268

NEBULIZATION THERAPY AS ADJUNCT TO CONVENTIONAL TREATMENT OF BOVINE RESPIRATORY DISEASE

by

MARK F. SPIRE

B. S., West Texas State University, 1971
D.V.M., Texas A & M University, 1974

A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1978

Approved by:

Major Professor

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

The author is appreciative of the help and guidance given to him by Drs. J. E. Mosier, J. G. E. Vestweber, and D. A. Schoneweis in the Department of Surgery and Medicine, Dr. H. W. Leipold in the Department of Pathology, and Dr. H. D. Anthony at the Kansas State Diagnostic Laboratory. Appreciation is also extended to Dr. S. M. Kruckenberg for his expertise in data accumulation and statistical analysis.

I would like to give special thanks to my wife and daughter. Their faith and support during this project was tremendous.

INTRODUCTION

The incidence of pneumonia may vary greatly in a given herd. Death loss is frequently high and surviving animals may be affected with chronic bronchopneumonia. Treatment of bovine bronchopneumonia is difficult and frequently unsuccessful.

The time interval for an animal to pass from the acute stage of bronchopneumonia to the chronic stage of bronchopneumonia may be as short as seven days (Leipold, 1977). This short interval may challenge the efficacy of treatment, even if the causative bacteria is sensitive to the chemotherapeutic agent.

A common histopathological finding in chronic bronchopneumonia is the occlusion of the lumen of the alveoli, bronchioles, and bronchi due to an exudate accumulation. The exudate, composed of mucus, bacteria, neutrophils, macrophages, and blood (Jensen et al. 1976), limits the activity of the mucociliary apparatus by limiting the amount of oxygen reaching the alveolar epithelium. The resulting pulmonary hypoxia impairs pulmonary clearance and macrophage function (Leak, 1964 and Stossel, 1974). In addition, the accumulated exudate protects bacteria from normally secreted respiratory immunoglobulins (Dulfano, 1973) and antibacterial agents.

Prompt elimination of tracheobronchial secretions may prevent the development of serious pulmonary complications in the patient with inflammation of the respiratory passage (Thomas and Treasure, 1977). Conventional treatment of

pneumonia with antibacterial agents have little or no effect on this common sequella to bovine bronchopneumonia. The benefit of aerosol therapy as an adjunct to conventional treatment is promising. The administration of antibacterial agents and mucolytic agents by nebulization through indwelling tracheal catheters will allow such agents to penetrate the obstructed bronchioles and alveoli of the lungs and to possibly minimize the pulmonary changes that are seen in chronic bronchopneumonia.

This study was undertaken to investigate the additive effect of aerosolized antibacterial and mucolytic agents, in conjunction, with the conventional treatment of bovine bronchopneumonia. The primary purpose of the study was to evaluate the clinical response of bovine subjects affected with acute bronchopneumonia.

REVIEW OF THE LITERATURE

Miller (1973) reviewed the use of inhalation therapy and found it dated back to the oldest written medical history. Presently, the therapeutic use of inhaled aerosols is recognized as an essential part of the total approach for the treatment of a wide variety of acute and chronic respiratory disorders in man. In man, aerosol therapy has been used in asthma, bronchitis, bronchiolitis, emphysema, cystic fibrosis, alveolar proteinosis, bronchopneumonia, and also to relieve bronchospasm, decrease mucosal edema, and to liquefy bronchial secretions.

Lourenco (1974) states that because of the large surface area of the lung and because of accessibility, the respiratory tract is ideal for treatment with aerosols. It is difficult to measure the exact location where an aerosol will exert its activity. Lourenco (1974) also states that theoretical models have been designed to determine distribution of particles, but individual patient variance, disease alteration of respiratory pathways, and bronchospasm make it impossible to predict the site of pulmonary deposition of a therapeutic aerosol.

