (neither production of a large capsule nor releasing of extracellular toxins have been described). Only lipo-oligosaccharide (LOS), Fc receptors (receptors that bind to bovine IgG) and two outer membrane proteins (OMPs) have been described as possible virulence factors (1, 4).

In some cases of pneumonic mannheimiosis, **H. somni** might have been the primary pathogen, but was not so identified because of the faster growing Pasteurella spp. or because of the antimicrobial therapy, which would mask the slower growing and more vulnerable **H. somni**.

Different well known factors make of **H. somni** a bacteria that has been traditionally misdiagnosed in Europe.

**CLINICAL SIGNS AND LESIONS**

Regarding the impact in reproduction, the protagonism of **H. somni** in any kind of reproductive failure in the male is only occasional, being able to cause poor semen quality or infertility, and being the prepuce the preferred site for sampling. Some studies have reported **H. somni** to be the cause of infertility, prolonged open intervals and repeat breeding but more research is needed to confirm the role of **H. somni** in these cases, as this bacterium is a common inhabitant of the uterus. The most reliable location for culturing the bacteria is the clitoral fossa (4).
In the upper respiratory tract it can cause laryngitis as well as tracheitis. In the lower respiratory tract it can cause pneumonia, which is generally difficult to differentiate, from a clinical point of view, from other bacterial etiologies. The course of disease, hyperthermia, salivation, eye discharge, depression, increased respiratory rate, ..., all is found during a clinical case. Environment, immunity and coinfection all play a role in modulating the severity of each case. Coinfection with other bacteria is common, and can aggravate the clinical presentation, and previous viral pneumonia infection is actually quite common, particularly in feedlots, where big groups of animals are put together at the same time, so rapid transmission of respiratory viruses (IBR, BRSV, BVD, Parainfluenza-3 and Adenovirus) are usually present and become the triggering event in new cases of BRD.

The pneumonic form can evolve into a septicemia and subsequent invasion of other organs. In our challenge experiments we demonstrated that intratracheal inoculation of *H. somnus* in unstressed, conventional calves caused severe pneumonia and death in some animals. *H. somnus* was re-isolated from lung and brain tissues, thus indicating a bacteremic distribution (septicemic lesions were observed in the spleen and auricles) and a tropism for some areas of the nervous system (vasculitis and edema in meninges were observed).

Regardless of the target organ that is primarily affected, the pathological lesions that occur in *H. somnus* infections are usually characterized by vasculitis with diffuse thrombi that contain fibrin, inflammatory cells (especially neutrophils) and large numbers of bacteria (7).

The lesional impact of *H. somni* in pneumonia is described as fibrinous pleuritis and pleuropneumonia. The macroscopic findings of fibrinous pleuritis consist in a pale straw coloured liquid with exudates of fibrin in thoracic cavity, with generalized deposits of fibrin on the pleura. More commonly pleuroneumonia is presented (inflammation of pleura and pulmonary parenquima) characterized by consolidation of cranioventral pulmonic lobes, dilated interlobular septa, with presence of fibrin on the pleural surfaces of the affected lobes. Lung lesions are bilateral and mainly located on cranial lobes, although large areas or both caudal lobes may be involved. Viewed macroscopically, the affected areas do not differ too much from those caused by *M. haemolytica* and they are characterized by an exudative bronchopneumonia with pneumonic tissue, usually deep-red in color, and slight to markedly swollen and firm at palpation. Small airways could be delineated by purulent exudate and small necrotic foci present superficially and, upon sectioning, interlobular septa are often seen to be distented and oedematous. Nodular abscesses and fibrinous pleuritis may be present. The trachea may be hyperemic with foamy exudate and the regional lymph nodes edematous and swollen. Epicardial petechiation and accumulation of pericardial fluid have also been described.

