

RESPIRATORY DISEASE OF NEONATAL DAIRY CALVES: SEROLOGICAL,  
BACTERIOLOGICAL AND PATHOLOGICAL STUDIES

by

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D.V.M., Universidad Centro Occidental, Venezuela, 1973

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A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY

Manhattan, Kansas

1978

Approved by:

  
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Document 1

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1972

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## INTRODUCTION

Despite the effort that has been devoted to understanding, preventing and controlling respiratory tract disease of cattle, and the huge volume of literature on this subject, it still remains the most costly and troublesome disease problem in cattle in most parts of the world. The heavy economic losses associated with these infections are due, in part, to the fact that they affect cattle of all types and ages, these diseases tend to recur and they lend themselves poorly to preventive or therapeutic measures (McKercher, 1968). There is a three-way economic loss incurred in combatting this group of maladies: first by death of the animal, second by treatment of sick animals and third by weight loss in sick animals or those with a subclinical or unapparent infection.

In 1973, Oxender et al. surveyed 77 Michigan dairy herds and reported that pneumonia (41% of the herds) was one of the major health problems in young calves. Lillie (1974) estimated that 40% to 80% of all cattle diseases involve the respiratory tract. In 1976, Jensen et al. reported a survey of 407,000 yearling feedlot cattle and found that 75% of the clinical diagnoses and 64% of the necropsy diagnoses were respiratory tract diseases.

Willadsen et al. (1977) found that the overall respiratory disease attack rate among calves from birth to six

months was 23%; the respiratory disease case fatality rate was 40%, and the mortality rate was 9%. Also, according to the same studies, the mortality rate due to ailments other than respiratory disease was 11% and the overall mortality rate during the first six months of life was 20%.

Respiratory diseases rank first in economic importance (McKercher, 1968). These infections are extremely costly for several reasons: immunity is generally poor and as a result, they tend to recur periodically; vaccination is of limited value; and antibiotic therapy must be extensively applied to control the disease. Treatment may be life-saving, but loss in production by surviving animals may result in economic liability.

Anon (1974) estimated the total losses involved in relation to bovine respiratory tract diseases at 225 million dollars per year, and Herrick (1969) estimated that these maladies cost \$10 to \$20 for every calf in a feedlot.

New information has been obtained in relation to the etiology, pathogenesis and epizootiology of respiratory diseases in cattle. This information has given promise of practical solutions, however, we are confronted with the fact that these infections still constitute a big problem to the bovine industry. This situation re-emphasizes the magnitude and complexity of the problem.

The present study was carried out in an effort to clarify some of the problems regarding the bovine respiratory complex.



## LITERATURE REVIEW

### Serology and Immunology

#### I. Epizootiology

Bovine respiratory infections have been recognized for many years as one of the bigger problems with which persons connected with the cattle industry have to deal with. An exact estimate of the economic losses to this industry caused by clinical and subclinical respiratory disease is difficult to assess. Respiratory infections are not reportable which makes it difficult to determine their distribution and incidence other than by isolation and serological studies. However, by these means, it has been demonstrated that bovine respiratory infections are widespread throughout the world.

The etiology and related factors of bovine respiratory diseases are complex and imperfectly understood, however, most of the work done on the subject seems to agree with the fact that different factors associated with onset of the syndrome fall into three categories: stress, viral infection and bacterial infection. Some authors have implied other factors in the production of respiratory disease in cattle, i.e., chronic or hereditary pulmonary lesions which may serve as a deposit for bacteria and viruses and so, enhanced susceptibility to disease (Rosner, 1968).

Many bacteria and viruses have been isolated and associated with respiratory disease in cattle, however, some



have been reported in many parts of the world with significant frequency for many years. Included in this group are Infectious Bovine Rhinotracheitis virus (Miller, 1955; Madin et al., 1956; York, 1968; McKercher, 1968; Jensen, 1971; Bruner and Gillespie, 1973; Durham, 1977); Bovine Viral Diarrhea virus (Horlein, 1959; McKercher, 1968; Jensen, 1971; Rosenquist, 1974); Parainfluenza 3 virus (Reisinger et al., 1959; Woods, 1968; Sweat, 1967; Rosenquist, 1970 and 1974; Durham, 1977) and Pasteurella spp. bacteria (Rosner, 1971; Jensen, 1976; Bitsh, 1976). The epizootiology of these agents will be reviewed next.

A. Infectious Bovine Rhinotracheitis Virus (IBR).

Infectious Bovine Rhinotracheitis virus, a herpesvirus, is cited by McKercher (1968) as one of two viruses capable to produce disease in the bovine respiratory tract by itself. The virus is known mainly as a respiratory tract pathogen, but it has also been related to conjunctivitis, infectious pustular vulvovaginitis, abortion, balanoposthitis and encephalitis (Merck Manual, 1973; Phillip, 1970; Kahrs, 1977).

The virus affects mainly cattle (Merck Manual, 1973), but infection has been reported in mule deer (Bruner and Gillespie, 1973), goat (McKercher, 1973), swine (Nelson, 1972), and water buffalo (St. George, 1972). The morbidity is high because the virus tends to induce persistent infection (Carter, 1973; Hyland, 1974; Kahrs, 1977) and because large quantities of virus are shed in respiratory, ocular and reproductive secretions of infected cattle (Snowdon,

1965; Kahrs, 1977) thus, providing a large inoculum for other cattle.

Several authors state that the virus affects all breeds and ages of cattle (Custis, 1966; Harbourne, 1966; Hyland et al., 1974) and the virus is persistent or latent in a herd once a field strain or a live virus vaccine has been introduced. Many animals respond several times per year to infections with IBR.

Curtis (1966) found the morbidity rate in infected feedlot cattle to be 50% whereas the mortality was only 1%. On the other hand, when the disease involved young calves, the morbidity reached 100% and the mortality 50%. Kahrs (1977) supports these figures saying that the case fatality rate is considerably higher in young calves (less than two weeks old) than in adults.

In contrast to the former reports, Harbourne (1966) published a serological survey of paired samples of cattle suffering from a respiratory disorder and his results demonstrated low IBR antibody levels in the three farms tested. Reed et al. (1973) published a paper on a systemic form of IBR infection in young calves with low morbidity but with a high death rate among clinically ill calves. The author was unsuccessful in isolating IBR virus from pulmonary tissue, but isolated the virus from gut, liver, kidney and cerebrum. Burgess (1977) reported from an intensive study of six young calves over a period of 14 months that active infection with IBR virus was not demonstrated

and this infers that IBR virus infections occur more commonly later in life.

In relation to the incidence of IBR virus serum antibodies, Kahrs et al. (1963) reported a 12% incidence of IBR from herds in New York state. Fastier and Hansen (1966) reported in their studies on the distribution of IBR serum antibodies in dairy herds with a history of persistent respiratory illness. They found that 81.6% of the surveyed animals possessed antibodies against IBR virus. They also surveyed a herd of 60 cows in which respiratory disease was not considered endemic and found 36% of the animals with antibodies against IBR virus. In the same survey, regardless of clinical history and possible earlier IBR virus vaccination, 73% of the animals were positive to IBR virus serum antibodies.

Chow (1961) surveyed 42 counties in California and reported that 34 counties contained range cattle with antibodies titers to IBR virus (greater than 50 titer); 5 counties were classified as doubtful (32 to 50 titer); and three counties negative (less than 32 titer). However, he pointed out that the small number of samples taken in the negative counties in relation to the other counties could be the reason for the negative results.

In 1974, Durham and Forbes-Faulkner reported that 32% of the serum submitted over an 18 month period from most areas of New Zealand possessed antibodies against IBR virus. They pointed out that 33% of animals with enteric disease and 50%

of the animals with respiratory disease had positive IBR virus titers. Dean and Burgess (1976) surveyed cattle older than 1-1/2 years and found 97.5% of samples positive (titers of 2 and more) to antibodies against IBR virus.

#### B. Bovine Viral Diarrhea - Mucosal Disease Virus.

The name Bovine Viral Diarrhea-Mucosal disease was adopted in 1971 during a Bovine Respiratory Symposium of the American Veterinary Medical Association. Under that denomination are included a group of syndromes described earlier as two different entities (Olafson et al., 1946; Ramsey and Chivers, 1953). Currently, the etiological identity of the two diseases is recognized and commonly referred to as Bovine Virus Diarrhea (BVD).

The disease is worldwide in distribution (Horlein, 1959; McKercher, 1968; Jensen, 1971; Phillip, 1971; Rosenquist, 1974; Durham, 1977) and affects cattle of all breeds and ages but young animals are said to be most susceptible to the disease (Bruner and Gillespie, 1973). Blod and Henderson (1976) state that the greatest incidence occurs in animals between 8 months and two years of age and some authors report the disease occurring most commonly in animals between 6 to 24 months of age. BVD is transmitted by contact under natural conditions (McKercher, 1968; Merck Manual, 1973; Blood and Henderson (1974) and cattle seem to be the only affected specie (Blood and Henderson, 1974), but Kahrs (1964) found neutralizing antibodies in the sera of white tailed deer from New York state. Serum antibodies to BVD in sheep

have also been found in Germany (Bogel, 1964), Australia (French and Snowden, 1964), New Zealand (Robinson, 1971), U.S.A. (Seibol and Dougherty, 1967) and Central Africa (Provost et al., 1967). Stewart et al. (1971) suggested that BVD virus occurs as a natural infection without signs of illness in domestic swine in the United States. Recently, Schipper et al. (1978) reported the isolation of BVD virus from a 1 week old foal.

In relation to serological incidence, Newberne et al. (1961) reported the per cent of positive serum in animals from the states of Illinois, Iowa and Nebraska and found 59%, 69% and 73% respectively. Pritchard (1963) stated that BVD virus infection is one of the most common in the U.S.A. Knaizeff (1963), in his analysis of serum samples in 22 counties of Florida, found 65% of beef cattle and 61% of dairy cattle were positive for BVD antibodies.

Kahrs et al. (1963) reported that 53% of the animals in the average herd in New York state had antibodies to BVD virus. Taylor (1968), working in Nigeria, found 19% of native cattle were positive to BVD virus by serum determinations. St. George et al. (1969) stated that 50% of the cattle in Great Britain and 89% in Australia are serologically positive to BVD infection. Robinson (1971) reported an incidence of 66% (1:8 dilution) or greater in serum tested from New Zealand. Hafez et al. (1976) reported from Germany that 48% of the serum had neutralizing activity against six strains of BVD virus.



C. Parainfluenza 3 Virus (PI3). Following the first isolation and identification of PI3 virus from cattle (Reisinger et al., 1959), the virus was isolated from several species of domestic animals (horses, sheep and goat). PI3 virus has also been associated with persistent respiratory infection (Gross et al., 1973 and 1974) and bloody diarrhea (Arunson et al., 1974) in man; has been isolated from the prepuce of bulls (Dennet et al., 1973) and also has been reported in association with encephalopathy in cattle (Munday et al., 1976).

The incrimination of the virus in bovine respiratory disease has been reported for many years (Reisinger et al., 1959; Abinanti, 1961; Horlein, 1957; McKercher, 1968; Jensen, 1971; Rosenquist, 1974; Durham, 1977) and generally speaking, no herd has escaped infection from this virus (McKlurkin, 1976). Serological evidence and isolation from widely separated areas indicates that PI3 virus is worldwide (Betts, et al., 1964; Omar, 1966; Ide, 1970; Kramer, 1973; Kahrs, 1976).

Mortality rates are said to be small compared with morbidity (Burroughs, 1967a). Patterson (1962) suggested that the first infection is the most serious while subsequent infections are either mild or not productive of disease. The morbidity and incidence of PI3 are well established, however, its pathogenicity has been questioned (Potgeiter, 1977).

In 1966, Harbourne reported as a result of his experiments that the overall morbidity rate for PI3 virus was 58%

and the mortality rate was 6%. Betts et al. (1964) were unable to obtain calves free of antibodies against PI3 virus for use in experimental studies (cited by Burroughs, 1967a) suggesting a high morbidity for PI3 virus infection.

In relation to serological incidence, several papers have been published on this subject. In Sweden, Bakos and Dinter (1960) demonstrated antibodies in 70% of cows and in 50% of calves tested. Abinanti et al. (1961) found in the United States a distribution by states ranging from 53% to 95%. They reported the presence of P 3 antibodies in at least 70% of the market cattle samples.

Kramer et al. (1961) reported that of 2843 cattle tested in Nebraska, 86% had been exposed and reacted immunologically to PI3 virus. Kahrs et al. (1963) reported a 48% average incidence per herd of PI3 antibodies in New York state.

Dawson and Darby (1964) demonstrated in the United Kingdom that approximately 85% of the cattle population and 95% of cattle of breeding age had serum antibodies to PI3 virus. Fastier and Hansen (1966), working in New Zealand, found that 98% of 118 cows with respiratory disease and 58% of relatively healthy herds showed serum titers against PI3 virus. Harbourne (1966) reported that 82% of cattle in herds where there had been an outbreak of pneumonia showed positive titers to PI3 virus. Burroughs (1967), studying natural infection of dairy cattle, found that at least 96% of the milking cows tested and 50% of the calves over 5 months had hamagglutination-inhibition antibodies to PI3 virus.



St. George (1971) has shown that at least 87% of sheep flocks in Australia have antibodies to PI3. Kramer et al. (1963) surveyed 2843 cattle blood samples in Nebraska submitted for brucellosis examination and found that 86% of the sampled serum had antibodies of 1:20 or more to PI3 virus. Taylor et al. (1975) reported from Nigeria that using a base line of 1:8, approximately 65% of cattle, 60% of sheep and 50% of goat had evidence of previous exposure to PI3 virus. Moreno-Lopez et al. (1976) found that from 230 calves 3- to 4-weeks old, 199 had antibodies against PI3 virus.

## II. Immunocompetence of the Bovine Fetus

The bovine fetus has been shown to be immunologically competent for a variety of antigens before birth.

Klaus et al. (1969), working with young calves, found that the calf is not agammaglobulinemic at birth. Kniazef and Rimer (1967) tested a pool of serum from fetal calves to gammaglobulins and reported that approximately 40% of the sera tested contained significant amounts of gammaglobulins. McCoy et al. (1967) found a small amount of gammaglobulins in calves before suckling colostrum and stated that calves do not obtain all gammaglobulins by colostrum absorption. Kirbride et al. (1977) made a comparison of immunoglobulin concentration between aborted and abbatoir fetuses and found that both showed immunoglobulins levels.

McEwan et al. (1970) suggested that the ability to produce antibodies in response to certain forms of antigenic

stimulation is present at birth in the bovine specie. Schultz et al. (1971a), using the radial immunodiffusion test found that 90% of the fetuses from 235 days of gestation to birth had immunoglobulins in their serum. Schultz also demonstrated in 1973 that the calf, like the adult, is able to produce immunoglobulins. Mohenda and Merriman (1971), analyzing pre-colostral and post-colostral serums of Holstein calves, found immunoglobulins in their serum and suggested that the developing fetus may be capable of independent immune response. In 1973, Schultz concluded that fetuses become immunologically competent to IBR, BVD, and PI3 at approximately 90 to 120 days of gestation.

Conversely, some authors have failed in detecting immunoglobulins in the serum of calves before feeding colostrum. Kendrick and Franchi (1974), working on BVD, stated that antibodies are not present in serum samples of calves before feeding colostrum. Mohar and Gonzalez-Rubiera (1976) did not find gammaglobulins before colostrum feeding in any of their tested calves and cited Brambel (1958), Hommings (1961) and Marinescus (1971) as agreeing with their findings. Stone and Gitter (1969), Rice and Carrier (1969) and Thorton et al. (1972) also reported failure in demonstrating immunoglobulins in the serum of calves that had not received colostrum.

### III. Origin and Type of Colostral Immunoglobulins

The fact that transfer of antibodies from dam to fetus

in the domestic ruminants species does not occur is generally accepted, therefore, calves are generally agammaglobulinemic or hypoglobulinemic at birth (Frontiers of Biology, 1971).

Cellular immunity may be suppressed for a time after birth due to production of glucocorticoids associated with parturition (Osburn, 1974). In addition, a response to antigenic stimulation may require several days to produce significant number of sensitive lymphocytes. Thus, passive transfer of colostral immunoglobulins from the dam is the most important immediate immunologic protection available to the newborn calf.

Several studies in test suckle calves have shown that low levels of immunoglobulin increase the risk of infectious diseases and subsequent death and calves with high serum immunoglobulin concentration are able to better resist the common neonatal infectious diseases. In relation to the kind of immunoglobulins transferred, it is worthwhile to recall that three different classes of immunoglobulins have been identified in cattle: immunoglobulin G (IgG), immunoglobulin M (IgM) and immunoglobulin A (IgA) (Butler, 1971). Two subclasses of IgG are currently recognized: IgG1 and IgG2. IgG1 is normally the most abundant immunoglobulin in the serum and lacteal secretion of the bovine species (Butler, 1970 symposium). Oyeniya and Hunter (1978) found that up to 86% of immunoglobulins in colostrum are immunoglobulin G.

Bovine IgG1 accumulates in very high levels in colostral and precolostral lacteal secretions by a mechanism which

selectively transports it from the serum. Oyeniya and Hunter (1978) stated that the bulk of colostrum immunoglobulins are derived by active transport across the alveolar epithelium rather than by synthesis in the gland. Mach et al. (1970) stated that the bovine mammary gland has acquired a special function of transporting IgG from serum to colostrum or milk because of the impossibility of transferring immunoglobulins to the fetus through the placenta. Smith (1970) showed that the hormones, estrogen and progesterone, are involved in the control of this selective transport of immunoglobulins.

Conversely, Yurchak et al. (1970) postulated that the mammary gland is unique in that it apparently both produces immunoglobulins locally and also transports large amounts of IgG1 from the serum. Lascelles (1966 and 1970) showed that besides the substantial serum transfer of IgG1, immunoglobulins such as IgA and perhaps some IgM may be synthesized locally.

#### IV. Absorption of Immunoglobulins by the Fetus

Several authors have demonstrated that after ingestion of colostrum there is a marked increase in the total serum protein concentration in the calf due primarily to absorption of colostral immunoglobulins. This immunoglobulin absorption occurs significantly only during a brief interval after birth reaching a peak immunoglobulin concentration in the serum of calves at 24 hours after birth (Staley, 1971).

Klaus et al. (1969) reported from their experiments

that ingestion of colostrum led to a rapid increase in serum IgM and IgG concentrations within 24 hours after birth and these antibodies reached a peak level within the first 48 hours of life. They also reported that both IgG and IgM were absorbed equally well and that the degree of immunoglobulin absorption varies considerably from calf to calf. Some calves may remain virtually agammaglobulinemic despite the ingestion of colostrum.

