

511  
EPIDEMIOLOGY AND PROPHYLAXIS  
OF DISEASE AND MORTALITY  
IN HOUSED DAIRY CALVES

by

BRUCE RICHARD WATT

B.V.Sc., University of Sydney, 1976

---

A MASTER'S THESIS

Submitted in partial fulfillment of the  
requirements for the degree

MASTER OF SCIENCE

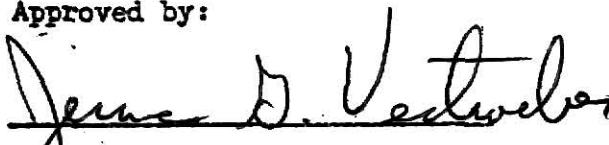
Department of Surgery and Medicine

KANSAS STATE UNIVERSITY

Manhattan, Kansas

1980

Approved by:

  
Major Professor

**THIS BOOK  
CONTAINS  
NUMEROUS PAGES  
THAT HAVE INK  
SPLOTCHES IN THE  
MIDDLE OF THE  
TEXT. THIS IS AS  
RECEIVED FROM  
CUSTOMER.**

**THESE ARE THE  
BEST IMAGES  
AVAILABLE.**

Spec. Coll.  
LD  
2668  
.T4  
1980  
W377  
c.2

#### ACKNOWLEDGEMENTS

I am grateful for the help of many people in completion of these studies. Rebecca Brownson provided an enormous amount of assistance in caring for the calves, in data collection and in helping with radial immunodiffusion. Drs. Morrill and Corbeil provided much early guidance and encouragement.

As members of my committee, Drs. Vestweber, Anderson and Morrill were most helpful and their critical appraisal of the studies and thesis was greatly appreciated. Dr. Dennis and the Department of Pathology, Dr. Coles and the Department of Laboratory Medicine and Dr. Anthony and the Diagnostic Laboratories were most cooperative and provided helpful advice. Dr. Bostwick allowed me to manage the health of the calves during the study period and, in addition, was most cooperative and helpful.

Drs. Bordt and Bramer from Syntex Agribusiness were generous in providing hyperimmune serum, Serogen, for the second study. Dr. Feyerherm from the Department of Statistics helped design the second study and his patient assistance in analysing and interpreting the data was invaluable. Dr. Mosier and the Department of Surgery and Medicine provided funding to enable this study to be undertaken.

I also wish to thank Mr. Pat Murphy of Extension Engineering for conducting ventilation studies, Mary Schmidt for assistance with the dairy calves and John Lyons who instructed me in the technique of electrophoresis.

## TABLE OF CONTENTS

PAPER I	page
An epidemiological study of mortality and disease in housed dairy calves	4
 PAPER II	
Parenteral immunoglobulin administration to hypogammaglobulinemic calves	34
 REVIEW OF LITERATURE	
Hypogammaglobulinemia in calves: Its incidence, causes, effects, diagnosis and treatment	61
 ABSTRACTS	1



PAPER I  
AN EPIDEMIOLOGICAL STUDY OF  
MORTALITY AND DISEASE IN  
HOUSED DAIRY CALVES

## INTRODUCTION

Neonatal calf mortality continues to be a serious problem to the cattle industry with mortality rates frequently estimated at from 8-25%.<sup>1-5</sup> Mortality is highest around parturition and in the first month of life.<sup>4,6,7</sup> In calves surviving parturition, diarrhea and pneumonia are the main causes of death.<sup>2,4</sup>

The many factors affecting neonatal calf health have been classified as (i) microbiological, (ii) immunological, (iii) nutritional, (iv) genetic, (v) physical and (vi) psychological.<sup>8</sup> These factors interact considerably and act collectively to adversely affect the health of the calf.

This investigation examined some of the factors influencing neonatal calf disease and mortality in a group of housed dairy calves.

## MATERIALS AND METHODS

This investigation, conducted from January 2, 1979 to May 21, 1979, involved the 98 Holstein calves born alive at the Kansas State University Dairy Teaching and Research Center (KSUDTRC) during that time.

### Management of the Calves

Parturition occurred in straw-bedded earth floor pens within an open-front maternity barn. Calves stayed with their dams for 24 hours except during the epizootic of severe neonatal diarrhea when calves were removed earlier. Colostrum was administered if calves appeared not to have nursed sufficiently.

The calf barn to which the calves were then moved consisted of two rooms, one holding 32 calves and the other holding 30 calves. Ventilation in each room was via exhaust fans with controlled air inlets. Supplemental heat was provided to maintain the temperature at a minimum of 13 C. Calves were kept in individual elevated crates constructed with sides and bottom of metal rod.

Calves received colostrum for the first three days of life and then were fed either milk and calf starter or an experimental milk replacer. Calves were fed twice daily when general attitude, feed consumption and fecal character was noted. Fecal character was graded from one (formed) to four (liquid diarrhea).<sup>9</sup> Rectal temperatures were taken once daily and calves judged to be sick were further examined and treated, if necessary, by one of the authors (B.W.). Calves consuming more than 0.7 kg of dry feed daily and having gained 9 kg above birth weight were weaned, and removed from the calf rooms.

## Diagnostic Procedures

### 1. Bacteriology

Lung and tissue samples submitted to the Diagnostic Laboratory (DL) at Kansas State University were plated onto blood agar, McConkey agar, Salmonella-Shigella agar and phenylethyl alcohol agar. Plates were incubated for 24 hours at 37°C. In addition nasal swabs were plated onto blood agar and McConkey agar in 10% carbon dioxide at 37°C. Intestinal and fecal swabs were also plated onto brilliant green agar and into gram negative broth. The gram negative broth was incubated for 24 hours then rechecked to brilliant green agar.

Colonies on blood agar which were typical of *Pasteurella* were identified on the basis of odor (*P. multocida*), hemolysis (*P. hemolytica*), indole production (*P. multocida*), reaction on triple iron sugar agar, lack of growth on McConkey agar and ability to produce cytochrome oxidase.

Colonies typical of *E. coli* (lactose fermenting) on McConkey agar were inoculated onto triple sugar iron agar, lysine iron agar and SIM medium (sulfide, indole, motility). Those colonies fermenting lactose and producing indole were considered to be *E. coli* and were then tested for heat labile and heat stable enterotoxin production.<sup>10</sup>

Fecal samples submitted to the Clinical Pathology laboratory were plated onto blood, McConkey and Salmonella-Shigella agar and incubated for 24 hours at 35°C. *E. coli* recovered for K-99 antigen testing were transferred daily for 3 days onto Minca agar plates, then tested for K-99 antigen. To test for the K-99 antigen a slide agglutination test was used. The growth from the third Minca plate was mixed with formalised saline and one drop of this suspension added to one drop of antigen on a slide. Agglutination indicated a positive result. One drop of normal rabbit serum plus one drop of antigen on a slide provided the control.

The isolate salmonella samples were inoculated onto selenite brilliant green agar and incubated overnight at 35°C. A small amount of broth was then inoculated onto McConkey and Salmonella-Shigella plates and incubated overnight.

Colorless colonies both directly after incubation on blood agar, McConkey or Salmonella-Shigella agar or following growth in selenite

brilliant green agar then McConkey and Salmonella-Shigella agar were inoculated onto biochemical media to determine presence of salmonella. Triple sugar iron agar, urea and citrate agar and indole and tyrosine broths were used.

To evaluate the importance of clostridia, fecal samples were inoculated onto blood agar plates and incubated anaerobically for 24-48 hours. A subjective assessment of the number of clostridial colonies growing was made.

## 2. Parasitology

Fecal specimens were placed in centrifuge tubes containing saturated zinc sulfate solution and centrifuged for 5 minutes at 100 x G with a glass cover slip in place. The glass cover slip was removed, placed on a glass slide and examined at 100 magnification for ova and coccidia. Giemsa stained fecal smears were examined for cryptosporidia.

## 3. Virology

Serum samples submitted to the DL were tested for antibodies to infectious bovine rhinotracheitis (IBR), bovine virus diarrhea virus (BVD), parainfluenza-3 virus (PI<sub>3</sub>) and adenovirus Type 3 virus (A-3). The serum neutralization test was performed on all samples.

Fluorescent antibody studies were performed on fecal and necropsy samples by the DL as described.<sup>11</sup>

Virus isolation procedure. - Tissues and feces from affected calves were homogenised using a mortar and pestle. A 10% suspension of the homogenate was made using Eagles basic salt solution with 1000 units of penicillin, 1000 micrograms of streptomycin sulfate and 50 micrograms of amphotericin B added to each milliliter of solution. This suspension was frozen and thawed once then centrifuged at 1000 x G for 10 minutes. The supernatant was passed onto 16 x 25 mm roller tubes containing embryonic bovine kidney cells. Cell cultures were observed daily for cytopathic effect. Three blind passages were made and a fluorescent antibody test done on the third passage for Rota, Corona and BVD virus before the sample was discarded.

Electron microscopy. - Electron microscopic examination of feces was performed by a modified method of Horne.<sup>12</sup> The fecal material was

diluted 1:5 in phosphate buffered saline and the crude material removed by centrifugation at 2500 x G for 10 minutes at 4°C. The supernatant was saved and centrifuged at 100,000 x G for one hour. The pellet obtained was resuspended in 5 drops of distilled water. A negative stain was prepared by mixing 20 drops of distilled water with 4 drops of 4% phosphotungstic acid and one drop of 0.1% bovine serum albumen. One drop of the pellet mixture was added to the negative staining solution and mixed with a Pasteur pipette. After 5 minutes the suspension was sprayed onto a carbon-coated collodion filmed copper grid using an all-glass nebulizer and examined immediately in the electron microscope.

#### Ventilation Measurement

Air velocities were measured using an air velocity meter.<sup>A</sup> To calculate air change rate a mean air velocity (over 9 measurements) was calculated at the exhaust fan grid after other major sources of air leakage were sealed. The mean air velocity at the grill was then multiplied by the area of the grid to give an exhaust volume per hour. This figure was then divided by the volume of the room to give the ventilation rate in air changes per hour.

#### Immunological Procedures

The immunoglobulin content of serum samples was determined using the Zinc Sulfate Turbidity<sup>13</sup> Test and protein electrophoresis.<sup>14</sup> Determination of quantity of individual classes of immunoglobulins was performed using single radial immunodiffusion.<sup>15</sup>

#### Indices of Disease and Mortality

Only observations made in the first 28 days of the calf's life were included in this study. Therefore, the indices of disease are all a pro-

---

A Kurz Air Velocity Meter  
Model 444  
Kurz Instruments, Incorporated  
Carmel Valley, California

portion of the calf's length of life or for 29 days if calves survived the first month.

1. Diarrhea incidence.

The diarrhea incidence was the number of days which the calf had a fecal score <sup>9</sup> of four at both morning and evening observation, as a percentage of the calf's length of life.

2. Incidence of blood in the feces.

The incidence of blood in the feces was the number of days in which blood was observed in the feces expressed as a percentage of the days of the calf's life.

3. Pneumonia incidence.

The pneumonia incidence was the number of days the calf exhibited clinical signs of pneumonia as a percentage of the days of the calf's life.

## RESULTS

It is intended to present the major clinical syndromes observed and the distribution of mortality and then to outline some of the contributing factors.

### 1. DISTRIBUTION OF MORTALITY

Of the 98 calves studied, 29 died - mortality rate of 29.6%. The age and sex distribution of the mortalities is presented in Figure 1. All but one of the calves which died, died within the first 28 days of life.

### 2. MAJOR SYNDROMES OBSERVED

#### 1. Acute neonatal diarrhea

This syndrome was characterised by severe depression, rapid (10-15%) dehydration with sunken eyes, profuse yellow watery diarrhea and hypothermia. The age of onset was between 10-60 hours and onset was very abrupt - often progressing from normality to collapse in six hours. 19 calves were affected severely enough to require intravenous fluid therapy. Of these 19 calves one died before treatment could be given, two died during treatment and the remaining 16 responded well to fluid therapy. Of the 16 survivors, however, 6 subsequently died at from 8-28 days of age. The incidence of diarrhea in surviving calves was not different from the incidence in calves which did not develop acute neonatal diarrhea.

#### 2. Chronic diarrhea

This syndrome was characterised by yellow fluid diarrhea, often with varying amounts of blood, mucus and occasionally intestinal casts. Calves were mildly depressed, with slight to moderate (5-7%) dehydration and in uncomplicated cases, a normal temperature. As shown on Figure 2 peak incidence of chronic diarrhea was at 10-12 days of age and was usually resolved by one month of age.

#### 3. Pneumonia

Pneumonia was characterised by fever (temperature  $39.7^{\circ}$  -  $42.7^{\circ}$  C), increased respiration rate ( $>30$ -40 breaths/min.), mild to moderate depression, coughing, serous to purulent nasal discharge, serous ocular discharge and dry or moist rales particularly in the ventral and anterior



lung field. Pneumonia was confirmed at necropsy in calves as early as one week of age and incidence plateaued from 2-4 weeks of age.

#### 1. MICROBIOLOGICAL FACTORS

E. coli isolates from cases of acute neonatal diarrhea and from chronic diarrhea were tested for K99 antigen and for toxin production. Four of eight isolates were K99 positive and five of 15 isolates were heat stable toxin producers. No Salmonella were isolated from any of the fecal samples cultured.

A very limited examination (2 samples) for cryptosporidia failed to reveal the presence of these organisms and six samples examined for clostridia were regarded as normal. No helminths or coccidia were found on fecal examination.

Most calves were vaccinated soon after birth with modified live rota-corona vaccine.<sup>A</sup> Since these calves shed vaccine strain rota- and corona virus, interpretation of virus isolation results was more difficult. Therefore, in March 1979, some calves were not vaccinated to facilitate virus studies. One non-vaccinated calf which died at 30 hours of age with acute neonatal diarrhea was fluorescent-antibody (FA) positive for rotavirus.

One non-vaccinated calf which died following an episode of hemorrhagic diarrhea was FA positive for corona virus (and negative for rotavirus). Nine fecal samples from calves with chronic diarrhea with or without blood were also submitted for virus isolation. Corona virus was successfully isolated from these samples and identified both by fluorescent antibody and electron microscope.

Three calves which died between 2½ to 3 weeks of age with chronic diarrhea plus or minus blood were FA positive for bovine virus diarrhea virus (BVD) at necropsy.

---

A    Scourvax II  
      Norden Laboratories  
      Lincoln, Nebraska

To determine the infectious agents involved in the pneumonia, nasal swabs for virus isolation and bacteriology were taken from 12 calves. In addition, blood samples were taken from 11 calves three weeks apart for serum neutralization tests for BVD, infectious bovine rhinotracheitis (IBR) virus, parainfluenza-3 (PI<sub>3</sub>) virus and adenovirus-type 3.

All calves tested either had pneumonia at the time of first examination or developed pneumonia just after first examination (3 calves). Virus isolation studies were uniformly negative. Results of the serum neutralization tests presented on Table 1 showed that significant seroconversion did not occur to any of the viruses studied.

Of the nine nasal swabs taken from calves with pneumonia at the time of sampling, eight yielded Pasteurella hemolytica while one yielded mixed flora suggestive of contamination. Of the three calves which had yet to develop pneumonia only E. coli, streptococci, staphylococci and Bacillus sp. were isolated. Pasteurella hemolytica and Pasteurella multocida were isolated from the lungs of calves with pneumonia at necropsy but no respiratory viruses were isolated.

No attempt was made to examine either clinical or necropsy cases for chlamydia or mycoplasma.

## 2. IMMUNOLOGICAL FACTORS

A limited number of calves were sampled to determine immunoglobulin status before onset of disease. The calves developing acute neonatal diarrhea usually developed the disease before 48 hours. Initial samples were not taken from these calves.

Table 2 demonstrates the relationship between total gammaglobulin values as determined by electrophoresis, individual immunoglobulin class levels as determined by single radial immunodiffusion and the Zinc Sulphate Turbidity Test (ZST) and cause of death. Calves surviving had significantly higher gammaglobulin levels ( $P < 0.05$ ), as measured by electrophoresis, than calves dying of pneumonia or pneumonia plus diarrhea. The ZST showed a similar trend but differences were not significant.

A significant relationship also existed between length of life and gammaglobulin value as measured by electrophoresis ( $P < 0.08$ ) and ZST ( $P < 0.1$ ).

During the time of study variations in total and individual class immunoglobulin values were noted with lowest values being recorded from late January to early March. Small sample size in many two week groups prevents meaningful analysis.

### 3. PHYSICAL ENVIRONMENT

The calves were housed in two rooms in which the temperature was controlled at a minimum of 13 C. Despite this environmental control, there was a significant seasonal variation in the incidence of diarrhea, bloody diarrhea and pneumonia. (Figure 4,5) A significant seasonal difference in weight gain in the first week and the first month of life was also observed, as demonstrated on Figure 5.

The variable factor was not temperature, which was controlled, but ventilation rate which was reduced in the winter to avoid excessive heat loss. A retrospective study of the ventilation was conducted on May 7, 1980. Winter settings on the exhaust fans of one room was estimated to have an air change rate of 2.7 changes/hour and the other 3.6 changes/hour. Air velocities measured at calf level were variable with measurements of from 3-7 m/min to 13-20 m/min being obtained.

A diurnal variation in relative humidity was observed. The relative humidity was lowest at 6-8 am at 50-60%, rose to a peak at 12 noon, fell slightly, then rose to a higher peak at 6-8 pm. After 6-8 pm the relative humidity fell steadily until 6-8 am. The 12 noon peak and the 6:00 pm peak followed the twice daily washing and hosing of the concrete floors.

### 4. GENETIC FACTORS

Since at least 10 sires were used, analysis of disease incidence and mortality in the calves related to sire was not conducted.

The sex of the calf, which can be regarded as genetic, was an important factor in disease and mortality. Male calves had a highly significantly greater incidence of diarrhea and significantly shorter average length of life. Male calves had a higher mortality rate (37%) than female calves (21%). Male calves, however, had no significantly different incidence of blood in the feces or of pneumonia. (Table 3) No significant difference in immunoglobulin levels between sexes was observed except for IgM (Table 4). The small sample size makes interpretation difficult.

The weight loss of males in the first week of life was significantly greater than the weight loss of females and the weight gain over the first month was also significantly lower in males. (Table 5)

#### 5. NUTRITIONAL FACTORS

Groups of calves were fed various different milk replacers. The results of these feeding trials and their influence on disease will be reported elsewhere.