Miller (1974) concludes that because aerosols are delivered best to the well-ventilated areas of the lung it is necessary to provide improved ventilation if antibiotic aerosols are to be delivered to diseased areas. Postural drainage, deep breathing, chest percussion and/or endotracheal suction may improve ventilation.

Miller (1973) outlined the spectrum of aerosol therapy established for man. Aerosol distribution and deposition, particle size and potential toxicity affects the method of aerosol therapy. This may be summarized to include the following:

1. Deposition of relatively minuscule amounts of very potent agents in smaller airways obtains optimal topical therapeutic effect with minimal systemic side effects. Particle droplet size is 0.3 microns to 3.0 microns.
2. Deposition of moderate amounts of certain agents where a topical effect is desired or where the agent is effective topically only avoids otherwise potentially toxic systemic effects. Particle size range is small enough to penetrate yet large enough to carry an effective volume of medication, approximately 1 micron to 20 microns.
3. Deposition of relatively large amounts of bland substances in the medium and large airways promoting bronchial evacuation with minimal mucosal irritation. Particle size range is 5 microns to 40 microns.
4. Humidification of the inspired air is done with large particles (greater than 10 microns) of water as heated or unheated mist.

When therapy is to be directed to the lower airways, a mouthpiece or at least breathing through the mouth with a mask should be the method of choice taking care to keep the teeth

and tongue out of the path of the aerosol. Nasal breathing will cause more than 95 percent of the aerosol to be deposited in the nose.

Morrow (1974) reviewed therapeutic particle size and stated that for therapeutic and diagnostic aerosols, particles need to be in the aerodynamic size range of 1-10 microns in diameter. Particles of this size range were easily produced, sufficiently stable aerosols, and massive enough to deposit and deliver the requisite amount of drug or agent. To include the alveolated regions of the lungs, the particle size range should be restricted to the 1 to 5 micron diameter.

Veit (1976) illustrated particle distribution and penetration of the normal bovine lung. The upper airway anterior to the larynx contained particles of all sizes, but especially those over 10 microns. Larger particles were removed by the mucociliary apparatus and turbinates. As air passes into the trachea the maximum particle size was reduced to 5-10 microns throughout the trachea. Particle size in the primary bronchi was in the range of 1-3 microns with few particles above 5 microns. Alveolar tissue was only penetrated by particles in the size range of 1-2 microns.

Bolton (1977) described the principals of aerosol therapy in small animal medicine and discussed particle size and stability. Larger particles (greater than 5 to 10 microns) were deposited in the upper airways. Only the smaller particles (0.5 to 5 microns) reached the lower airways. Particle stability was affected by the type of solution used. Concen-

trated solutions or hygroscopic solutions tended to take up water from the environment, increase in size and were deposited in the upper airways. Dilute solutions tend to evaporate and become smaller, reducing the amount of mist delivered to the patient, but reach deeper into the airways. Cool-mist aerosols evaporate upon warming and decrease in particle size, while warm-mist aerosols coalesce upon cooling, and increase in particle size.

Miller (1973) evaluated the use of aerosolized antibiotics and concluded that they are particularly effective against resistant gram-negative organisms in patients with a major problem of effective bronchial clearance. His evaluation was substantiated by High et al. (1958), Rose et al. (1970), Klastersky et al. (1974), and Feeley et al. (1974). Miller (1973) concluded that the technique should be reserved for patients with severe bronchopulmonary infection which fail to respond to intensive bronchial hygiene and parenteral or oral administration of antibiotics. Pine et al. (1970) and Williams (1974) concluded from clinical studies that aerosol antibiotic treatment was no more effective than parenterally administered antibiotics.

Miller (1974) states that an antibiotic which is administered as an aerosol should be one that has a potent topical effect, is poorly absorbed to minimize systemic effects, and is neither highly irritating nor allergenic. Dickie and deGroot (1973) state that aerosol therapy may have specific advantages over other methods of administration of the anti-

biotic particularly if therapeutic levels of the antibiotic can be achieved within airways and lung tissue without causing deterioration in lung function. Prisgal (1956) concluded that if antibiotics could be delivered to the lung tissue without significant blood levels of the antibiotic then toxic effects of these agents on other organs might be avoided.