Considering the site of immunoglobulin absorption, Comline et al. (1951) showed that in newborn calves the absorption of colostral immunoglobulins occur entirely in the small intestine and that none is absorbed from the abomasum or large intestine. They also showed that transport of the absorbed immunoglobulin to the circulation is entirely lymphatic and that none enters the fetal circulation directly. Jubb and Kenedy (1970) stated that there is good cytological evidence that immunoglobulins enter as globules of colostrum directly into the epithelial cells lining the small intestine by absorption of globules onto the cell surface followed by invagination and the enclosure in microdroplets.

There is evidence that the absence of proteolytic activity in the digestive tract of the newborn calf may facilitate the colostral proteins reaching the small intestine without degradation. Colostral trypsin inhibitor may contribute (Baintner, 1976) to this process and thus absorption is affected by the epithelial cells of both jejunum and ileum (Frontiers of Biology, 1971).



In relation to the duration of gut permeability to immunoglobulin absorption, Johnston et al. (1977) claimed that the mechanisms of absorption through the gut ceases by 24 to 36 hours of age and in some cases much earlier than this. Oyeniyi and Hunter (1978) stated that gut absorption of immunoglobulins ceases by 36 hours postpartum, but pointed out that they still can function partially in the gut lumen to control bacterial populations.

Selman et al. (1971) emphasize the value of very early feeding of colostrum. They showed that calves fed after six hours of birth had considerably lower immunoglobulins levels than calves fed colostrum before six hours of life.

#### V. The Decline of Colostral Immunoglobulins in the Calf's Serum

It has been cited that the normal calves that ingest colostrum will reach the maximum concentration of serum immunoglobulins by the second day of life. After that, there is a period when the decline in the passively acquired globulins overlaps the rise in autogeneous gammaglobulins and tends to obscure it. Determination of the rate of disappearance of the one is complicated by the rate of appearance of the other. There are numerous estimates of the age which a hypothetical average calf is certain to be free of colostrally acquired immunity and high variability has been reported. Jubb and Kenedy (1970) stated that passive immunity acquired through the colostrum is in large part lost by the third or

fourth week of age. Whereas Kahrs (1976) estimated 6 to 8 months of maternal serum antibodies persistence to BVD virus.

#### VI. Factors Influencing Immunoglobulins Levels in Young Calves

Several factors have been reported in association with the variability of immunoglobulin levels in young calves. Some of them are:

1. Timing of the first feeding of colostrum. As far back in history as 1921, Howe demonstrated that there was a large increase in the gammaglobulins of the serum of a calf that received a first feeding of colostrum 5 hours after birth. There was only a small increase above that level in those calves that had been fed colostrum 21 hours after birth.

Selman et al. (1971) reported significantly higher immunoglobulin concentrations in calves fed the first 6 hours postpartum in comparison to calves fed later. McClurkin (1976) reported that feeding colostrum in relation to experimental exposure revealed that colostrum had to be fed before experimental exposure if it were to protect the calf. Feeding colostrum within 30 minutes after exposure failed to protect the calf, and acute fatal disease developed. Oyeniya and Hunter (1978) found that colostrum given 12 and 24 hours postpartum contained only 78.3% and 47% levels of IgG as that secreted at parturition.

2. Calf's individual factors. All calves do not receive maternal immunity and it diminishes at different



ages in different calves (Kahrs, 1976). Fey and Margadant (1961) offer evidence that some calves have an inherent inability to establish or maintain a normal titer of gamma-globulins even when the immunoglobulins have been obtained in the colostrum of the dam.

Smith (1967) stated that it is probable that the immunoglobulins levels in the serum of calves kept under ordinary conditions are determined to a considerable extent by the ability of their alimentary tract to absorb immunoglobulins from colostrum or not to digest them, and that calves vary greatly in this respect. Genetical or congenital factors may be involved in this variability. Sawyer et al. (1977) working on lambs found that 14% of clinically normal lambs demonstrated some failure of passive transfer whereas 46% of 59 lambs dying of natural causes showed failure of passive transfer. Klaus et al. (1969) claimed that three of ten calves remained virtually agammaglobulinemic despite the ingestion of colostrum. Bush et al. (1971) reported that 4 of 27 calves remained hypogammaglobulinemic despite normal intake of colostrum during the first 24 hours of life.

3. Seasonal variations. Gay et al. (1965) showed that gammaglobulins levels in calves are high in the months of July, August and September but reach very low levels during November, December, January and February. They were of the opinion that the seasonal variations in immunoglobulins levels might offer some explanations for the seasonal differences in calf mortality that occurs in Scotland.

Selman et al. (1971) found that a seasonal variation did exist in the serum immunoglobulins concentrations of newborn dairy heifer calves.

Contrary to the former reports, Smith et al. (1967) found no relationship between the time of year when a calf was born and its immune globulin level.

4. Management. In 1971, Selman et al. reported that the mean serum immunoglobulins concentration of field-born calves was significantly higher than those of the box stall. They also reported significantly elevated serum immunoglobulins concentrations in those calves which were left with their dams for more than 12 hours.

Barber (1971) found that suckled calves had significantly higher gammaglobulins levels than pail-fed calves despite the fact that pail-fed calves were allowed to remain with their dams for 24 hours.

Logan (1977) found that poor husbandry did not have an apparent influence on immunoglobulin concentration in colostrum, but it had a profound effect on the colostrum yield of the first milking. Total colostrum immunoglobulins secreted by well-fed housed cows were nearly three times greater than immunoglobulins secreted by cows which had received no supplementary feeding and fed outdoors. Leech et al. (1968) emphasized that apparent regional differences in neonatal mortality might well reflect regional differences in management.

Selman (1971) suggested that management differences

associated with summer and winter calving might be responsible for the marked seasonal variation already noted in the serum immunoglobulins concentrations of newborn Ayrshire bull calves.

5. Breed. Johnson and Harpestad (1970) found that calf mortality is higher in Guernsey herds than in Holstein herds. Kruse (1970) reported that cows of the Danish black and white breed produced higher yields of colostrum with a lower per cent of immunoglobulins than cows of the Danish red and white breed.

Selman et al. (1971) found that the mortality rate for Ayrshire calves was 14% whereas that for Friesans and Friesan-cross - Ayrshire - was 6%. They pointed out that apparent breed differences in mortality rate might reflect variations in early calf management. They also cited Withers (1952 and 1953), Blackmore et al. (1968) and Leech et al. (1968) in relation to studies indicating breed variations in susceptibility to neonatal disease and death.

Schultz et al. (1971) reported from their in vitro experiments that Holstein-Friesian, Ayrshire, and Guernsey calves showed a similar grade of immune response whereas Brown Swiss calves were able to mount a greater response.

6. Other factors. Logan et al. (1972), feeding calves at approximately the same time after birth, found a marked variation in individual serum immunoglobulins levels and postulated that those differences were the result of both

intake and quality of colostrum.

Oyeniyi and Hunter (1978) found that the amount of IgG in Holstein colostrum from cows beginning their first, second or third lactation did not differ, but cows beginning their fourth through seventh lactation had more IgG in colostrum. They also reported that the rate of disappearance of IgG from colostrum was greater in the younger animals.

#### VII. Bovine Immune Response to Respiratory Infections of Viral Etiology

Viruses represent a structurally and biochemically diverse group of infectious agents and several mechanisms of defense have been developed in order to protect the host against viral infection and disease. There are three principal components which contribute to host defense against viral infections: antibodies, cell-mediated immunity and interferon (Fudenberg et al., 1976).

The formerly cited authors also stated that antibodies in secretions are better correlated with resistance to infection than serum titers followed by subsequent rechallenge with a live virus. Thus, immunity to many respiratory viruses which produce their disease locally in the mucosa seems to be mediated by IgA antibodies.

Todd (1971) postulated that viruses which replicate extensively in cells of the respiratory tract epithelium evoke both humoral and secretory response (PI3 and IBR viruses), whereas viruses such as BVD which do not depend upon respiratory tract cells for primary replication do not

induce the formation of secretory antibodies. He also postulated that secretory and humoral antibodies mechanisms are functionally independent.

Morein and Moreno-Lopez (1973a), dealing with a skin hypersensitivity test, showed that cell mediated immunity participates in the immune response of cattle to PI3, whereas Shope et al. (1976) suggested an essential role for humoral passive antibody, but not for cellular immunity in protection from primary systemic viral infection.

#### 1. Host defense against PI3 virus.

a) Passive immunity. Sweat (1967) showed evidence that maternal antibodies to PI3 virus are passed in the colostrum and provides a passive protection to the calves in levels equal to or even greater than those of the dam. Rosner (1971) also supports the former assumption. Moreno-Lopez et al. (1976) made a good differentiation between active and passive PI3 virus immunity in calves with a skin hypersensitivity test. They evaluated cell mediated immunity by their skin test in a relatively large population of calves 1 to 4 weeks old and found that most of the calves were seropositive.

The seropositive animals were negative by skin test demonstrating the maternal origin of serum antibodies. They also demonstrated that the presence of maternal antibodies did not inhibit the induction of skin hypersensitivity by intranasal vaccination.



b) Active immunity. Active immunity against PI3 virus develops in calves with no colostral protection when the animal becomes in contact with PI3 virus. Sweat (1967) postulated that colostral antibodies levels against PI3 virus decrease with age and are no longer detectable by weaning time at 6 to 8 months of age. Conversely, Dawson (1966) stated that passive immunity against PI3 in individual calves varies from 10 to 23 weeks.

Todd (1971) exposed 8 calves devoid of neutralizing antibodies against PI3 to experimental infection with PI3 virus or PI3 and IBR virus and found that antibodies were present in serum from 1 of 8 calves on day 7; 3 of 8 calves on day 8; 6 of 8 calves on day 9; and 8 of 8 calves on day 10. Titers of serum antibodies were maximal on days 12 to 14 and were receding by post-exposure day 21. He also reported that concurrent infections with IBR virus had no apparent effect on the time required for PI3 antibodies to appear; however, maximum serum antibodies titers to PI3 were 4-fold higher in calves with the combination infection than in calves infected with PI3 virus alone. Nasal antibodies against PI3 were present in all calves on days 14, 17 and 21 in titers of 1:3 to  $\geq 1:12$  (serum neutralization test).

Morein and Moreno-Lopez (1973a) demonstrated that cell mediated immunity participated in the immune response to PI3 virus, however, they suggested that active immunity is not present in young calves.

It seems that the first defense of the host against PI3

virus infection is the production of neuraminidase inhibition titers. According to Morein et al. (1973b), all animals which respond with a significant rise of hemoagglutination-inhibition titers in serum and nasal secretions to systemic or local infection respond also with an increase of neuraminidase-inhibition titers in these body fluids.

c) Serum titer and its relation to protection against infection. Lennet and Schmidt (1964) proposed a minimum dilution of 1:8 for use in human diagnostic tests for PI3 infection. St. George (1971), working in lambs, suggested that reaction at the dilution of 1:4 may not be evidence of infection. Taylor (1975) established a base line of 1:8 as an indicator of past infection. Rosner (1971) established a hemoagglutination-inhibition antibody titer of 1:32 or greater as being protective.

## 2. Host defense against IBR virus.

a) Passive immunity. Bruner and Gillespie (1973) postulated that maternal antibodies are readily detected in calves from immune dams and that those antibodies can persist in the calf's serum up to 4 months of age. Hyland et al. (1974) found IBR serum antibodies in calves ages 2-4 weeks. They pointed out that the antibody was lost within 4 months suggesting that it may have been colostrum antibodies.

Kahrs (1977) stated that colostrum antibodies are measurable in the serum of a calf that suckles an immune mother on the first day of life. He also postulated that some



calves lose their maternal antibodies as early as one month of age, but a few may still have detectable antibodies at 6 months of age.

Langer (1960) supported the protective value of maternal antibodies in resistance to infection and disease from IBR virus.

b) Active immunity, viral persistence and latency or carrier state. Studies on IBR-interferon-induced production and studies of the role of cell-mediated immunity in suppressing reactivation of latent infections indicate that immunity to IBR involve complex interactions which can not be explained on the basis of humoral antibodies alone (Kahrs, 1977; Sheffy and Rodman, 1973; Hall and Minocha, 1977).

Mohanty et al. (1972) supported the former statement reporting that calves recovered from respiratory infection with a virulent strain of herpesvirus had no detectable antibodies to the virus but were immune to challenge 8 weeks later. Curtis et al. (1966) stated that there is a poor correlation between circulating antibodies and immunity to IBR. They consistently isolated the virus from clinical cases exhibiting high virus neutralizing antibodies (1:64 - 1:256) and such levels would effectively prevent clinical disease to other virus diseases.

Gerber et al. (1978) showed that intranasal vaccination with a temperature-sensitive mutant of IBR stimulated local cell-mediated immunity and antibody response. Intramuscular

vaccination also stimulated local cell-mediated immunity and antibody response as well as systemic cell-mediated immunity and antibody response to IBR virus.

In relation to the beginning and the duration of immunity, McKercher (1959) indicated that immunity is present by the 12th day following exposure to the virus and resistance persists for at least 14 months. Average readings of the group indicate that antibodies in detectable quantity 8 to 12 days following exposure. After a slight decline, the titer continues to raise gradually for 10 months by which time it attains its peak.

Todd (1971) found that antibodies against IBR virus were first detected on post-exposure day 8 and that serum antibodies reached its maximal levels on days 14 to 21, titers receded somewhat by days 31 to 45. He also reported that concurrent infection with BVD virus apparently delayed the appearance of serum antibodies against IBR virus and resulted in maximal titers 4-fold lower than those detected in sera of calves exposed to IBR or to IBR and PI3 combination. The recovery of virus from calves experimentally infected with IBR lasted 10 to 13 days.

Snowdon (1965) stated that IBR virus is most frequently recovered from nasal secretion of susceptible animals 6-12 days after experimental infection, however, the virus can be recovered from nasal swabs up to 510 days after intravenous inoculation. Hyland (1975) found that cow herds that had recurrent to persistent disease seemed to have consistently

high IBR virus antibodies levels, perhaps due to constant antigenic stimulation of antibody forming cells. They also provided evidence that IBR occurred sporadically and appeared not to be related to vaccination and/or antibody concentration.

### 3. Host defenses against BVD virus.

a) Passive immunity. Kendrick and Franti (1974) showed a marked increase of serum antibodies against BVD in calves 24 hours after feeding colostrum whereas they were negative to detectable antibodies before feeding colostrum. The linear decay of the titers after parturition were considered by the authors as an indication that the immunity was passive and that it was received from colostrum. The duration of the titer ranged from 105 to 230 days and after the titer disappeared all calves developed an increase in titer, again indicating infection probably from contact with other infected cattle.

Lambert et al. (1974) pointed out the value of early feeding of colostrum from an immune dam in the prevention of BVD infection. They also claimed that one reason for relatively few isolations of BVD virus from colostrum-fed calves was the high serum antibody titers in most of the calves.

Burguess (1977) reported maternal antibodies to BVD virus at one month of age, and Kahrs (1976) found the duration at 6-8 months for the time in which an average calf is certain to be free of colostral antibodies against BVD.

b) Active immunity. The viremic nature of BVD virus infection and the high incidence of serum antibodies in cattle populations suggest the possibility of a long and solid immunity after exposure to BVD (Bruner and Gillespie, 1973).

Gutekunst and Malmquist (1964) demonstrated that infection with BVD virus was able to stimulate both complement fixing and serum neutralizing-antibody levels. The theory that BVD virus is able to compromise the process of delayed hypersensitivity and cellular immunity through its action on lymphocytes has been suggested (Braun et al. 1973; Muscoplat, 1973).

Kahrs (1968) suggested that carrier cattle are able to provide their own immunogenic stimulation against BVD because of continued external re-exposure. Lambert et al. (1974) reported the isolation of BVD virus in calves born from cows exposed intravenously to BVD virus in the last 25 days of pregnancy indicating either that BVD virus was transmitted in utero or via the dam's milk. They also showed the potential of a BVD virus infected neonatal calf to disseminate BVD virus to other susceptible calves or to their dams. McKlurkin (1976) stated that if the fetus is infected with BVD virus during the last trimester of pregnancy, it will be able to produce antibody and have resistance to BVD virus infection.

## BACTERIOLOGY

### I. Preface

The bacterial flora of the respiratory tract of cattle has been studied for years without definite conclusions as to its role in disease. It is generally believed that in normal circumstances, all component organisms are saprophytic, although some may possess disease production potential (McKercher, 1968).

Despite the fact that they are suspected to be only part of the etiologic spectrum of causative agents of bovine respiratory disease, *Pasteurella* spp. are the most common bacterial agents reported in association with illness of the respiratory tract of cattle (Horlein, 1961; Baldwin, 1967; Jubb and Kennedy, 1970; Omar, 1966; Carter, 1973; Bitsch, 1976; Mwanga, 1978).

In 1961, Horlein stated that *Pasteurella* spp. are usually found in cattle with respiratory infection, but pointed out that their role has not been clearly established. Rosner (1971) suggested that *Pasteurella* spp. seem to be ubiquitous in cattle populations and postulated that the microorganisms can be recovered from the upper (nasopharyngeal region) respiratory tract in a certain percentage of clinically normal cattle. There are many reports on *Pasteurella* spp. being involved in respiratory tract disease, but there are also separate citations for *Pasteurella multocida* and *Pasteurella*



hemolityca, the two most important members of the genus involved with bovine respiratory disease. Following the former differentiation, some reports will be cited next.

## II. Pasteurella Spp.

Carter (1956) reported that *Pasteurella* spp. are found in the upper respiratory tract of approximately 10% of normal cattle. Reisinger et al. (1959) isolated *Pasteurella* spp. from 65% of the cattle in herds affected with respiratory disease but also from 50% of animals in herds without clinical signs of disease.

Horlein et al. (1961) studied nasal swabs from apparently normal calves and from calves with different stages of respiratory disease, and found *Pasteurella* spp. in 3% of apparently normal calves; in 21% of calves with increased body temperature but without clinical signs; in 60% of calves clinically ill; in 14% of calves with antibiotic treatment; and in 40% of convalescent calves.

They explain the low incidence of *Pasteurella* spp. in the group of apparently normal calves under two points of view: a) most of the calves were free of these bacteria; and b) the number of bacteria was so small that the sampling methods used were unable to detect it.

The authors also suggested that the calves which later had signs of respiratory disease and positive cultures of *Pasteurella* spp. may have had only an infinitesimal number of microorganisms when first sampled, but a decrease in the

resistance of the mucous membrane allowed bacterial multiplication.

