The Role of *Haemophilus somnus* in Bovine Respiratory Disease (BRD)

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Introduction

Infection with *Haemophilus somnus* was first described in North America in the mid fifties.[1] In the early stages of the study of this disease, the most common manifestation of infection described, was a meningoencephalitis.[2] Subsequent authors emphasized the septicemic nature of the disease. It was readily apparent that many organs and systems were involved and to reflect this, a more suitable expression, **Haemophilus somnus septicemia** initially[3] and **Haemophilosis** subsequently[4] was suggested.

In earlier years, when *Haemophilus somnus* infection was considered to be predominantly a neurological disorder, it was observed to be only an occasional cause of mortality. In more recent times, there were increasing observations of other disease entities reported in Western Canadian Feedyards, (See Tables 1-3). If all the conditions supposedly caused by *H. somnus* are lumped together, Haemophilosis remains one of the most important causes of mortality in fall placed calves.[5,6,7]

Table 1. Specific causes of mortality in high-risk, full-placed calves in a Saskatchewan feedlot in 1990, (n=6280).[1]

Necropsy Diagnosis	Number of deaths	Proportion where Haemophilosis was confirmed
Pneumonia	55	3/10
Myocarditis	34	10/11
Other	18	0/12
Polyarthritis	15	1/12
Pleuritis	14	2/3
Bloat	8	0/2
TME	5	5/5
Haemophilus Septicemia	4	3/3

[1]From Van Donkersgoed (5)

Guichon, *et al*[7] reported that less than 1% of proportional mortality at necropsy examinations could be attributed to *Haemophilus somnus* pneumonia. This is in contrast to a proportion of 30% for fibrinous pneumonia.[7] The purpose of this paper is to examine the role of Haemophilus somnus in clinical pneumonia.

Table 2. Specific causes of mortality in high-risk, full-placed calves in a Saskatchewan feedlot in 1991, (n=5129) and in 1992 (n=6041).[1][1]

	Number of deaths	
Necropsy diagnosis	1991	1992
BRD	19	14
Myocarditis/Pericarditis	35	32
Pleuritis	3	10
TME/Septicemia	12	2
Polyarthritis	3	6

[2]From Van Donkersgoed *et al.* (6)

Table 3. Specific causes of mortality in high-risk, full-placed calves (n=118,828).[3]

Necropsy Diagnosis	Number of Deaths	Proportional Mortality
Bloat	228	11.7
Fibrinous pneumonia	574	29.5
Haemophilus myocarditis	182	9.4
Haemophilus pericarditis	46	2.4
Haemophilus pleuritis	187	9.7
Haemophilus pneumonia	16	0.8
Haemophilus septicemia	171	8.8
Thrombotic meningoencephalitis	31	1.6
Other metabolic causes	30	1.5
Miscellaneous	236	12.1
Polyarthritis	141	7.3
Other respiratory causes	102	5.2
Total	1944	100

[3]From Guichon, *et al.* (7)

Clinical Features Similar to Pneumonia

Haemophilus Myocardial Infarction (HMI)

There are several manifestations of Haemophilosis that under certain conditions can be confused with a pneumonia. A commonly observed cause of mortality is myocarditis.[4,5,6,7] If these animals are seen early in the course of the bacterial infarction, the main clinical features will be an elevated temperature and a subjective increase in depression. It is only when the myocardial infarcts begin to affect cardiac output, that more defini-

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tive clinical signs begin to emerge. Subsequent to identification in the pen, calves with a severe MI, will show poor exercise tolerance. They may "mouth breathe" with tongue extended. Frequently this is so dramatic, they collapse during movement from the "home" to hospital pen. Calves examined at this stage are extremely depressed, the heart rate is elevated and upon auscultation of the thorax, few respiratory sounds may be heard.

Many calves diagnosed with an HMI have a previous history of treatment for an undifferentiated fever and depression within the last 10-14 days. They are returned to their "home pen" only to be "found dead" or in severe respiratory distress. When necropsied the lungs are enlarged and the severe interlobular edema and hemorrhage of left sided heart failure is present, Figure 1. If these calves are euthanized as "downers" before the heart fails, this pulmonary edema is not there. The cause of the heart failure is one or more myocardial lesions, Figure 2-3.