![Photo 1](https://example.com/photo1.jpg) - Pneumonic lesion produced by an intranasal experimental infection with *H. somni* – 2 days post infection

![Photo 2](https://example.com/photo2.jpg) - Lung section from calf experimentally infected with *H. somni* showing the extension of pneumonic tissue in the left caudal lung lobe (80 % approximately) – 24h post infection

![Photo 3](https://example.com/photo3.jpg) - Congestion and vascular lesions on brain of a calf (field case) where *H. somni* was isolated.

![Photo 4](https://example.com/photo4.jpg) - Congestion, suffusion and haemorrhage on myocardial surface of a calf (field case) where *H. somni* was isolated.
The thromboembolic meningoencephalitis (TEME) caused by *H. somni* is considered to gain importance as the diagnostic approach to the disease is also developing. Of low incidence but usually high lethality this nervous presentation is characterized by central nervous system (CNS) signs: blindness, recumbency, depression and death 1-2 days after the onset of clinical signs. High fever and deep depression are the landmarks of this CNS presentation of *H. somni* or TEME. At postmortem abnormalities might be restricted to meninges and brain, with a pattern of multiple vascular lesions and hemorrhages, and vasculitis (2).

One manifestation of the septicemic form that is observed more frequently is myocarditis. Cardiac lesions in necropsy material are usually described as endocardial hemorrhages, myocarditis and pericarditis. Affected animals might die suddenly or may follow a chronic course of disease for some days. The cause of death is acute heart failure, and in addition to myocarditis there may be evidence of pulmonary congestion and oedema from left heart failure. These pulmonary findings can easily be mistaken as interstitial pneumonia and unless the heart is properly examined the correct diagnosis may be missed. This manifestation is restricted not only to feedlot animals; affected cattle of varying ages and on pasture have also been described.

As well as the respiratory, myocardial, nervous, reproductive and septicemic form of *H. somni* disease or *histophilosis*, there are other, less reported, clinical and subclinical presentations in cattle that include: Mastitis, polyarthritis, conjunctivitis and otitis.

**DIAGNOSIS**

Diagnosis based on bacteriological isolation and identification of *H. somni* is poorly sensitive even when the clinical presentation and anatomopathology become a strong orientation of *histophilosis*. Difficulty on classic diagnosis is due to different factors:

1- *H. somni* is a bacteria with a slow growth (48-72 hours), unlike *M. haemolytica* and *P. multocida* which grow faster (16-24 hours). These two very common bacteria in BRD and the contaminating bacteria which reach the lung during manipulation for sampling do mask and negatively affect in the end the isolation and identification of *H. somni*.

2- The germ is fragile and samples must reach the laboratory fairly quickly under refrigeration, as this extends the survival rate of bacteria from 1 to 3 days, if kept at 4ºC during transport to the lab.

3- Bacterial cultures must be incubated on presence of 10% CO₂, as this is a requirement of this facultative anaerobic bacterium.

4- *H. somni*’s colonies are quite small in size and pale yellow in colour and this, linked to the fact of being a slow grower, make quite common the fact that *H. somni* colonies are overgrown by other bacteria like *Pasteurella* sp. *Mannheimia* sp. or *Proteus* sp.

5- Antibiotic treatments administered to the animal before death might decrease the rate of successful *H. somni* isolations. A Danish study showed that 32% of pneumonic lungs that reach the lab for diagnostic work contain antibiotic residues.

Our recommendation in BRD cases is to employ more than one culture media, to incubate for up to three days the primary cultures, to employ specific biochemical tests for identification and to confirm identification with PCR. We are actually combining, routinely in BRS cases, bacteriological culture in different conditions and PCR for *H. somni*. If one of the two methods is positive to *H. somni* the sample gets a positive result. Molecular diagnosis of *H. somni* based on PCR techniques can be done on different type of samples: Tissue (lung, heart, brain, synovial fluid, …), swab (parenchimal and bronchial from lung, pericardial sac…), bacterial culture. For all the explained above, amplification of DNA of 16s confers PCR higher sensitivity than bacteriology tests and also than other immunohistochemical or immuno-fluorescence techniques.