Gourlay et al. (1970) reported the isolation of *Pasteurella* spp. in 31% of pneumonic lungs from apparently healthy calves and in 30% of death or killed in extremis calves. They stated that it was not possible to attempt any exact correlation between laboratory observations and the presence or absence of clinical disease or death.

Jensen et al. (1976b) reported an incidence of 62% of *Pasteurella* spp. from pneumonic lungs in yearling feedlot cattle.

### III. *Pasteurella Multocida*

Scott and Farley (1932) isolated *Pasteurella bovis septica* from 80% of the clinical cases of bovine respiratory disease studied. Carter and Rowsell (1958) isolated *Pasteurella multocida* from 12 of 31 lungs with chronic pneumonia. They failed to isolate *Pasteurella hemolytica* and suggested that *Pasteurella hemolytica* is most frequently associated with acute respiratory diseases.

Saunders et al. (1964) reported 19.7% isolations of *Pasteurella multocida* from nasal swabs of clinically healthy animals. They also reported the isolation of 17 strains of *Pasteurella multocida* from pneumonic lesions present in normal calves at slaughter. Burroughs (1967b) isolated *Pasteurella multocida* from nasal swabs in 23.5% of cattle with respiratory infection and in 12.5% of animals without clinical signs of



respiratory disease. The author stated that evaluation of the role of *Pasteurella multocida* in respiratory infections in respiratory infections in the bovine specie remains a difficult problem.

Magwood et al. (1969) studied nasal swabs of 790 calves and found *Pasteurella multocida* of 61.3% isolations. Their results also showed that calves in herds with enzootic pneumonia did not have a bacterial flora which differed quantitatively or qualitatively from that in calves from normal herds. They also found no significant difference in the per cent of frequency of isolations between calves less than 3 months old and calves older than that. They concluded that there was no consistent association between presence and number of microorganisms in the nasal passage and the presence of pneumonia.

Carter (cited in Carter, 1973) tested 60 sera from shipped calves for antibodies to *Pasteurella multocida*. On arrival, only 3 were positive but two months later, 59 had antibodies. Bitsch et al. (1976) studied the lungs of 50 calves with respiratory disease and isolated *Pasteurella multocida* from 8 lungs.

Vestweber et al. (1977) reported the isolation of *Pasteurella multocida* from 20 lung samples from calves with chronic pneumonia. The authors assumed that the failure in isolating *Pasteurella hemolytica* from those lung samples could be due to the chronicity of the lesions.

#### IV. Pasteurella Hemolytica

Saunders et al. (1964) found an incidence of 23% of *Pasteurella hemolytica* in both calves with respiratory disease and normal animals. Wessman and Hilker (1968) claimed that *Pasteurella hemolytica* is carried with impunity in the respiratory tract of normal animals. They also isolated *Pasteurella hemolytica* from the respiratory tract of cattle with respiratory disease and from healthy cattle.

Magwood et al. (1969) found an incidence of 23% of *Pasteurella hemolytica* in the nasal bacterial flora of normal calves. They also surveyed 43 bulls at a test station and found that on arrival, 33% of the animals yielded *Pasteurella hemolytica*; on periodic tests, 49% were positive, and the organism was isolated in 79% of pneumonic animals. They reported some controversy on their results and pointed out that *Pasteurella hemolytica* was isolated from 11 of 14 cases of pneumonia, but at the same time 9 of 12 animals in one of the surveyed herds yielded these bacteria in large numbers but pneumonia did not ensue in this herd.

Grey and Thomson (1971) reported the isolation of *Pasteurella hemolytica* from the nasal swabs of 21 of 28 normal calves and from tracheal air of 17 of the same animals. They found that the animals which had no *Pasteurella hemolytica* in the nasal swabs yielded none in the tracheal air. They stated the probability that the organisms found in the tracheal air originated from the nasal passages of animals with positive nasal swabs as only these animals yielded the

organisms in the tracheal air.

Thomson et al. (1975) found high levels of *Pasteurella hemolytica* in the nasal flora of sick animals compared with normal animals and indicated that this organism proliferates to a great extent in the sick animals. Bitsch et al. (1976) reported the isolation of *Pasteurella hemolytica* in 8 of 50 pneumonic lungs. Mwangota et al. (1977) isolated *Pasteurella hemolytica* from the nasal passages of 200 healthy cattle.

In the bovine specie, Thurley et al. (1977) reported the isolation of *Pasteurella hemolytica* from the upper respiratory tract of lambs and pointed out the seasonal variation in isolation. Jones et al. (1978) published their isolation of *Pasteurella hemolytica* from pneumonic lungs and concluded that *Pasteurella hemolytica* and *Mycoplasmas* may commonly be the etiological agents involved in atypical pneumonia.

## PATHOLOGICAL ASPECTS

The extent and characteristics of the macroscopic and microscopic lesions usually found in lungs from calves dead or dying from bovine respiratory disease vary greatly. There is no established pattern because they depend upon the agents involved and the course of the disease. Also, as fatal pneumonia usually results from secondary bacterial infection, it is not surprising that both anatomical and histological descriptions are very similar.

There is a lot of literature published on the subject and some will be cited next.

Carter and Rowsell (1958) reported that 25% of lungs from calves 3 to 4 months old had some degree of pneumonia. They found that the right apical lobe was most frequently affected. In relation to the microscopic lesions, they found that changes in lungs from which *Pasteurella multocida* was not isolated were characterized by peribronchiolar hyperplasia of lymphoid tissue with lymphocytes infiltrating the muscular layer of the bronchioles and plugging them in most cases. The bronchial epithelium showed excessive goblet cells formation and the lack of exudate in the bronchioles was very common. The alveoli were either collapsed or they contained macrophages or, occasionally, small giant cells. Alveolar epithelialization was scattered throughout the sections.

On the other hand, the sections from the lungs yielding *Pasteurella multocida* regularly showed bronchioles plugged with polymorphonuclear (PMN) leukocytes, fibrin and cellular debris. Evidence of exudative changes were obvious by the presence of neutrophils and fibrin in the alveoli.

McKercher (1959), working with IBR virus, considered pneumonia a complication of IBR virus infection and stated that most fatal cases display characteristics of bronchopneumonia. He also stated that usually the bronchioli are filled with purulent exudate while the peribronchiolar alveoli are edematous and contain fibrin, leukocytes and erythrocytes.

Palotay (1953) reported that 96% of autopsied calves showed consolidation of one-third or more of the lung and 77% showed pleuritis. Smith and Jones (1961) suggested that the reaction of the lung to viral infection could be expected to be characterized by a serous and mononuclear reaction whereas in bacterial pneumonia, the small lymphocytes or neutrophils and fibrin are expected to be the predominant changes.

Jolly and Ditchfield (1965) showed that the typical lesions of field and experimentally produced cases of pneumonia are the organization of the apical and cardiac lobes. Histologically, they found bronchiolitis, alveolitis, serocellular exudate in the lung and alveolar macrophages. Woods et al. (1965) exposed colostrum-deprived calves to PI3 virus and their histopathological findings consisted of interlobular edema and diffuse thickening of the alveolar septums with



accumulation of erythrocytes and mononuclear leukocytes.

Omar (1966) supported the conjecture that the overall picture of pneumonia in calves is very similar. He stated that there are anatomical and gravitational reasons for the bilateral involvement of the antero-ventral lobes and that some differences exist in both the gross and macroscopic picture from outbreak to outbreak, depending on the type of secondary invaders. He postulated that purulent or fibrinous pneumonias are most commonly a result of infection with organisms like *C. pyogenes* and *Pasteurella hemolytica*, whereas, proliferative pneumonias are the common picture when viral agents are involved; however, the author points out that a typical proliferative pneumonia does not need necessarily be of viral origin since it is a basic response of pulmonary tissue to a mild irritant.

Trapp et al. (1966) published their findings on pulmonary lesions in lungs from calves experimentally exposed to agents associated with diseases of the bovine respiratory tract (PI3, PPL0 and *Pasteurella*) and reported that the inflammatory response in calves were variable in intensity and type. In the very acute cases, an exudate in the alveolar walls composed of RBC, neutrophils and predominantly large mononuclear cells was present. Other cases considered more chronic in nature showed relatively fewer neutrophils and more macrophages and fibroblasts in the lung tissue.

Darbyshire et al. (1969), working with bovine adenoviruses, reported lesions in large areas of the right apical and

cardiac lobes as well as in the posterior regions of both diaphragmatic lobes in calves dead from pneumonia. Histopathologically, their principal findings were proliferative cellular reaction in collapsed alveoli situated around small bronchioles. In well developed lesions, the alveolar walls were thickened and the nuclei of alveolar cells were conspicuously swollen and hyperchromatic. The areas of collapse were interspread with microemphysema, but in adjacent lobules the emphysema was more pronounced. There were many localized patches of necrosis of the bronchiolar epithelium which were accompanied by small amounts of bronchial exudate composed mainly of lymphocytes, alveolar macrophages and a few neutrophil leukocytes.

A constant feature in the lungs of calves 4 days after infection was peribronchiolar collapse. The exudation of fluid into the alveoli was clearly seen. On the other hand, at seven days after infection the alveoli wall thickening had increased as a consequence of an increased number of cells so that little exudate could be found.

Mohanty et al. (1969) inoculated 14 bulls of different breeds with Bovine Rhinovirus and claimed that many large areas of the lungs had changes indicating pneumonias of variable severity. Many alveoli were filled with eosinophilic exudate and contained cellular debris. The alveolar walls were thickened by mononuclear infiltration. Several of the areas of infiltration contained a mixture of neutrophils and monocytes. The bronchiolar lumen were relatively

free of exudate.

Gourlay et al. (1970) examined abbatoir pneumonia lungs from apparently healthy 3-month old calves and found that the right lung showed pneumonic lesions in 98% of the cases whereas the left lung was only affected in 42%. Macroscopic consolidation was associated with varying degrees of collapse or atelectasis. Collapsed alveoli appeared normal in other respects or they had a cellular reaction consisting of infiltration of the alveolar wall and alveolar exudate. Pulmonary collapse was assessed to be a significant feature in 73% of pneumonic lungs. This pulmonary collapse was accompanied by lesions of acute bronchiolitis or by peribronchial lymphoid hyperplasia with stenosis of the bronchi. In general, they found an alveolar exudate that contained large alveolar epithelial type cells as well as a varying number of neutrophils, eosinophils and small round cells. Bronchiolitis was seen in 75.5% either as acute bronchiolitis with the lumen of the airway plugged with neutrophils or less frequently as subacute bronchiolitis in which the lumen contained organising exudate or bronchial material having a reticulin and collagen framework with neutrophils and round cell reactions. These changes were also apparent in the bronchial wall.

They also found some degree of alveolar involvement but extensive fibrinous or purulent alveolitis was not seen. On the basis of alveolar or bronchial reactions, 62% of the cases were classified as showing purulent bronchopneumonia.

Peribronchial lymphoid hyperplasia was found in 75.5% of the cases and about 50% of pneumonic lungs had pronounced follicular lymphoid hyperplasia.

The authors also studied lungs from calves of different ages which had died or been killed in extremis with pneumonitis and found that some of the lungs showed no areas of consolidation but the whole lung was congested. In these cases both lungs were usually equally affected. Pulmonary collapse was assessed to be significant in 55% of the cases. Alveolar epithelial cell exudate was the rule and in 55% of the cases there was significant giant cell formation in alveoli and some interstitial pneumonia with eosinophilic or hyaline membrane formation and alveolar epithelialization. In 30% of the cases there was fibrinous or necrotizing alveolitis of the type usually associated with infection by *Pasteurella* spp. There was bronchiolitis in 85% of the cases and lesions of subacute bronchiolitis or bronchiolitis obliterans occurred in some animals. Sixty-five percent of the cases showed purulent bronchopneumonia similar to the first series.

Ide (1970) points out the similarity of the pulmonary lesions from different outbreaks and stated that most are characterized by atelectasis or consolidation. He also postulated that in early cases the lesions are primarily seen in the ventral aspects of the anterior lobes of the lungs but later may extend deeply into all lobes and extensive lesions are usually accompanied by emphysema. It is the

author's opinion that bacterial invasion produces a variable picture like purulent bronchopneumonia, lung necrosis, abscessation and pleuritis.

Jubb and Kennedy (1970) stated that bronchiolitis is the central and basic lesion in the bronchopneumonic syndrome. According to these authors, leukocytes, mucus and desquamated cells fill the bronchiolar lumen. Peribronchial spread is usual and inflammatory infiltrations are present in all levels of the bronchial wall, in the peribronchial connective tissue and lymphatics and in the alveolar septa. Later on a progressive fibrinous thickening of the alveolar septa leads to a chronic bronchopneumonia.

Rosner (1971) stated that in field cases of PI3 virus infection complicated by *Pasteurella* spp., a fibrinous exudate on the visceral pleura which at times adheres to the parietal pleura, is common. He also stated that an exudative bronchial pneumonia with a histopathologic cellular reaction is indicative of bacterial infection.

Musa et al. (1972) studied pathological changes in calves given *E. coli* endotoxin and *Pasteurella multocida* and reported that the lungs had the most prominent changes in both groups. Petechial hemorrhages were seen on the outer surface of the lungs of both groups. Hyperemia, edema, and interstitial pneumonia were widespread in the group of calves infected with *Pasteurella multocida*, whereas hyperemia, leukocytic infiltration, edema and thrombosis were the rule in the group of calves infected with *E. coli*.



Thomson (1974) suggested that there is some similarity in the gross lesions caused by different agents, particularly in the chronic stages. In the very acute stages, the predominant lesion is a bronchiolitis in the small and medium sized bronchioles. The severity of the disease will be determined by the degree of damage to the epithelial lining of the bronchioles. If the epithelium becomes ulcerated, the bronchioles are likely to become plugged by necrotic debris and inflammatory exudate. These lesions may be secondarily infected and lead to mucopurulent bronchiolitis or abscesses. In addition, there is danger of organization of the exudate in the bronchioles from the connective tissue below the ulcerated epithelium. Permanent organized plugs of exudate may then remain in the bronchioles and cause persistent respiratory insufficiency.

Epstein et al. (1976) reported lymphocytosis around bronchi, bronchioles, and arterioles in lambs with proliferative pneumonia. They also reported nonspecific lesions caused by *Pasteurella hemolytica* alone: nodular areas with peribronchiolar and perivascular reactions alternating with areas of pulmonary consolidation. When *Pasteurella hemolytica* is associated with other microorganisms the picture is also nonspecific: an exudative pneumonia with hemorrhages, bronchiectasia, exudates and polymorphonuclears in the bronchiolar lumen and parenchymal infiltration by inflammatory elements. If the association is with *Staphylococcus*, *Streptococcus* or *Fusiforms*, there is abundant polymorphonuclears in

the alveolar lumen and more marked exudative processes.

In relation to lesions by PI3, the author reported areas of consolidation with thickening of the bronchial wall and presence of mucofibrinous exudate in the ventral portions with areas of emphysema in the apical and cardiac lobes. There is also proliferation and infiltration of the alveolar wall. The bronchial lumen is plugged with exudates.

Blood and Henderson (1974) stated that extensive hepatization, interlobular accumulation of a serofibrinous exudate and fibrinous pleuresy are common in pneumonia caused by *Pasteurella* spp. infection. On the other hand, consolidation and suppuration are lesions more commonly associated with infections by *Corynebacterium progenes* and *Spherophorus necrophorus*.

Jensen et al. (1976c) reported a chronic degenerative deformation of the lower airways (bronchiectasis) in 1.6% of 407,000 samples from yearling feedlot cattle with signs of illness or from necropsy. They found that the permanently dilated small bronchi and bronchioles were located in ventral parts and that they were filled with accumulations of exudates and microorganisms.

The same group of workers (Jensen et al., 1976d) reported in the same year their results on pathological lesions. They found that most pneumonias were bilateral and that the lesions were localized in the ventral parts of the lung, whereas the dorsal parts were usually normal. Advanced and fatal lesions involved most ventral tissues of the apical, cardiac and

diaphragmatic lobes. The cardiac lobes were invariably the most severely affected.

Microscopically, the alveoli were filled with fluids and semisolid exudates. Hemorrhagic infarcts and areas of coagulative necrosis were common complications. Exudate was composed of mucus, bacteria, neutrophils, macrophages and blood plugged bronchi and bronchioles. Epithelial cells were often necrotic and desquamated over small or large areas of mucosa and congested blood vessels in bronchial and bronchiolar laminae propria resulted in hemorrhages into tissues and lumens.

Rarely were entire walls or adjacent alveoli infiltrated with leukocytes and serum whereas exudate and bacteria was present in the lumen of terminal bronchioles and alveolar ducts. They also reported filling of alveoli with exudate during acute phases of disease. This early exudate was composed of fibrin with admixtures of serum, RBCs and bacteria. In more advanced stages, macrophages and neutrophils super-vened the fibrin. In some lobules the exudates in alveolar ducts and alveoli consisted entirely of fibrin, leukocytes and bacteria as this exudate is more commonly present at the periphery of lobules.

In relation to the vascular tissue, variable intra-vascular clots were present in many blood vessels. Occluded capillaries presented evidence of necrosis, disintegration and dissolution. This lesion was present in all lungs with acute pneumonia. The necrotic focus were demarcated by a

peripheral reactive zone where large numbers of bacteria and leukocytes accumulated. Advanced stages of necrosis were characterized by chromatolysis and coagulation of both tissue and exudate.

Cases with obvious chronicity showed clear organization of fluids and exudates. Fibrocytes grew into fibrinous exudates of alveolar lumens, pleural surfaces, fibrinous thrombi of lymphatics, and into the transudate of interlobular stroma. Connective tissue formed a capsule around the foci of necrosis.

Lopez et al. (1976), working on the role of PI3 virus in the clearance of *Pasteurella hemolytica* from the lung reported that the exudate observed in bronchi, bronchioles and alveoli consisted essentially of neutrophils and sometimes macrophages. The grade of infiltration was very variable. Lymphoid hyperplasia was common and a mild degree of alveolar edema was present in all calves. Atelectasis was present in all calves and inflammatory cell infiltration of the alveolar septa was very common.