#### 6. INTRAUTERINE AND OBSTETRICAL FACTORS

Calf birth weight was the only factor studied which could be directly related to the intrauterine environment. No significant relationship was demonstrated between calf birth weight and length of life, diarrhea score or pneumonia score. There was a significant ( $P < .07$ ) negative relationship between birth weight and the presence of blood in the feces.

The difficulty at calving was rated from 1 (easy calving) to 4 (very difficult calving) and 5 (requiring cesarean section). No relationship was found between calving score and length of life or diarrhea, pneumonia or bloody feces scores.

No significant relationship was demonstrated between parity and length of life or diarrhea, pneumonia or bloody diarrhea scores.

#### 7. PSYCHOLOGICAL FACTORS

No attempt was made to evaluate psychological factors as influencing calf mortality and disease. Since these calves were subjected to uniform management practices no differences in the calves' psychological environment was expected.

## DISCUSSION

It has been said that "every disease and epidemic is a complex of numerous variable factors".<sup>16</sup> Some of these factors have been examined in this disease outbreak. However, while it is difficult to list and explore the various factors in a disease outbreak, determining their relative importance and interaction is more difficult.

If we consider that infectious disease is a manifestation of the interaction between the host and the parasite or pathogen, then examination of host resistance and determination of the presence of pathogens would appear to be the first step in disease investigation. In this study numerous known pathogens were isolated. These pathogens included enterotoxigenic E. coli, Rota, Corona and BVD viruses and Pasteurellas. The antibody component of host resistance was studied and the well described relationship between immunoglobulin values and disease<sup>17-20</sup> was again demonstrated. In this study calves which survived had significantly higher immunoglobulin values than calves which died of pneumonia or pneumonia plus diarrhea. Calves which died of chronic diarrhea had lower values of immunoglobulins at 48 hours of age than calves which survived, but this difference was not significant.

However, it has been stated that the saying attributed to Claude Bernard, "Le microbe n'est rien, le milieu est tout" or "the microbe is nothing, the environment is everything" is very appropriate when considering calf enteric and respiratory disease.<sup>8</sup> In the calf barn in which these calves were housed, a compromise was necessary in that winter ventilation rates were reduced to prevent excess heat loss. At the winter exhaust fan setting, ventilation rates of 2.7 and 3.6 air changes per hour were calculated in each of the two rooms in which the calves were housed. This is below the recommended 4-8 air changes per hour.<sup>21,22</sup>

Air velocity control and the avoidance of drafts has been shown to be important in calf health. Recommendations of a maximum of 10-12 m/min. air velocity have been made.<sup>23,24</sup> In this study air velocities of up to 20 m/min. were recorded.

Breed differences in immunoglobulin absorption and resistance to

calfhood diseases, suggests a genetic predisposition.<sup>8</sup> A within breed analysis would be valuable in determining the possibility of selection for calves resistant to these diseases. As mentioned, the large number of sires used in this herd precluded this analysis.

The influence of sex of the calf on disease incidence is most interesting. Several studies have shown a higher disease incidence and mortality in male calves.<sup>26-28</sup> In this study male calves had a much higher mortality (37% versus 21%) than female calves and the incidence of diarrhea was highly significantly different ( $P < .0006$ ) in males than females. Male calves are often managed quite differently than female calves so the comparison of mortality rates and disease incidence is often difficult. In this case, the only deliberate difference in management of males compared to females was that more males were included in certain diet groups than females. The effect of the different diets on the incidence of diarrhea and mortality will be reported elsewhere, however, this male-female difference has been observed at KSUDTRC in previous years in the absence of dietary differences.<sup>29</sup>

If we can discount management differences as accounting for the sex predisposition to diarrhea and mortality, then we must consider other factors which might differ in males and female calves. Two such factors are birthweight (and subsequent obstetrical problems) and intrinsic physiological or endocrine factors. The mean birthweight of the male calves in this study was significantly higher ( $P < .004$ ) than the females (44.5 kg vs 40.7 kg). However, there was no significant correlation between birthweight and either diarrhea, pneumonia or the length of life (there was a significant relationship between birth-weight and the presence of blood in the feces). There was also no significant relationship between calving difficulty and length of life or incidence of diarrhea.

There is a possibility that endocrine differences in males compared to females is the basis for the difference in diarrhea and mortality. Hyperthyroidism at birth has been associated with a higher incidence of fatal diarrhea although immunoglobulin absorption was not affected.<sup>30</sup> Elevated pre-partum progesterone values in the dams have been associated with a higher incidence of dystocia<sup>24,25</sup> and weak calves and progesterone

can result in flaccidity when injected into pre-natal lambs.<sup>33</sup>

There is possibly a sex difference in these hormone levels. The hormones most obviously different in male compared to female calves are the sex hormones, so the possibility exists that they are involved in the observed sex difference in disease and mortality.

Although not included in Roy's list of factors<sup>8</sup> on "environments" affecting calf health, it is felt that intrauterine and obstetrical factors should be considered. These factors are perhaps less important in dairy calves than beef calves, and the influence of the intra-uterine environment in particular is difficult to measure. However, in certain circumstances these factors are most important. Undernutrition of the dam has been implicated in producing weak calves and reduced colostral absorption in calves.<sup>34</sup> Several diseases including leptospirosis,<sup>35</sup> brucellosis<sup>35</sup> and bovine virus diarrhea,<sup>36</sup> which by infecting the fetus or placenta, have been found to produce weak calves with a high mortality rate. Dystocia may induce brain damage and meningeal hemorrhage in neonatal calves and so reduce viability.<sup>37</sup>

It was considered that in this study intra-uterine and obstetrical factors were not important in subsequent calf disease and mortality. No relationship was demonstrated between calving difficulty or parity and disease or mortality. The infectious agents known to produce weak calves at birth were not isolated (although BVD virus was isolated from cases of chronic diarrhea). Birthweight which is influenced by fetal nutrition was not significantly related to mortality or the incidence of disease (except as previously mentioned - blood in the feces).

Psychological and nutritional factors would both be considered in an investigation of calf health problems. As mentioned, the nutritional influences on calf health observed in this study will be reported elsewhere.

There was no deliberate difference in the way calves were handled or managed. While it could be argued that stress occurred in calves individually penned in raised crates, the marked seasonal differences in disease and mortality suggest that environmental or microbiological factors were most important in this disease outbreak.



An investigation into the cause of disease and mortality in housed Holstein calves within the first month of life was conducted.

The mortality rate was 29.6% with all but one calf dying in the first month of life. Acute neonatal diarrhea affecting calves from 10-60 hours of age, chronic diarrhea frequently with blood and mucus and pneumonia were the main disease syndromes observed.

Enterotoxigenic K99 positive Escherichia coli (E. coli) and rotaviruses were isolated from neonatal diarrhea cases. E. coli, corona viruses and bovine virus diarrhea viruses were isolated from chronic diarrhea cases. Pasteurella hemolytica was the main isolate from calves with pneumonia. Virus isolation and serological studies revealed no evidence of viral respiratory pathogens.

Calves that died from pneumonia or chronic diarrhea plus pneumonia had significantly lower immunoglobulin levels at 48 hours of age than calves that survived. Calves dying of chronic diarrhea had lower levels of immunoglobulins than survivors but the difference was not significant.

Pneumonia incidence was highest in February while diarrhea and bloody feces incidence was highest in March and April.

The calf barn was maintained at a minimum of 13° C. Air exchange was measured at 2.7 air changes per hour in one room and 3.6 exchanges per hour in the other. Air velocity readings ranged from 3-7 m/min to 13-20 m/min in various parts of the room. Relative humidity ranged from 50% to 80% and exhibited a diurnal variation.

Male calves had a significantly higher mortality and incidence of diarrhea than female calves. There was no sex predisposition to pneumonia or bloody feces.

Parity, calving difficulty or birth weight had no relationship with disease or mortality except that the appearance of blood in the feces was negatively correlated with birth weight.

The interrelationship and importance of the various factors in calf mortality and disease is discussed.



## REFERENCES

1. Amstutz HE: Calf Diseases. V International Meeting on Diseases of Cattle. Opatija, Yugoslavia. pp 33-39, 1968
2. Prenatal and Postnatal mortality in Cattle. National Academy of Sciences, 2101 Constitution Avenue, Washington D.C. pp 1-129, 1968
3. Speicher JA, Hepp RE: Factors associated with calf mortality in Michigan. JAVMA 162: 463-466, 1973
4. Oxender WD, Newman LE, Morrow DA: Factors influencing calf mortality in Michigan. JAVMA 162: 458-460, 1973
5. Grunsell CS: Mortality and morbidity in calves. Vet Rec 68: 788, 1956
6. Dennis SM: Perinatal mortality in ruminants. Compendium on Continuing Education, Large Animal Supplement 1: 517-526, 1979
7. Withers FW: Mortality rates and disease incidence in calves in relation to feeding, management and other environmental factors, Part VI. Brit Vet J 109: 122-131, 1953
8. Roy JHB: Decision making and calf health. J Royal Agricultural Society of England. 132: 81-105, 1971
9. Larsen LL, Owen FG, Albright JL, et al: Guidelines toward more uniformity in measuring and reporting calf experimental data. J Dairy Sci 60: 989-991, 1977
10. Phillips RM, Kelley B, Anthony HD: The identification of enterotoxigenic Escherichia coli as a routine diagnostic procedure. 20th Annual Proceedings, Amer Assoc Vet Lab Diag, 1977
11. Howard DR: Fluorescent antibody techniques for diagnosing animal disease conditions. 22nd Annual Proceeding, Amer Assoc Vet Lab Diag 283-302, 1979
12. Horne RW, Magington J: Electron microscope studies of the development and structure of poliomyelitis virus. J Mol Biol 1: 333-335, 1959
13. McEwan AD, Fisher EW, Selman IE; et al: A turbidity test for the estimation of immune globulin levels in neonatal calf serum. Clin Chim Acta 27: 155-163, 1970
14. Serum protein electrophoresis procedure, Helena Laboratories, 1530 Lindborgh Drive, P.O. Box 752, Beaumont, Texas, 77704, 1977

15. Mancini G, Carbonara AO, Heremans JF: Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry* 2: 235-254, 1965
16. Dudley SF: Ecological outlook of epidemiology. *Proc Roy Soc Med* 30: 57, 1936
17. Gay CC, Anderson N, Fisher EW, et al: Gammaglobulin levels and neonatal mortality in market calves. *Vet Rec* 77: 148-149, 1965
18. Fisher EW, Selman IE, McEwan AD, et al: Some causes of and some factors affecting mortality in newborn calves. V. International meeting of diseases of cattle. Opatija, Yugoslavia, pp 41-54, 1968
19. Boyd JW, Baker JR, Leyland A: Neonatal diarrhea in calves. *Vet Rec* 95: 310-313, 1974
20. McEwan AD, Fisher EW, Selman IE: Observations on the immune globulin levels of neonatal calves and their relationship to disease. *J Comp Path* 80: 259-265, 1970
21. Bates DW, Anderson JF: Calculation of ventilation needs for confined cattle. *JAVMA* 174: 581-589, 1979
22. Webster J: Personal communication
23. Martig J, Boss PH, Nicolet J, et al: Etiology and predisposing factors in respiratory disease of milk-fattened veal calves. *Livestk Prod Sci* 3: 285, 1976
24. Murphy JP: Personal communication
25. Tennant B, Harrold D, Reina Guerra M, et al: Neonatal alterations in serum gammaglobulin levels in Jersey and Holstein-Friesian calves. *Am J Vet Res* 30: 345-354, 1969
26. Davis HP: Dairy calf birth and disposals. *Neb Agr Exp Sta Bull* 411, 1952
27. Withers FW: Mortality rates and disease incidence in calves in relation to feeding, management and other environmental factors. *Br Vet J* 109: 122-131, 1953
28. Woodward RR, Clark RT: A study of stillbirths in a herd of range cattle. *J Anim Sci* 18: 85-90
29. Morrill JL: Personal communication

30. Cabello G, Levieux D: The effects of thyroxine and climatic factors on colostral immunoglobulin absorption in newborn calves. *Ann Rech Vet* 9: 309-318, 1978
31. Jochle W, Esparza T, Gimenez T, et al: Inhibition of corticoid induced parturition by progesterone in cattle: Effect on delivery and calf viability. *J Reprod Fert* 28: 407-412, 1972
32. O'Brien T, Stott GH: Prepartum serum hormone concentrations related to dystocia in Hostein hieifers. *J Dairy Sci* 60: 249-253, 1976
33. Crenshaw MC, Merchia G, Barron Dm: Role of progesterone in inhibition of muscle tone and respiratory rhythm in foetal lambs. *Nature* 212: 842, 1966
34. Bull RC, Ron RH, Olson DP: Effects of maternal protein restriction on blood composition and pathological lesions in neonatal calves. *Proc West Sect ASAS* 29: 343, 1978
35. Prenatal and Postnatal mortality in cattle. National Academy of Sciences, Washington, DC, 1968
36. Heuschele WP: New perspectives on the epidemiology of BVD. 94th Meeting Ohio Veterinary Medical Association, Colombus, Ohio, 1978
37. Haughey KG: Meningeal hemorrhage and congestion associated with perinatal mortality of beef calves. *Aust Vet J* 51: 22-27, 1975

TABLE 1

SERUM NEUTRALIZATION TESTS PERFORMED FOR IBR, BVD, PI<sub>3</sub> AND  
ADENOVIRUS - 3 VIRUS ANTIBODIES

Calf	IBR <sub>I</sub> - IBR <sub>II</sub>	BVD <sub>I</sub> - BVD <sub>II</sub>	PI <sub>3</sub> <sub>I</sub> - PI <sub>3</sub> <sub>II</sub>	A-3 <sub>I</sub> - A-3 <sub>II</sub>
1	1:8 - 1:8	>1:256 - 1:8	1:28 - 1:16	1:32 - 1:4
2	<1:2 - 1:2	1:128 - 1:8	1:64 - 1:8	1:64 - 1:32
3	<1:2 - 1:2	1:128 - 1:32	1:128 - 1:8	1:4 - <1:2
4	<1:2 - 1:2	1:32 - <1:2	1:32 - 1:8	1:32 - 1:16
5	<1:2 - 1:8	1:8 - 1:8	1:64 - 1:2	1:64 - 1:16
6	1:2 - 1:4	1:8 - 1:8	>1:256 - 1:64	1:32 - 1:16
7	1:2 - 1:4	1:4 - 1:4	1:128 - 1:16	1:16 - 1:4
8	<1:2 - 1:4	>1:256 - 1:4	1:64 - 1:8	1:128 - 1:32
9	<1:2 - 1:2	1:128 - 1:32	1:128 - 1:16	1:128 - 1:64
10	<1:2 - *	1:16 -	1:32 -	1:16 -
11	<1:2 - 1:2	1:32 - 1:4	>1:256 - 1:8	1:64 - 1:16

\* Calf 10 died prior to second sample.

TABLE 2

## IMMUNOGLOBULIN VALUES AT 48 HOURS AND CAUSE OF DEATH

	IgA	N	IgM	N	IgG <sub>1</sub>	N	IgG <sub>2</sub>	N	TOTAL G- GLOBULIN	N	ZINC SULFATE	
SURVIVING	182.0 <sup>A</sup>	21	195.0 <sup>A</sup>	21	1286.1 <sup>A</sup>	19	171.0 <sup>A</sup>	22	1.57 <sup>A</sup>	20	12.75 <sup>A</sup>	2
CHRONIC DIARRHEA	130.7 <sup>A</sup>	3	255.0 <sup>A</sup>	3	255.0 <sup>A</sup>	3	137.7 <sup>A</sup>	3	1.00 <sup>AB</sup>	3	9.0 <sup>A</sup>	
ACUTE DIARRHEA	--	--	--	--	--	--	--	--	--	--	--	--
PNEUMONIA	66.0 <sup>A</sup>	2	290.0 <sup>A</sup>	1	290.0 <sup>A</sup>	1	61.0 <sup>A</sup>	2	0.60 <sup>B</sup>	2	5.0 <sup>A</sup>	
PNEUMONIA plus DIARRHEA	93.75 <sup>A</sup>	4	86.0 <sup>A</sup>	4	86.0 <sup>A</sup>	4	137.0 <sup>A</sup>	4	0.86 <sup>B</sup>	7	11.33 <sup>A</sup>	

- Values in columns with different letters significantly different (P < 0.05)
- Immunoglobulin levels (mg/dl)
- Total gammaglobulin (grams/dl) determined by electrophoresis
- Zinc Sulfate expressed in Zinc Sulfate Turbidity Units

TABLE 3

## CALF SEX AS A FACTOR IN DISEASE AND MORTALITY

	LENGTH OF LIFE	DIARRHEA SCORE	BLOOD IN FECES	PNEUMONIA SCORE	N
FEMALE	26.0	15.5%	8.3%	14.2%	53
MALE	23.2	32.8%	9.9%	13.8%	45
LEVEL OF SIGNIFICANCE OF DIFFERENCE	0.07	.0006	N.S.	N.S.	

TABLE 4

## CALF SEX AND IMMUNOGLOBULIN LEVELS

	IMMUNO- GLOBULIN TOTAL (gr/dl)	ZST:	IgA mg/dl	IgM mg/dl	IgG <sub>1</sub> mg/dl	IgG <sub>2</sub> mg/
FEMALE	1.45 (6)	13.4 (5)	171.8(4)	299.5(4)	1502.5(4)	194.5(4)
MALE	1.26(26)	11.2(27)	155.2(26)	171.9(25)	1066.2(22)	150.7(27)
LEVEL OF SIGNIFICANCE OF DIFFERENCE	N.S.	N.S.	N.S.	.02	N.S.	N.S.

- number in brackets is number of calves in sample

TABLE 5

Calf SEX AND WEIGHT GAIN OR LOSS (POUNDS)

	GAIN 1st WEEK	N	GAIN 1st 4 WEEKS	N
FEMALE	-0.14	51	8.51	43
MALE	-4.24	41	1.44	27
LEVEL OF SIGNIFICANCE OF DIFFERENCE	.0003		.005	



Fig. 1.