Serology tests are available, although most of them at an experimental level, and are usually difficult to get a precise interpretation of the results obtained. As *H. somni* is a comensal bacterium and is found in the upper respiratory tract of healthy animals, positive results on serology do not always correlate completely with presence of disease.

**CONTROL**

Medical treatment of BRD based on antibiotics, antiinflamatories, bronchodilators, etc is the most common approach to this disease, and means the individual treatment of diseased animals as soon as symptomatology is detected. Although a viral component is very often present and, as said above, is the triggering event in BRD, generally the treatment is directed towards bacteria, as they are the ones conditioning the severity of the clinical presentation and are the main target of the ethiological treatment. For *H. somni* the success rate of antibiotic treatments is usually high, based in *in vitro* sensitivity testing. The performance *in vivo*
is not so high, but still higher than for other bacterial pathogens. A Danish study on antibacterial sensitivity of *H. somni* strains collected between 1990 and 2002, showed good sensitivity for ampicillin, ceftiofur, ciprofloxacin, erythromycin, florfenicol, penicillin, espectinomicin, tetracycline, tiamuline, tilmicosine and sulfa + trimetroprim.

Humoral antibodies have been shown to be a necessary protection mechanism against *H. somni* infections, and immunization with a bacterin enhances this resistance by stimulating high serum concentrations of specific antibodies and bactericidal activity (4, 6, 9). Several experimental and commercial bacterins seem to have demonstrated efficacy against challenge infection by TME as well as against the pneumonic form of histophilosis (3, 4).

Until recently, *H. somni* immunization was usually done with autovaccines that used the bacterial strain isolated on a clinical case, it was taken to the lab to reproduce it and prepare a vaccine, and was eventually used to actively immunize all the animals of the farm of origin.

A combined commercial vaccine containing *M. haemolytica* A1 leukotoxin and *H. somni* (Hiprabovis Pneumos”) has shown positive results of protection both in front of experimental infections and field studies.

A group of 130 calves of 2 months of age were included in a study to evaluate the efficacy of such vaccine. All the animals (64 vaccinated with the bacterial vaccine and 66 as control) received a tetravalent viral vaccine that included BRSV, IBR, BVDV and PI-3. The test group received then two doses of this new bacterial vaccine (*M. haemolytica lkt* + *H. somni*), and the control group received placebo instead. The monitorisation of clinical parameters for 8 months, until slaughter, showed the following results:

**Respiratory clinical signs:** Vaccinated animals with the commercial bacterial vaccine showed less respiratory problems than the non-vaccinated (p<0.05). The reduction of clinical signs was superior to 50% (44% vaccinated, 20% control).

**Treatments:** Significant reduction of medical treatments in both groups. Vaccinated calves required 5 times less treatments than the control (144 treatments in front of 26 treatments, p<0.05).

**Pulmonary lesions:** The percentage of pneumonic tissue was reduced by 50% for vaccinated animals (20.4% for vaccinated calves, 41.3% for controls, p<0.05).

**Mortality:** Vaccinated calves showed a tendency to reduce mortality compared to controls (0% compared to 3%, p>0.05, considered only losses with clinical symptomatology and pulmonary lesions which agreed with a respiratory process).

Statistical significant reduction of the clinical respiratory symptomatology, of the number of medical treatments and of the percent of pulmonary damage caused by pneumonia were found in such trial with this bacterial vaccine. Mortality also showed a tendency to reduction.

**CONCLUSIONS**

*H. somni* is responsible for respiratory, nervous, septicemic and myocardial clinical signs and lesions, while its detection rate in pneumonic lungs is estimated to be of 41-43%. Its requirements for growth and other characteristics are the reason why this bacteria has been for some time been misdiagnosed in many diagnostic labs. PCR techniques prove to be more adequate for ethiological diagnosis on biological samples from field cases. Finally, amongst other measures to control environment, vaccination is now feasible in EU with a vaccine that proves reduction of clinical signs and lung lesions by 50% and use of medical treatments by 80%.

**BIBLIOGRAPHY**