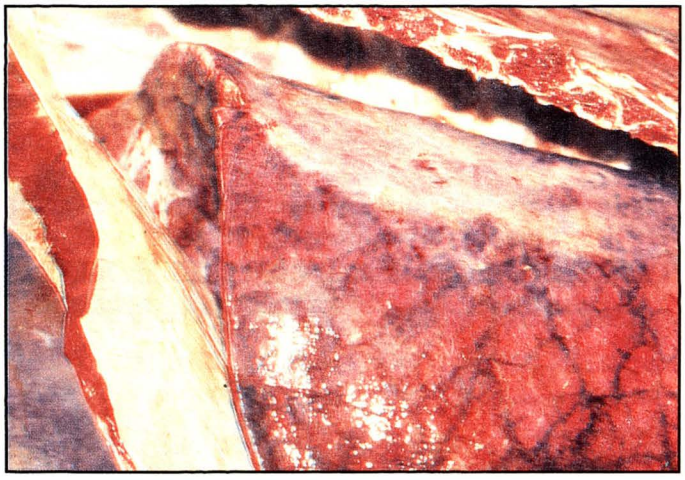

Figure 1. Extreme interlobular edema and blood of left sided heart failure. The lung is also non-collapsed and covered with petechial hemorrhages. The liver appears fibrotic.

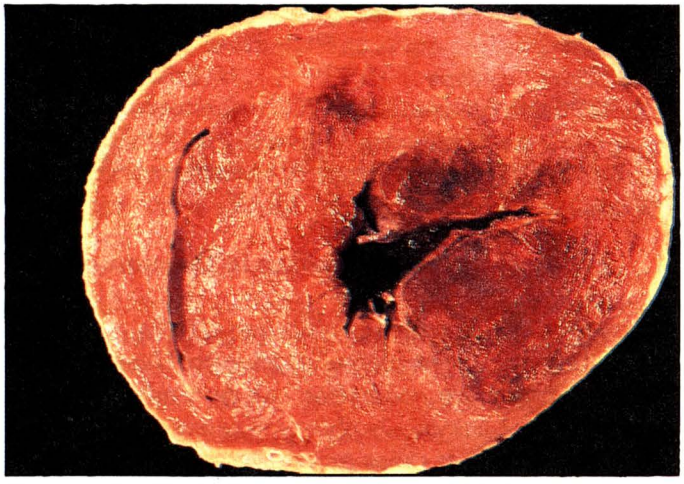

Figure 2. Early bacterial myocardial infarction; approximately 48 hours. The location in the papillary muscles is typical.

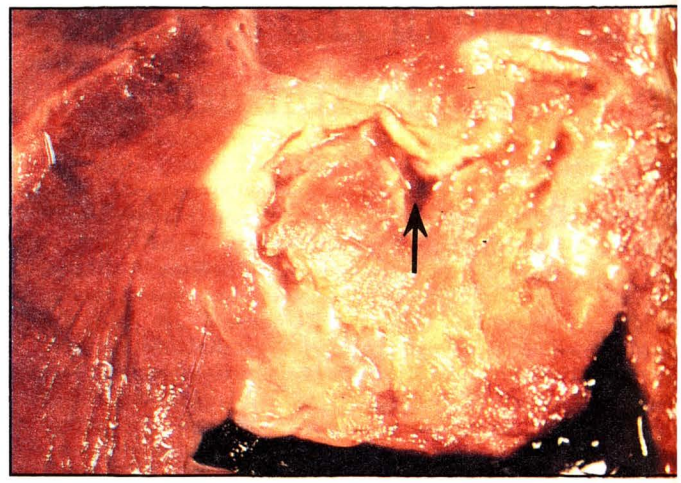

Figure 3. Left ventricular papillary muscle with a chronic septic infarct resulting in sequestration (see arrow). It is estimated that this lesion is greater than 14 days of age.

Pleuritis

Many calves affected with either septicemic, encephalitic, myocardial or pleuritic Haemophilosis are often found dead without any prior selection for treatment. This is especially true of the pleuritic form. Few calves are clinically diagnosed with pleuritis and greater than 50% die in the pen without ever having been treated.[5] This would suggest that the pleural space can fill very quickly to the extent that calves succumb to ***unilateral or bilateral compression atelectasis*** and die of acute hypoxemia.