Wiseman et al. (1976) reported pathological lesions from an outbreak of acute pneumonia in young, single-suckled calves. They found a fibrinous pleuresy affecting parts of the apical, cardiac and diaphragmatic lobes. Microscopically, an exudative interstitial pneumonia of the type often associated with *Pasteurella* spp. infection was detected. In the involved areas, there was marked involvement of the interlobular septa and the adjacent alveoli in an acute

inflammatory reaction with congestion and edema, dilatation of septal lymphatics, many of which contained plugs of fibrin, and infiltration by neutrophils and macrophages. Alveoli adjacent to these areas were often either congested and contained edema fluid, sometimes with extensive fibrin formation, or a necrotic cellular infiltrate in which it was difficult to identify the cell types. Thrombosis of intra-lobular branches of the pulmonary artery and vein was detected in some lobules.

Davies et al. (1977) exposed lambs to PI3 virus and *Pasteurella hemolytica* and reported a higher incidence of pneumonic lesions in the right apical and cardiac lobes.

Stevenson (1977) reported on proliferative interstitial pneumonia in lambs. The lesions involved all lobes of the lung. Generally, the apical and intermediate lobules of both lungs were totally involved as were about three-quarters of all cardiac lobes and the anteroventral portions of the diaphragmatic lobe.

A distinctive feature of the gross lesions was the relatively sharp line of demarcation between normal and affected parts of the lung. Occasionally there were small foci of consolidation or linear areas of collapse in the dorsal parts of the diaphragmatic lobes. In the atelectatic portions individual lobes were usually discernible which gave the affected part a granular appearance.

Histologically, the predominant reaction was classified as a proliferative interstitial pneumonia. The major bronchi



were not affected to any appreciable degree but the small bronchi and bronchioles showed marked hyperplasia of the epithelium. Alveoli with minimal changes contained free alveolar macrophage whereas in others, free and attached large alveolar cells were observed along with thickening of interlobular septa. In other areas, the author was unable to discern individual alveoli because of the proliferative reaction.

Kim (1977), working on Holstein dairy cattle between six months and two years of age, showed that a suppurative pneumonic condition may be elicited in cattle by antigen-antibody complexes mainly localized in sub-endothelial and epithelial tissues. Numerous polymorphonuclear were found in the blood vessels. Generally speaking, the lung tissue examined had diffuse red hepatization and some nodular abscessations. One lobe may be completely consolidated whereas others remained completely unaffected.

The author summarized by saying that proliferation of interstitial cells, edema, accumulation of polymorphonuclears and leukocytes with increased reticular fibrin, and interstitial fibrosis were basic elements of the histologic changes found in his study.

Vestweber et al. (1977), studying calves affected with chronic pneumonia found that the right apical lobe usually showed the most dramatic changes. Bullous emphysema was a common finding in the dorsal aspects of the lungs, especially the diaphragmatic lobes. Lobular and interlobular emphysema

in these areas were confirmed by histological studies. Atelectasis, fibrosis, abscess formation and necrosis were seen in the ventral parts of the lungs. Also, purulent bronchiolitis and peribronchiolar organization were common findings. Obliterative bronchiolitis was common to all cases.

Jones et al. (1978), working on lambs, obtained lungs with consolidated lesions from the abbatoir and histological examination showed a proliferative exudative pneumonia, the principal features of which were lymphoid hyperplasia, bronchiolar hyperplasia, macrophagies and polymorphonuclear exudation, giant cells, hyaline scar formation and areas of alveolar collapse. The authors inoculated other animals with a suspension of lung tissue from these lesions and were able to reproduce a proliferative pneumonia very similar to that seen in the diseased tissue used as inoculum.

Those non-consolidated areas showed mild to moderate infiltration of the interalveolar septa with mononuclear cells. They also found necrosis of the bronchiolar epithelium, capillary congestion, serums alveolar exudation and inflammatory cell infiltration of the parenchyma. Some animals developed pleuritis.

Kiorpes et al. (1978) inoculated Holstein calves 4 to 8 weeks of age with IBR virus and reported pathological lesions mainly in the upper airways. However, they found bronchial congestion associated with focal hemorrhages. Gross appearance of the lungs were normal, however, some calves showed

patchy lobular consolidation over approximately 10% of the lung surface and another 10% showed focal, petechial hemorrhagic lesions. They found lobular atelectasis in several microscopic sections.

## MATERIALS AND METHODS

### Animals

Ninety-six Holstein calves 3 to 9 days old were brought from southwestern Wisconsin farms during the months of February through May, 1978. The calves arrived in four groups i.e., I, II, III and IV, groups of 24 calves each at intervals of 21 days. All groups of calves were transported nonstop for 18 hours from Wisconsin to Manhattan, Kansas. These calves had originated from many farms and were part of a larger group of 168 calves (7 groups of 24 calves each) which had been assembled for studies of drug efficacy on diarrhea in calves.

The usual conditions of management in the area of origin supposed that the calves had ingested colostrum. After their arrival, the calves were housed individually in wooden hutches (1.2m x 1.2m x 1.2m, roof slope 16 cm) in an outdoor area and were fed twice a day with milk replacer. Each calf was identified and nasal swabs (for bacteriological isolations) and serum samples (for serological tests) were collected from the calves within 24 hours after arrival. A second serum sample was taken 15-16 days later from the surviving calves.

### Serology

Blood samples were collected by jugular puncture within

24 hours after arrival. Five ml. of blood were collected into a glass vial, left to clot and the serum harvested within one hour after bleeding. Serum was harvested by centrifugation of the sample at 3000 r.p.m. for 5-10 min. and passed to a new glass vial using a Pasteur's pipete.

Second samples were also taken from the survivors in groups II, III and IV within 15-16 days after the first sampling. Identical procedures were used in handling these second samples. All samples were sent to the Diagnostic Laboratory of Kansas State University within two hours after collection and tested for antibodies against IBR, BVD and PI3 viruses. The standard serum neutralization test as described by Lennette and Schmidt (1969) was used.

In relation to the serum protein values, the SMA 6/60 microsystem method was used for the determination of total proteins and immunoelectrophoresis on cellulose acetate was performed in order to determine globulin and gammaglobulin serum concentrations.

An arbitrary classification of Low ( $<1:4$  and  $1:4$ ), Medium ( $1:8$  to  $1:64$ ) and High ( $1:128$  to  $\geq 1:512$ ) dilutions was used in order to establish reference points for the analysis of the data. Besides, the  $1:8$  dilution was considered as the threshold of positiveness for all three viruses.

### Bacteriology

Nasal swabs were procured from the calves within 24 hours



after arrival. Sterile cotton-tipped 15 cm. length<sup>1</sup> nasal swabs were used and the samples collected by introduction (approximately 13 cm. in depth) and rotation of the swab in both sides of the nasal cavity, care being taken to avoid contact with the skin of the anterior nares. The swabs were then immersed in transport media<sup>1</sup> and taken to the Bacteriology Laboratory at Kansas State University immediately.

Within 30 minutes after collection, the swabs were cultured by application and rotation of each swab onto one-squart of a tryptic soy blood agar and McConkey plates. The inoculum was then streaked out over the rest of the plate with a platinum loop. Plates were incubated at 37 C in an atmosphere of 5% CO<sub>2</sub>. After 24 and 48 hours of incubation, the plates were examined for colonies suspected of being *Pasteurella* spp. and were also selected from the tryptic soy blood agar and subcultured by streaking for isolation on the same media.

After being subcultured, colonial morphology was reported for each strain isolated. Each culture was identified with the aid of generally accepted procedures and Keys (Buchanan and Gibbons, 1974; Gordon et al., 1973). Morphological identification of *E. coli* from McConkey agar was reported.

Antibiotic sensitivity tests were performed on colonies

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<sup>1</sup>TRANS-CUL. Microbiological Collection and Transport System, Wampole Laboratories, Dist. Div. Denver Chemical Mfg. Co., Stamford, Ct., 06904.

of *Pasteurella* spp. isolated from nasal swabs and on colonies isolated from lung samples taken from pneumonic lesions of dead or killed in extremis calves.

The isolation of colonies from pneumonic lungs was performed as follows. Samples were taken at the necropsy room following sterile procedures and transported immediately to the bacteriology laboratory. The surface of each sample was seared with a hot spatula and an incision was made into the underlying tissue with scissors sterilized by flaming in 70% alcohol. A sterile swab was used to transfer material from the tissue to a plate of trypticase soy blood agar. All cultures were maintained at 37 C and in an atmosphere of 5% CO<sub>2</sub>. Cultures were examined at 24 and 48 hours after inoculation and those that grossly appeared to be *Pasteurella* spp. were isolated into new plates.

The procedure used for antibody sensitivity was the disc susceptibility test as described by Matsen and Barry (1974). The reference organisms used were stock cultures of *Staphylococcus aureus* (ATCC 25923) and *E. coli* (ATCC 25922).

The following antibiotics<sup>3</sup> and concentrations were tested: Cephalothin (30 mg.); Trimethoprim/sulfomethoxazole (23.75 mcg.); Chloramphenicol (30 mcg.); Triple sulfa: equal parts of sulfodiazine, sulfamerazine and sulfamethazine (300 mg); Polymyxin B (300 units); Nitrofurazone (100 mcg.);

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<sup>3</sup>Pfizer Disks Inc., Barceloneta, P.R., 00617.

Tetracycline (30 mcg.); Kanamycin (30 mcg.); Neomycin (30 mcg.); Gentamycin (10 mcg.); Streptomycin (10 mcg.) and Ampicillin (10 mcg.).

### Pathology

Calves were necropsied within a short time after death or immediately after euthanasia. Euthanasia was performed by intravenous injection of 10 cc. of N-[2-(m-Methoxy-phenyl)-2-Ethyl-butyl-(1)]-Gamma-Hydroxybutyramide (T61<sup>4</sup>) in those animals considered improbable to recover.

Gross changes in the lungs of 26 dead calves with macroscopic pulmonary lesions were recorded on a sheet as shown in drawing number one. These lesions were classified by the method reported by Friend et al. (1977).

Microscopic studies were performed as follows. At necropsy, the lungs were removed and significant portions of macroscopic lesions were collected, fixed in 10% buffered formalin solution, embedded in parafin, sectioned at four to six microns and stained with hematoxylin and eosin. The histological slides (six for each calf) were observed at 40X by light microcopy. Some of the most common lesions are shown in Figs. 6 through 14.

The following code was used to define the microscopic lesions (see Table 16):

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<sup>4</sup>Taylor Pharmacol Co., Dacatur, Illinois, 62525.

- Absence of the lesion in the six slides
- + Presence of the lesion in one or two slides
- ++ Presence of the lesion in three or four slides
- +++ Presence of the lesion in five or six slides

## RESULTS

### I. Serology

1. Infectious Bovine Rhinotracheitis Virus (IBR). The distribution of antibody titers for IBR from two collections of samples and for mortality rate are shown in Fig. 2.

For the first sampling (samples taken at arrival of all calves), 44.8% of samples possessed antibodies to IBR virus at dilutions of 1:8 or more. On the other hand, 42.6% of samples were positive (1:8 or more) at the second sampling for titer performed 15 days later, a decreased difference of 2.2% was found between those samples.

The highest incidence of samples was found to be at the low antibody titer dilutions level for both trials, with 55.2% for the first sampling and 57.4% for the second sampling. There was an increase of 2.2% of incidence at the second sampling in low antibody titer dilutions. Conversely, the incidence in medium antibody titer dilutions decreased from 40.6% at the first sampling to 38.9% for the second sampling. High antibody titer dilutions also decreased from 4.2% to 3.7%.

Mortality rate was highest at low antibody titer dilutions, diminishing through increasing antibody titer dilutions with 61.6%, 34.5% and 3.8% for low, medium and high dilutions, respectively.

Only 5.6% of animals had a fourfold or greater increase



in antibody titer at the second sampling. Of the animals, 11.1% had a twofold increase, 42.6% had a decreased antibody titer and 40.7% showed the same antibody titer.

2. Bovine Viral Diarrhea Virus (BVD). The results of both serum samplings and of mortality rate are shown in Fig. 3.

Of the first sampling, 61.5% of the samples possessed antibodies to BVD virus whereas 66.7% of the samples were positive at the second sampling, 15 days later, showing an increase of 5.2% for positive animals.

The highest incidence of samples was found to be in the low antibody titer dilutions with 38.5% for the first sampling, however, in the second sampling only 33.3% of samples were within this range meaning a decrease of 5.2% of incidence at this level.

At the level of medium antibody titer dilutions, there also was a decrease. From 30.2% of incidence at the first sampling, there was a decay to 27.8% at the second sampling, meaning a decrease of 2.4% of incidence at this range. On the other hand, at the level of high antibody titer dilutions, an increase of 7.6% of incidence was found. The incidence increased from 31.3% at the first sampling to 38.9% for the second sampling.

Mortality rate was high at low antibody titer dilutions with a 61.6% of incidence. The incidence of death at medium dilutions was 34.5% and at high dilutions only 3.8%.

The comparison between the bars representing first

sampling and those representing mortality rate shows that with the exception of the <1:4 dilution, the bar representing mortality rate is higher than that representing first sampling up to the 1:32 dilution where the situation reverses and the bar representing first sampling is higher than that representing mortality rate.

The changes in individuals serum antibody titers from those animals with two samples showed that 48.1% of the animals did not change their titer; 22.2% showed a decrease; 9.3% had a twofold dilution increase and 20.4% had fourfold dilution increase or greater.

3. Parainfluenza 3 Virus (PI3). The results from PI3 virus serology are summarized in Fig. 4.

The overall incidence for the first sampling was 84.4% whereas the overall incidence for the second sampling, despite the fact that it remained high, decreased to 81.5% of positive sera which meant a difference of 2.9% of positiveness between both trials.

The low antibody titer dilutions exhibited an incidence of 15.6% and 18.5% for the first and second sampling, respectively, with an increase of 2.9%.

A variation of incidence in relation to IBR and BVD viruses (highest incidence of titers was found at the level of low dilutions) as the highest incidence of titers for PI3 virus antibodies was distributed in the medium dilutions with 65% for the first sampling and an increased 75.9% for the second sampling with a clear difference of 10.3% between both

trials.

High antibody titer dilutions displayed a clear decrease of 13.2% as the titer changed from 18.8% at the first sampling to only 5.6% at the second sampling.

Mortality rate was distributed principally within the low and medium antibody titer dilutions with 30.8% in the low range but with an incidence of 61.5% in the medium antibody titer dilution. High dilutions showed a mortality rate of 7.6%.

Only 1.9% of animals had a fourfold increase in antibody to PI3 titer whereas 59.3% had decreased PI3 antibody titers and 38.9% maintained the same serum PI3 antibodies concentration.

Total protein, globulin and gammaglobulin values of 96 calves 1 to 9 days old are shown in Table 6.

Total protein mean value was in the order of 5.6 g/100 ml ( $\pm 0.8$ ) in the whole group. The mean values for globulin and gammaglobulin fractions were 2.29 g/100 ml ( $\pm 0.8$ ) and 0.86 ( $\pm 0.5$ ), respectively.

Tables 7, 8, 9 and 10 show the same values but for individual groups. As the results show, in group I the mean values for globulin and gammaglobulin fractions are higher in the subgroup of dead calves than in the subgroups of both total calves and survivor calves.

The total protein values were similar in all groups. Only group IV had a mean value for gammaglobulins below the mean value reported for this fraction for the total group.

Group I, with the lowest total protein mean value (5.47 g/100 ml), had the highest gammaglobulin fraction mean value (0.97 g/100 ml). Group II, with the highest total protein mean value (5.86 g/100 ml), had lower immunoglobulin values than those of groups I and III. The highest mortality rate (8 calves, see Tables 2 and 5) was found in groups I (highest immunoglobulin mean values) and IV (lowest immunoglobulin mean values).

## II. Bacteriology

The microbiological findings are summarized in Tables 2, 3, 4, 5, 11, 12 and 13. The distribution of 59 strains of *Pasteurella* organisms isolated from nasal swabs from young calves are shown in Table 11.

*Pasteurella* organisms were recovered from the nasal swabs of 55 animals (57.3%). However, the total strains isolated were 59 because 4 calves yielded both *Pasteurella multocida* and *Pasteurella hemolytica*. Of the 59 isolations made from the calves, 35 were identified as *Pasteurella multocida* (59.3%); 19 as *Pasteurella hemolytica* (34.5%); 3 as *Pasteurella* spp. (5.5%) and 2 as *Pasteurella gallinarum* (3.6%) (see Table 11).

Of 26 calves that died during the trial, 14 yielded *Pasteurella* organisms from the nasal swabs taken at arrival. These organisms were identified as *Pasteurella multocida* and *Pasteurella hemolytica*. The former was recovered from 7 animals (26.9%) and the later from 9 animals (34.6%).

These percentages were calculated in relation to the 26 dead calves. Two calves which yielded both organisms were in this group (see Table 11).

Of 70 survivor calves (72% of the whole group), 41 (58.6%) yielded *Pasteurella* organisms from the nasal swabs. *Pasteurella multocida* was isolated from 12 calves (17.1%); *Pasteurella hemolytica* from 26 (37.1%); *Pasteurella* spp. from 3 (4.3%) and *Pasteurella gallinarum* from 2 (2.9%). The incidence of each strain was calculated in relation to the 70 survivor calves. Two calves from which both organisms had been isolated were in this group.

*Pasteurella multocida* or *Pasteurella hemolytica* were isolated from 11 (42.3%) lungs of 26 dead animals. As shown in Table 12, all the strains were identified as *Pasteurella multocida*.

*Escherichia coli* was isolated from 43.8% of the total animals.

Table 13 shows the correlation found when *Pasteurella* isolations from nasal swabs and from lung tissue were compared.

Calves number 26, 79, 91 and 119 yielded *Pasteurella hemolytica* but no *Pasteurella multocida* from the nasal swabs whereas *Pasteurella multocida* and no *Pasteurella hemolytica* was isolated from the lungs (Table 13).

Calves 28 and 114 yielded *Pasteurella multocida* from both nasal swabs and lung tissue whereas attempts to isolate *Pasteurella hemolytica* from either nasal swabs or lung tissue



were negative.

Calves 43, 46, 96 and 114 did not yield *Pasteurella* from nasal swabs but *Pasteurella multocida* was isolated from the lungs. In calf 73, *Pasteurella multocida* and *Pasteurella hemolytica* were isolated from the nasal swabs but only *Pasteurella multocida* was isolated from the lungs.

Table 14 shows that of 20 strains of *Pasteurella multocida* isolated, only 2 were susceptible to triple-sulfa, whereas, 18 were resistant. Only one strain showed sensitivity to Neomycin and the same situation occurred with Streptomycin. All strains were susceptible to Cephalothin, Chloramphenicol and no strain was resistant to Polymycin B.

The majority of *Pasteurella hemolytica* isolates were sensitive to the antibacterial tested (Table 15). All strains were susceptible to Ampicillin, Chloramphenicol, Gentamycin, Polymycin B, Tetracycline and Trimethoprim/Sulphamethoxazole.