Kanamycin has been demonstrated by High (1958) and Bilodeau et al. (1966) to be safe and effective when administered as an aerosol. Kanamycin was found by Bilodeau et al. (1966) and Prokhorova II (1963) to be poorly absorbed into the systemic circulation resulting in a decreased possibility of auditory and renal toxicity. Prokhorova II (1968) showed that with repeated nebulization, a high and accumulative antibiotic level occurs in the lung tissue.

Lifschitz and Denning (1971) investigated three aspects of the pharmacology of kanamycin aerosol. The three areas were absorption, effect on airway resistance, and sputum viscosity. Absorption of kanamycin from the tracheobronchial airways was found to be so low that toxicity was not considered a problem. Kanamycin had no effect upon airway resistance. Sputum viscosity was reduced 52 percent following use of kanamycin aerosol.

Ayres et al. (1972) detected kanamycin in the urine of patients following its delivery as an aerosol, but could not detect levels in the venous or arterial serum, thus indicating that small amounts are absorbed and cleared rapidly from the bloodstream. Low serum levels of kanamycin have been reported

by Huang et al. (1959) and Bilodeau and Roy (1963) following aerosol therapy.

Dickie and deGroot (1973) studied the ventilatory effects of aerosolized kanamycin in patients with chronic lung disease of varying etitology. Forced expiratory volume was decreased slightly, but appeared physiologically insignificant in regards to ventilatory function. Dickie and deGroot (1973) concluded that insofar as its effect on the airway, kanamycin would be an excellent therapeutic agent by aerosol.

Potter et al. (1965) found that kanamycin precipitates with deoxynucleic acid from purulent sputum, and it may lower sputum viscosity. The mucolytic effects of kanamycin was confirmed by Lifschitz (1971) in patients with nonpurulent sputum. Lifschitz (1971) concluded that the mucolytic effect of kanamycin could enhance its clinical usefulness.

In man, the recommended dosage levels for aerosol use of kanamycin varies from 100 mg per treatment (Matthews, et al. 1964) to 250 mg (Bilodeau, 1966). In view of the evidence that only a small fraction of an inhaled aerosol is deposited in the lower respiratory tract, Spier et al. (1961) states that the concentration should be adequate to assure therapeutic levels in the lung tissue.

Bolton (1977) states that antibiotic aerosols are irritating and may cause bronchial swelling and constriction. For this reason, antibiotics are always used in conjunction with bronchodilators, such as, isoproterenol or racemic epinephrine. Walker and Stephen (1977) consider the elimination of the

total biomass of infective organisms the primary objective of aerosol therapy and that the need for bronchodilators are probably of little value in most causes of infectious pneumonia.

Sheffner (1963) studied the in vitro effects of N-acetylcysteine. Acetylcysteine is the N-acetyl derivative of the amino acid cysteine. Acetylcysteine, a clear liquid with a sulfur odor, is more stable than its parent compound but can be inactivated by oxidation. In vitro efficiency is enhanced by an alkaline pH. The mucolytic action of acetylcysteine is related to the sulfhydryl group which reduces the viscosity of mucoprotein solutions and bronchial secretions in vitro. The free sulfhydryl group acts upon the disulfide bonds of mucoprotein thereby reducing the viscosity of mucus (Sheffner, 1965).

Clinically, acetylcysteine has been shown to be therapeutically useful in the elimination of tracheobronchial secretions as a result of its mucolytic properties by Reas (1963), Hurst et al. (1967), Lieberman (1970), and Utkin et al. (1972). Lieberman (1970) concludes that a 10 or 20 percent solution is adequate for achieving a mucolytic effect. Reas (1963) states that acetylcysteine delivered to the bronchial airways by nebulization is adequate to reduce sputum consistency.