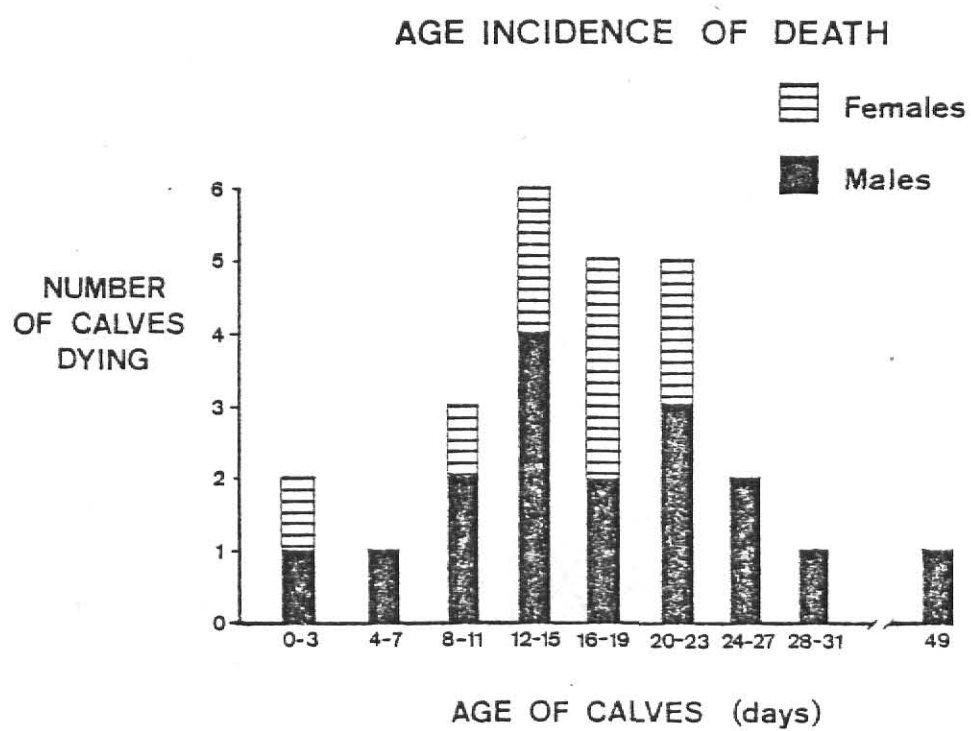


Fig. 2.

## DIARRHEA - INCIDENCE WITH AGE

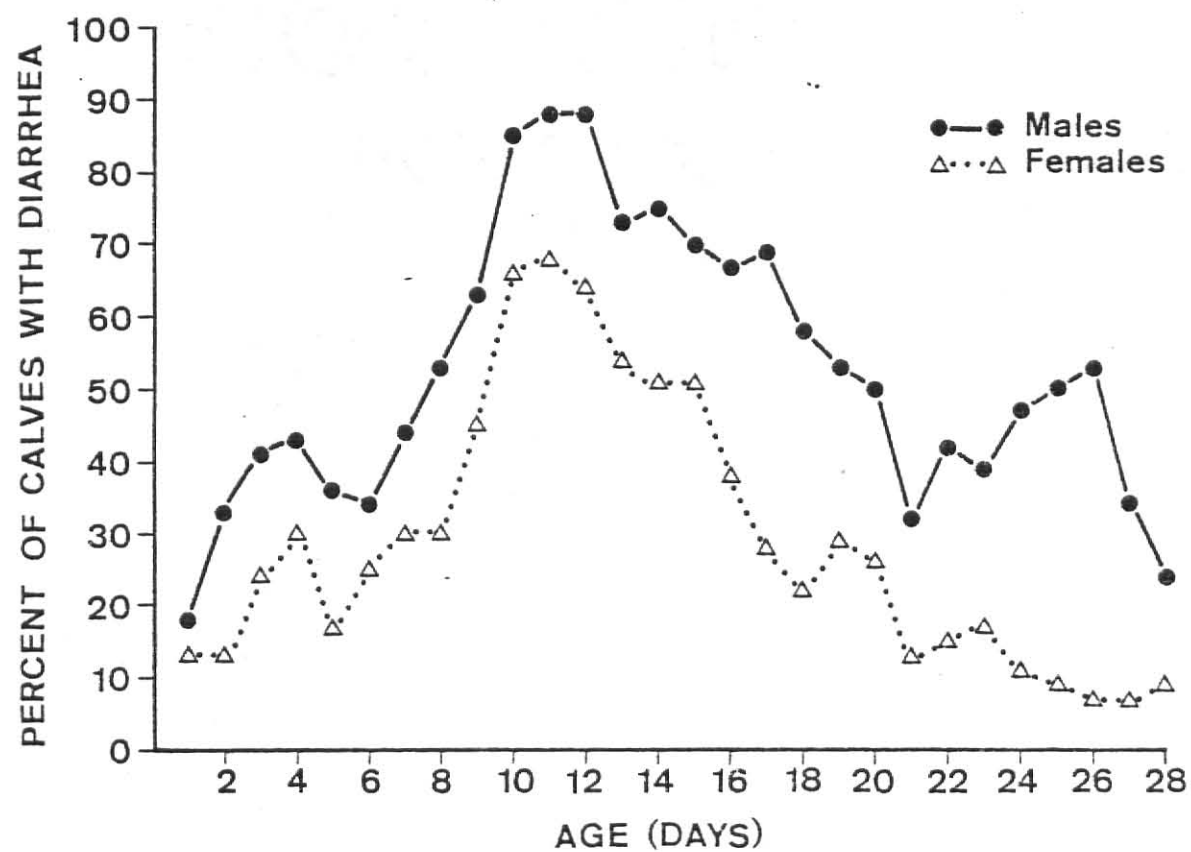


Fig. 3.

## PNEUMONIA - INCIDENCE WITH AGE

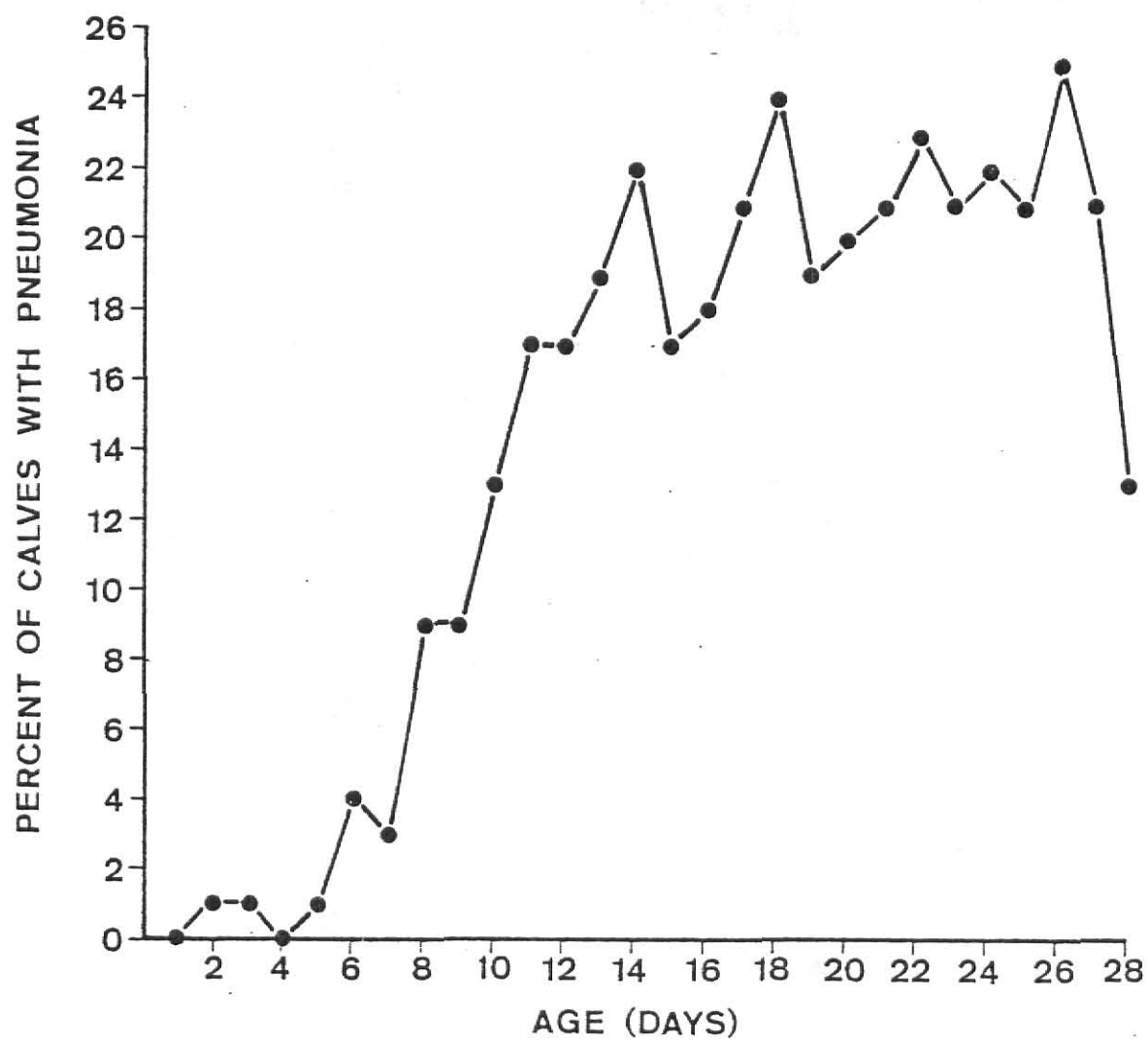


Fig. 4.

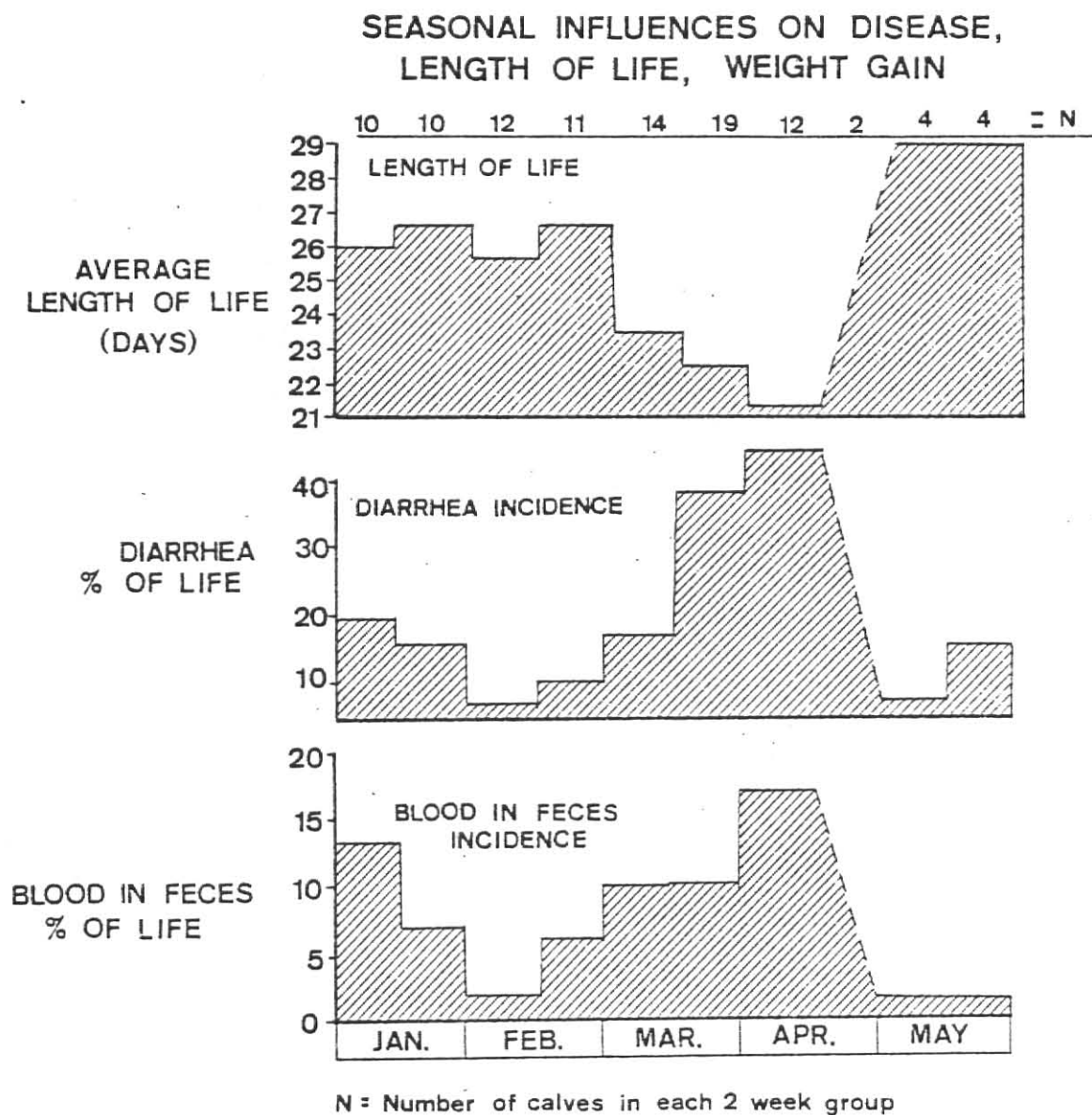
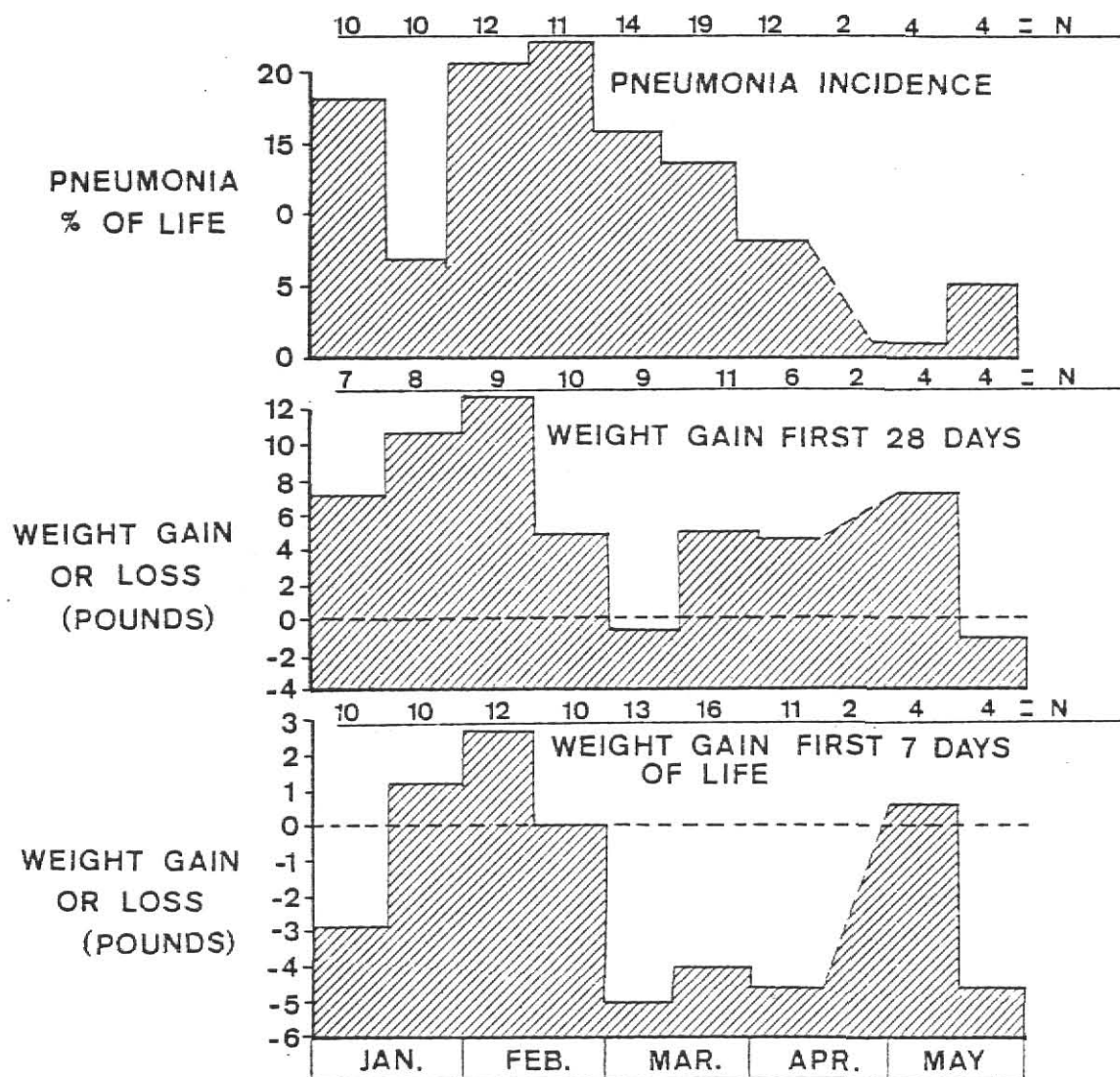


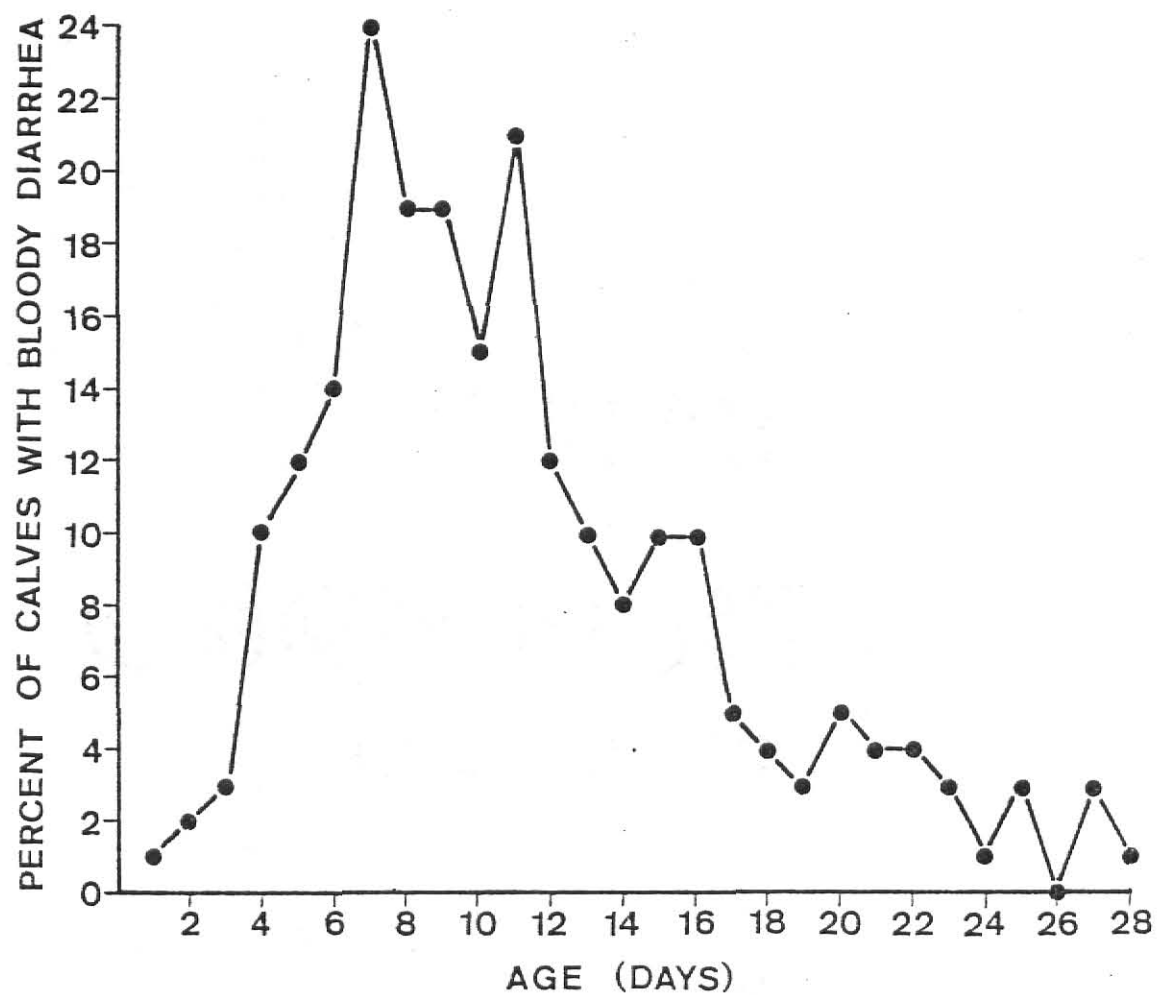
Fig. 5.