### III. Pathology

The pathological findings are summarized in Table 16 and Figure 5.

The distribution of the Pathological lesions and its relation with *Pasteurella* organisms isolation and serum titers against IBR, BVD and PI3 viruses are shown in Table 16. Figure 5 shows the incidence of the most common lesions as well as its degree of compromise.

At necropsy, 23 of 25 surveyed calves showed different

degrees of pneumonia. Extensive lesions were found in 6 of 25 calves. Thirteen cases of pneumonia were bilateral and macroscopic consolidation of lung tissue was frequently found to be associated with varying degrees of collapse or atelectasis. The right apical lobe usually was affected most severely.

A distinctive feature of the gross lesions was the relative sharp line of demarcation between normal and affected parts of the lungs. Occasionally, there were small foci of consolidation or linear areas of collapse in the dorsal parts of the cardiac lobes. The affected parts usually had a granular appearance.

It was not possible to correlate collapse consistently with bronchial obstruction due to the variability of the lesions. Most of the lungs were red (dark), but a greyish coloration could be seen in some of them. Dark areas were usually covered by variable amounts of fibrin on the pleural surface.

Microscopically, atelectasis and interstitial pneumonia were the most common findings (see Table 16). Pleuritis was also very common as were other specific lesions such as fibrin, purulent material, emphysema and hemorrhages. Plugging of alveoli with neutrophils was invariably seen in the most severe cases. In many of the sections of pneumonic lungs examined there was an alveolar exudate containing some epithelioid cells as well as varying numbers of other cells, neutrophils and round cells.

## DISCUSSION

### I. Serology

The results from the serology of IBR, BVD and PI3 viruses are consistent with the results of previous surveys and support the widespread nature of these agents within the cattle population (Curtis, 1966; Knaizeff, 1963; Dawson, 1964).

The antibody titers found upon arrival are considered to be maternal origin, however, the possibility of early infection can not be discarded. If we take into consideration the following fact: we are not sure that the calves were fed colostrum in adequate amounts and quality and under natural conditions; there is a period of approximately 4 hours following birth when a calf is agammaglobulinemic and theoretically susceptible to infection (Logan, 1978). Also, IgG1 is present in nasal secretions at approximately 24 hours after first suckling (Smith, 1976).

The mortality rate was high at low serological dilutions for IBR virus, however, no clear correlation was found between individual serum antibody dilutions and mortality rate (see Fig. 2). This finding can be related to the statement of Curtis (1966) that the factor determining immunity to herpes viruses is the antibody concentration in the film of fluid covering the respiratory mucous membrane and there is poor correlation between circulating serum antibodies and immunity to IBR virus. The actual immunity against IBR virus infection

is probably based upon the host's immune response to stop the spread of virus from cell to cell (Gerber, 1978) which is local immunity.

There was not clear evidence of active IBR virus infection within the tested calves because only 5.6% of animals with a fourfold or greater rise in antibody titer at the second sampling were found. Only occasionally antibody titers reached 1:124 or greater. This finding is in agreement with other published data (Bruner and Gilliespie, 1973).

The mortality rate for BVD virus was also high at low serum antibodies titers. Of the animals, 20.4% had an increase of fourfold dilutions or greater which suggested that active infection took place in several animals. This finding is in contradiction with the data reported by Burgess (1977) which suggested that infections with BVD virus occur more commonly later in life. It is important to point out that the highest incidence of animals with sero-conversion occurred in group II (see Table 3). This group was exposed to the most adverse climatic conditions of all groups.

It is the author's opinion that the role of BVD virus as pathogen of the respiratory tract is not well elucidated. Evidence has been obtained that BVD virus has an apparent affinity for cells of the immune system (Muscoplat, 1973) and the virus does not depend upon respiratory tract cells for primary replication (Todd, 1971). Evidence by Muscoplat (1973) suggests that BVD virus may compromise an animal's immune response and result in secondary infection by bacteria

and other viruses. Frequent isolations of BVD virus from the nasal passages can be explained on the basis of the viremic condition of this viral infection as demonstrated by Lambert et al. (1974). They isolated BVD virus from blood, nasal swabs and rectal swabs for 103 days following exposure.

If we take into consideration the fact that BVD virus does not induce the formation of secretory antibodies, as stated by Todd (1971), the importance of colostral immunoglobulins in conferring protection against BVD virus infection during early life is very obvious (Shope et al., 1976).

The results of PI3 virus serology indicate a high infection rate among adult cows in the herds of origin. The serologic data obtained did not demonstrate active PI3 virus infection among the calves since a fourfold or greater increase in antibody titer was found in only one calf. The finding that 59.3% of the animals had decreased titers also supported the former assumption.

The lack of correlation between the different serum antibody dilutions and mortality rate (see Fig. 4) could suggest that maternal serum antibody titers against PI3 virus are not indicative of protection. In relation to the former suggestion, it is the author's opinion that the importance of passive serum immunoglobulin in prevention of infection of the respiratory tract epithelium from PI3 virus is not well established. If we take into consideration, as demonstrated by Morein (1975), that the first attack by PI3



virus, as well as the first defense area against the virus, are found in the gel phase (which has similar receptors as those of the cell) of the respiratory secretion, and the mechanism of defense is carried out by IgA antibodies (Morein, 1973). This is not usually present in the nasal secretion until 2 to 3 weeks of age (Smith, 1976) and only present in minimal amounts (Rossen, 1971). We find that the importance of colostral immunoglobulins in blocking primary PI3 virus infection of the epithelial cell is not clear. It has been suggested that viruses multiply in the respiratory mucosa in the absence of local immunity and if high antibody titers of IgG antibodies (main component of colostral immunoglobulins) are present in the serum, transudation may occur onto the local site and the interaction of serum IgG (complement fixing) with antigens in the lungs produces a hypersensitivity reaction of the Arthus (immune complex) type (Fudenberg, 1976). Kim (1977) presented evidence that antigen antibody complexes may play an important role in Bovine respiratory diseases.

It is possible that the respiratory epithelium has no defense to viral infections during the first days of life. During this time, PI3 or other viral agents may exert their pathologic effect on the cells and/or enhance the pathogenicity of other viruses; for example, the activation of IBR virus after infection with PI3 virus (Mensik, 1976). Such events and others (stress, diarrhea) are going to impair the defense mechanisms of the lung against other infectious

agents allowing the exacerbation and pathogenic action of usually nonpathogenic organisms.

Summarizing the serologic results, no correlation was found between the serum titers of BVD and PI3 viruses and the mortality rate. For IBR, however, most of the dead animals had low serum antibody titers against the virus (see Table 16). We were unable to establish specific correlation between the serologic values and post-mortem lesions. The author suggests that probably a mild infection was present in several of the surveyed calves. The suggestion is supported by the following facts:

a) It has been established that in the neonatal calf, the gut absorption of immunoglobulins ceases completely by 36 hours post-partum (Oyeniyi, 1978).

b) All calves were at least 3 days old, so we can infer that the gut closure to absorption of immunoglobulins had occurred and that the first serum samples reflected the highest maternal antibody concentration at sampling time.

c) In respect to all three viruses, some calves maintained the same titer while others had a twofold rise in titer which is not considered proof of infection.

d) The half life of IgG1 which is the most important immunoglobulin in colostrum (Jensen, 1978) is approximately 10 days (Butler, 1971).

e) If the two samples were taken with a difference of 15-17 days and the calves had been fed colostrum at least 3 days before the first sampling and only maternal antibodies

were present, all the calves should have had a lower serum titer on second sampling considering the rate of decay, however, several calves maintained the same titer or had a slight increase. This may signify infection in several calves with the production of antibodies by the calf.

## II. Serum Proteins

The results for total serum proteins (total calves and surviving calves) are in agreement with those obtained by Schultz et al. (1971) and Thornton et al. (1972) in normal calves. However, the values found for the gammaglobulin fraction are lower than those reported by the former authors. This can be explained by the great variation found between the immunoglobulin levels in the serum of young calves (Smith, 1967). It has been suggested (Smith, 1967) that the differences between one survey and another survey may be a reflection of different regional management practices used in rearing calves.

If we take into consideration that 6 g/dl is the lower limit for total serum proteins above which disease and death are less likely to occur (Naylor et al., 1977), the mean value for total serum proteins obtained in the present study (5.6 g/dl) would suggest some predisposition to disease in the groups of tested calves.

The results for serum immunoglobulin values from groups II, III and IV (Tables 8, 9 and 10) support the observation by many authors that survival of calves is related to the

serum gammaglobulin concentration. However, in group I (Table 7), the subgroup of dead calves yielded a higher gammaglobulin concentration than values for the surviving calves and for the total group. This finding is difficult to explain. This group had the highest mortality rate (8 of 24 calves died), and perhaps can be explained by the fact that some of the calves which later died had some degree of dehydration at arrival and this may be the cause of the higher gammaglobulin concentration. The higher mortality rate in this group with relatively high gammaglobulin levels could also be explained by the lack of specific antibodies against the pathogen involved in the cause of death.

No clear relationship was found between total serum protein values and gammaglobulin values among the different groups (Tables 7, 8, 9 and 10). If we take into consideration the results of Tennant et al. (1969), suggesting that colostrum feeding does not affect serum albumin and alpha-globulin concentrations and the increase in serum proteins in neonatal calves is a measure of serum immunoglobulin, the discrepancy could be explained by differences in the immune status of the dams.

### III. Bacteriology

The bacteriology results suggest that *Pasteurella* spp. organisms are a common inhabitant of the nasal passages of calves as indicated by the finding of 57.3% of animals yielding these organisms. It is important to point out that

a negative nasal swab does not necessarily mean the absence of the organism in the nasal passages. Animals with negative nasal swabs may harbor the organisms in small numbers which are not detectable by the method used.

There was no correlation between the specie of *Pasteurella* isolated from the nasal swabs and the specie isolated from lung tissue of dead calves (Table 13). *Pasteurella hemolytica* was isolated from the nasal swabs of 9 calves of the total of 26 calves which later died. However, the organism was not isolated from the pneumonic lungs of these animals. On the other hand, *Pasteurella multocida* was isolated from the nasal swabs of 7 calves of the total 26 calves which later died, whereas, this organism (*P. multocida*) was isolated from all the lungs of dead animals which yielded *Pasteurella* at bacteriological examinations (Table 13).

The specie of *Pasteurella* isolated from lung tissues did not demonstrate specific correlation with the type of lesions found at histopathological examination. For example, calf number 91 (Table 16) displayed a picture of acuteness and *Pasteurella multocida* (usually associated with more chronic lesions) was isolated from the lungs. These findings are in contrast with those of Carter (1958) and Schiefer (1978) who found correspondence between the organisms isolated and the characteristics of the histopathologic picture.

The results suggest that *Pasteurella* spp. organisms in the nasal passages of calves fluctuate widely in regard to



type and number with occasional periods of time when one type of *Pasteurella* prevails over the species. A common state of dynamic change of prevalence, probably explained by bacteriocin activity (Chengappa, 1977) or by immunological phenomena (Mukkur, 1977), may play a role in these changes. There is also a complex host-bacterial relationship in the normal bovine. Some strains of bacteria seem capable of establishing themselves within the host's tissues without apparently causing clinical disease. Highly virulent strains of *Pasteurella* organisms can apparently establish residence within the nasopharynx and exist there for long periods of time without apparent harm to the carrier (Collins, 1976). Clinical disease may only occur following exposure to another pathogen or following some type of unusual stress.

#### IV. Antimicrobial Tests

The antimicrobial tests performed indicated that *P. hemolytica* was sensitive to most of antibiotics tested, whereas *P. multocida* demonstrated an unusual resistance to several of the same antimicrobial agents (Tables 14 and 15). For example, 18 of 20 strains of *P. multocida* isolated during this study were resistant to triple sulfa whereas this antimicrobial has been recognized as effective against the *Pasteurella* organisms (Carter, 1967). In regard to Streptomycin and Neomycin, only one strain of *multocida* was susceptible to each of these antibiotics. However, these antibiotics have also been recognized as effective in the

treatment of bovine respiratory disease (Carter, 1967; Seemann, 1977).

#### V. Pathology

It was not possible to attempt precise correlation between macroscopic or microscopic pathologic lesions and the isolation of *Pasteurella* organisms from nasal swabs or lung tissues. For example, calf number 53 (Table 16) demonstrated pulmonary lesions ranging from congestion to necrosis whereas *Pasteurella* organisms were not isolated from the lungs. In contrast, calf number 73 demonstrated relatively mild lesions in histopathologic examination; however *Pasteurella multocida*, which is usually associated with chronic lesions (Carter 1958, was isolated from the lungs of this calf.

The results emphasize the complexity of the bovine respiratory syndrome and illustrate the fact that the mere presence or absence of a specific microbial agent is not what is required in order to produce a specific pathological picture or disease. Viruses appear to be the key to the respiratory disease problem; however, many other factors have been associated: genetic deficiencies in cell enzymes and chronic disease of the lung or other organs (Green, 1970); antigen antibody complex depositions (Kim, 1977); stress and high glucocorticoids concentrations (Gwazdavskas, 1978); and other factors which increase the chance of a pathogen finding a susceptible host.

Whatever primary factor or microbiological agent is found, the major gross pathological lesions are usually caused by secondary invaders (usually bacteria, but also mycoplasmas and chlamydia). In the final analysis, severe clinical respiratory disease is nearly always the result of interaction between viruses and bacteria. For this reason the overall pathological picture of pneumonia in calves is generally very similar. Macroscopically, there is a uni or bilateral involvement of the anteroventral aspects of the lung because of anatomical and gravitational reasons. Microscopically, the end result usually is a combination of bronchopneumonia, bronchiolitis obliterans, bronchiectasis, abscess formation and necrosis.

It is the author's opinion that chronic diffuse non-specific pulmonary disease develops as various combinations and permutations of multiple etiologic factors meet, and slowly, but progressively, impair the multiple defense mechanisms of the respiratory tract. Lesions suggestive of the original etiological agent can not usually be recognized in field cases, nor can the original agent (usually virus) be isolated. The extent of damage in the lung will be related to the immune status of the host and the virulence of the agent (a) involved (Thomson, 1974).

## CONCLUSIONS

1. The results support the theory that IBR, BVD and PI3 viruses are ubiquitous in most bovine herds.

2. Serum titers against IBR and PI3 viruses do not necessarily imply protection against primary infection with these viruses in the respiratory tract epithelium in young calves.

3. More work needs to be accomplished in discerning the role of maternal antibodies in protection against IBR and PI3 infection of the respiratory tract epithelium and demonstrating the protective effect of colostrum immunoglobulins on the epithelium of the respiratory tract.

4. Neither the isolation of a specific bacteria nor the level of antibody serum titers against the most common viruses associated with respiratory disease are indicative of susceptibility or resistance to the onset of disease.

5. Studies to determine the effectiveness of mucosal immunity and cell mediated immunity at early age need to be encouraged.

6. Serum gammaglobulin concentrations are usually associated with the protection of the calf from disease; however, according to the results of the present study, it seems that the degree of protection also depends on the quality and quantity of specific antibodies transferred from the mother to the newborn. Antibodies are specific and high

serum immunoglobulin values in calves should not imply protection against all pathogen infection or disease.

7. A maintenance or slight increase in the serum antibody titers against IBR and PI3 viruses in young calves for more than three weeks could be indicative of early infection with these viruses. BVD virus does not follow the same pattern because of its special characteristics (see page 65 ).

8. There is not a consistent association between the presence of *Pasteurella* organisms in the nasal passages and the onset of disease.

9. According to the results of this study, there is no clear correlation between the type of *Pasteurella* spp. isolated and the microscopic histopathological findings.

10. The results of bacteriological isolations from nasal swabs and from lung tissue of dead calves (Tables 2 through 5) suggested that the bovine respiratory tract possesses a dynamic flora which seems to be constantly fluctuating in a series of equilibria.

11. The specific lesions of viral agents are not observed in the natural clinical respiratory disease. Lesions suggestive of etiology are not usually recognized in field cases. There is a great similarity in the macroscopic and microscopic lesions caused by the most common bacterial agents associated with bovine respiratory disease, particularly in the chronic stages (see page 74 ).

12. According to the present study, microscopic lesions



did not allow the identification of the causal agent(s).

13. Infection with *P. multocida* or *P. hemolytica* does not establish the final characteristics of the microscopic lesions when bovine respiratory disease occurs under natural conditions.

14. The results suggest that there is a difference in antimicrobial susceptibility between *P. multocida* and *P. hemolytica*. According to the obtained results, it can be suggested that any treatment of bovine respiratory disease should be treated according to the prevalence of type and incidence of the most common causal agents of bovine respiratory disease in any specific region.

15. The solution of the respiratory disease problem in the bovine specie lies initially in the determination of the relative importance of the individual factors involved in the development of the syndrome.

## ACKNOWLEDGMENTS

I would like to express my deep appreciation and gratitude to my advisor, Dr. Jerome Vestwebér, for his scientific guidance and example and for his personal patience and understanding.

It is a pleasure to acknowledge the help, advice and friendship of Drs. Horst W. Leipold, Neil V. Anderson and Harish C. Minocha, members of my committee.

Sincere appreciation is also extended to Elwayne (Bill) Stowe and Freddy Parra for their contribution to this work.

Finally, the author wants to express his gratitude to Universidad Centro Occidental of Venezuela and to the Department of Surgery and Medicine of the Veterinary School of Kansas State University for their economical support.

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## APPENDICES

## APPENDIX I

## FIGURES

Taken from:  
Bovine Anatomy,  
W.M. McLead, 1958.