Adverse side effects are seldom seen, but the danger of acute bronchospasm in rare cases has been recognized by Bernstein and Ausdenmore (1964). Lieberman (1970) suggested

that the bronchospasm is induced by bronchial irritation arising from its hypertonicity. A 10 percent solution is probably less irritating than a 20 percent solution. Kory and Hirsch (1965) and Miller (1973) suggest the administration of bronchodilators, such as, isoproterenol or racemic epinephrine, preceding or accompanying the use of acetylcysteine.

Jenkins and van Ovost (1974) successfully treated viral pneumonia in the equine using intermittent positive-pressure with a commercial respirator and nebulization therapy. Racemic epinephrine and water were nebulized several times daily, in conjunction, with positive-pressure therapy. A marked decrease in congestion of the lungs and improved blood gas values were noted following two days of therapy.

Bemis and Appel (1977) used antibiotic aerosol therapy and demonstrated a reduction in bacterial density of Bordetella bronchiseptica in dogs. Erythromycin, chloramphenicol, ampicillin, tetracycline and tylosin given orally, and kanamycin or gentamicin, given parenterally, were unable to reduce bacterial numbers in the trachea and bronchi of infected dogs. Clinical signs appeared to be related to bacterial numbers in the bronchial airways. A properly administered aerosol antibiotic regimen may reduce the bacterial density in the trachea and bronchi, and thereby reduce the occurrence and severity of clinical signs.

Lebedev et al. (1976) concluded that for group treatment of respiratory disease in calves, and especially in

acute bronchopneumonia, that the use of antibiotics in aerosol form was very effective. The method was more economical in time and materials, than parenteral injection.

Morel (1971) using two commercial preparations of essential oils, applied as aerosols, showed they had an antiseptic effect in the lungs. Promising results were obtained in a stable of horses with influenza, a calfhouse with an outbreak of pasteurellosis, and a herd of unthrifty pigs with coughing.

Goldhamer et al. (1970) used a mucoevacuant solution containing 0.125 percent tyloxapol, 2 percent sodium bicarbonate, and 5 percent glycerin in cats to study effects on mucus flow. Significant increases in mucus flow rates occurred at 20 and 60 minutes following exposure. In cats with respiratory pathology the amelioration of the reduced mucus flow rate, accompanied by or caused by increased viscosity of the mucus blanket, appeared to be amenable to agents which reduced interfacial tension, reduced viscosity, and allowed mucus to be moved in a normal fashion.

MATERIALS AND METHODS

Fifteen castrated male calves (4-Angus-Hereford cross, 5-Charolais cross, 2-Angus, 2-Hereford cross, and 2 Hereford) averaging 213 kg. were utilized in this study. The animals were part of a group of 105 mixed breed calves that were received from central Texas. The total group was gathered over a three day period by a commercial cattle buyer, and transported to central Kansas on the fourth day. Processing the day following receipt consisted of intranasal vaccination for infectious bovine rhinotracheitis and parainfluenza,[a] vaccination for Clostridium chauvoei, septicum, novyi, and sordelli,[b] deworming with thiabendazole,[c] treatment for ectoparasites using an organophosphate pour-on,[d] branding and dehorning.

Clinical cases were drawn from the total group as clinical signs of bronchopneumonia developed over a two day period. Selection of the animals on the farm was based upon labored breathing, depression, anorexia, rectal temperature of 39.5° C or greater, and/or nasal discharge. The calves exhibiting clinical signs of bronchopneumonia were randomly divided into a seven animal control group and an eight animal nebulized (test) group.