If ever examined clinically, calves are febrile, severely dyspneic and demonstrate poor exercise tolerance. The presence of "fluid splashing sounds" in the pleural space is often easily audible upon auscultation. At necropsy,

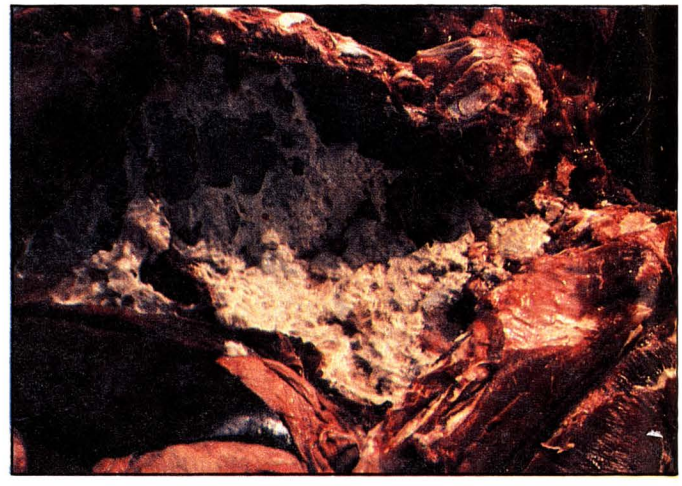

Figure 4. The pleural space on the right side of a fall placed calf, filled with fibrin and fluid. Note both visceral and parietal pleura involved.

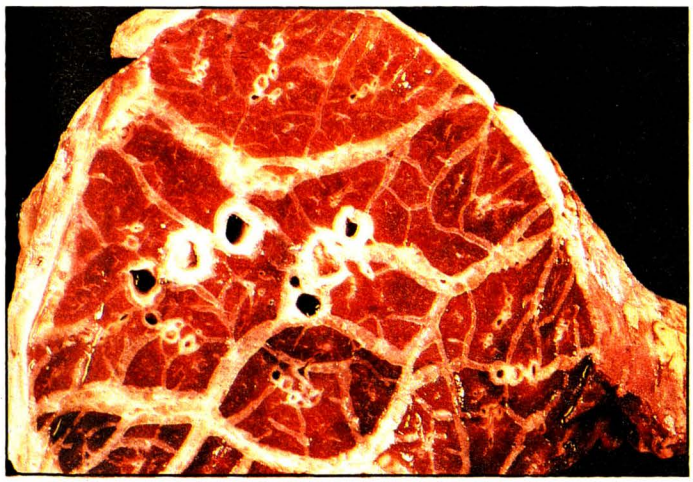

Figure 5. The main lesion in the lung is atelectasis with severe interlobular fibrin. There often is no pneumonia. Note the lack of inflammatory debris in the bronchi.

there is a large amount of fluid in the pleural cavities, Figure 4, often without any pneumonia, Figure 5.

Laryngitis

The prevalence of laryngeal lesions in cattle at slaughter was reported to be 13.1%[8] yet clinical laryngitis in feedlot cattle is not considered common. While the above group[8] made no attempt to identify probable pathogens of laryngitis, another group[9] surveyed tracheal bacterial flora and their results are summarized in Table 4. Similar observations,[10] suggest that while it would be difficult to definitely associate laryngitis with Haemophilosis, a necrotizing vasculitis (thrombophlebitis) very similar to that caused by *Haemophilus somnus* is often present and considered by some to be the initiating process.

Table 4. Rate of isolation (%) of Bacteria from the Trachea of feedlot Cattle in relation to clinical state.[4]

	n	Rate of *H. somnus* isolation	Rate of *P. heme* isolation	Rate of *Mycoplasma* isolation
BRD	281	3.2	30.2	59.1
Healthy	87	3.4	24.1	27.6

[4]From Corstvet, *et al.* (9)

Laryngitis, whatever the etiology, does still arise as a differential diagnosis in cases of severe dyspnea in feedlot cattle and in younger calves out on pasture as well. Often there is a pronounced laryngeal stertor to the extent that all other respiratory sounds are masked. Affected cattle are febrile, dyspneic to the extent that they are mouth breathing and inappetant. Where surveillance of young calves is intermittent, the syndrome may become so severe that by the time the calf is selected for treatment, it is unable to nurse or feed and is presented gaunt and dehydrated.

Pneumonia

Practitioners have based their understanding of bovine pneumonia and its causes on studies like the one where Schiefer et al, report on the correlation between the putative pathogens of fibrinous and bronchopneumonia.[11] *Pasteurella hemolytica* was associated with fibrinous pleuropneumonia and *Pasteurella multocida* with a suppurative bronchopneumonia. Further examinations exploring the isolation rate of *Haemophilus somnus* in cases of pneumonia are presented in Tables 5 and 6 and show that *Haemophilus somnus* can probably be a primary pathogen anywhere from 30 - 50% of the time. While Andrews reported that *Haemophilus somnus* alone could cause fibrinous pleuropneumonia in 7/68 cases examined[11] it is more common for the lesion to be that of a suppurative bronchopneumonia, Figure 6.