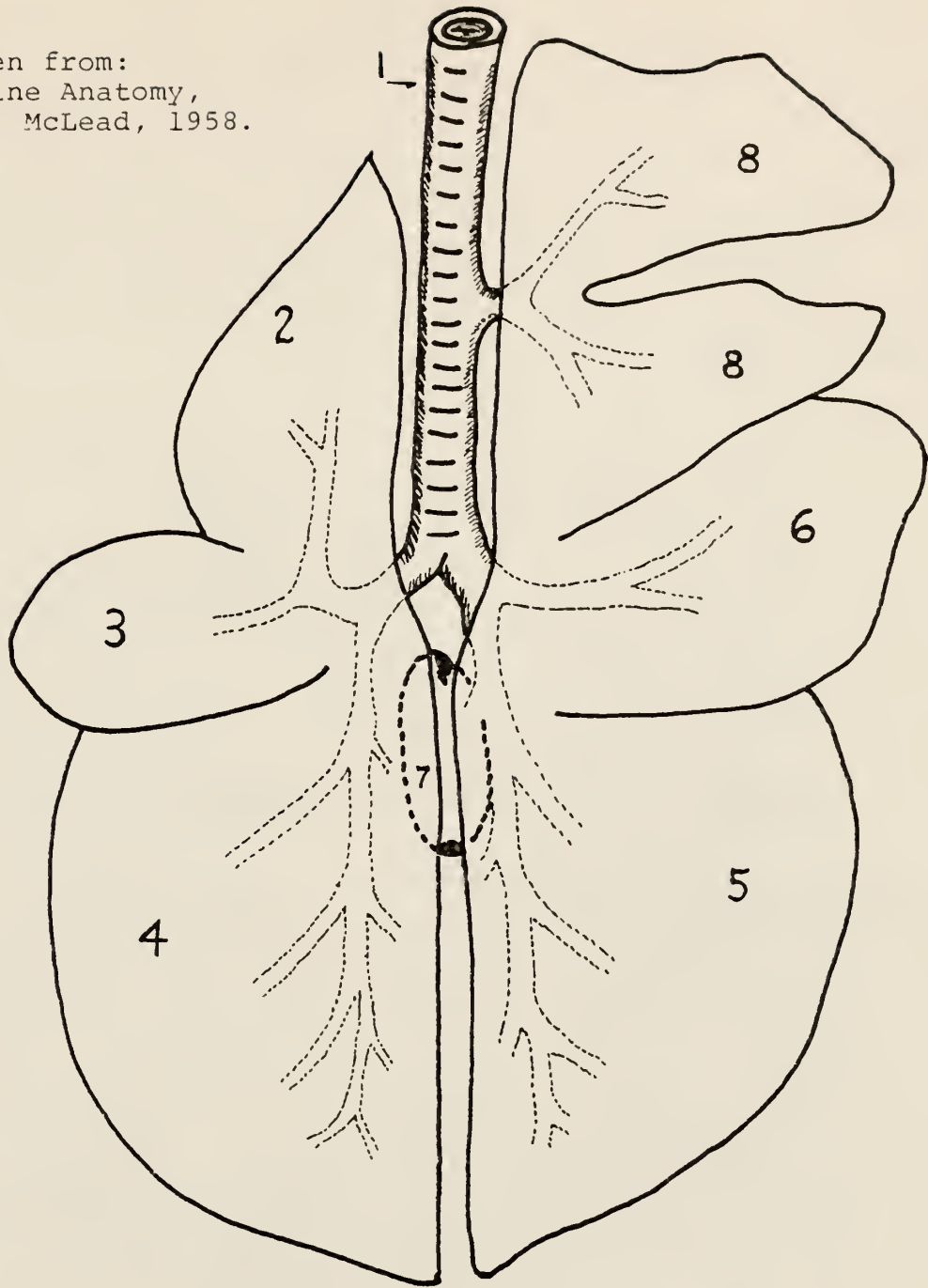


Fig. 1. Lung

1. Trachea
2. Left apical lobe
3. Left cardiac lobe
4. Left diaphragmatic lobe
5. Right diaphragmatic lobe
6. Right cardiac lobe
7. Intermediate lobe
8. Right apical lobe

Fig. 2. Infectious Bovine Rhinotracheitis Virus

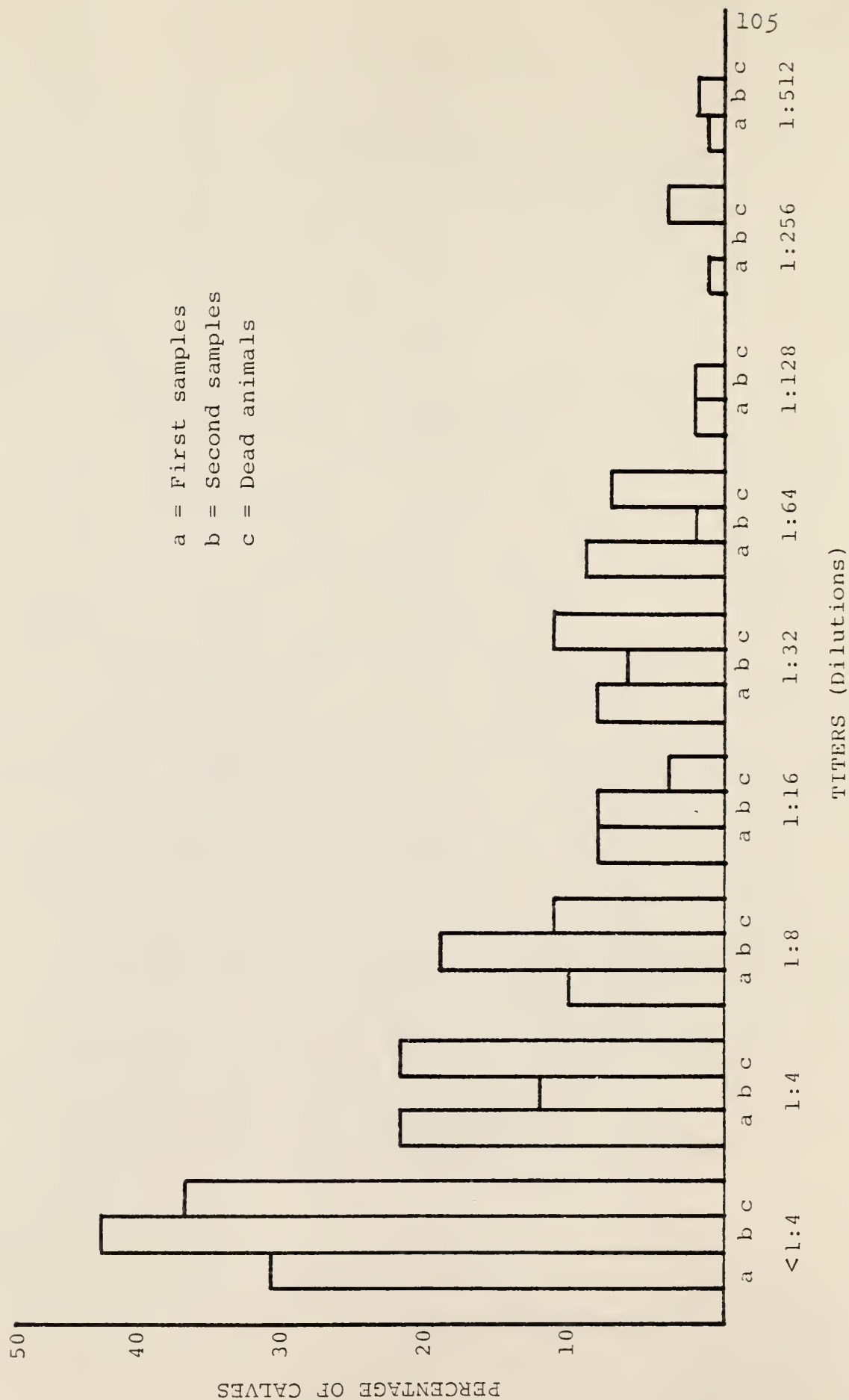


Fig. 3. Parainfluenza 3 Virus





Fig. 4. Bovine Virus Diarrhea

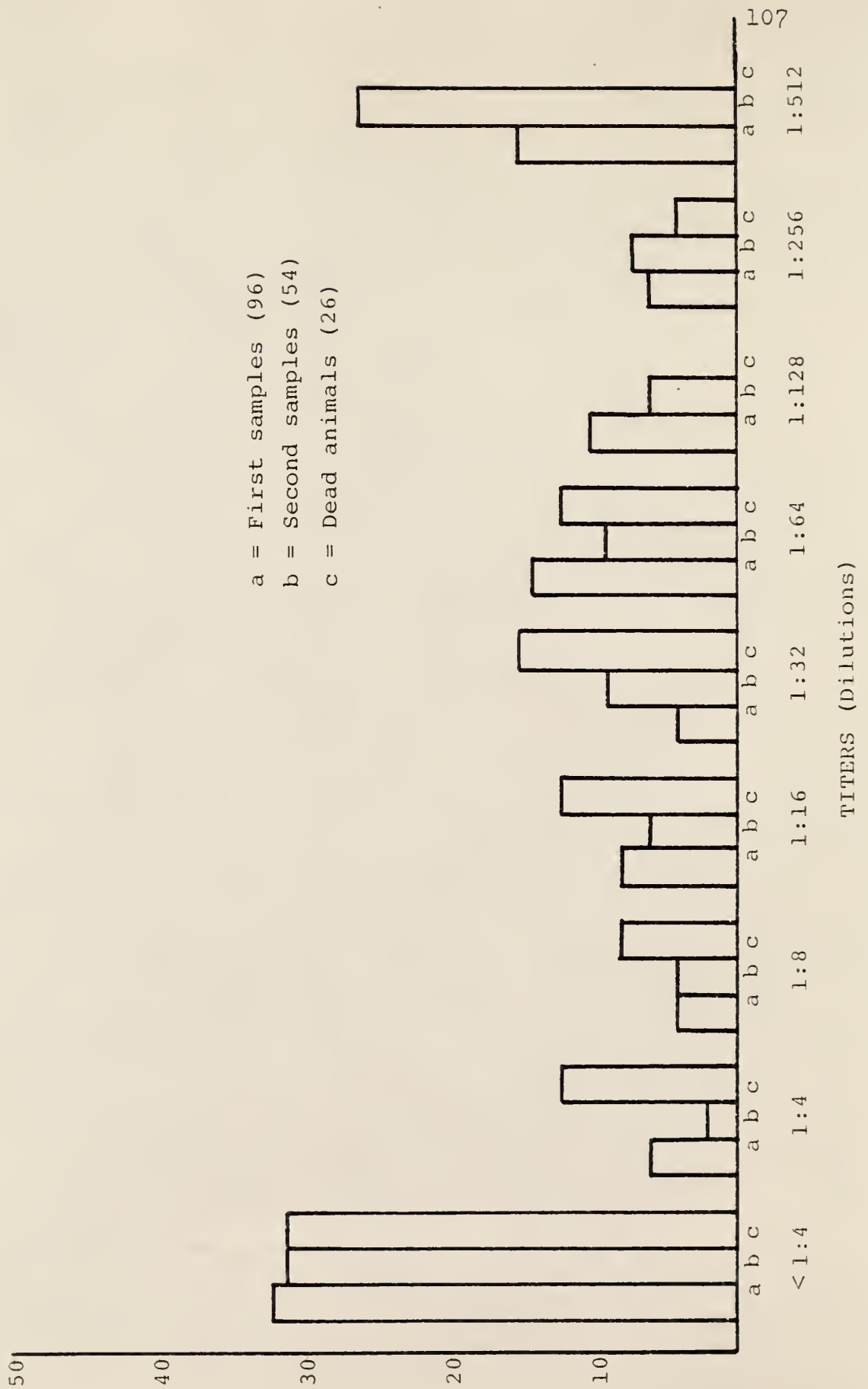


Fig. 5. Incidence of the most common microscopic lesions and its degree of compromise.

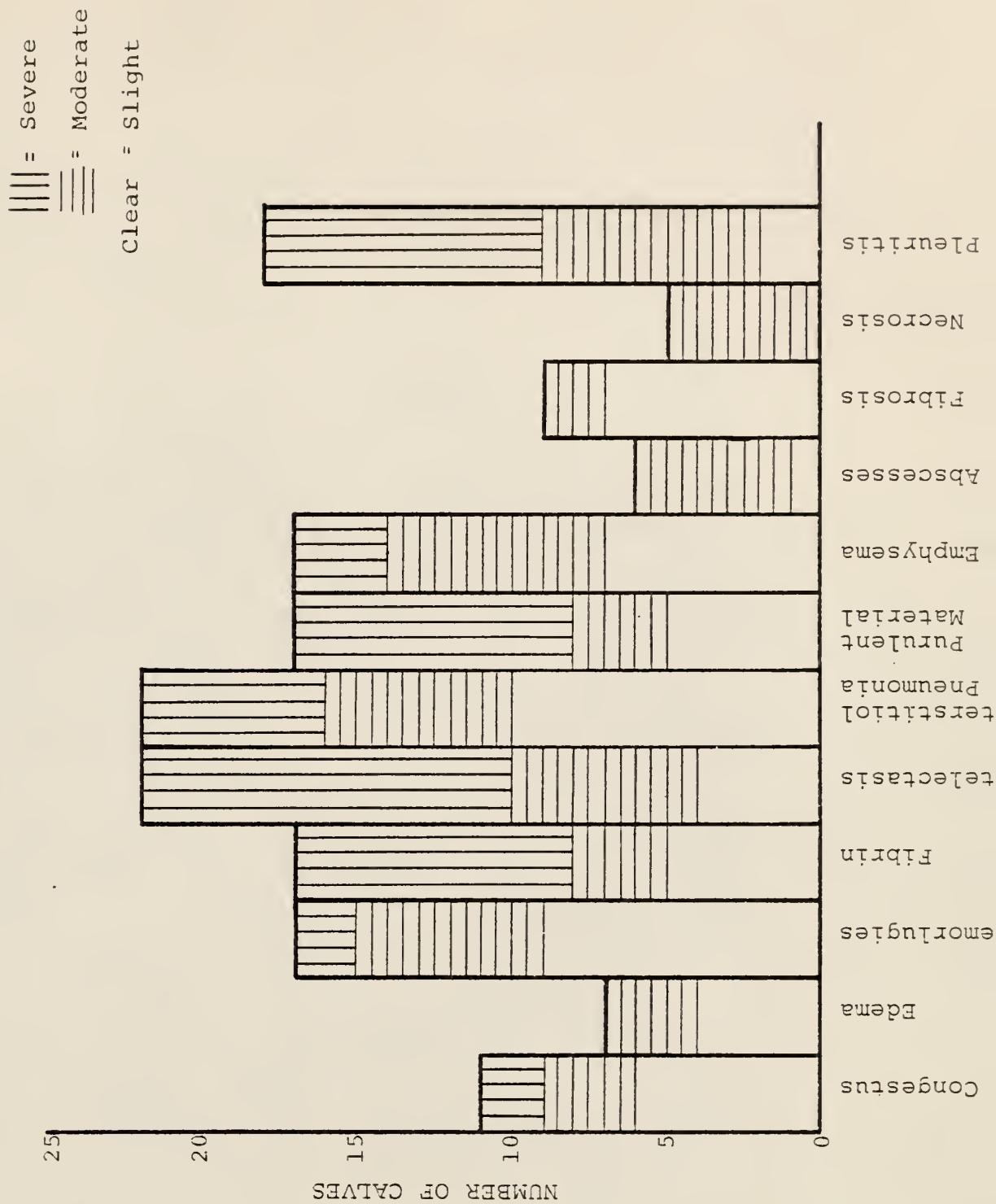


Fig. 6. Acute purulent bronchopneumonia in a calf.  
H & E, 200X. Notice plugging of bronchi by  
purulent exudate (a).

Fig. 7. Acute bronchopneumonia in a calf. Notice  
bronchitis (a) and alveoli (b) filled with macro-  
phages. H & E, 200X.

Fig. 8. Pleuritis in a calf. Notice organizing fibrin  
(a). H & E, 200X.

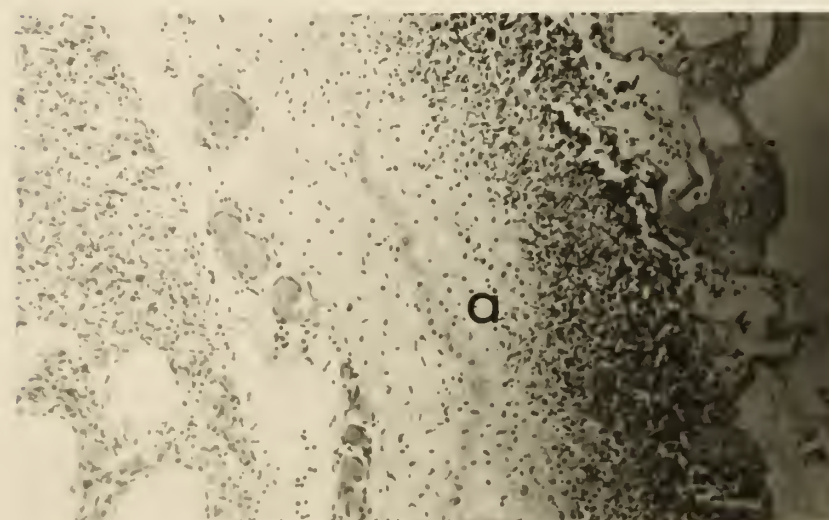
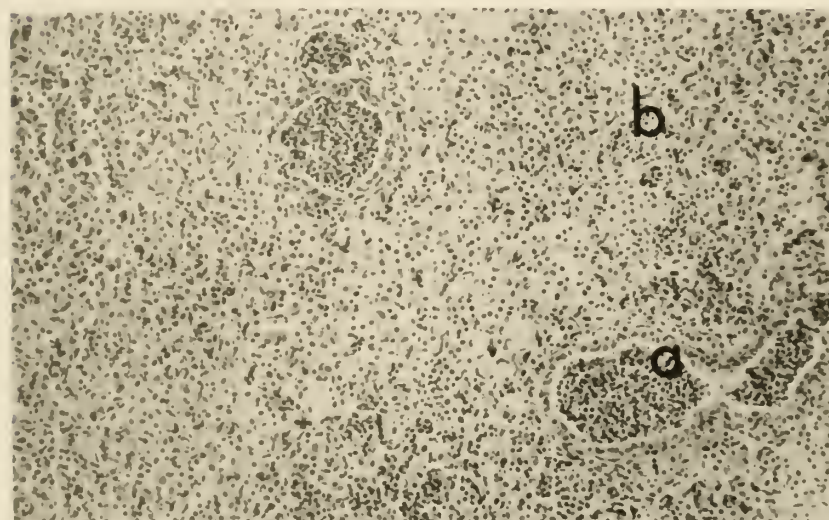
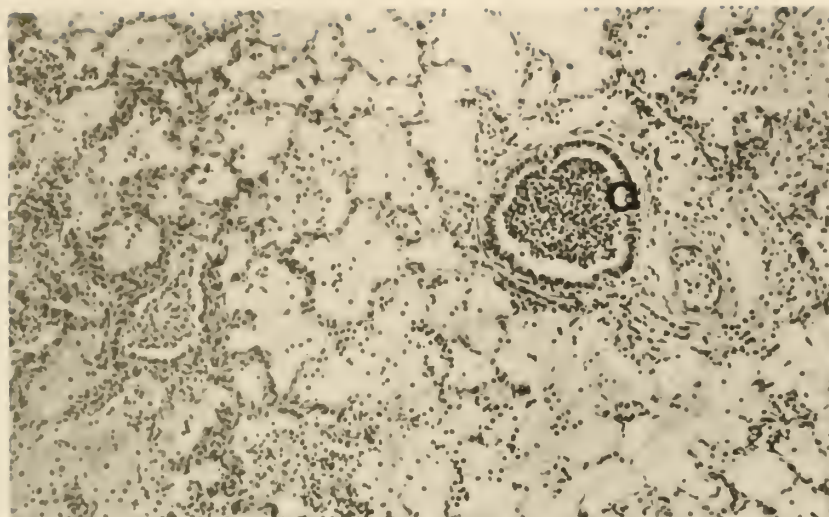


Fig. 9. Chronic bronchopneumonia. Notice fibrous thickening of alveolar septa. H & E, 200X.