All calves were given a general physical examination and

---

a Nasalgen, Jensen-Salsbery Laboratories, Kansas City, Mo.
b Electroid CSNS, Jensen-Salsbery Laboratories, Kansas City, Mo.
c Thibenzole Cattle Wormer Paste 43%, Merck and Company, Inc., Rathway, N.J.
d Co-Ral - Chemagro Corp., Kansas City, Mo.

classified subjectively as to "Degree of Illness" (Hjerpe, 1975). A numerical score of one was given to slightly ill or well animals, two to moderately ill (moderately depressed, gaunt, rough hair coat, acclerated respiratory rate) animals, and three to severely ill (weak, very depressed, labored breathing) animals. Each animal was evaluated daily throughout the course of the trial as to "Degree of Illness."

Following the initial clinical examination of all animals, an arterial blood sample was collected anaerobically from the ventral coccygeal artery using a heparinized glass syringe. Additional samples were collected daily in the same manner until completion of the trial. The samples were analyzed for the blood gas parameters of pH, PO_2, PCO_2, total CO_2, HCO_3, and base excess within two minutes of collection using a Corning pH blood gas analyzer.[e] The analyzer was standardized at 0800 hours and 1300 hours daily with adjustments made for changes in barometric pressure. Standardization and sample analysis were made in accordance with the manufacturer's recommended procedure.

A blood sample containing disodium ethylene-diamine-tetra acetic acid (NaEDTA) for hematological studies was obtained from the external jugular vein at the time of initial examination and on the day of discharge from the trial. Determinations of packed cell volume (PCV), hemoglobin content, total plasma protein, plasma fibrinogen, and total white blood cell count were made from each sample. PCV was determined using a

---

e Corning pH/Blood Gas Model 165, Scientific Instruments, Corning Glass, Medford, Mass.

microhematocrit tube. The hemoglobin content was calculated through the use of the cyanomethemoglobin technique. Total plasma protein levels were estimated through the use of a hand refractometer.[f] White blood cell totals were computed using an electronic particle counter.[g] Fibrinogen assay was determined by heating a microhematocrit tube filled with blood containing EDTA for three minutes in a 50 degree centigrade waterbath. This will precipitate the fibrinogen which is then removed by centrifugation in a high speed microhematocrit centrifuge for five minutes. Total protein in the heated tube is then determined using a hand refractometer. The fibrinogen concentration is calculated by subtracting the protein value in an unheated tube from the protein value in the heated tube.

Bacterial specimens from the lower respiratory tract were collected from calves number 1 and 12 using a transtracheal aspiration technique. An area near the junction of the proximal and middle one-third of the trachea was shaved and surgically prepped. 3-5 cc of 2% lidocaine[h] was infused subcutaneously along the ventral surface of the trachea. A skin incision approximately 2-3 centimeters in length was made along the line of anesthetic infusion. An 8 gauge sterile bleeding trochar was then introduced and directed between adjacent tracheal rings into the lumen of the trachea. A

---

f Goldberg Refractometer, American Optical Corp., Buffalo, N.Y.

g Coulter Counter model ZBI, Coulter Electronics Ind., Hialeah, Fla.

h 2% Lidocaine HCL, Vitarine Co., New York, N.Y.

polypropylene catheter[i] was then directed through the trochar and into the tracheal lumen. The trochar was removed prior to the catheter being passed distally down the trachea. As soon as the cough reflex was stimulated a 35 cc syringe containing 25 cc of sterile saline was attached to the catheter. The saline was introduced into the lumen of the trachea and then aspirated. If air was collected into the syringe, the syringe was removed and the air was expelled prior to being reattached to the catheter. Approximately 5 cc of aspirate was obtained from each calf. Routine culture and antibiotic sensitivity tests were performed on the transtracheal aspirations.