Table 5. Isolation of other organisms from a selected sample of bovine lungs at necropsy where H. somnus was also present.[5]

Organism	(n)	(%)
H. somnus (total)	162	--
H. somnus and P. multocida	37	22.8
H. somnus and P. hemolytica	14	8.6
H. somnus alone	92	56.7

[5]From Andrewst, *et al.* (12)

Table 6. Examination of Selected Cases of Broncho-Pneumonia With the View of Etiological Determination[6]

Etiology	Number of Cases	percent
H. somnus	12	34
BRSV	2	5.5
A. Pyogenes	2	5.5
A.I.P.	2	5.5
IBR	3	8.3
Pasteurellosis	2	5.5
H. somnus + M. bovis	2	5.5
H. somnus +/- P. hemolytica	5	13.8
Unable to classify	6	16.6
	36	

[6]From Clarke. (13)

Haemophilus somnus can also cause a suppurative pneumonia, not uncommonly in association with *Mycoplasma bovis*, Figure 7. Occasionally multifocal red lesions are distributed diffusely throughout the entire parenchyma of the lung thereby suggesting a hematogenous spread because of a septicemia, Figure 8.

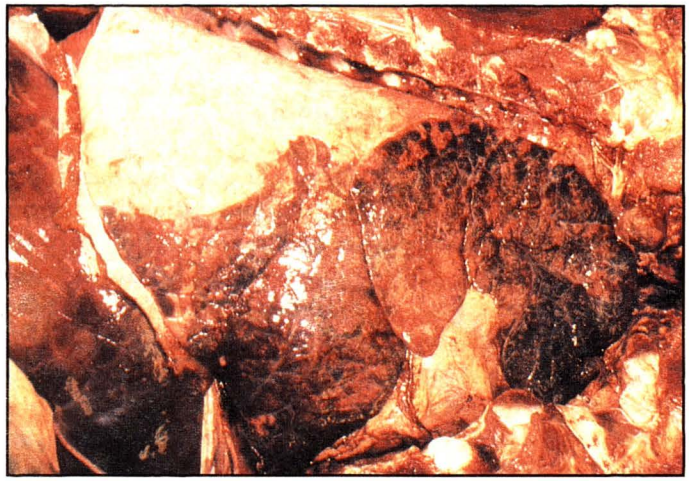

Figure 6. Bronchopneumonia where Haemophilus somnus was the primary pathogen isolated.

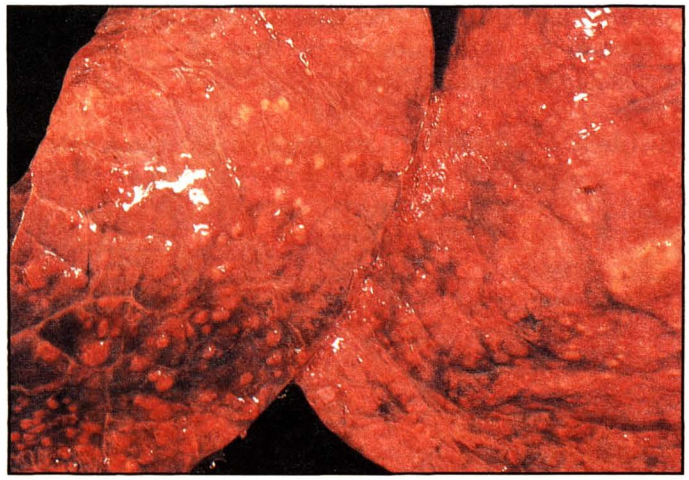

Figure 7. Bovine lung with bronchiectasis and bronchopneumonia where Haemophilous somnus and Mycoplasma bovis were both isolated. Note the raised nodular masses above the pleural surface are Mycoplasma bovis lesions.