Fig. 10. Chronic changes encountered in bronchopneumonia. Notice epithelialization of alveoli (arrow). H & E, 200X.

Fig. 11. Chronic bronchopneumonia. Notice fibrous tissue. H & E, 200X.



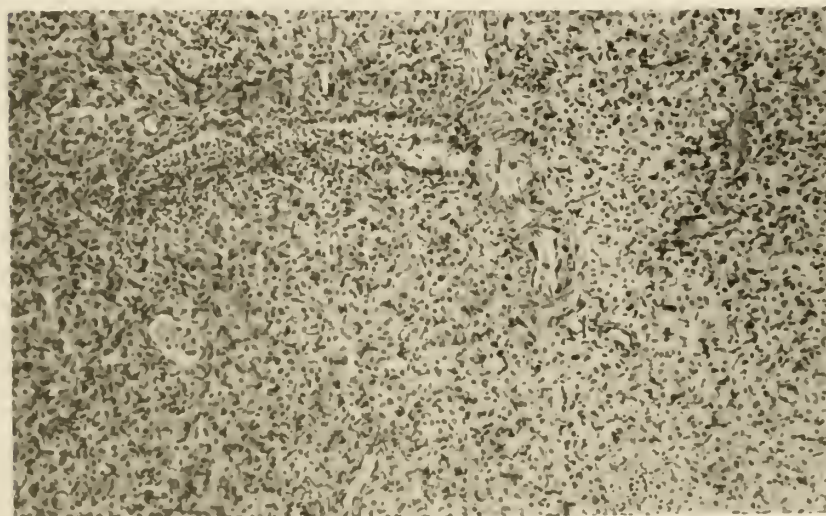
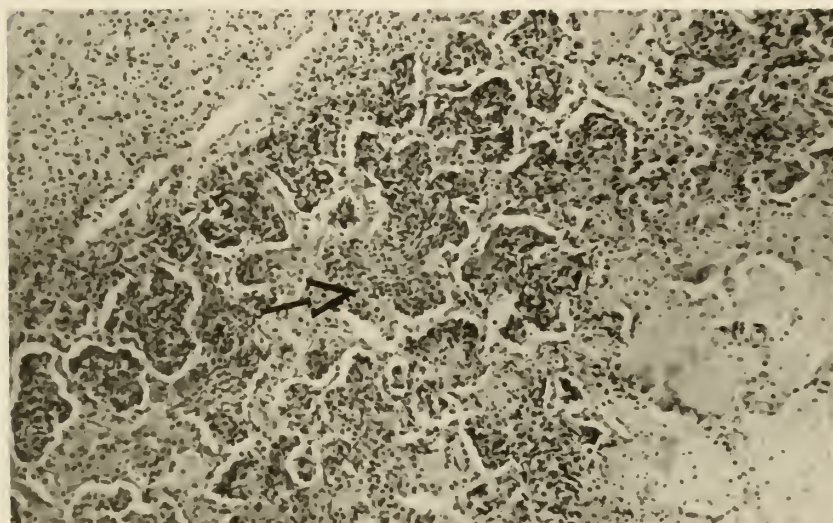
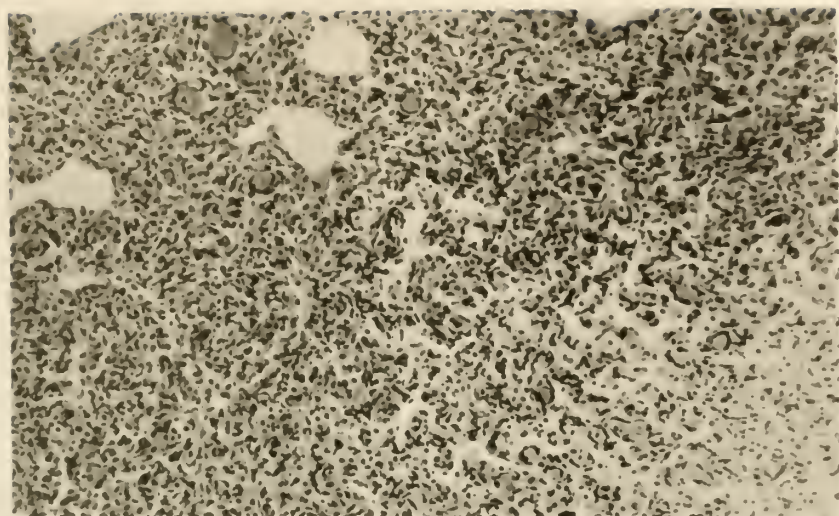
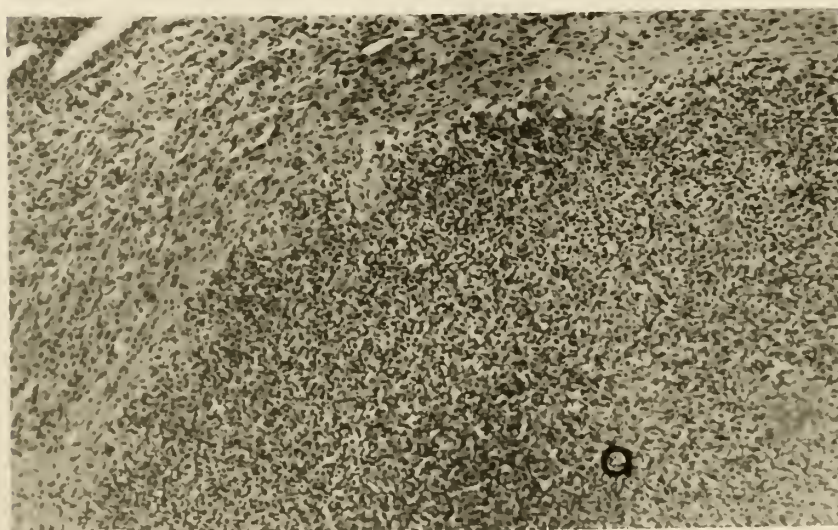
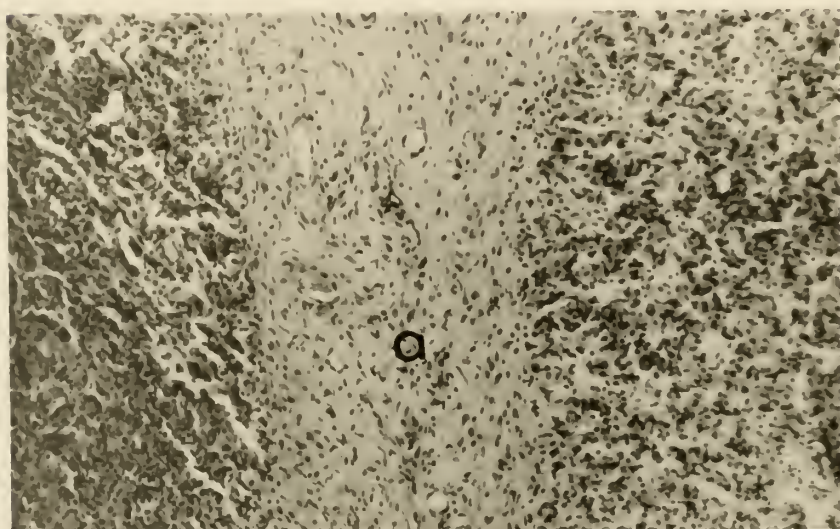
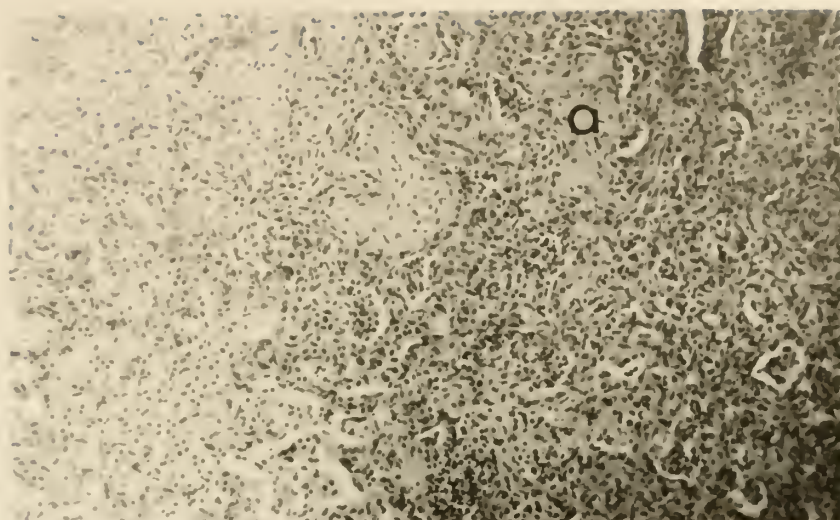


Fig. 12. Chronic bronchopneumonia. Notice fibrous tissue (a).

Fig. 13. Chronic bronchopneumonia. Notice proliferation of fibrous tissue in interlobular septum (a).  
H & E, 200X.

Fig. 14. Abscess formation (a) in a chronic bronchopneumonia. H & E, 200X.





## APPENDIX II

## TABLES

TABLE 1

PATTERN FOR IDENTIFICATION OF *P. MULTOCIDA* AND *P. HEMOLYTICA*

ORGANISM	COLONY MORPHOLOGY (BLOOD AGAR)	CATALASE	KOH	TSI 1 Acid/Acid or Acid/No Change	OXIDASE	NITRATE	UREA	INDOL	CITRATE	SUGARS 2
<i>Pasteurella multocida</i>	Round, gray colonies of 1-5mm. Some of them up to 8mm. Musty odor.	+	+	Acid/Acid or Acid/No Change	+	+	-	+	-	
<i>Pasteurella hemolytica</i>	Usually small colonies 0.5-1mm. Some with a halo of hemolysis.	+	+	Acid/Acid or Acid/No Change	+	+	-	-	-	D: +; X: -; M: +; L: -; S: +; M: +; or D: +; X: +; M: +; L: -; S: +; M: +.

1 Triple sugar iron agar

2 D: Dextrose; X: Xylose; M: Mannitol; L: Lactose; S: Sucrose; M: Maltose



TABLE 2

SEROLOGY, SERUM PROTEINS, BACTERIAL ISOLATIONS AND PATHOLOGICAL LESIONS IN CALVES FROM GROUP 1

CALF NO.	SERUM SAMPLES <sup>1</sup>						REMARKS	SERUM PROTEINS <sup>3</sup>			BACTERIAL ISOLATION				PULMONARY LESIONS	
	IBR BVD Pi3							Total Serum proteins	Globulins	Gamma-globulins	Nasal Swabs				Macroscopic	Microscopic
	Sample No.										Lung Tissues					
	1	2	1	2	1	2					PH	PM	PH	PM		
25	4	256	512				Dead-Diarrhea <sup>4</sup>	4.9	1.7	0.75	-	+	-	-	+++	3
26	4	4	16				Dead-Diarrhea	4.7	1.9	0.91	+	-	-	+	++	1
27	64	32	32				Dead-Diarrhea	5.1	1.3	0.51	-	+				
28	64	512	8					5.1	1.7	0.90	-	+	-	+	+	2
29	8	4	4					5.1	1.5	0.75	-	+				
30	4	4	128					6.0	2.7	1.29	-	-				
31	512	128						7.6	4.1	2.23	-	-				
32	32	64	64					4.8	1.8	0.76	+	-				
33	4	4	4					5.1	1.3	0.33	-	+				
34	4	4	4					4.4	0.9	0.30	+	-				
35	32	4	128					6.4	2.4	0.86	-	-				
36	4	256	8					6.1	2.9	1.37	-	-				
37	128	8	256					5.4	2.1	0.93	-	-				
38	8	16	128					5.8	2.1	1.07	-	+				
39	64	4	128					5.2	1.9	0.80	-	+				
40	16	128	64					6.1	2.5	1.13	-	-				
41	4	4	128					4.9	1.9	0.93	-	-				
42	16	256	64					4.7	1.4	0.51	-	-				
43	256	8	128				Dead-Diarrhea	5.9	2.4	1.13	-	-	-	+	+++	3
44	4	16	32				Dead-Diarrhea	4.7	1.2	0.45	-	+	-	-	+++	3
45	16	512	16				Dead-Diarrhea	6.3	3.4	2.24	-	-	-	-	+++	2
46	4	64	64				Dead-Diarrhea	6.5	3.2	1.63	-	-	-	+	++	1
47	32	16	8				Dead	5.5	2.3	1.15	-	-	-	-	+++	2
48	4	16	256					4.9	1.3	0.40	-	-				

1 Titers expressed as the reciprocal of the highest dilution.

2 First sample taken at arrival, second sample 15-17 days later.

3 Tested on the day of arrival.

4 It means that the calf had some degree of diarrhea at dead time.

5 Pasteurella gallinarum.

IBR: Infectious Bovine Rhinotracheitis virus

BVD: Bovine viral diarrhea virus

Pi3: Parainfluenza 1 virus

PH: Pasteurella hemolytica

PM: Pasteurella Multocida

TABLE 3

SEROLOGY, SERUM PROTEINS, BACTERIAL ISOLATIONS AND PATHOLOGICAL LESIONS IN CALVES FROM GROUP II

CALF NO.	SERUM SAMPLES 1						REMARKS	SERUM PROTEINS 3			BACTERIAL ISOLATION			PULMONARY LESIONS		
	IBR		BVD		PI3			Total Serum Proteins	Globulins	Gamma-globulins	Nasal Swabs		Lung Tissues		Macroscopic	Microscopic
	Sample No. 2										PH	PM	PH	PM		
	Sample No. 2															
	1	2	1	2	1	2										
49	<4	---	32	---	4	---	Dead - Diarrhea <sup>4</sup>	4.9	1.7	0.20	+	-	-	0	1	
50	<4	<4	64	256	64	64	BVD Seroconversion	5.4	1.5	0.60	+	-	-			
51	<4	<4	4	≥512	<4	<4	BVD Seroconversion	5.1	1.3	0.10	-	+	-			
52	<4	<4	128	≥512	64	32	BVD Seroconversion	6.1	2.1	0.80	+	-	-			
53	4	---	8	---	4	---	Dead	5.0	1.2	0.40	-	-	-	+++	3	
54	<4	---	128	---	32	---	Dead	5.3	1.7	0.80	-	-	-	0	2	
55	4	<4	<4	<4	128	128		7.0	5.5	1.70	+	-	-			
56	<4	<4	256	≥512	128	64		7.3	2.9	1.10	+	-	-			
57	8	<4	128	128	32	32		5.3	1.9	0.80	-	-	-			
58	64	32	128	≥512	32	32	BVD Seroconversion	6.6	3.0	1.51	+	-	-			
59	4	8	>512	≥512	64	64		6.2	2.8	1.21	-	+	-			
60	128	≥512	≥512	≥512	256	256	IBR Seroconversion	7.1	3.9	1.77	-	-	-			
61	64	128	128	>512	16	16	BVD Seroconversion	5.8	2.6	0.94	-	-	-			
62	32	8	64	128	16	16		6.2	2.8	0.94	+	-	-			
63	8	4	8	32	4	4	BVD Seroconversion	5.7	2.3	0.26	-	-	-			
64	<4	<4	<4	<4	32	16		5.2	1.9	0.19	-	-	-			
65	16	4	<4	<4	32	16		5.5	1.9	0.34	+	-	-			
66	<4	---	<4	---	<4	<4	Dead - Diarrhea	4.5	1.4	0.18	+	-	-	+	2	
67	4	<4	128	>512	64	64	BVD Seroconversion	6.5	3.9	1.80	-	-	-			
68	<4	---	4	---	4	---	Dead - Diarrhea	4.6	1.6	0.14	-	-	-	+	1	
69	4	<4	64	256	64	64	BVD Seroconversion	6.2	3.4	1.31	-	-	-			
70	<4	<4	256	≥512	128	128		6.5	3.5	1.47	-	-	-			
71	<4	<4	64	>512	32	32	BVD Seroconversion	5.7	2.8	0.93	-	-	-			
72	64	16	<4	<4	32	16		7.0	3.9	1.81	+	-	-			

1 Titers expressed as the reciprocal of the highest dilution

2 First sample taken at arrival, second sample 15-17 days later

3 Tested on the day of arrival

4 It means that the calf had some degree of diarrhea at dead time

IBR: Infectious Bovine Rhinotracheitis virus

BVD: Bovine viral diarrhea virus

P13: Parainfluenza III virus

PH: Pasteurella Hemolytica

PM: Pasteurella Multacida

TABLE 4

SEROLOGY, SERUM PROTEINS, BACTERIAL ISOLATIONS AND PATHOLOGICAL LESIONS IN CALVES FROM GROUP III

CALF NO.	SERUM SAMPLES 1					REMARKS	SERUM PROTEINS 3			BACTERIAL ISOLATION				PULMONARY LESIONS				
	IBR	BVD					Gamma-globulins	Total Serum Proteins	Globulins	Nasal Swabs	Lung Tissues		Macroscopic	Microscopic				
		Sample No. 2									pH	PM			pH	PM		
		1	2	1	2												1	2
73	<4	---	32	---	16	---	Dead	4.5	2.1	0.52	+	-	+	++	2			
74	<4	4	64	16	16	<4		4.5	1.1	0.27	-							
75	4	8	<4	<4	32	8		4.7	1.7	0.46	-							
76	<4	<4	≥512	≥512	256	64		6.2	2.8	0.97	+							
77	16	4	128	32	128	64		6.0	2.7	1.19	5	1						
78	<4	---	128	---	4	---	Dead	5.0	1.6	0.52	-		-	+++	2			
79	32	---	64	---	16	---	Dead	4.0	1.6	0.26	+		-	+++	2			
80	64	16	<4	<4	64	64		5.3	2.3	0.84	+							
81	16	16	128	32	8	4		4.9	2.0	0.68	-							
82	8	8	<4	<4	8	4		5.5	1.6	0.45	+							
83	4	4	≥512	≥512	32	16		5.8	2.2	0.53	-							
84	32	32	≥512	64	32	16		5.6	2.5	0.87	-							
85	<4	<4	<4	<4	64	64		5.6	2.7	1.02	-							
86	16	16	≥512	64	32	16		5.9	3.0	1.57	+							
87	<4	<4	<4	<4	16	8		4.7	1.7	0.39	+							
88	<4	8	≥512	32	64	64		6.7	3.3	1.51	+							
89	32	8	256	64	8	4		5.1	1.9	0.34	-							
90	4	8	≥512	≥512	256	64		7.5	4.7	2.05	-							
91	64	---	64	---	64	---	Dead - Diarrhea 4	6.8	3.9	1.85	+		-	+	1			
92	<4	64	64	256	8	32	IBR, BVD & PI3 Seroconversion	6.9	3.8	1.86	-							
93	8	8	<4	<4	8	8		5.5	2.4	0.87	+							
94	<4	<4	<4	<4	64	32		5.9	2.6	1.19	-							
95	8	4	≥512	64	128	64		5.9	2.8	1.25	+							
96	32	---	<4	---	64	---	Dead	6.3	3.1	0.99	-		-	+++	2			

<sup>1</sup> Titers expressed as the reciprocal of the highest dilution<sup>2</sup> First sample taken at arrival, second sample 15-17 days later<sup>3</sup> Tested on the day of arrival<sup>4</sup> It means that the calf had some degree of diarrhea at dead time<sup>5</sup> Pasteurella spp.