N = Number of calves in each 2 week group

Fig. 6.

## BLOODY DIARRRHEA - INCIDENCE WITH AGE



PAPER II

PARENTERAL IMMUNOGLOBULIN

ADMINISTRATION TO HYPOGAMMAGLOBULINEMIC

CALVES

## INTRODUCTION

Calves are normally agammaglobulinemic at birth and depend on absorption of colostrum antibodies for passive immunity to the ubiquitous neonatal diseases.<sup>1-3</sup> The relationship between low gamma-globulin values and calf mortality has been demonstrated in many studies.<sup>4-9</sup>

Calves deprived of colostrum or severely hypogammaglobulinemic have a high mortality from colisepticemia.<sup>4,10-15</sup> The immunoglobulin M (IgM) component of colostrum has been found to be specifically protective against this disease.<sup>16,17</sup> Moderately hypogammaglobulinemic calves are more susceptible to fatal diarrhea.<sup>13,15,18,19</sup> While immunoglobulin G<sub>1</sub> (IgG<sub>1</sub>) is reported to be the major defense against fatal neonatal calf diarrhea,<sup>20</sup> IgM and immunoglobulin A (IgA) appear also to be important and may act in synergy with IgG<sub>1</sub>.<sup>15</sup>

An association between low serum immunoglobulin values in young calves and pneumonia within the first five months of life has also been demonstrated.<sup>21-23</sup> Colostral IgG<sub>1</sub> and IgA appear to be most protective against pneumonia.

Even with good management not all calves absorb adequate colostrum antibodies. From 10-40% of calves remain hypogammaglobulinemic after cessation of intestinal permeability to immunoglobulins.<sup>6,8,9,24-28</sup>

Techniques are available to screen calves for hypogammaglobulinemia, including the Zinc Sulfate Turbidity Test,<sup>5,6,13,19,21,22,29,30</sup> the Sodium Sulfite Precipitation Test,<sup>31,32</sup> the Glutaraldehyde Coagulation Test,<sup>9</sup> and serum protein refractometry.<sup>7</sup> Accurate quantification of gammaglobulin levels is possible using Single Radial Immunodiffusion,<sup>6,22,26,35</sup> and protein electrophoresis.<sup>36,37</sup>

Many products have been utilized to increase passive immunity in calves, including whole blood,<sup>38-40</sup> bovine plasma or serum,<sup>41-44</sup> hyperimmune bovine serum,<sup>45-47</sup> hyperimmune equine serum<sup>48</sup> and gammaglobulin rich fractions derived from blood<sup>49,50</sup> or colostrum.<sup>17,51</sup> Specific replacement therapy in hypogammaglobulinemic neonates has been more widely practiced in foals,<sup>52,53</sup> than in calves. In hypogammaglobulinemic foals and man a dose of 20 ml of plasma/kg has been demonstrated



to be adequate. <sup>52,54</sup> It has been calculated that a minimum dose of 40 grams of gammaglobulin or approximately 700 ml of serum is necessary to adequately raise the blood gammaglobulin value in hypogammaglobulinemic calves. <sup>55</sup>

The objective of this study was to investigate absorption, efficacy and ease of administration of a commercial hyperimmune serum given by several routes to hypogammaglobulinemic calves.

## 1. EXPERIMENTAL DESIGN

36 calves were utilized in the study, six of which were treated subcutaneously, six intraperitoneally, six intravenously and 18 of which were left as paired controls. A concurrent study on maternal vaccination with an Escherichia coli bacterin necessitated the division of the calves into two groups, but otherwise calves were assigned randomly into the three treatment groups then randomly for either treatment or as a control.

An additional trial was conducted in which an intramuscular dose of 20 ml of hyperimmune serum was given to four calves.

## 2. THE CALVES

The calves were Holsteins of both sexes belonging to the Kansas State University Dairy Teaching and Research Center (KSUDTRC). 113 calves were included in this study.

## 3. ESTIMATION OF GAMMAGLOBULIN STATUS OF CALVES

On the evening of the second day of life of each calf a blood sample was collected by jugular venipuncture. Total plasma protein was determined using refractometry as described by McBeath et al.<sup>33</sup> This method has been shown to accurately predict gammaglobulin values.<sup>33,34</sup>

A study the previous winter at the KSUDTRC revealed that one third of the calves had total serum protein values below 5.5 grams/dl at 24 hours of age. This figure was chosen as the upper limit for calves to be included in this study since it was intended to include only the third of the calves with the lowest gammaglobulin levels.

## 4. TREATMENT GROUPS

A commercial hyperimmune serum preparation<sup>A</sup> was used as the source of gammaglobulin. The preparation was administered at 0.5 grams of gamma-globulin per kilogram. The amount of gammaglobulin in the hyperimmune

---

A Serogen LA  
Corynebacterium pyogenes. Pasteurella hemolytica-multocida antiserum.  
Diamond Laboratories, Incorporated.  
Des Moines, Iowa, 50304.

serum was determined by protein electrophoresis to be 4.43 grams/dl. Using radial immunodiffusion it was determined that the IgA value was 47 mg/dl, IgM 402 mg/dl, IgG<sub>1</sub> 3140 mg/dl and IgG<sub>2</sub> 5516 mg/dl. Serum from a second batch was used on the final calf treated intravenously, however, the gammaglobulin and immunoglobulin class values were very similar to those determined for the first batch.

Treatments were administered as follows:

i. Subcutaneous treatment.

The hyperimmune serum, initially cold and later warmed to body temperature, was injected subcutaneously with 60 ml per site. Up to 10 sites were necessary in a large calf.

ii. Intraperitoneal treatment.

Intraperitoneal administration was through the right paralumbar fossa using a 15 gauge 1½" needle and rubber infusion tube.

iii. Intravenous treatment.

Initial intravenous treatments were given using undiluted hyperimmune serum through a rubber infusion tube. Serious complications, including depression, ataxia, dyspnea, and cardiac arrest, precluded delivery of the calculated dose. The final two intravenous treatments were administered over approximately 2 hours using an intravenous catheter and with the hyperimmune serum diluted in 1-1½ liters of saline.

iv. Intramuscular treatment.

Intramuscular treatments were given in two 10 ml doses in the muscles on either side of the neck.

## 5. TOTAL PROTEIN AND IMMUNOGLOBULIN DETERMINATION

Blood samples were collected 1, 3 and 5 days post-treatment except for the intravenously treated calves which were sampled 1 and 5 days after treatment. Control calves were sampled 5 days after the initial sampling. Serum was collected from the clotted blood samples.

Total serum protein values were determined using refractometry. The technique was as for total plasma protein determination.<sup>33</sup> Total gamma-globulin values were measured using protein electrophoresis.<sup>54</sup> Individual immunoglobulin values were determined using single radial immunodiffusion.<sup>55</sup>

## 6. CALCULATION OF EXPECTED INCREASE IN BLOOD IMMUNOGLOBULIN VALUES

Calculation of expected increase in  $\text{IgG}_2$  following administration of 11.11 ml/kg of serum containing 5.5 grams/dl of  $\text{IgG}_2$  was as follows:

Volume of total dose = 555 ml or 5.55 dl

$\text{IgG}_2$  content of dose = 5.55 dl x 5.5 grams/dl  
= 30.5 grams  $\text{IgG}_2$

Serum volume of 50 kg calf = 6% body weight  
(9% blood volume - 3% PCV, fibrinogen)  
= 3 liters or 30 dl

30.5 grams distributed in 30 dl serum = increase of 1.02 grams/dl

However, if only 45%  $\text{IgG}_2$  is distributed in serum,<sup>59</sup> calf's

$\text{IgG}_2$  would be elevated by 0.46 grams/dl.

In comparing the three methods of administration of hyperimmune serum to calves the following were considered:

- i. ease of administration and complications
- ii. relative absorption
- iii. efficacy in protecting from diarrhea, pneumonia and mortality

#### 1. EASE OF ADMINISTRATION AND COMPLICATIONS

Intraperitoneal administration was the most rapid and simple technique. 500 ml of the product could be administered in less than one minute without assistance. Subcutaneous administration was more time consuming (2-3 minutes) and was resented by the calf. Intravenous administration was difficult without assistance and was time consuming, requiring preparation of the skin of the neck and intravenous catheter introduction. Rapid administration of the undiluted hyperimmune serum produced severe side-effects while administration of the product diluted in saline took 2-2½ hours.

Subcutaneous administration produced no serious immediate side-effects. Most calves resented the repeated injections necessary and half the calves exhibited mild shivering following treatment. The calves also appeared more subdued following treatment. Subcutaneous treatment produced large subcutaneous lumps which usually disappeared over two weeks. In one calf, however, these injection sites became infected. The calf developed chronic enteritis and pneumonia and died at 18 days of age. The infected injection sites no doubt contributed to the calf's death.

Intraperitoneal administration produced shivering and mild to moderate depression in all cases. Half the calves salivated excessively and exhibited chewing behavior and half the calves blinked frequently. These abnormalities were transient, lasting at most 30 minutes except the depression which persisted for several hours in some cases. No cardiac or respiratory abnormalities were noted and no chronic complications developed as a result of intraperitoneal administration.

Intravenous administration of the hyperimmune serum produced dramatic side-effects. One calf developed acute respiratory distress with excess salivation, dyspnea, polypnea (respiration rate 128 breaths/

minute) and open mouthed breathing following administration of 90 ml of the serum. On discontinuation of treatment the calf returned to normal in five minutes. One calf developed tachycardia and arrhythmia following administration of 50 ml of the serum at which point treatment was stopped. Complete heart and respiratory block occurred in one calf following rapid administration of 35 ml of the serum. Respiration recommenced then the heart spontaneously commenced beating 30 seconds after cessation. The calf at this stage was cyanotic, flaccid and semiconscious. After an episode of deep rapid respiration and tachycardia the calf recovered and five minutes after treatment cessation was much improved. In one calf very slow intravenous administration of the serum produced no side-effects but perivascular leakage precluded administration of the dose.

In the final two calves allocated for intravenous treatment the dose was diluted in  $1-1\frac{1}{2}$  liters of saline and infused through an intravenous catheter over  $1\frac{3}{4}$  to  $2\frac{1}{2}$  hours. One calf exhibited no side-effects while another calf showed transient mild salivation and shivering. No adverse effects were noted following administration of 20 ml of hyper-immune serum intramuscularly.

## 2. ABSORPTION OF SERUM IMMUNOGLOBULINS

No significant difference ( $P < 0.05$ ) was demonstrated in immunoglobulin values between the groups of calves whose dams had been vaccinated with an Escherichia coli (E. coli) bacterin and those whose dams had not. These groups of calves were therefore analysed together and the data are presented without regard to maternal vaccination status. Significant difference was also not observed in immunoglobulin levels between the calves in the two groups before treatment.

### i. Total immunoglobulin absorption as measured by electrophoresis. (Table 1)

Subcutaneous treatment elevated gammaglobulin levels by 0.023 grams/dl on day 3. This elevation was not significant ( $P < 0.05$ ). In the two calves which received a complete intravenous dose of hyperimmune serum, gammaglobulin values were elevated by 0.30 grams/dl. This is an inadequate sample size for determination of significance but is useful for comparison.

Intraperitoneal treatment significantly elevated immunoglobulin values on day 3 ( $P < 0.1$ ) by 0.46 grams/dl and on day 5 ( $P < 0.01$ ) by 0.48 grams/dl.

### ii. IgA absorption. (Table 2)

In all cases except on day 5 following intravenous treatment, hyperimmune serum administration resulted in decreased IgA levels. This decrease achieved significance on day 3 ( $P < 0.05$ ) and on day 5 ( $P < 0.1$ ) following subcutaneous treatment.

### iii. IgM absorption. (Table 3)

No method of treatment produced significant changes in IgM levels in treated versus control calves.

### iv. IgG<sub>1</sub> absorption. (Table 4)

No method of treatment produced significant changes in IgG<sub>1</sub> levels in treated versus control calves. In the two calves in which the calculated dose was given intravenously an elevation in IgG<sub>1</sub> of 0.38 grams/dl was achieved but due to the small sample size this was not tested for significance.

v. IgG<sub>2</sub> absorption (Table 5)

All methods of treatment produced significant elevations of IgG<sub>2</sub>. Subcutaneous treatment produced a highly significant elevation ( $P < 0.01$ ) on days 1, 3 and 5 post-treatment with the highest increase, 0.32 grams/dl, being observed on day 5.

Intraperitoneal treatment also resulted in significant increases in IgG<sub>1</sub> ( $P < 0.05$ ) with the highest increase, 0.37 grams/dl, being observed on day 1 post-treatment. The calculated dose of hyperimmune serum given intravenously resulted in an increase in IgG<sub>2</sub> levels of 0.39 grams/dl.

The difference in levels achieved by each treatment method was not significant.

Intramuscular treatment with 20 ml of hyperimmune serum did not significantly alter calf serum gammaglobulin levels. Alteration in individual classes of immunoglobulins was not measured, and no further data on response to intramuscular treatment are presented.



### 3. PROTECTION FROM DISEASE AND MORTALITY

#### (i) Mortality

Of the 36 calves in the trial, 16 died, a mortality rate of 44.4%. Seven control calves and nine treated calves died--a non-significant difference. Of the remaining 77 calves sampled (but not included in the trial because their total protein plasma value was above 5.5 grams/dl) nine died, a mortality rate of 11.7%. The mortality figures for each treatment and control are presented on Table 6. Due to small sample size the significance of the variation in mortality was not determined.

Length of life was averaged with calves surviving the first month regarded as living 29 days. No significant differences in length of life were noted between treated or control calves. (Table 6)

#### (ii) Disease

No significant differences in the incidence of diarrhea or pneumonia was noted for any treatment group compared with each other or with the controls. (Table 6)

In comparing the three methods of administration of a large volume of hyperimmune serum (approximately 11 ml/kg in this case), intraperitoneal administration offered several advantages. It was the most rapid and simple means of delivering a large volume of serum, was well tolerated by the calf and was free from serious short or long term side-effects.

Subcutaneous administration would be a convenient means of administration of a small volume of serum but was not well suited to administration of large volumes since it was time consuming, was resented by the calf and, in one calf, was followed by infection.

Intravenous administration was hampered by serious side-effects which may have been due to the serum itself or to the preservatives added (phenol and thimerosal). Intravenous administration is also time consuming and difficult without assistance or restraint of the calf.

The methods used in this trial did not enable detection of small increases or decreases in immunoglobulin levels. Therefore, since colostrum and therefore the serum of young calves is normally low in IgG<sub>2</sub>,<sup>22,58</sup> but the product used was high in IgG<sub>2</sub> (5.5 grams/dl), IgG<sub>2</sub> determination gave the best indication of immunoglobulin absorption. Significant increases in IgG<sub>2</sub> occurred following each treatment method with no significant difference being noted between methods. Maximum IgG<sub>2</sub> increases following subcutaneous treatment were 0.32 grams/dl, for intraperitoneal treatment 0.37 grams/dl and for the two effective intravenous treatments 0.39 grams/dl. As can be seen these increases are very similar for each method and are close to the expected increase of 0.46 grams/dl, calculated previously.

Absorption of other immunoglobulins was not significant. This may have been a feature of experimental design and small sample size rather than failure of absorption. The IgG<sub>1</sub> and total immunoglobulin content of the serum following subcutaneous treatment increased in the treated calves by 0.1 grams/dl. For intraperitoneal and the two effective intravenous treatments the change from day 0 to day 1 was 0.16 grams/dl and 0.35 grams/dl respectively. This suggests that absorption occurred but nonetheless was still less than the expected increase of 0.23 grams/dl (calculated as for IgG<sub>2</sub>).

Analysis of the data demonstrated no significant absorption of IgM. However, the expected elevation of IgM if 80% was distributed in the blood, <sup>60</sup> is only 59.2 mg/dl. An elevation of this magnitude would be unlikely to reach significance with the methods used in this trial.

The level of IgA in the hyperimmune serum used was very low (42 mg/dl). Even if all the IgA was distributed in the blood this would only produce an elevation in IgA of 7.7 mg/dl. It is not surprising that no significant absorption was demonstrated by any method. It is, however, surprising that treatment by all methods actually decreased IgA values compared with controls. The decrease reached significance following subcutaneous treatment. This result may have been due to chance but if not, a possible explanation is that parenteral immunoglobulin administration may have caused a redistribution of IgA out of the blood.