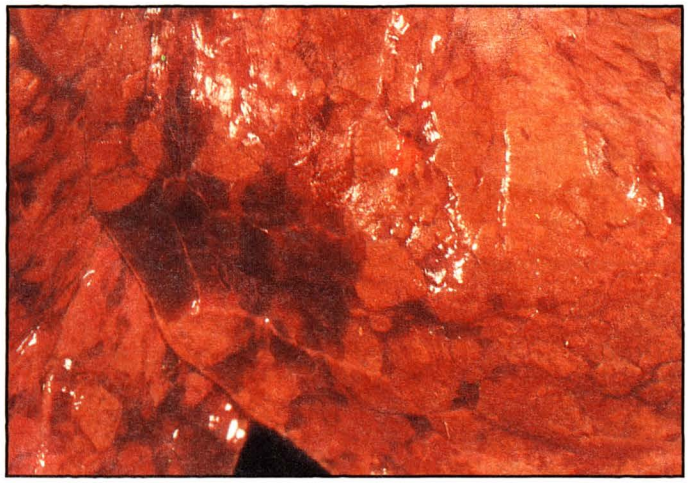

Figure 8. Multifocal lobular and coalescing patches of atelectasis, secondary to Hemophilus septicemia with thrombophlebitis.

Histopathologically, these are due to pulmonary thrombophlebitis.

An additional stage of pulmonary involvement is that of severe pulmonary congestion and edema usually associated with the encephalitic form of Haemophilosis, Figure 9. This suggests that a neurogenic mechanism in moribund cattle may act to produce the lung lesions secondary to the CNS involvement and is known as neurogenic edema, Figure 10.

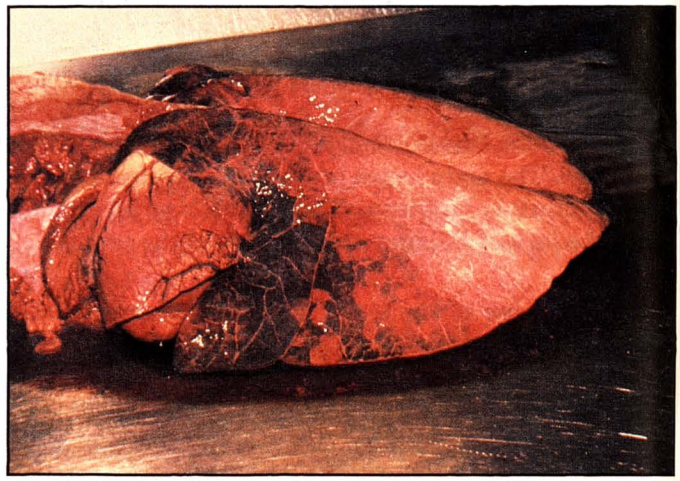

Figure 9. Pulmonary congestion and edema associated with encephalitic Haemophilosis, (ITEME).

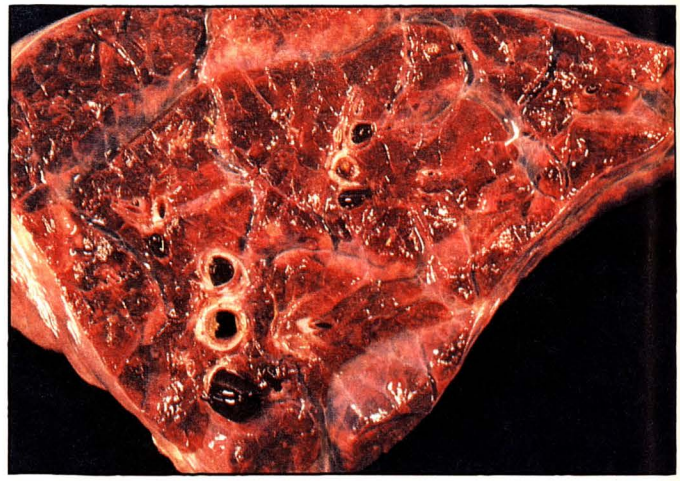

Figure 10. Pulmonary congestion and edema observed in a bovine where a definitive diagnosis of Rabies was made. A similar pulmonary lesion is often observed with encephalitic Haemophilosis or any other extensive CNS disease.

Clinically, pneumonia presents with a nonspecific pattern of signs. Whether the primary pathogen is *Haemophilus somnus*, *Pasteurella hemolytica* or *Pasteurella multocida*, calves are selected for subjective signs of depression. If calves are thereafter found to be febrile (≥ 40.0°C), they are considered to fit the working case definition of bovine respiratory disease. **This lack of pathogen specificity has meant writ-**

ers often label bovine respiratory disease as *undifferentiated.*

Diagnosis

A clinical diagnosis of *Haemophilus somnus* pneumonia is almost impossible to make using the broad case definition of ***undifferentiated fever and depression***. Eventually, additional signs like dyspnea, poor exercise tolerance, swollen joints or recumbency may develop that are more specific for Haemophilosis, yet not definitive. Laboratory evidence to support a diagnosis of Haemophilosis is usually unrewarding. Routine microbiological examination for *Haemophilus somnus* in the bacterial flora of the respiratory tract from healthy and BRD designated cattle showed little difference, Table 4.