IBR: Infectious Bovine Rhinotracheitis virus

BVD: Bovine viral diarrhea virus

PT3: Parainfluenza 3 virus

PM: Pasteurella hemolytica

PM: Pasteurella multocida

TABLE 5

SEROLOGY, SERUM PROTEINS, BACTERIAL ISOLATION AND PATHOLOGICAL LESIONS IN CALVES FROM GROUP IV																
CALF NO.	SERUM SAMPLES 1					REMARKS	SERUM PROTEINS 3			BACTERIAL ISOLATION				PULMONARY LESIONS		
	IBR		BVD				Total Serum Proteins	Globulins	Gamma-globulins	Nasal Swabs		Lung Tissues		Macroscopic	Microscopic	
	Sample No. 2									PII	PM	PII	PM			
	1	2	1	2	1											2
97	4	---	<4	---	4	Dead-Diarrhea <sup>4</sup>	4.4	1.3	0.27	+	-	-	-	Lost	2	
98	4	---	<4	---	32	Dead-Diarrhea	5.6	2.4	0.95	-	-	-	-	++	2	
99	8	---	<4	---	32	Dead-Diarrhea	4.8	1.8	0.49	-	-	-	-	++++	2	
100	4	<4	<4	8	32	BVD seroconversion	5.7	2.0	0.79	+	+	+	+			
101	64	16	64	32	32		5.3	2.5	0.86	-	+					
102	4	---	<4	---	16	Dead	5.1	1.6	0.56	+	+	-	-	Lost	3	
103	4	4	16	16	16		6.2	2.1	0.42	5	-					
104	8	8	<4	<4	8		4.5	1.1	0.18	-	+					
105	4	8	<4	4	64		5.6	2.5	0.96	-	-					
106	<4	<4	<4	<4	16		5.2	1.7	0.42	+	-					
107	4	<4	4	<4	4		5.3	1.5	0.35	+	+					
108	16	8	16	8	16		5.9	2.1	0.64	+	-					
109	<4	<4	<4	<4	32		6.4	2.9	0.82	5	-					
110	4	<4	<4	<4	32		6.5	3.3	1.31	+	-					
111	64	32	>512	256	64		6.1	2.9	1.11	+	-					
112	32	32	>512	>512	64		6.4	2.5	1.00	-	-					
113	4	<4	64	128	<4		6.0	2.3	0.72	+	-					
114	8	---	32	---	<4	Dead-Diarrhea	6.4	2.2	0.30	-	-	-	+	Lost	1	
115	4	<4	<4	<4	8		4.8	1.5	0.26	-	-					
116	<4	<4	64	64	64		5.5	2.1	0.81	-	+					
117	4	---	<4	---	4	Dead	5.1	1.5	0.36	-	+	+	+	Lost	Lost	
118	<4	---	<4	---	8	Dead	4.6	1.5	0.72	-	+	-	-	Lost	1	
119	8	---	16	---	16	Dead-Diarrhea	6.1	2.1	0.45	+	-	-	+	Lost	3	
120	16	4	16	16	16		6.4	2.8	1.08	+	-					

IBR: Infectious Bovine Rhinotracheitis virus

BVD: Bovine viral diarrhoea virus

PI3: Parainfluenza 3 virus

PII: Pasteurella hemolytica

PM: Pasteurella multocida

PG: Pasteurella gallinarum

1 Titers expressed as the reciprocal of the highest dilution

2 First samples taken at arrival, second samples 15-17 days later

3 Tested on the day of arrival

4 It means that the calf had some degree of diarrhoea at dead time

5 Pasteurella spp were isolated

6 Only one slide was studied from calves 97, 102, 114, 118 and 119

TABLE 6

TOTAL PROTEIN, GLOBULIN AND GAMMAGLOBULIN VALUES IN 96 CALVES

Determination	Minimum	Maximum	Mean	SD <sup>1</sup>
Total Serum Proteins	4.0	7.6	5.6	0.8
Globulins	0.9	3.9	2.3	0.8
Gammaglobulins	0.1	2.2	0.9	0.5

<sup>1</sup> Standard Deviation



TABLE 7  
TOTAL PROTEIN, GLOBULIN AND GAMMAGLOBULIN VALUES IN CALVES FROM GROUP I

CALVES	TOTAL PROTEINS				GLOBULINS				GAMMAGLOBULINS			
	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>
Total Group	4.4	7.6	5.5	0.7	0.9	4.1	2.1	0.8	0.3	2.2	1.0	0.6
Dead Calves	4.7	6.5	5.5	0.7	1.2	3.4	2.2	0.8	0.5	2.2	1.2	0.6
Survivor Calves	4.4	7.6	5.5	0.8	0.9	4.1	2.0	0.8	0.3	2.2	0.9	0.5

<sup>1</sup> Standard Deviation

TABLE 8

TOTAL PROTEIN, GLOBULIN AND GAMMAGLOBULIN VALUES IN CALVES FROM GROUP II

CALVES	TOTAL PROTEINS					GLOBULINS					GAMMAGLOBULINS				
	Minimum	Maximum	Mean	SD	<sup>1</sup>	Minimum	Maximum	Mean	SD	<sup>1</sup>	Minimum	Maximum	Mean	SD	<sup>1</sup>
Total Group	4.5	7.3	5.86	0.8		1.2	3.9	2.5	0.9		0.1	1.8	0.9	0.6	
Dead Calves	4.5	5.3	4.9	0.3		1.2	1.7	1.5	0.2		0.2	0.8	0.3	0.3	
Survivor Calves	5.1	7.3	6.1	0.7		1.3	3.9	2.7	0.8		0.1	1.8	1.0	0.6	

<sup>1</sup> Standard Deviation

TABLE 9  
TOTAL PROTEIN, GLOBULIN AND GAMMAGLOBULIN VALUES IN CALVES FROM GROUP III

CALVES	TOTAL PROTEINS					GLOBULINS					GAMMAGLOBULINS				
	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean
Total Group	4.0	7.5	5.6	0.8	1.1	3.9	2.5	0.8	0.3	2.0	0.9	0.5			
Dead Calves	4.0	6.8	5.3	1.2	1.6	3.9	2.5	1.0	0.3	1.9	0.8	0.6			
Survivor Calves	4.5	7.5	5.7	0.8	1.1	3.8	2.5	0.8	0.3	2.0	1.0	0.5			

<sup>1</sup> Standard Deviation

TABLE 10

TOTAL PROTEIN, GLOBULIN AND GAMMAGLOBULIN VALUES IN CALVES FROM GROUP IV

CALVES	TOTAL PROTEINS				GLOBULINS				GAMMAGLOBULINS			
	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>	Minimum	Maximum	Mean	SD <sup>1</sup>
Total Group	4.4	6.5	5.6	0.7	1.1	3.3	2.1	0.6	0.2	1.3	0.7	0.3
Dead Calves	4.4	6.4	5.3	0.7	1.3	2.4	1.8	0.4	0.3	1.0	0.5	0.2
Survivor Calves	4.5	6.5	5.7	0.6	1.1	3.3	2.2	0.6	0.2	1.3	0.7	0.3

<sup>1</sup> Standard Deviation

TABLE 11

DISTRIBUTION OF 59 STRAINS OF PASTEURELLAE ISOLATED FROM NASAL SWABS FROM CALVES

CATTLE SAMPLED		POSITIVE ANIMALS	PERCENTAGE OVER THE TOTAL	STRAINS OF PASTEURELLA <sup>1</sup> (number of isolations)			
Type	Number			P. Multocida	P. Hemolytica	P. spp.	P. Gallinarum
Total Group	96	55	57.3	35	19	3	2
Dead Calves	26	14	53.8	7	9	---	---
Survivor Calves	70	41	58.6	12	26	3	2

<sup>1</sup> Four animals yielded both Pasteurella Multocida and Pasteurella Hemolytica



TABLE 12

DISTRIBUTION OF 11 PASTEURELLA STRAINS  
ISOLATED FROM THE LUNGS OF 26 DEAD CALVES

NUMBER OF DEAD CALVES	NUMBER OF ISOLATIONS	PERCENTAGE	STRAINS OF PASTEURELLA <sup>1</sup>	
			P. MULTOCIDA	P. HEMOLYTICA
26	11	42.3	11	----

<sup>1</sup> Number of Isolations

TABLE 13

COMPARISON BETWEEN PASTEURELLA ISOLATED FROM NASAL SWABS AND LUNG TISSUE OF DEAD CALVES

CALF NUMBER	NASAL SWAB		LUNG TISSUE	
	P. hemolytica	P. multocida	P. hemolytica	P. multocida
26	+	-	-	+
28	-	+	-	+
43	-	-	-	+
46	-	-	-	+
73	+	+	-	+
79	+	-	-	+
91	+	-	-	+
96	-	-	-	+
114	-	-	-	+
117	-	+	-	+
119	+	-	-	+

TABLE 14

ANTIMICROBIAL SENSITIVITY OF 20 ISOLATES OF PASTEURELLA MULTOCIDA  
ON MUELLER-HINTON BOVINE BLOOD AGAR

DETERMINATION	ZONE DIAMETER (mm)			INTERPRETATION (N <sup>o</sup> of isolates)		
	Observation Range	Mean	SD <sup>1</sup>	Susceptible	Intermediate	Resistant
Ampicillin	6-34	22.8	8.6	16	---	4
Cephalathin	18-36	32.3	9.0	20	---	---
Chloramphenicol	26-36	28.8	2.7	20	---	---
Gentamycin	10-20	13.4	2.4	13	---	7
Kanamycin	6-20	14.0	4.7	4	10	6
Neomycin	6-27	12.4	4.8	1	9	10
Polymycin B	11-16	12.9	1.4	16	4	---
Streptomycin	6-24	9.9	3.7	1	4	15
Tetracycline	6-32	22.3	7.51	15	---	5
Trimethoprim/ Sulphathiazole	6-32	17.7	10.3	12	---	8
Triple Sulfa	6-30	8.2	6.67	2	---	18

<sup>1</sup> SD: Standard Deviation

TABLE 15

ANTIMICROBIAL SENSITIVITY OF 12 ISOLATES OF PASTEURELLA  
HEMOLYTICA ON MUELLER-HINTON BOVINE BLOOD AGAR

DETERMINATION	ZONE DIAMETER (mm)			INTERPRETATION (N <sup>o</sup> of isolates)		
	Observation Range	Mean	SD <sup>1</sup>	Susceptible	Intermediate	Resistant
Ampicillin	6-42	29.7	5.9	12	---	---
Cephalathin	25-46	31.0	7.7	11	1	---
Chloramphenicol	29-48	37.3	8.3	12	---	---
Gentamycin	13-22	16.9	4.6	12	---	---
Kanamycin	12-25	19.5	3.8	10	1	1
Neomycin	13-21	15.8	2.2	4	8	---
Polymycin B	12-18	14.3	2.0	12	---	---
Streptomycin	10-20	13.8	2.6	2	9	1
Tetracycline	26-36	29.0	3.4	12	---	---
Trimethoprim/ Sulphamethoxazole	23-37	27.6	4.6	12	---	---
Triple Sulfa	6-42	22.0	11.6	8	1	3

<sup>1</sup> SD: Standard Deviation

TABLE 16

PATHOLOGICAL LESIONS, PASTEURILLA ORGANISMS ISOLATED FROM LUNGS OF  
DEAD CALVES AND ANTIBODY TITERS AGAINST IBR, BVD AND PI3 VIRUS  
AT ARRIVAL

CALVES NO.	MACROSCOPIC LESIONS	MICROSCOPIC LESIONS								PASTEURILLA ISOLATIONS			SERUM TITERS					
		CONGESTION	EDEMA	HEMORRHAGES	FIBRIN	ATELECTASIS	INTERSTITIAL PNEUMONIA	PURULENT MATERIAL	HEPATOMA	ABSCESSES	EMBOSI	NECROSIS	PLEURITIS	P <sub>m</sub>	Ph	IBR	BVD	P13
25	+++	-	-	++	++	+++	+	++	+	++	++	++	+++	-	-	<4	256	≥512
26	++	+	+	+	++	+++	+++	-	++	-	-	-	-	+	-	4	4	16
28	+	-	-	++	+++	++	++	+++	-	-	-	-	++	+	-	64	≥512	8
43	+++	-	-	-	+++	+++	+	++	+	++	++	++	+++	+	-	256	8	128
44	++++	-	-	-	+++	+++	+	+++	+	++	+	+	+++	-	-	<4	16	32
45	++++	-	-	++	+++	+++	+	+++	-	+	-	+	+++	-	-	16	≥512	16
46	++	+	+++	-	+++	+++	+++	+	-	-	-	-	++	+	-	<4	64	64
47	+++	+	++	+	++	++	++	+++	-	-	-	-	+++	-	-	32	16	8
49	0	+++	++	+	-	+++	-	-	-	-	-	-	-	-	-	<4	32	4
53	++++	++	-	++	+++	+++	-	++	++	++	++	++	+++	-	-	4	8	4
54	0	-	+	+	+++	+++	+++	-	++	-	-	-	-	-	-	<4	128	32
66	+	-	+	-	+++	+++	+	+	-	-	-	-	-	-	-	<4	<4	<4
68	+	-	+++	-	+	+	+	-	-	-	-	-	-	-	-	<4	4	4
73	++	++	+	+++	+++	++	++	+	-	-	-	-	++	+	-	<4	32	16
78	++++	-	-	-	++	+++	+	+++	-	-	-	-	+++	-	-	<4	128	4
79	++++	+	-	+	+++	++	++	+++	-	-	+	-	+++	+	-	32	64	16
91	+	+++	+	+	+	+	-	+	-	+	-	-	-	+	-	64	64	64
96	+++	-	-	-	+++	+++	++	+++	++	++	-	-	++	+	-	32	<4	64
97 <sup>3</sup>	Lost	+	+	+	+++	+	+	-	-	+	-	-	-	-	-	4	<4	4
98	++	-	-	-	+++	+++	+++	+	++	++	-	-	++	-	-	4	<4	32
99	++++	-	-	-	++	++	++	+++	++	++	-	-	+++	-	-	8	<4	32
102 <sup>3</sup>	Lost	-	-	++	-	++	-	+++	-	+	+	+	++	-	-	4	<4	16
114 <sup>3</sup>	Lost	+	-	+++	-	++	+	+	-	+	-	-	++	+	-	8	32	<4
117	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	Lost	+	-	4	<4	4
118 <sup>3</sup>	Lost	++	+	+	+	+	+	-	+++	-	-	-	+	-	-	<4	<4	8
119 <sup>3</sup>	Lost	-	+	-	-	-	-	-	-	+	+	+	++	+	-	8	16	16

1 Expressed as the inverse of the highest dilution

2 From lung tissue

3 Only one slide studied



RESPIRATORY DISEASE OF NEONATAL DAIRY CALVES: SEROLOGICAL,  
BACTERIOLOGICAL AND PATHOLOGICAL STUDIES

by

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AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY

Manhattan, Kansas

1978

## ABSTRACT

Serum samples from 96 young (3 to 9 days old) dairy calves were taken at arrival and again 15-17 days later from the survivor calves. High incidence of maternal antibodies against IBR, BVD and PI3 viruses was found among the surveyed calves suggesting that infections with these viruses are common in cattle populations.

There was an indication of active infection within the calves only for BVD virus. The former finding suggests that early viral infection can occur in young calves and also that they are able to develop an immunologic response. No clear relationship could be established between mortality rate and serum antibody titers.

The mean values for total proteins, globulins and gammaglobulins were determined and compared with former reports. The lack of a steady correlation between the values obtained for the different groups and mortality rate suggests that total serum protein concentration not always is directly related to protection from disease in young calves but that other factors as immune status of the dam are involved.

The isolation of *Pasteurella* organisms from the nasal cavity of apparently healthy calves suggests that these organisms are common inhabitants of the nasal passages of young calves. It appears that there is a complex host-bacterial interaction and that the kind of microorganisms

fluctuate widely in regard to type and number. The former assumption can be inferred from the fact that there was not a clear correlation between the type of *Pasteurella* isolated from the nasal swabs and the type isolated from the lungs.

The isolation of *P. multocida* and no *P. hemolytica* from the lungs of dead calves with a wide variety of lesions would suggest that *P. multocida* can be associated to the respiratory pathology regardless of the acuteness or chronicity of the lesions.

Antibiotic susceptibility tests were performed on the strains of *P. multocida* and *P. hemolytica* isolated from the nasal swabs and/or lung tissues. *P. multocida* exhibited an unusual resistance to the antibacterial tested; for example 18 of 20 strains tested were resistant to triple sulfa.

The results of pathologic studies showed that, macroscopically, the lesions were localized on the anteroventral aspects of the lungs which is the result of anatomical and gravitational phenomena. Microscopically, a wide variety of pathologic lesions were found without any apparent association with the presence or type of *Pasteurella* organisms suggesting that chronic diffuse nonspecific pulmonary disease develops as a result of combinations and permutations of multiple etiologic factors.