Only intraperitoneal treatment produced a significant increase in total immunoglobulins. Subcutaneous treatment also resulted in an increase in immunoglobulins when a comparison was made of treated calves before and after treatment. However, the control calves in this group had higher immunoglobulin levels (by 0.3 grams/dl) than treated calves on day 0. This may have cancelled any increase when comparison was made between treated and control calves. The two effective intravenous treatments did raise immunoglobulin levels but significance was not determined due to small sample size.

Failure of protection from disease and mortality with the hyperimmune serum may have been because too little was given, too late, at the wrong site or because specific antibodies were lacking.

The level of immunoglobulins needed to protect against disease and mortality varies depending on environmental, microbiological and other factors. <sup>58</sup> The concept of a threshold or minimum level of immunoglobulins has also been presented. <sup>7,61</sup> A total serum protein of 5.5 grams/dl was suggested as a cutoff figure. Findings in this study are in agreement with previous studies since the mortality was 44.4% for calves below this figure and 11.9% for calves above 5.5 grams/dl. The dosage given rarely raised total serum protein above 5.5 grams/dl and so may not have been adequate to protect hypogammaglobulinemic calves in this environment.

The treatment may also have been given too late. It has been demonstrated that colonisation of the anterior small intestine with E. coli occurs early in life but in calves with diarrhea the population in the duodenum is much higher than for normal calves. Colostral antibodies have been shown to be important in modifying colonization of the anterior small intestine with E. coli.<sup>58,62,63</sup> A similar phenomenon may exist within the respiratory tract. It has been shown that calves with low serum immunoglobulin levels in the first weeks of life are more susceptible to pneumonia 4-6 weeks later.<sup>21,22</sup> It has been postulated that in the young calf immunoglobulins influenced the microbial and/or immune status so that subsequent immunity was enhanced.<sup>22</sup>

The serum used in this trial was derived from steers hyperimmunised with Pasteurella hemolytica, Pasteurella multocida and Corynebacterium pyogenes but not against enteric pathogens. The importance of specific immunity against enteric pathogens has been demonstrated.<sup>64,65,66</sup> The importance of local versus systemic specific immunity has also been stressed.<sup>65</sup>

## SUMMARY

Absorption, efficacy and ease of administration of a commercial hyperimmune serum when administered by various routes to calves was studied. 36 hypogammaglobulinemic calves were studied with 18 controls and six calves each treated subcutaneously, intraperitoneally and intravenously.

The intraperitoneal method was rapid and simple with only mild side effects. The subcutaneous method was more time consuming and resented by the calf but was free of short term side effects. One calf developed infected injection sites, however. Severe side effects including heart and respiratory blockage, dyspnea and ataxia precluded administration of the complete intravenous dose unless it was diluted in saline and administered over approximately 2 hours.

No significant absorption of IgA, IgM or IgG<sub>1</sub> was demonstrated. All three methods resulted in significant absorption of IgG<sub>2</sub> with no significant difference being detected between methods of administration. Only intraperitoneal treatment significantly elevated gammaglobulin levels as measured by protein electrophoresis.

Treatment with hyperimmune serum did not significantly alter mortality or incidence of diarrhea or pneumonia.

Possible reasons for the differences in absorption for the different immunoglobulin classes and for the failure of hyperimmune serum to protect against diarrhea, pneumonia or death are discussed.

## REFERENCES

1. Howe PE: An effect on the ingestion of colostrum on the composition of the blood of newborn calves. *J Biol Chem* 49: 115-118, 1921
2. Hansen RG, Phillips PH: Studies on proteins from bovine colostrum. 1. Electrophoretic studies on the blood serum proteins of colostrum free calves and of calves fed colostrum at various ages. *J Biol Chem* 171: 223-227, 1947
3. Polson A: Comparative electrophoretic studies of bovine and human colostrum in relation to neonatal immunity. *Onderstepoort J Vet Res* 25: 7-12, 1952
4. Hurvell B, Fey H: Comparative studies on the gammaglobulin levels in sera of market calves in relation to their health. *Acta Vet Scand* 11: 341-360, 1970
5. McEwan AD, Fisher EW, Selman IE: Observations on the immune globulin levels of neonatal calves and their relationship to disease. *J Comp Path* 80: 259-265, 1970
6. Selman IE, Fisher EW, McEwan AD: The serum immune globulin concentration of newborn dairy heifer calves: A farm survey. *Vet Rec* 88: 460-464, 1970
7. Naylor JM, Kronfeld DS, Bech-Nielsen S, et al: Plasma total protein measurement for the prediction of disease and mortality in calves. *JAVMA* 171: 635-638, 1977
8. Fallon RJ: The effect of immunoglobulin levels on calf performance and methods of artificially feeding colostrum to the newborn calf. *Ann Rech Vet* 9: 347-352, 1978
9. Tennant B, Baldwin BH, Braun RK, et al: Use of the glutaraldehyde coagulation test for detection of hypogammaglobulinemia in neonatal calves. *JAVMA* 174: 848-853, 1979
10. Smith T, Little RB: The significance of colostrum to the newborn calf. *J Exp Med* 36: 181-198, 1922
11. Aschaffenburg R, Bartlett S, Kon SK, et al: The nutritive value of colostrum for the calf. 1. The effect of different fractions of colostrum. *Brit J Nutrit* 3: 187-196, 1949

12. Fey H, Margadant A: Zer pathogenese der kälbercolisepsis. IV. Agammaglobulinämie als disponierender faktor. Zbl Vet-Med 9: 653-663, 1962
13. Gay CC, Anderson N, Fisher, EW, et al: Gamma globulin levels and neonatal mortality in market calves. Vet Rec 77: 148-149, 1965
14. Fey H: Die bedeutung des gammaglobulins für das neugeborene kalb. Int tierärztl Arbeitsgemeinschaft Tierernährung Symposium, Salzburg pp 17-28, 1967
15. Fisher EW, Selman IE, McEwan AD, et al: Some causes of and some factors affecting mortality in newborn calves. V. International Meeting of Diseases of Cattle. Opatija, Yugoslavia. pp 41-54, 1968
16. Penhale WJ, Christie G, McEwan AD, et al: Quantitative studies on bovine immunoglobulins. II. Plasma immunoglobulin levels in market calves and their relationship to neonatal infection. Br Vet J 126: 30-36, 1970
17. Logan EF, Penhale WJ: Studies on the immunity of the calf to colibacillosis. I. The influence of colostral whey and immunoglobulin fractions on experimental colisepticemia. Vet Rec 88: 222-228, 1971
18. Fisher EW, de la Fuente GH: Antibiotics and calf diarrhea--the effect of serum immune globulin concentrations. Vet Rec 89: 579-582, 1971
19. Boyd JW, Baker JR, Leyland A: Neonatal diarrhea in calves. Vet Rec 95: 310-313, 1974
20. Fisher EW, Martinez AA, Trainin Z, et al: Studies of neonatal calf diarrhea. VI. Serum and faecal immune globulin in calves with mixed infections. Br Vet J 132: 252-258, 1976
21. Thomas LH, Swann RG: Influence of colostrum on the incidence of calf pneumonia. Vet Rec 92: 454, 1973
22. Williams MR, Spooner RL, Thomas LH: Quantitative studies on bovine immunoglobulins. Vet Rec 96: 81-84, 1975
23. Ford EJH, Boyd JW, Hogg RA: Investigation into possible relation-

- ship between the quality of colostrum and the subsequent performance of calves. Index Res Meat and Livestock Commission pp 4, 1978
24. Penhale WJ, Logan EF, Selman IE, et al: Observations of the absorption of colostral immunoglobulins by the neonatal calf and their significance in colibacillosis. *Ann Rech Vet* 4: 223-233, 1973
  25. Irwin VCR; Incidence of disease in colostrum deprived calves. *Vet Rec* 94: 105-106, 1974
  26. Logan EF, McBeath DG, Lowman BG: Quantitative studies on serum immunoglobulin levels in suckled calves from birth to five weeks. *Vet. Rec* 94: 367-370, 1974
  27. McBeath DG, Logan EF: Influence of neonatal management on serum immunoglobulin levels of suckled calves. *Vet Rec* 95: 466, 1974
  28. Logan EF, Gibson T: Serum immunoglobulins in suckled beef calves. *Vet Rec* 97: 229-230, 1975
  29. Smith HW, O'Neill JA, Simmons EJ: The immune globulin content of the serum of calves in England. *Vet Rec* 80: 664-666, 1967.
  30. McEwan AD, Fisher EW, Selman IE, et al: A turbidity test for the estimation of immune globulin levels in neonatal calf serum. *Clin Chim Acta* 27: 155-163, 1970
  31. Stone SS, Gitter M: The validity of the sodium sulphite test for detecting immunoglobulins in calf sera. *Br Vet J* 125: 68-72, 1969
  32. Pfeiffer NE, McGuire TC: A sodium sulfite precipitation test for assessment of colostral immunoglobulin transfer to calves. *JAVMA* 170: 809-811, 1977
  33. McBeath DG, Penhale WJ, Logan EF: An examination of the influence of husbandry on the plasma immunoglobulin level of the newborn calf, using a rapid refractometer test for assessing immunoglobulin content. *Vet Rec* 88: 266-270, 1971
  34. Naylor JM, Kronfeld DS: Refractometry as a measure of the immunoglobulin status of the newborn dairy calf: Comparison with the zinc sulphate turbidity test and single radial immunodiffusion. *Am J Vet Res* 38: 1331-1334, 1977



35. Logan EF, McMurray CH, O'Neill DG, et al: Absorption of colostral immunoglobulins by the neonatal calf. *Br Vet J* 134: 258-262, 1978
36. Tennant B, Harrold D, Reina-Guerra M, et al: Neonatal alterations in serum gamma globulin levels in Jersey and Holstein-Friesian calves. *Am J Vet Res* 30: 345-354, 1969
37. Thornton JR, Willoughby RA, McSherry BJ: Studies on diarrhea in neonatal calves: The plasma proteins of normal and diarrheic calves during the first ten days of age. *J Comp Med* 36: 17-25, 1972
38. Mac Donald DW, Oakley GA: The prophylactic use of blood in colibacillosis in calves. *Vet Rec* 73: 415-416, 1961
39. Watts RE: Blood transfusions for reducing calf losses. Fifth Annual Field Day, University of Arizona, Tucson, 1963
40. Rafferty GC: Blood from a donor cow. *Vet Rec* 90: 166, 1972
41. Smith T, Little RB: Cow serum as a substitute for colostrum in new-born calves. *J Exp Med* 36: 453-468, 1922
42. Wise GH, Anderson GW: The control of diarrhea ("white scours") of new-born dairy calves by means of serum and sulfaquanidine. *J Dairy Sci* 27: 965-979, 1944
43. Watt JG: The use of fluid replacement in the treatment of neonatal diseases in calves. *Vet Rec* 77: 1474-1482, 1965
44. Watt JG: Fluid therapy for dehydration in calves. *JAVMA* 150: 742-750, 1967
45. Dollahite JW: An experimental study of homologous hyperimmune serum in the prevention of acute dysentery of new-born calves. *Vet Med* 34: 652-654, 1939
46. Lambert G, Mueller DJ, Welter CJ: Field evaluation of antiserum for prevention of the neonatal calf pneumonia enteritis complex. *Vet Med Small Anim Clin* 65: 795-797, 1970
47. McBeath DG: Prophylactic use of hyperimmune serum in experimental colisepticemia in calves. *Vet Rec* 100: 259-262, 1977
48. Dam A: Immunoprophylaxie dans la colibacillose du veau, principalement par la serotherapie. *Ann Rech Vet* 4: 181-189, 1973

49. Penhale WJ, Logan EF, Stenhouse A: Studies on the immunity of the calf to colibacillosis. II. Preparation of an IgM-rich fraction from bovine serum and its prophylactic use in experimental colisepticemia. Vet Rec 89: 623-628, 1971
50. Logan EF, Penhale WJ: Studies on the immunity of the calf to colibacillosis. IV. The prevention of experimental colisepticemia by the intravenous administration of a bovine serum IgM rich fraction. Vet Rec 89: 663-667, 1971
51. Fey H, Margadant A, Nicloet J, et al: Prophylaxie der experimentellen colisepsis des kalbes mit einem colostrum serumpool. Schweiz Arch Tierheilk 105: 361-370, 1963
52. Rumbaugh GE, Ardans AA, Ginno D, et al: Identification and treatment of colostrum-deficient foals. JAVMA 174: 273-276, 1979
53. Rumbaugh GE, Ardans AA: Field determination of the immune status of the new born foal. Equine Practice 1: 37-41, 1979
54. Buckley RH: Plasma therapy in immunodeficiency diseases. Amer J Dis Child 124: 376-381, 1972
55. Fisher EW: Vet Rec 77: 1482-1486, 1965
56. Serum protein electrophoresis procedure, Helena Laboratories, 1530 Lindborgh Drive, P.O. Box 752, Beaumont, Texas, 77704, 1977
57. Mancini G, Carbonara AO, Heremans JF: Immunochemical quantitation of antigens by single radial immunodiffusion, Immunochemistry 2: 235-254, 1965
58. Roy JHB: Decision making and calf health. J Royal Agric Soc England 132: 81-105, 1971
59. MacDougall DF, Mulligan W: The distribution and metabolism of fast IgG immunoglobulin in the neonatal calf. J Physiol 201: 77-79, 1969
60. Roy JBH: Factors affecting susceptibility of calves to disease. J Dairy Sci 63: 650-664, 1980

61. Boyd JW: The relationship between serum immune globulin deficiency and disease in calves. A farm survey.. Vet Rec 90: 645-649, 1972
62. Reisinger RC: Pathogenesis and prevention of infectious diarrhea (scours) of newborn calves. JAVMA 147: 1377-1386, 1965
63. Corley LD, Staley TD, Bush LJ, et al: Influence of colostrum on transepithelial movement of Escherichia coli 055. J Dairy Sci 60: 1416-1421, 1977
64. Myers LL, Newman FS, Wilson RN, et al: Passive immunization of calves against experimentally induced enteric colibacillosis by vaccination of dams. Am J Vet Res 34: 29-33, 1973
65. Wood GN, Jones J, Bridger J: Levels of colostral antibodies against neonatal calf diarrhea virus. Vet Rec 97: 148-149, 1975
66. Acres SD, Radostits OM: The efficacy of a modified live reo-like virus vaccine and an E. coli bacterin for prevention of acute undifferentiated neonatal diarrhea of beef calves. Can Vet J 17: 197-212, 1976

TABLE 1

SERUM GAMMAGLOBULIN VALUES FOLLOWING ADMINISTRATION OF  
HYPERIMMUNE BOVINE SERUM BY THREE ROUTES (mg/dl)

		DAY			
		0	1	3	5
METHOD 1 (SQ)	T	0.431	0.532	0.708	0.661
	C	0.731	0.716	0.685	0.655
	DIFF. (T-C)	-0.30	-0.185	0.023	0.006
METHOD 2 (IP)	T	0.70	0.983	0.967	0.94
	C	0.587	0.560	0.508	0.4567
	DIFF. (T-C)	0.11	0.423	0.458 $\Delta$	0.483**
METHOD 3 (N)	T	0.647	0.83		0.722
	C	0.677	0.65		0.590
	DIFF. (T-C)	-0.03	0.18		0.13
METHOD 3(a)	T	0.585	0.96		0.62
	C	0.68	0.66		0.55
	DIFF. (T-C)	-0.095	0.30		0.07

$\Delta$  significant at .1 level

\* significant at .05 level

\*\* significant at .01 level

Method 3(a) - Two intravenous treatments where complete dose  
given.

Note - Control values for days 1, 3 interpolated from days 0, 5.

TABLE 2

SERUM IgA VALUES FOLLOWING ADMINISTRATION OF HYPERIMMUNE  
BOVINE SERUM BY THREE ROUTES (mg/dl)

		DAY				mg/dl
		0	1	3	5	
METHOD 1 (SQ)	T	64.5	15.33	3.17	0.833	
	C	65.5	53.33	29.16	4.83	
	DIFF. (T-C)	-1.0	-38.0 <sup>Δ</sup>	-26.0*	-4.0 <sup>Δ</sup>	
METHOD 2 (IP)	T	55.0	40.67	22.83	9.33	
	C	82.0	72.33	49.0	33.5	
	DIFF. (T-C)	-27.0	-31.67	-26.17	-24.16	
METHOD 3 (IV)	T	42.0	19.3		8.66	
	C	64.67	56.17		9.16	
	DIFF. (T-C)	-22.67	-36.83		-0.5	
METHOD 3(a)	T	31.0	8.5		20.5	
	C	13.5	13.0		10.5	
	DIFF. (T-C)	17.5	-4.5		10.0	

<sup>Δ</sup> significant at .1 level

\* significant at .05 level

\*\* significant at .01 level

Method 3(a) - two intravenous treatments where complete  
dose given

Note - Control values for days 1, 3 interpolated from  
days 0, 5.

TABLE 3

SERUM IgM VALUES FOLLOWING ADMINISTRATION OF HYPERIMMUNE  
BOVINE SERUM BY THREE ROUTES (mg/dl)

		DAY			
		0	1	3	5
METHOD 1 (SQ)	T	40.3	38.8	74.0	50.2
	C	97.3	93.8	86.3	79.7
	DIFF. (T-C)	-57.0	-55.0	-12.3	-18.5
METHOD 2 (IP)	T	109.5	114.5	87.8	66.5
	C	45.0	50.5	61.2	71.33
	DIFF. (T-C)	64.5	64.0	26.2	-4.83
METHOD 3 (IV)	T	45.3	65.8	--	51.0
	C	-88.7	94.8	--	118.8
	DIFF. (T-C)	43.4	-29.0	--	-67.3
METHOD 3(a)	T	31.5	94.5	--	43.5
	C	61.5	65.0	--	77.5
	DIFF. (T-C)	-30	29.5	--	-34.0

△ significant at .1 level

\* significant at .05 level

\*\* significant at .01 level

Method 3(a) - Two intravenous treatments where complete  
dose given.

Note - Control values for days 1, 3 interpolated from days  
0, 5.