Indeed, the isolation of *Haemophilus somnus* in the flora of the respiratory tract or blood stream is rare, whether done on weaned calves upon arrival or when they are selected as *sick*.[6] This low isolation rate is not at all in proportion with the cause specific mortality rates (Tables 1-3) unless infection and mortality rates are much the same.

This same difficulty in making a definitive diagnosis is present at necropsy as well. While the presence of *Haemophilus somnus* alone in the lungs can vary from 30-50%, (Tables 5-6) a definitive (differentiated) diagnosis of *Haemophilus somnus* pneumonia is rare. At least 50% of the time, the etiology is a mixture of agents and whether the differentiating technique is conventional histology and microbiology or the more precise immunoperoxidase stained histology,[15] Table 7, exact categorization remains elusive.

Table 7. Confirmation of H. somnus as an etiological agent in 49 selectively euthanized, chromically affected cattle by histopathology and immuno-histochemistry.[7]

	confirmed by	
Gross Diagnosis	**Histopathology**	**Immunohistochemistry**
Polyarthritis	4/17	3/17
Pleuritis	0/6	1/6
Bronchopneumonia	4/7	2/7
Fibrinous Pneumonia	3/13	3/13
Broncho Interstitial Pneumonia	1/1	0/1
Pericarditis	2/3	1/3
Cellulitis	0/1	0/1
Myocarditis	0/1	0/1

[7]From Janzen, *et al.* (14)

The use of necropsy examinations should be encouraged even if definitive individual diagnoses can not always be made. Often a ***group diagnosis*** made on a pen or block of pens can reveal underlying reasons, like *Mycoplasma bovis*, Figure 11,[16] immunocompetent *Bovine Virus diarrhea infection,*[17] (Figure 12, 13), like the post caval thrombotic syndrome, Figure 14, or other reasons, Figure 15, for an elevated treatment and mortality rate.

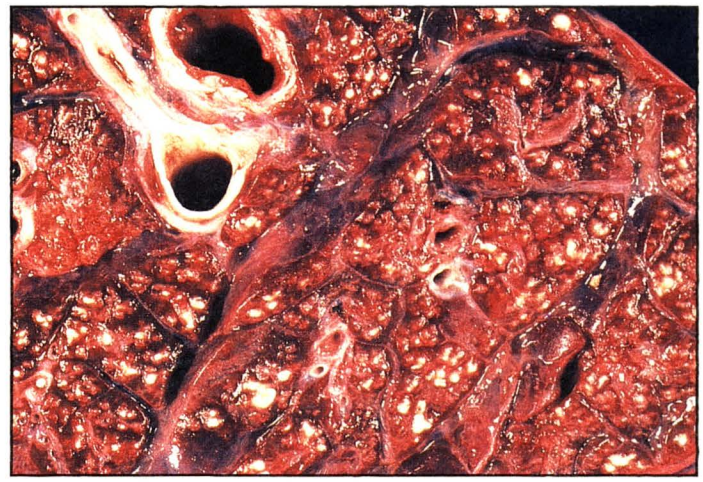

Figure 11. Lung with bronchiectasis typical of chronic Mycoplasma bovis involvement.