TABLE 4

SERUM IgG<sub>1</sub> VALUES FOLLOWING ADMINISTRATION OF HYPERIMMUNE  
BOVINE SERUM BY THREE ROUTES (mg/dl)

		DAY			
		0	1	3	5
METHOD 1 (SQ)	T	776.7	846.7	878.3	863.3
	C	1033.3	1008.7	959.3	910.0
	DIFF. (T-C)	-256.7	-162.0	-81.0	-46.7
METHOD 2 (IP)	T	975.0	1126.7	1136.7	1078.3
	C	1158.3	1133.0	1080.7	1031.7
	DIFF. (T-C)	-183.3	-6.3	56.0	46.6
METHOD 3 (IV)	T	883.3	1010.0	--	878.0
	C	898.3	891.3	--	863.3
	DIFF. (T-C)	-15.0	118.7	--	14.7
METHOD 3(a)	T	710.0	1060.0	--	680.0
	C	685.0	681.0	--	1330.0
	DIFF. (T-C)	25.0	379.0	--	-650.0

△ significant at .1 level

\* significant at .05 level

\*\* significant at .01 level

Method 3(a) - Two intravenous treatments where complete  
dose given.

Note - Control values for days 1, 3 interpolated from days  
0, 5.

TABLE 5

SERUM IgG<sub>2</sub> VALUES FOLLOWING ADMINISTRATION OF HYPERIMMUNE  
BOVINE SERUM BY THREE ROUTES (mg/dl)

		DAY			
		0	1	3	5
METHOD 1 (SQ)	T	129.5	333.5	431.5	475.5
	C	174.5	171.3	164.8	158.5
	DIFF. (T-C)	-45.0	162.2**	266.7**	317.0**
METHOD 2 (IP)	T	218.7	557.0	499.0	505.8
	C	189.3	186.2	179.8	173.3
	DIFF. (T-C)	28.8	370.8*	312.4**	324.8**
METHOD 3 (IV)	T	174.5	360.0		334.0
	C	210.3	206.0		195.0
	DIFF. (T-C)	-35.8	154.0		138.7
METHOD 3(a)	T	121.5	538.5		445.5
	C	311.0	150.0		151.0
	DIFF. (T-C)	-189.5	388.5		294.3

Δ significant at .1 level

\* significant at .05 level

\*\* significant at .01 level

Method 3(a) - Two intravenous treatments where complete  
dose given.

Note - Control values for days 1, 3 interpolated from  
days 0, 5.



TABLE 6

DISEASE AND MORTALITY IN CALVES TREATED WITH HYPERIMMUNE  
BOVINE SERUM VERSUS CONTROLS

	METHOD 1 (SQ)		METHOD 2 (IP)		METHOD 3 (IV)	
	T	C	T	C	T	C
LENGTH OF LIFE <sup>a</sup>	24.83	26.33	29.0	25.5	19.33	24.5
DIARRHEA SCORE <sup>b</sup>	19.30	17.99	14.94	20.56	42.88	23.41
PNEUMONIA SCORE <sup>b</sup>	18.55	12.06	9.77	12.11	9.96	7.53
MORTALITY	3	1	1	4	5	2
CALVES PER GROUP	6	6	6	6	6	6

- a. Calves surviving one month were recorded as having length of life of 29 days.
- b. Diarrhea and pneumonia scores arrived at by dividing number of days with diarrhea or pneumonia within the first month by length of life - expressed as percent (ie. percent of the calf's life that it had diarrhea or pneumonia).

## REVIEW OF LITERATURE

Hypogammaglobulinemia in calves:  
Its incidence, causes, effects,  
diagnosis and treatment.

- I. Hypogammaglobulinemia in calves--incidence
- II. Hypogammaglobulinemia in calves--causes
  - i. Colostral factors
  - ii. Environmental factors
  - iii. Maternal factors
  - iv. Maternal - calf factors
  - v. Calf factors
- III. Hypogammaglobulinemia in calves--effects
  - i. Immunoglobulin values and calf mortality
  - ii. Immunoglobulin values and colisepticemia
  - iii. Immunoglobulin values and diarrhea
  - iv. Immunoglobulin values and pneumonia
  - v. Immunoglobulin values and other calf diseases
- IV. Hypogammaglobulinemia in calves--diagnosis
- V. Hypogammaglobulinemia in calves--treatment
- VI. References

## I. HYPOGAMMAGLOBULINEMIA IN CALVES - INCIDENCE

Calves have been judged to be hypogammaglobulinemic if their blood immunoglobulin levels are below 15 to 20 zinc sulphate turbidity units<sup>1-3</sup> or when the IgG values are below 500mg/dl and the IgM values below 110mg/dl.<sup>4</sup>

The incidence of hypogammaglobulinemia in calves is usually above 10%<sup>5</sup> with from 20-30% incidence being frequently recorded.<sup>2,4,6-8</sup> Herd instances as high as 40-60% hypogammaglobulinemia have been reported.<sup>1-3,9</sup>

## II. HYPOGAMMAGLOBULINEMIA IN CALVES - CAUSES

The three most important mechanisms in causing hypogammaglobulinemia in neonatal calves are:

- i. delayed feeding of colostrum
- ii. ingestion of an inadequate amount of colostrum, and
- iii. impaired absorption of colostral immunoglobulins.

Adequate amounts of colostrum must be ingested while the calf's intestine is still permeable to macromolecules. Closure, or "the cessation of absorption of macromolecules from the gut to blood in neonates,"<sup>10</sup> is a spontaneous, gradual, progressive phenomenon, which may be independent for each immunoglobulin class, and is complete in 12 to 48 hours.<sup>4,11-13</sup>

Feeding at least 5% of the calf's body weight in colostrum in the first five hours, followed by a further 5% in the next 4-6 hours has been shown to produce adequate immunoglobulin levels in the blood of calves.<sup>1,14</sup> The ingestion of an adequate quantity of colostrum is critical and 68% of the variation in blood immunoglobulin levels in the calf have been attributed to differences in the amount of colostral immunoglobulin consumed per unit weight of the calf.<sup>11</sup>

### 1. Colostral Factors

Some authors feel colostral immunoglobulin concentration is a critical factor affecting the amount of immunoglobulin absorbed by a calf.<sup>15,16</sup> Others have found no relationship between colostral

concentration and the calf's subsequent blood immunoglobulin level. 17-19 Bush et al <sup>20</sup> observed that the concentration of gammaglobulin in colostrum, studied as an independent variable, had a negligible effect on the concentration in the calf's serum. These authors felt that the mass of immunoglobulin consumed was the main factor influencing the calf's serum immunoglobulin level.

Substances have been found in colostrum whey which facilitate immunoglobulin absorption. These substances include inorganic phosphate, glucose-6-phosphate and a low molecular weight protein fraction. <sup>21</sup> Salts of volatile fatty acids, and in particular potassium isobutyrate, accelerated absorption more than colostrum whey. <sup>22</sup> However, in intact calves no chemical compounds, when added to colostrum, were able to increase the rate of immunoglobulin absorption. <sup>23,24</sup>

Bovine colostrum trypsin inhibitor is a factor which deserves attention as an influence on subsequent calf immunoglobulin levels. This substance inhibits trypsin and weakly inhibits chymotrypsin in the intestine of calves <sup>25</sup> and thus protects colostrum antibodies from digestion. It has been shown that the IgA and IgG levels in newborn suckled pigs are influenced by the concentration of colostrum trypsin inhibitor. <sup>26</sup>

No difference in colostrum intake or immunoglobulin absorption was observed when colostrum was fed at room temperature, compared with body temperature. <sup>1</sup> Less immunoglobulin was, however, absorbed from fermented than fresh colostrum. <sup>27,28</sup> Adjustment of pH to that of fresh colostrum partially improved immunoglobulin absorption. <sup>27</sup>

## 2. Environmental Factors

A marked seasonal effect on calf immunoglobulin levels has been demonstrated with lowest levels being recorded from December to April. 8,17,29-32 Not all authors have noted this seasonal variation, however, 19,33 and Thornton et al <sup>33</sup> suggested that when calves are fed colostrum soon after birth there is no significant seasonal variation in calf serum gammaglobulin levels.

Temperature appears to affect immunoglobulin absorption or colostrum ingestion. Workers in Arizona <sup>34</sup> and France <sup>35</sup> have shown that high ambient temperatures suppress immunoglobulin absorption.

High stocking rates of cattle with reduced supervision and mothering of the calf have been shown to reduce immunoglobulin levels <sup>7,36</sup> and increased care of calves has been shown to increase calf immunoglobulin levels. <sup>8,32</sup>

The influence of micro-environment (and management practices) on calf immunoglobulin levels was demonstrated by Selman et al. <sup>8</sup> They showed that mean serum immunoglobulin levels were higher for field born calves than box-born calves, whose levels, in turn, were higher than for "byre-born" calves.

The microbiological environment and, in particular, the level of pathogens to which the calf is exposed, is important for calf health and immunity. Not only does a high number of pathogens provide a serious challenge to the immune defenses of the calf, but it appears that the presence and multiplication of bacteria in the calf's intestine may suppress immunoglobulin absorption by reducing "closure time." <sup>37,38</sup>

### 3. Maternal Factors

Large bulbous teats, low milk production, <sup>6</sup> poor conformation with low-hanging udders and teats <sup>17,39</sup> and the general health and physiological status of the cow <sup>16</sup> have been shown to affect calf serum immunoglobulin levels.

Some workers have demonstrated that the calves of primiparous cows have lower gammaglobulin levels than those of older cows. <sup>31,39</sup> This may be because heifers produce less colostrum or that heifers are poorer mothers. <sup>14,17</sup> Smith et al, <sup>19</sup> however, found no effect of parity on the calf immunoglobulin levels. These workers also showed no relationship between the serum immunoglobulin level of the cow and the subsequent level in her calf's serum.

### 4. Maternal-Calf Factors

A number of factors which are neither dam or calf factors alone

have been shown to influence the subsequent immunoglobulin level of calves.

Cows on a protein deficient pre-partum diet produced weak calves.

<sup>40</sup> Affected calves were unable to absorb colostral immunoglobulins normally. This may have been because the dam had reduced mothering ability or colostral quality/quantity or because the calf was less vigorous or had impaired absorptive capacity.

Mild reductions in feeding level may not influence calf immunoglobulin levels, however. Dardillat et al <sup>16</sup> found that a 15% reduction in feed intake of cows in late gestation had no effect on calf mortality or calf weight.

Corticosteroids injected into cows to induce parturition inhibited colostral immunoglobulin absorption by the calf. <sup>41</sup> It might therefore be expected that elevated corticosteroid values in the calf might also suppress immunoglobulin absorption. However contrary to findings in the rat, <sup>42</sup> corticosteroids have been shown not to suppress immunoglobulin absorption <sup>35,43,44</sup> in calves and, in fact, may slightly enhance it. <sup>45</sup>

Dardillat et al <sup>16</sup> observed that diseased cows, mainly affected with mastitis and metritis, produced "weak calves, poor quality colostrum" and that their calves had considerably higher mortality than calves from healthy cows. They commented that the immunoglobulin concentration of colostrum reflects the physiological status of the mother, which in turn affects the physiological status of the fetus.

Cabello and Levieux <sup>35</sup> found that calves which were hyperthyroid at birth had reduced immunoglobulin absorption and a higher disease incidence. They found thyroxin injections at birth, however, did not alter IgG absorption. Hyperthyroidism in calves may be an indication of the physiological status of their dams.

Both the length of pregnancy and the difficulty of parturition have been shown not to influence subsequent calf serum immunoglobulin levels <sup>19,44</sup> but calves delivered by cesarean section have reduced immunoglobulin levels. <sup>31</sup>

## 5. Calf Factors

While it has been shown that the sex of a calf did not affect serum immunoglobulin levels,<sup>46</sup> the size of the calf may. Hurvell and Fey<sup>30</sup> showed that a higher percentage of hypogammaglobulinemia occurred in lighter calves.

Any calf disease, weakness or deformity which hinders a calf's ability to nurse will obviously also affect subsequent immunoglobulin levels. In a study previously alluded to<sup>40</sup> it was shown that "weak" calves had lower gammaglobulin levels. Logan et al<sup>6</sup> noted that one calf they studied had weak forelegs and had lower immunoglobulin levels.

The presence of the dam has been shown to increase immunoglobulin absorptive efficiency.<sup>1,47,48</sup> Calves muzzled after birth but left with their dams and fed from a teat bucket absorbed a similar quantity of gammaglobulins to those suckling their dams. However, calves separated from their dams at birth and fed from a bucket absorbed less immunoglobulins.<sup>47,48</sup>

Consumption of food markedly affects time of closure of the immunoglobulin absorptive mechanism in other species<sup>49</sup> but is less important in the calf. McCoy et al<sup>50</sup> noted no difference in absorption of immunoglobulins between calves fed glucose and calves from which all food was withheld for 24 hours.

Stott et al<sup>11</sup> demonstrated that while closure occurred spontaneously an average of 24 hours after birth, early feeding of colostrum resulted in more rapid cessation of absorption and delayed feeding of colostrum also delayed closure. Amount of colostrum fed was found not to influence time of closure.

The possibility of inherited or acquired malabsorption as contributing to hypogammaglobulinemia has frequently been raised.<sup>18,19,51</sup> Since calves vary widely within and between breeds in ability to absorb immunoglobulin<sup>39</sup> genetic variation is likely. Smith<sup>19</sup> did not observe a breed difference in immunoglobulin levels in his survey but Tennant et al<sup>46</sup> demonstrated markedly higher gammaglobulin levels in Jersey calves compared to Holstein calves. These workers speculated on the reason for this variation and suggested that absorptive differences included a

greater intrinsic ability of Jersey calves to absorb immunoglobulin. They also considered differences in colostrum or rate of catabolism of immunoglobulins as possibilities.

As mentioned, endocrine or bacterial factors may be involved in hastening closure or producing malabsorption, and probably the most important factor in reduced absorption is delayed feeding of colostrum.  
4,6,8,18

### III. HYPOGAMMAGLOBULINEMIA IN CALVES - EFFECTS

Since the demonstration by Smith and Little in 1922<sup>52</sup> of the importance of colostral antibodies in preventing neonatal calf disease; numerous authors have shown a direct relationship between the blood immunoglobulin levels of calves and the incidence of disease and mortality.<sup>1,3,5,8,18,29-31,53-60</sup> In this review it is intended to discuss the importance of colostral immunoglobulins in relation to mortality and then to the most significant calf diseases.

#### 1. Immunoglobulin Levels and Calf Mortality

Several surveys relating calf immunoglobulin levels to mortality have shown a highly significant relationship. Tennant et al<sup>5</sup> surveyed 281 calves and found a 3.4% mortality in calves with high immunoglobulin levels ( $> .6$  grams/dl), a 7.7% mortality at intermediate levels (.41-.6 grams/dl), and a 16.7% mortality in calves with low immunoglobulin levels ( $< .4$  grams/dl).

Selman and others<sup>8</sup> demonstrated the relationship of environmental and management practices to serum immunoglobulin levels and subsequent mortality. These workers surveyed 327 two- to seven-day-old dairy calves. They reported a mortality rate of 3% in field born calves, which had an average immune globulin concentration of 24.4 zinc sulphate turbidity (ZST) units, compared with stall born calves which had a mortality of 8% and an immune globulin concentration of 12.0 ZST units. The calves with the highest mortality rate (15%) were the "byre born" calves which also had the lowest immune globulin concentration (9.0 ZST units).



In a survey of 3901 calves, Swedish workers<sup>30</sup> found that the mortality risk was three times greater in calves with the lowest gamma-globulin levels. McEwan et al<sup>29</sup> studied 415 calves which they divided into seven groups on the basis of gamma globulin levels. The calves in the lowest group had a mortality rate of 59.8%, the second lowest 20.9%, the third lowest 6.5%, the middle group 3.7%, while the calves in the three highest gammaglobulin groups had no mortalities.

Not all authors have observed a relationship between immunoglobulin levels and subsequent mortality in calves. Barber<sup>9</sup> found no significant difference in gammaglobulin levels between dying and surviving purchased calves raised in a rearing units. Other authors<sup>61,62</sup> similarly have found no such relationship in dairy calves in Israel or Canada.

## 2. Immunoglobulin Levels and Colisepticemia

In 1922, Smith and Little<sup>63</sup> showed that calves deprived of colostrum had a high mortality rate and died from the systemic invasion of "Bacillus coli." Aschaffenburg et al<sup>64</sup> repeated this finding in experimenting with colostrum-deprived calves. Since that time a number of investigators have shown that agammaglobulinemic or hypogammaglobulinemic calves are highly susceptible to colisepticemia.

Gay et al<sup>53</sup> surveyed market calves in Scotland and found that 11% of 178 calves died of septicemia. Of this 11%, 95% were markedly deficient in gammaglobulins. Fey<sup>65</sup> reported that 138 of 149 calves that died of colisepticemia were entirely lacking in, or had very inadequate levels of immunoglobulins in their serum. In a further study, Hurvell and Fey<sup>30</sup> examined 3901 calves and found that of the calves dying of septicemia, 75% were hypogammaglobulinemic.

Fisher et al<sup>17</sup> also showed that septicemic deaths occurred primarily in calves with very low levels of immunoglobulins and that other deaths (mainly from diarrhea) occurred in calves with low and medium levels of immunoglobulins. They grouped calves according to immunoglobulin levels and noted their subsequent fate. 90% of calves with less than 8 grams/dl of immunoglobulin died of septicemia. An average of 75% of calves with .8 - 2.0 grams/dl of immunoglobulins died but these calves died of

diarrhea. Of the calves with immunoglobulin levels of greater than 2 grams/dl only 5% died (one omphalophlebitis and one pneumonia.)

Fey and Margadant<sup>66</sup> found that 21 of 22 calves which died of Escherichia coli septicemia were hypo- or agammaglobulinemic. They were unable to induce colisepticemia in calves if colostrum was fed immediately after birth and if gammaglobulin levels were normal.

The IgM component of colostrum has been shown to be most important in protection against colisepticemia. Logan and Penhale<sup>55</sup> administered IgM concentrate to calves before challenge with pathogenic Escherichia coli and demonstrated significantly prolonged survival time and delay in the onset of colisepticemia. Penhale et al<sup>54</sup> discovered that in calves in which IgM was either absent or minimal, death, usually from colisepticemia, was inevitable.

### 3. Immunoglobulin Levels and Diarrhea

The relationship between immunoglobulin levels and neonatal diarrhea is not as clear as is the case with septicemia. Nonetheless, numerous workers have demonstrated that in certain circumstances, blood immunoglobulin levels reflect susceptibility to diarrhea.

In a survey of 178 market calves, Gay et al<sup>53</sup> observed that although the incidence and severity of diarrhea was unrelated to gammaglobulin levels, those calves which died as a result of diarrhea had low levels. Fisher et al<sup>17</sup> presented two sets of data showing much higher death rates from colibacillosis in calves with low to moderate immunoglobulin levels than calves with high levels. Almost all calves with gammaglobulin levels above 2 grams/dl survived, whereas calves below this level had high mortality rates (25-90%) from both diarrhea and septicemia. They further mentioned that calves with high serum immune globulin concentrations often developed diarrhea but did not become severely dehydrated and did not die.

McBeath et al<sup>56</sup> compared "suckler" calves with purchased and home reared dairy calves. They noted much higher immunoglobulin levels and shorter, less severe diarrhea in "suckler" calves, compared with dairy calves. In this case, however, differences between the environment of

"suckler" calves compared with dairy calves could account, at least in part, for the differences in diarrhea incidence.

Boyd et al <sup>59</sup> studied the incidence of neonatal diarrhea in home-raised calves over four seasons. They found that calves which remained healthy had an average immunoglobulin concentration of 23.6 ZST units, those which developed non-fatal diarrhea averaged 19.3 ZST units, and those suffering fatal diarrhea averaged 16.1 ZST units. They found the immunoglobulin difference between calves which died and calves which remained healthy to be highly significant ( $P < 0.001$ ) but that the difference in immunoglobulin levels between fatal and non-fatal cases of diarrhea was not statistically significant.

Boyd et al also studied the role of antibiotics in prevention of death from diarrhea and concluded that antibiotics had no beneficial effect in preventing death from diarrhea and that survival depended on a high serum immunoglobulin concentration. This finding concurred with those of Fisher and de la Fuente. <sup>57</sup>

Thornton et al <sup>33</sup> observed that calves with diarrhea that died, had lower levels of gammaglobulins than other calves. Radostits <sup>67</sup> found 11 of 13 calves presented with diarrhea to be hypogammaglobulinemic. Radostits et al <sup>68</sup> further noted that, in their clinical experience in treating calves with undifferentiated neonatal diarrhea, those calves with gammaglobulin levels of less than .5 grams/dl usually died despite vigorous treatment, while those calves with less than 1 gram/dl were difficult to treat and suffered relapses. Calves with levels of greater than 1.5 grams/dl usually responded completely to treatment and were unlikely to suffer relapses.

Frerking and Aeikens <sup>31</sup> also noted a correlation between blood immunoglobulins and diarrhea. They noted that healthy three day old calves had an average gammaglobulin level of 1.118 grams/dl, calves with mild diarrhea averaged .6 grams/dl, calves with severe diarrhea averaged .3 grams/dl and dying calves had an average of .253 grams/dl of gammaglobulins. They observed that calves which died had consumed colostrum an average more than 10 hours after parturition.

Tennant et al <sup>5</sup> provided a further example of the association between immunoglobulin levels and death from diarrhea (and pneumonia). Although they did not specify the death rate from each disease, these authors noted a much higher death loss from diarrhea (and pneumonia) in calves with low gammaglobulin levels than those with high levels.

Fisher et al <sup>17</sup> studied the correlation between specific gamma-globulin levels and diarrhea in calves. They found a significant difference ( $P < 0.05$ ) between the serum IgA levels of calves which survived diarrhea compared with calves dying of diarrhea. They also found a significantly increased ( $P < 0.01$ ) total immunoglobulin and IgG level between surviving diarrheic and non-diarrheic calves, and between non-diarrheic compared with diarrheic dying calves. A relationship also existed between fecal output and initial IgA levels. These workers found a highly significant negative correlation between daily fecal output and initial total and individual immunoglobulin levels. A highly significant correlation was also found between fecal output and IgG excreted in the feces. The authors considered that this implied a "mechanical leak" of IgG. It was concluded that all three classes of immunoglobulins may act together and are perhaps synergistic.

The above authors also studied immunoglobulin levels in calves with salmonellosis. <sup>70</sup> They found that initial serum immunoglobulin levels were significantly lower in dying than in surviving or healthy calves. They commented that while high serum immunoglobulins did not protect the calf from developing salmonellosis, survival was increased and the disease was less severe in those calves with higher levels. It was concluded that protection against salmonellosis was largely mediated through IgM and IgG<sub>1</sub> and was non-specific. They considered the virulence of salmonellosis to be the reason why much higher, non-specific antibody levels were needed to protect against salmonellosis compared with colisepticemia.

Further studies by Fisher et al <sup>71</sup> supported the findings previously reported <sup>30</sup> that high serum immunoglobulins prevent death but not diarrhea in newborn calves. These authors considered that IgG provides the major defense against fatal neonatal calf diarrhea.

Not all investigations, however, have noted a correlation between

high immunoglobulin levels and protection from fatal neonatal diarrhea. Barber and MacLennan <sup>72</sup> studied 351 single suckled beef calves and found no relationship between total circulating immunoglobulin level and the development of a form of neonatal calf diarrhea referred to as the "collapse syndrome."

Bradley et al in Canada <sup>73</sup> surveyed 346 beef calves at 48 ( $\pm$  12) hours of age. It was found that immunoglobulin levels failed to predict the chance of development of, or death from undifferentiated neonatal diarrhea in beef calves.

Fallon, <sup>1</sup> in a survey of 1250 purchased calves, found no relationship between initial immunoglobulin levels and incidence of diarrhea. As previously mentioned, however, this author did show a positive relationship between immunoglobulin levels and mortality. These authors did not indicate the causes of mortality, but it can be assumed that diarrhea was significant, so it is speculated that an association was present between death from diarrhea and immunoglobulin levels.

#### 4. Immunoglobulin Levels and Pneumonia

An association between serum immunoglobulin levels at one to two weeks of age and pneumonia within the first five months of age was demonstrated by Thomas and Swan. <sup>58</sup> These workers found that the percentage of animals requiring treatment for pneumonia was 37% in the ZST range of 1 to 10 units and 19% at above 20 units. They also recorded a mortality rate of 5% in the range 1 to 30 with no deaths above 30 ZST units.

In the previously mentioned study by Tennant et al, <sup>5</sup> the mortality rate observed was 16.7% for calves with low immunoglobulin levels (as measured by the glutaraldehyde coagulation test), 7.7% for calves with intermediate levels and 3.4% for calves with high levels of gammaglobulins. Deaths were attributed to both pneumonia and diarrhea.

Further evidence of an association between immunoglobulin levels and subsequent pneumonia was provided by Williams et al. <sup>74</sup> Low serum levels of IgG<sub>1</sub>, IgG<sub>2</sub> and IgA in calves at around 2½ weeks of age was found to be correlated with a higher incidence of clinical pneumonia in calves at around 2½ months of age. No such correlation with IgM levels was found.

The relationship was exemplified by the IgG<sub>1</sub> values. Only 9.5% of calves in the non-pneumonic group had IgG<sub>1</sub> values of below .8 grams/dl, whereas 45.5% of pneumonic calves had IgG<sub>1</sub> values below .8 grams/dl.

Roy <sup>75</sup> cited the work of Ford et al <sup>36</sup> who demonstrated that high serum immunoglobulin levels at 24 hours of age were associated with subsequent protection against pneumonia and delayed its onset.

These results suggest that colostral immunoglobulins, particularly IgG<sub>1</sub> and IgA are important in protecting calves against subsequent pneumonia. However, as pointed out by both Thomas and Swan <sup>58</sup> and Williams et al, <sup>74</sup> immunoglobulins may simply be markers for susceptibility to respiratory disease and may not be protective themselves.

Not all authors have observed a relationship between immunoglobulins and pneumonia. Lomba et al <sup>76</sup> in Belgium found that immunoglobulin levels at 48 hours of age were not correlated with the subsequent incidence of pneumonia (or diarrhea).

#### 5. Immunoglobulin Levels and Other Calf Diseases

Frerking et al <sup>31</sup> showed considerably lower levels of immunoglobulins in calves affected with omphalitis compared with normal calves.

Roy <sup>75</sup> commented that high blood immunoglobulin levels are important in the protection of calves against arthritis. In support of this statement he cited the work of Stone and Deyoe <sup>77</sup> who demonstrated that colostral antibodies appeared in the synovial fluid of lambs within 4-8 hours of colostrum ingestion.

#### IV. HYPOGAMMAGLOBULINEMIA IN CALVES - DIAGNOSIS

Several techniques have been utilized to assess the blood immunoglobulin levels of calves. These include:

##### 1. Zinc Sulphate Turbidity Test

This test, described by McEwan et al, <sup>78</sup> has been widely used in calf studies. <sup>3,8,19,29,53,58,59,74</sup> Globulins form a turbid precipitate with zinc ions. The turbidity can be measured using a spectrophotometer. Turbidity is influenced by temperature and dissolved carbon dioxide.



## 2. Single Radial Immunodiffusion

Accurate quantitation of individual classes of immunoglobulins has made this a widely used technique.<sup>6,8,74,79</sup> Serum to be tested is placed in wells cut in agar gel containing specific antiserum. The test serum diffusing into the agar gel matrix forms a precipitation ring with the specific antibody. The size of the precipitation ring is compared with a known standard enabling quantification of individual classes of immunoglobulin.

## 3. Sodium Sulfite Precipitation

The principle involved in this test is the same as for the Zinc Sulphate Test. The usual form of this test does not allow quantitative determination of immunoglobulin concentration but it has been shown to accurately detect hypogammaglobulinemia in calves.<sup>80,81</sup> An advantage of this technique is that it does not require a spectrophotometer.

## 4. Serum Electrophoresis<sup>33,46</sup>

The differential migration of serum proteins in an electrical field is the basis of this test. Quantification of total immunoglobulin levels is possible but there is evidence that not all immunoglobulins migrate in the gammaglobulin fraction, thus underestimating total immunoglobulin.<sup>82,83</sup>

## 5. Total Serum Protein Refractometry

Refractometry utilizes the principle that the refractive index of a solution is determined the concentration of solute and that that of serum or plasma depends mainly on the protein concentration, since proteins are the major constituents. This test is an indirect measurement of calf immunoglobulin levels and relies on the gammaglobulin constituent being the major variable in neonatal calf serum. Nonetheless, this test has been shown to be a fairly accurate guide to a calf's immunoglobulin status,<sup>56,84</sup> so long as the special instance of hemoconcentration is discounted. An advantage of this test is that it is rapid and simple to perform.

## 6. Glutaraldehyde Coagulation Test

This test is based on the coagulation of gammaglobulin by glutaraldehyde and enables classification of calf serum samples as high, intermediate or low in gammaglobulins.<sup>5</sup> An advantage of this test is that many samples can be run at one time and no instrumentation is required.

## V. HYPOGAMMAGLOBULINEMIA IN CALVES - TREATMENT

In 1922, Smith and Little<sup>85</sup> demonstrated that bovine serum was an effective substitute for colostrum in new-born calves. These authors found that approximately 20 ml of serum subcutaneously, 20 ml intravenously with 20 ml repeated subcutaneously the following day plus feeding 60 ml of serum in milk, prevented calf mortality in colostrum deprived calves.

Since the time of Smith and Little, many workers have used gammaglobulin products in the treatment or prevention of neonatal calf diseases associated with hypogammaglobulinemia.

The least refined gammaglobulin-containing product administered parenterally is whole blood. Several authors<sup>86-88</sup> have commented on the efficacy of blood administration in outbreaks of neonatal diarrhea. Dosages of from 20-30 mls<sup>86</sup> to approximately one liter intravenously<sup>87</sup> and 50 mls subcutaneously<sup>88</sup> have been recommended.

Bovine serum and plasma has been used to treat neonatal calf diseases both as a volume expander in dehydration,<sup>89,90</sup> and to supply gammaglobulin. Wise and Anderson<sup>91</sup> found that 10-20 ml of bovine plasma injected subcutaneously failed to protect calves against diarrhea but that plasma used both prophylactically and therapeutically significantly reduced mortality from diarrhea.

Lister and MacKay<sup>61</sup> used either 250 or 500 ml of plasma intravenously and compared its benefit with antibiotics in prevention of neonatal calf diarrhea. They found antibiotics alone to be superior and that 250 ml of plasma was more effective than 500 ml in reducing disease and improving growth rate and feed efficiency.

Many workers have used concentrated gammaglobulin products, either derived from colostrum or serum in the treatment of hypogammaglobulinemia in calves.



Hyperimmune bovine serum given intravenously <sup>92,93</sup> soon after birth has markedly reduced mortality from colisepticemia and diarrhea. Hyperimmune bovine serum given subcutaneously to 3-5 day old calves before entering a veal operation also reduced deaths from diarrhea. <sup>94</sup> Dam <sup>95</sup> used serum from horses hyperimmunized with pathogenic Escherichia coli suspensions. The serum, when administered subcutaneously immediately after birth, was shown to prevent neonatal calf diseases.

An IgM rich fraction derived from bovine serum was demonstrated to be protective against colisepticemia. <sup>96,97</sup> One gram of IgM given intravenously was shown to be protective, although very small amounts gave some benefit. Intraperitoneal administration also successfully protected calves. Parenteral IgM administration, while being very effective against colisepticemia, was only slightly effective against enteric disease.

Gammaglobulin rich preparations derived from colostrum have also been utilized in hypogammaglobulinemic calves. <sup>55,98</sup> These products, given intraperitoneally, intramuscularly or intravenously were beneficial in the prevention of or delaying of colisepticemia.

Not all authors have reported success with gammaglobulin immunoprophylaxis in calves. Lotan et al <sup>99</sup> found that parenteral immunoglobulins were successful one year, but not the next in reducing diarrhea in Israeli calves. Cohen and Trainin, <sup>62</sup> also in Israel, treated calves with 3.5 grams of a gammaglobulin product intraperitoneally. They found no marked difference in the mortality of treated versus control calves.

Specific replacement therapy in hypogammaglobulinemic neonates is more widely practiced in foals <sup>100-102</sup> than in calves. In man and in foals a dosage of 20 ml of plasma/kg has been shown to be adequate. <sup>101,103</sup> Fisher <sup>104</sup> calculated that a minimum dose of 40 grams of gammaglobulin or approximately 700 mls of bovine serum was necessary to adequately raise gammaglobulin levels in a hypogammaglobulinemic calf.

## REFERENCES

1. Fallon RJ: The effect of immunoglobulin levels on calf performances and methods of artificially feeding colostrum to the newborn calf. *Ann Rech Vet* 9: 347-352, 1978
2. Logan EF, Gibson T: Serum immunoglobulins in suckled beef calves. *Vet Rec* 97: 229-230, 1975
3. Irwin VCR: Incidence of disease in colostrum deprived calves. *Vet Rec* 94: 105-106, 1974
4. Penhale WJ, Logan EF, Selman IE, et al: Observations on the absorption of colostrum immunoglobulins by the neonatal calf and their significance in colibacillosis. *Ann Rech Vét* 4: 223-233, 1973
5. Tennant B, Baldwin BH, Braun RK, et al: Use of the glutaraldehyde coagulation test for detection of hypogammaglobulinemia in neonatal calves. *JAVMA* 174: 848-853, 1979
6. Logan EF, McBeath DG, Lowman BG: Quantitative studies on serum immunoglobulin levels in suckled calves from birth to five weeks. *Vet Rec* 94: 367-370, 1974
7. McBeath DG, Logan EF: Influence of neonatal management on serum immunoglobulin levels of suckled calves. *Vet Rec* 95: 466, 1974
8. Selman IE, Fisher EW, McEwan AD: The serum immune globulin concentration of newborn dairy heifer calves: A farm survey. *Vet Rec* 88: 460-464, 1971
9. Barber DML: Serum immune globulin status of purchased calves: an unreliable guide to viability and performance. *Vet Rec* 102: 418-420, 1978
10. Leece JG, Morgan DO: Effect of dietary regimen on cessation of intestinal absorption of large molecules (closure) in neonatal pigs and lambs. *J Nutr* 78: 265-268, 1962
11. Bush LJ, Aquilera MA, Adams GD, et al: Absorption of colostrum immunoglobulins by new born dairy calves. *J Dairy Sci* 54: 1547-1553, 1971
12. Stott GH, Marx DB, Menefee BE, et al: Colostral immunoglobulin transfer in calves. I. Period of absorption. *J Dairy Sci* 62: 1632-1638, 1979

13. McCoy GC, Reneau JK, Hunter AG, et al: Effects of diet and time on blood serum proteins in the newborn calf. *J Dairy Sci* 53: 358-362 1970
14. Kruse V; Yield of colostrum and immunoglobulin in cattle at the first milking after parturition. *Anim Prod* 12: 619-626, 1970
15. Molla A: Immunoglobulin levels in calves fed colostrum by stomach tube. *Vet Rec* 103: 377-380, 1978
16. Dardillat J, Trillat G, Larvor P: Colostrum immunoglobulin concentration in cows: Relationship with their calf mortality and with the colostrum quality of their female offspring. *Ann Rech Vét* 9: 375-384, 1978
17. Fisher EW, Selman IE, McEwan AD, et al: Some causes of and some factors affecting mortality in new born calves. V. International meeting of diseases of cattle. Opatija, Yugoslavia: 41-54, 1968
18. McGuire TG, Pfeiffer NE, Weikel JM, et al: Failure of colostral immunoglobulin transfer in calves dying from infectious disease. *JAVMA* 169: 715-718, 1976
19. Smith HW, O'Neil JA, Simmons EJ: The immune globulin content of the serum of calves in England. *Vet Rec* 80: 664-666, 1967
20. Bush LJ, Mungle MB, Corley LD, et al: Factors affecting absorption of immunoglobulins by newborn dairy calves. *J Dairy Sci* 56: 312, 1973
21. Balfour WE, Comline RS: Acceleration of the absorption of unchanged globulin in the new-born calf by factors in colostrum. *J Physiol* 160: 234, 1962
22. Hardy RN: The influence of specific chemical factors in the solvent on the absorption of macromolecular substances from the small intestine of the new-born calf. *J Physiol* 204: 607, 1969
23. Baumwart AL, Bush LJ, Mungle M, et al: Effects of potassium isobutyrate on absorption of immunoglobulins from colostrum by calves. *J Dairy Sci* 60: 759-765, 1977
24. Patt JA, Zarkower A, Eberhart RJ: Effect of histamine on intestinal absorption of gammaglobulin in newborn calves. *J Dairy Sci* 55: 645-651 1972