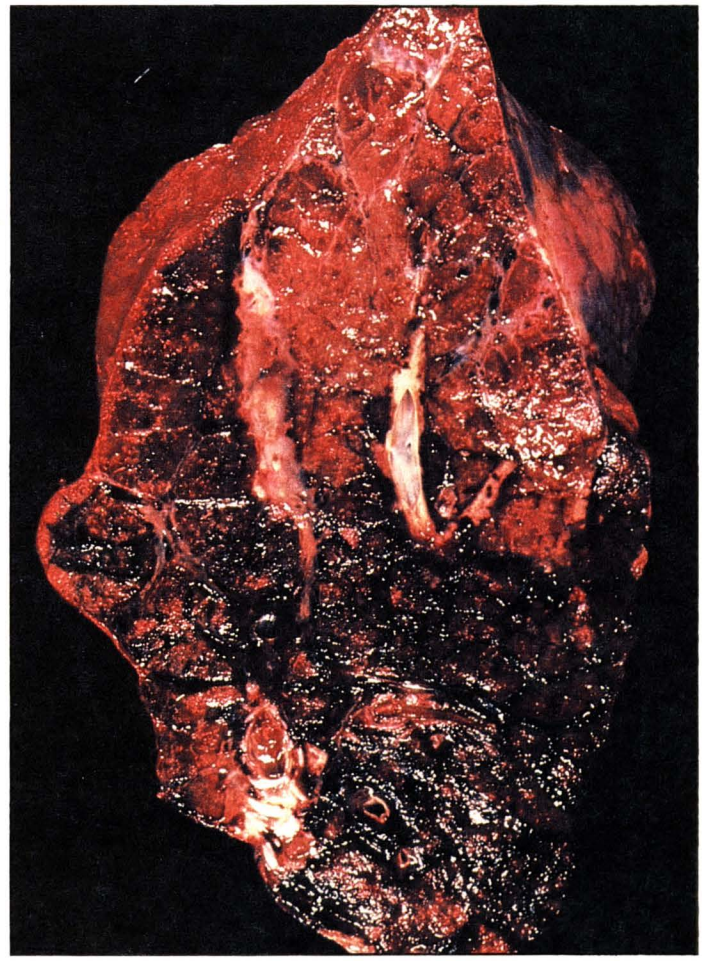

Figure 12. Bovine lung with severe hemorrhage into the alveoli, bronchi and interlobular spaces. This lesion is often associated with the hemorrhagic diathesis typical of infection with immunocompetent Bovine Virus Diarrhea Virus, Type II.

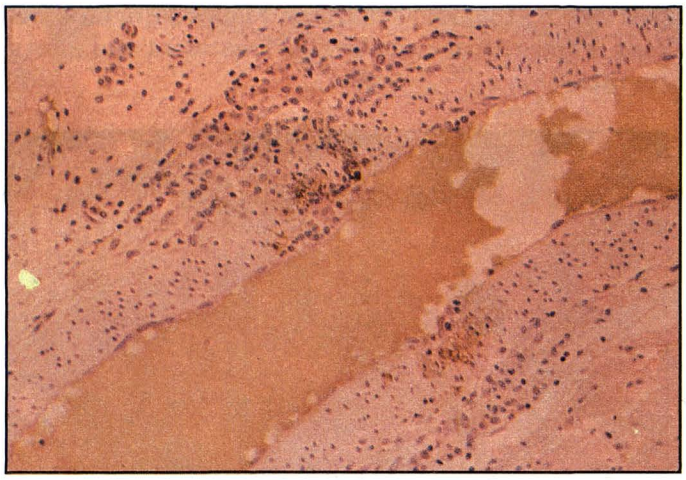

Figure 13. Photograph of a blood vessel that has been positively stained using immunoperoxidase for the Bovine Virus Diarrhea Virus

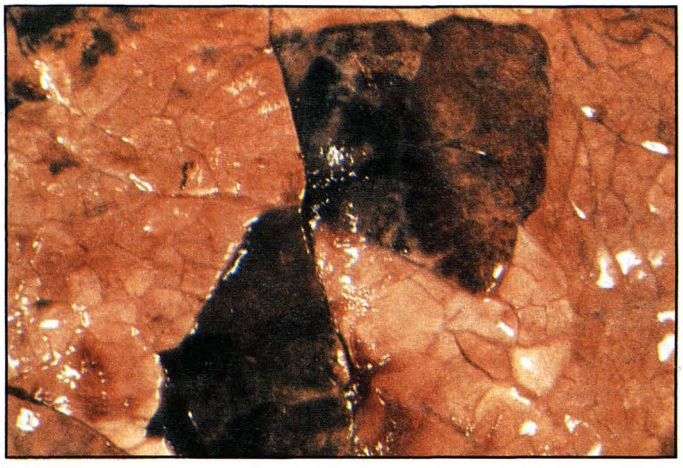

Figure 14. Lung with multiple locally extensive areas of suppurative pneumonia caused by micro-organisms carried by the posterior vena cava from an adjacent liver abscess.

Control

The case fatality rate remains very high in calves where a definitive diagnosis of pleuritic, myocardial or encephalitic Haemophilosis has been made. Mass individual injections of sustained action oxytetracycline do not appear to control Haemophilosis as well as they reduce respiratory disease mortality.[6] Some recent evidence[18,19] would suggest that mass medication in the feed may spare calves some mortality, in this case suggested to be Haemophilosis.

Vaccination with *Haemophilus somnus* bacterins[20,21,22,23] has been shown to significantly spare mortality, even if the significance of that sparing effect is lost as the feeding period progresses.[23] The bacterins available until the present time produced a serological

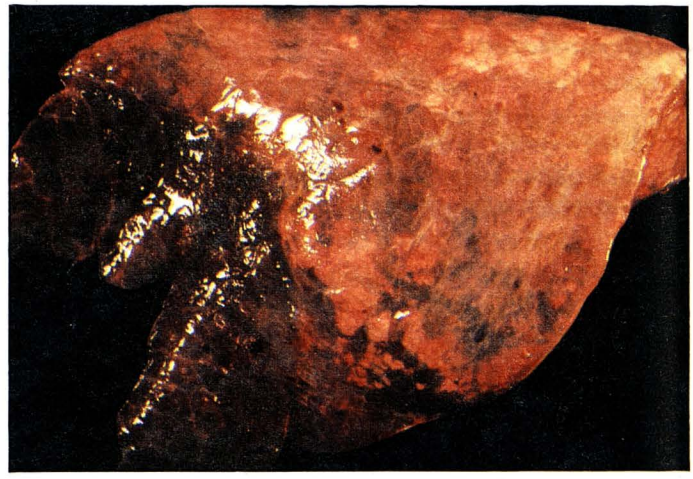

Figure 15. Lung typical of what some practitioners call "**upstairs-downstairs**" pneumonia. The upper ("upstairs") portion has a severe interstitial pneumonia, while the lower ("downstairs") lobes have an extensive bronchopneumonia.

response in 57% of single vaccinates and 80% of double vaccinates.[20]

Discussion

Haemophilosis would seem to be an important infection wherever large numbers of weaned calves are purchased and placed. The more dramatic manifestations of Haemophilus somnus (eg. HMI, pleuritis and TEME) infection would seem to be quite specific and therefore unlikely to be confused with other conditions. In addition, they can be easily ruled out by conventional laboratory means.

The same cannot be said for pneumonia. Investigators have reported that in some cases a pneumonia can be attributed to *Haemophilus somnus* alone. However, it is much more likely to report *Haemophilus somnus* as an organism that probably acts concomitantly with others in a pneumonic infection. It has been suggested by some[24] that based on serological evidence, *Haemophilus somnus* and *Pasteurella hemolytica* may act synergistically, and together increase the risk of fatality significantly.

There are several questions that remain about the biology of *Haemophilus somnus* infections. Over the years, investigators[6,9,20] have found a low prevalence of *Haemophilus somnus* isolation. This low rate of isolation almost mirrors the mortality rate often attributed to Haemophilosis. Does this mean that isolation of the organism and fatality are in some way associated and reflects an immunocompromise mechanism in the pathogenesis?

The distribution of lesions throughout all organ systems[2,3] and the characterization thereof led to the

conclusion that septicemia was the critical pathogenic mechanism. It was assumed that the infection began in the lungs after the organisms had entered via the bronchiolar tree. When the nervous system was the apparent primary target of *Haemophilus somnus*, pulmonary lesions were distributed similar to lesions in other organs. This same *pan* distribution of characteristic lesions is not as commonly observed now. Lesions would seem to be restricted to the thoracic cavity. This may be because lesions in other locations have healed, (the encephalitic form of the infection killed calves quicker; thus a diffuse distribution of lesions remained) or it takes longer for a "killer" HMI or pleuritis to develop.

It is also biologically possible that small changes in the genome of *Haemophilus somnus*, often barely detectable, may significantly alter its virulent expression. Some 30 years ago, Haemophilus somnus was a pathogen with a predilection for vascular and nervous tissue, whereas currently its primary pathology is often found and probably begins in the lung.

It is often speculated that the extensive use of "on arrival" mass mediation in BRD management programs in Western Canada has selected for an increased prevalence of Haemophilus somnus infections. While it is true that in recent years mortality caused by Haemophilosis has become more notable, the association between the two has not been firmly established.

Haemophilous somnus would appear to be an opportunist in the bovine respiratory tract. Its virulence might even be enhanced by a concomitant infection with *Pasteurella hemolytica*. Clinically, which pulmonary pathogen is to be incriminated with certainty is almost impossible and may not really be appropriate because it would hardly change the disease management strategy. A definitive diagnosis of Haemophilosis at necropsy often is enigmatic as well, given the collage of possible pathogens, to the extent that Bovine Respiratory Disease remains truly undifferentiated.

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