25. Piñeiro A, Brock JH, Esparza I: Isolation and properties of bovine colostral trypsin inhibitor. *Ann Rech Vét* 9: 281-286, 1978
26. Jensen PT, Pederzen KB: Studies on immunoglobulins and trypsin inhibitor in colostrum and milk from sows and in serum of their piglets. *Acta Vet Scand* 20: 60-72, 1979
27. Foley JA, Hunter AG, Otterby DE: Absorption of colostral proteins by newborn calves fed unfermented, fermented or buttered colostrum. *J Dairy Sci* 61: 1450-1455, 1978
28. Snyder AC, Schuh JD, Wegner TN, et al: Passive immunization of the newborn dairy calf via fermented colostrum. *J Dairy Sci* 57: 641, 1974
29. McEwan AD, Fisher EW, Selman IE: Observations on the immune globulin levels of neonatal calves and their relationship to disease. *J Comp Path* 80: 259-265, 1970
30. Hurvell B, Fey H: Comparative studies on the gammaglobulin levels in sera of market calves in relation to their health. *Acta Vet Scand* 11: 341-360, 1970
31. Frerking H, Aeikens I: About the importance of colostrum for the newborn calf. *Ann Rech Vét* 9: 361-365, 1978
32. Barber DML: Control of diarrhea and death in home-bred calves by bucket feeding pooled colostrum. *Vet Rec* 104: 385-386, 1979
33. Thornton JR, Willoughby RA, McSherry BJ: Studies on diarrhea in neonatal calves: The plasma proteins of normal and diarrheic calves during the first ten days of age. *J Comp Med* 36: 17-25, 1972
34. Stott GH, Wierman F, Menefee BE, et al: Influence of environment on passive immunity in calves. *J Dairy Sci* 59: 1306-1311, 1976
35. Cabello G, Levieux D: The effects of thyroxine and climatic factors on colostral gammaglobulin absorption in newborn calves. *Ann Rech Vét* 9: 309-318, 1978
36. Ford EJH, Boyd JW, Hogg RA: Investigation into possible relationships between the quality of colostrum and the subsequent performance of calves. *Index Res Meat and Livestock Commission*, 1978, p 4
37. James RE, Polan CE: Effect of orally administered duodenal fluid

- on serum proteins in neonatal calves. J Dairy Sci 61: 1444-1449, 1978
38. James RE, Polan CE, Bibb TL, et al: Effect of orally administered duodenal fluid on susceptibility of newborn calves to an Escherichia coli challenge. J Dairy Sci 59: 1495-1501, 1976
  39. Roy JHB: Decision making and calf health. Journal of the RASE 132: 81-105, 1971
  40. Bull RC, Ross RH, Olson DP, et al: Effects of maternal protein restriction on blood composition and pathological lesions in neonatal calves. Proc West Sect ASAS 29: 343-356, 1978
  41. Husband AJ, Brandon MR, Lascelles AK: The effect of corticosteroid on absorption and endogenous production of immunoglobulins in calves. Aust J Exp Biol Med Sci 51: 707-710, 1973
  42. Halliday R: The effect of steroid hormones on the absorption of antibodies by the young rat. J Endocr 18: 56-66, 1959
  43. Deutsch HF, Smith VR: Intestinal permeability to proteins in the newborn herbivore. Am J Physiol 191: 271-276, 1957
  44. Stott GH, Reinhard EJ: Adrenal function and passive immunity in the dystocial calf. J Dairy Sci 61: 1457-1461, 1978
  45. Johnston NE, Oxender WD: Effect of altered serum glucocorticoid concentrations on the ability of the newborn calf to absorb colostrum immunoglobulin. Am J Vet Res 40: 32-34, 1979
  46. Tennant B, Harrold D, Reina-Guerra M, et al: Neonatal alterations in serum gamma globulin levels in Jersey and Holstein-Friesian calves. Am J Vet Res 30: 345-354, 1969
  47. Selman IE, McEwan AD, Fisher EW: Studies on natural suckling in cattle during the first eight hours post partum. I. Behavioral studies (dams). Anim Behav 18: 276-283, 1970
  48. Selman IE, McEwan AD, Fisher EW: Studies on natural behavior in cattle during the first eight hours post-partum. II. Behavioral studies (calves). Anim Behav 18: 284-289, 1970
  49. Leece JG: Effect of dietary regimen on cessation of uptake of macromolecules by piglet intestinal epithelium (closure) and transport to the blood. J Nutr 103: 751-756, 1973

50. McCoy GC, Renean JK, Hunter AG, et al: Effects of diet and time on blood serum proteins in the new-born calf. J Dairy Sci 53: 358-362 1970
51. Klaus GGB, Bennett A, Jones EW: A quantitative study of the transfer of colostral immunoglobulins to the newborn calf. Immunology 16: 293-299, 1969
52. Smith TW, Little RB: Cow serum as a substitute for colostrum in new born calves. J Exp Med 36: 453-468, 1922
53. Gay CC, Anderson N, Fisher EW, et al: Gamma globulin levels and neonatal mortality in market calves. Vet Rec 77: 148-149, 1965
54. Penhale WJ, Christie G, McEwan AD, et al: Quantitative studies on bovine immunoglobulins. II. Plasma immunoglobulin levels in market calves and their relationship to neonatal infection. Br Vet J 126: 30-36, 1970
55. Logan EF, Penhale WJ: Studies on the immunity of the calf to colibacillosis. I. The influence of colostral whey and immunoglobulin fractions on experimental colisepticemia. Vet Rec 88: 222-228, 1971
56. McBeath DG, Penhale WJ, Logan EF: An examination of the influence of husbandry on the plasma immunoglobulin level of the newborn calf, using a rapid refractometer test for assessing immunoglobulin content. Vet Rec 88: 266-270, 1971
57. Fisher EW, de la Fuente GH: Antibiotics and calf diarrhea - the effect of serum immune globulin concentrations. Vet Rec 89: 579-582, 1971
58. Thomas LH, Swann RG: Influence of colostrum on the incidence of calf pneumonia. Vet Rec 92: 454, 1973
59. Boyd JW, Baker JR, Leyland A: Neonatal diarrhea in calves. Vet Rec 95: 310-313, 1974
60. Carroll EJ, Crenshaw GL: Bacteriocidal activity of bovine neonatal serums for selected coliform bacteria in relation to total protein and Immunoglobulin G<sub>1</sub> and Immunoglobulin M concentrations. Am J Vet Res 37: 389-394, 1976
61. Lister EE, MacKay RR: Effect of medication with antibiotics and

- mature bovine plasma on mortality, morbidity, rate of growth and serum immunoglobulins of Holstein calves. *Can J Anim Sci* 50: 645-650, 1970
62. Cohen R, Trainin Z: Serum gammaglobulin levels of newborn calves in two dairy herds and some observations on the effect of prophylactic administration of gammaglobulin products. *Refuah Vet* 26: 18-25, 1969
  63. Smith T, Little RB: The significance of colostrum to the new-born calf. *J Exp Med* 36: 181-198, 1922
  64. Aschaffenburg R, Bartlett S, Kon SK, et al: The nutritive value of colostrum for the calf. I The effect of different fractions of colostrum. *Brit J Nutrit* 3: 187-196, 1949
  65. Fey H: Die bedeutung des gammaglobulins fur das neugeborene kalb. *Int tierärztl Arbeitsgemeinschaft Tierernährung. Symposium, Salzburg* 17-28, 1967
  66. Fey, H, Margadant A; Zur pathogenese der kälber - colisepsis. IV. Agammaglobulinämie als disponierender faktor. *Zbl Vet Med* 653-663, 1967
  67. Radostits OM: Clinical management of neonatal diarrhea in calves, with special reference to pathogenesis and diagnosis. *JAVMA* 147: 1367-1376, 1965
  68. Radostits OM, Rhodes CS, Mitchell, et al: A clinical evaluation of antimicrobial agents and temporary starvation in the treatment of acute undifferentiated diarrhea in newborn calves. *Can Vet Jour* 16: 219-227, 1975
  69. Fisher EW, Martinez AA, Trainin Z, et al: Studies of neonatal calf diarrhoea. II. Serum and faecal immune globulins in enteric colibacillosis. *Br Vet J* 131: 402-414, 1975
  70. Fisher EW, Martinez AA, Trainin Z, et al: Studies of neonatal calf diarrhoea. IV. Serum and faecal immune globulin in neonatal salmonellosis. *Br Vet J* 132: 39-48, 1976
  71. Fisher EW, Martinez AA, Trainin Z, et al: Studies of neonatal calf diarrhoea. VI. Serum and faecal immune globulin in calves with mixed infections. *Br. Vet J* 132: 252-258, 1976



72. Barber DML, MacLennan W: Immune globulin studies of the "collapse syndrome" in suckled calves. Vet Rec 97: 403-405, 1975
73. Bradley JA, Niilo L, Dorward WJ: Some observations on serum gamma-globulin concentration in suckled beef calves. Can Vet J 20: 227-232, 1979
74. Williams MR, Spooner RL, Thomas LH: Quantitative studies on bovine immunoglobulins. Vet Rec 96: 81-84, 1975
75. Roy JHB: Factors affecting the susceptibility of calves to disease. 74th meeting of American Dairy Science Association. Conference, Logan, Utah, 1979
76. Lomba F, Fumiere I, Tshibangu M, et al: V. Immunoglobulin transfer to calves and health problems in large bovine units. Ann Rech Vét 9: 353-360, 1978
77. Stone SS, Deyoe BL: Appearance of brucella specific immunoglobulins in synovia of neonatal calves after colostrum feeding. Am J Vet Res 35: 1259-1261, 1974
78. McEwan AD, Fisher EW, Selman IE, et al: A turbidity test for the estimation of immune globulin levels in neonatal calf serum. Clin Chim Acta 27: 155-163, 1970
79. Logan EF, McMurray Ch, O'Neill DG, et al: Absorption of colostral immunoglobulins by the neonatal calf. Br Vet J 134: 258-262, 1978
80. Stone SS, Gitter M: The validity of the sodium sulphite test for detecting immunoglobulins in calf sera. Br Vet J 125: 68-72, 1969
81. Pfeiffer NE, McGuire TG: A sodium sulfite precipitation test for assessment of colostral immunoglobulin transfer to calves. JAVMA 170: 809-811, 1977
82. MacDougall DF: Immunoglobulin metabolism in the neonatal foal. J Reprod Fertil (Suppl) 23: 739-742, 1975
83. Reilly WJ, MacDougall DF: The metabolism of IgG in the newborn foal. Res Vet Sci 14 136-137, 1973
84. Naylor JM, Kronfeld DS: Refractometry as a measure of the immunoglobulin status of the newborn dairy calf: Comparison with the zinc sulphate turbidity test and single radial immunodiffusion. Am J Vet Res 38: 1331-1334, 1977



85. Smith T, Little RB: Cow serum as a substitute for colostrum in new-born calves. J Exp Med 36: 453-468, 1922
86. Watts RE: Blood transfusions for reducing calf losses. Fifth Annual Dairy Field Day November 14th, 1963, University of Arizona, Tucson
87. Rafferty GC: Blood from a donor cow. Vet Rec 90: 166, 1972
88. MacDonald DW, Oakley GA: The prophylactic use of blood in colibacillosis of calves. Vet Rec 13: 415-416, 1961
89. Watt JG: The use of fluid replacement in the treatment of neonatal diseases in calves. Vet Rec 77: 1474-1482, 1965
90. Watt JG: Fluid therapy for dehydration in calves. JAVMA 150: 742-750, 1967
91. Wise GH, Anderson GW: The control of diarrhea ("white scour") of new born dairy calves by means of serum and sulfaquanadine. J Dairy Sci 27: 965-979, 1944
92. Dollahite JW: An experimental study of homologous hyperimmune serum in the prevention of acute dysentery of newborn calves. Vet Med 34: 652-654, 1939
93. McBeath DG: Prophylactic use of hyperimmune serum in experimental colisepticemia in calves. Vet Rec 100: 259-262, 1977
94. Lambert G, Moeller DJ, Wetter CJ: Field evaluation of antiserum for prevention of the neonatal calf pneumonia enteritis complex. VMSAC 65: 795-797, 1970
95. Dam A: Immunoprophylaxie dans la colibacillose du veau principalement par la sérothérapie. Ann Rech Vétér 4: 181-189, 1973
96. Penhale WJ, Logan EF, Stenhouse A: Studies on the immunity of the calf to colibacillosis. II. Preparation of an IgM-rich fraction from bovine serum and its prophylactic use in experimental colisepticemia. Vet Rec 89: 623-628, 1971
97. Logan EF, Penhale WJ: Studies on the immunity of the calf to colibacillosis. IV. The prevention of experimental colisepticemia by the intravenous administration of a bovine serum IgM-rich fraction. Vet Rec 89, 663-667, 1971
98. Fey H, Margadant A, Nicolet J, et al: Prophylaxe der experimentellen

- Colisepsis des Kalbes mit einem Colostrum-Serum pool. Schweiz Arch Tierheilk 105: 361-370, 1963
99. Lotan E, Berman A, Tadmor A, et al: The efficiency of pooled gamma-globulins in preventing scours in Israeli-Holstein calves. Br.Vet J 120: 576-579, 1964
100. Crawford TB, McGuire TC, Hallowell AL, et al: Failure of colostral antibody transfer in foals: Its effect, diagnosis and treatment.
101. Rumbaugh GE, Ardans AA, Ginno D, et al: Identification and treatment of colostrum-deficient foals. JAVMA 174: 273-276, 1979
102. Rumbaugh GE, Ardans AA: Field determination of the immune status of the newborn foal. Equine Practice 1: 37-41, 1979
103. Buckley RH: Plasma therapy in immunodeficiency diseases. Amer J Dis Child 124: 376-381, 1972
104. Fisher EW, Vet Rec 77: 1482-1486

EPIDEMIOLOGY AND IMMUNOPROPHYLAXIS  
OF DISEASE AND MORTALITY IN  
HOUSED DAIRY CALVES

by

BRUCE RICHARD WATT

B.V.Sc., University of Sydney, 1976

---

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

1980

## ABSTRACT PAPER 1

### AN EPIDEMIOLOGICAL STUDY OF MORTALITY AND DISEASE IN HOUSED DAIRY CALVES

This investigation was conducted on 98 Holstein calves born from January 2 to May 21, 1979 at the Kansas State University Dairy Teaching and Research Center. During this time 29 calves died, a mortality rate of 29.6%. All but one calf died within the first month of life and the mean age of death was 14.4 days.

Three major disease syndromes were encountered. Acute neonatal diarrhea of high morbidity but low mortality (with fluid therapy) affected calves from 10-60 hours of age. Chronic diarrhea was the major cause of mortality with peak incidence of 68% in females and 88% in male calves at 11 days of age. Bloody diarrhea was also frequently seen. Pneumonia developed as early as one week of age, reached an incidence of 20-30% between weeks 2 and 3½ and declined by the fourth week.

Enterotoxigenic K99 positive Escherichia coli and rota viruses were isolated from neonatal diarrhea cases. E. coli, corona viruses and bovine virus diarrhea viruses were isolated from chronic diarrhea cases. Pasteurella hemolytica was consistently isolated from nasal swabs of calves with pneumonia and from pneumonic calves at necropsy. Pasteurella multocida and Corynebacterium pyogenes were also isolated from pneumonic lungs at necropsy. Virus isolation and serological studies revealed no evidence of viral respiratory pathogens.

Calves that died from pneumonia or chronic diarrhea plus pneumonia had significantly lower immunoglobulin levels at 48 hours of age than calves which survived. Calves dying of chronic diarrhea had lower levels of immunoglobulins than surviving calves but the difference was not significant. Calves which died had lower levels of IgA, IgG<sub>1</sub> and IgG<sub>2</sub> than survivors but the difference was not significant.

A significant seasonal variation in incidence of diarrhea, bloody feces and pneumonia was observed. Pneumonia incidence was highest in February which diarrhea and bloody feces incidence was highest in March and April. This trend was reflected by the mean length of life which was lowest in late March and early April although this difference was not significant.

The environment of the calf barn was investigated. Temperature was maintained at a minimum of 13 C. Air change occurred at the rate of 2.7 changes per hour in one calf room and 3.6 changes per hour in the other. Air velocity readings ranged from 3-7 m/min to 13-20 m/min in various parts of the calf rooms. Relative humidity exhibited a diurnal variation from 50-60% at 6:00 am rising to 70-80% at 6:00 pm then falling steadily again.

Male calves had a higher mortality rate (37%) than female calves (21%). Male calves also had a significantly higher incidence of diarrhea than female calves but no difference in incidence of pneumonia or bloody feces.

## ABSTRACT PAPER 2

### PARENTERAL IMMUNOGLOBULIN ADMINISTRATION TO HYPOGAMMAGLOBULINEMIC CALVES

This study aimed to investigate absorption, efficacy and ease of administration of a commercial hyperimmune serum given by various routes to hypogammaglobulinemic calves. 36, 48 hour old Hostein calves were studied with 18 calves as controls, six calves receiving intraperitoneal treatment, six calves receiving subcutaneous treatment and six calves receiving intravenous treatment. The hyperimmune serum containing 47 mg/dl of IgA, 402 mg/dl of IgM, 3140 mg/dl of IgG<sub>1</sub> and 5516 mg/dl of IgG<sub>2</sub> was used at a dose rate of 11.11 ml/kg.

Intraperitoneal treatment was the most rapid and simple technique of administration. Mild side effects of shivering and depression were observed but these lasted only 1-2 hours. Subcutaneous treatment was more time consuming but no immediate side effects were evident. One calf treated subcutaneously developed infected injection sites. Serious side effects such as dyspnea, heart or respiratory blockage and ataxia precluded delivery of the full dose of serum intravenously. When the dose was diluted in 1-1½ liters of saline and infused slowly no side effects were observed.

Significant absorption of IgA, IgM or IgG<sub>1</sub> was not demonstrated. All three methods resulted in significant absorption of IgG<sub>2</sub> with no significant difference being detected between methods of administration.

Only intraperitoneal administration produced significant elevation of gammaglobulin levels. However, intravenous treatment was not fairly evaluated since in 4 of 6 cases serious side effects prevented delivery of the calculated dose.

16 of the 36 calves in the trial died - 9 treated calves and 7 control calves. This represents a 44.4% mortality rate compared with 11.7% mortality rate for the remaining calves born during the study. Treatment with the hyperimmune serum did not significantly alter mortality or incidence of diarrhea or pneumonia.