Eight calves assigned to the test group were prepared for the installation of an indwelling tracheal catheter following completion of the physical examination and blood sample collection. Catheterization was performed using the procedure for transtracheal aspiration. The 55 centimeter polypropylene catheter was replaced with a 20 centimeter length of polypropylene catheter. The 5 centimeter exteriorized portion of the catheter was sutured to the skin using 0.3 synthetic suture material.[j]

Aerosol therapy was conducted for five minutes duration B.I.D. with the animal in standing restraint for each individual in the test group. Five cc. of sterile saline followed by five cc of air were flushed through the catheter prior to each aerosol procedure to remove accumulated debris and mucus.

---

i Sovereign^{R} Polypropylene Catheter, 10 Fr., 55 cm. Sherwood Medical Industries, St. Louis, Mo.

j Vetafil, Bengen R., Dr. S. Jackson, Washington, D.C.

Administration was accomplished by using a small air compressor capable of producing 14 p.s.i. and 20 L/minute attached to a commercial inline nebulizer.[k] The aerosol solution consisted of five cc of 20% N-acetyl-L-cysteine[l] and five cc of kanamycin sulfate[m] placed in the nebulizer vial. The aerosol solution was estimated to be delivered at a rate of 3 cc per individual treatment. Therapy was continued daily until the day of discharge from the trial.

A commercial nebulizer was modified from its original design for its adaptation to this trial. In order for the unit to be attached to the indwelling tracheal catheter, a 15 centimeter section of patient supply hose replaced the exhalation manifold. An inline reducer was attached to the patient supply hose, which then could readily be inserted into the tracheal catheter. Further modification of the original unit consisted of occluding the patient supply inlet on the nebulizer manifold by using a synthetic stopper. The nebulizer tube was then connected to the synthetic stopper by means of a 14 gauge disposable needle. This final adaptation was made in order for any baffled solution to be returned to the aerosol resevoir and to have a completely closed system.

Conventional treatment of bronchopneumonia as defined in this trial consisted of antibacterial agents, B-complex vitamins, palatable diet, and shelter. Conventional treatment was initiated on day 0 of the trial for all animals in the test.

---

k Lifeline Disposable, Model 1600, Monahgan, Littleton, Colo.
l Mucomyst, Med Johnson Lab., Evansville, Ind.
m Kantrim 200 mg/cc, Bristol Lab., Syracuse, N.Y.

Antibacterial agents used in the trial were oxytetracycline[n] at a dosage level of 11 mg/kg administered intravenously, sulfadimethoxine sustained release boluses[o] at a dosage level of 137.5 mg/kg administered per os, sulfadimethoxine (12.5% solution[p]) at a dosage level of 55 mg/kg administered intravenously, and Tylosin[q] at a dosage level of 13 mg/kg administered intravenously. Scheduling of the therapeutic regime is outlined in Table 1. In Table 1, five calves (numbers 7, 8, 18, 19, and 20) on day 0 were placed on the same treatment regime as the remaining calves on day 1 of the trial. These clinical cases were selected the day following receipt of the first group due to delayed development of the clinical signs of bronchopneumonia. This adjustment to the therapeutic regime was utilized to standardize treatment.

Changes to different antibacterial agents in the treatment regime were based upon a lack of response to treatment as guided by rectal temperatures and/or "Degree of Illness." A failure to respond as indicated by rectal temperature was based upon declines of less than 1.2 degrees Centigrade, no change, or an increase in rectal temperature. Failure of response as dictated by "Degree of Illness" was failure to change to a lower number group. A positive response to treatment was interpreted as rectal temperature declines of greater than 1.2 degrees Centigrade or a rectal temperature

---

n Liquamycin 50 mg/cc, Pfizer Inc., New York, N.Y.
o Albon SR boluses 12.5 gm/bolus, Hoffmann-LaRoche Inc., Nutley, N.J.
p Albon 12.5% Solution, Hoffmann-LaRoche Inc., Nutley, N.J.
q Tylan 200, 200 mg/cc, Eli Lilly & Co., Indianapolis, In.

less than 39.5 degrees Centigrade, and/or a change to a lower number group based upon "Degree of Illness." If an animal exhibited a positive response to treatment, the antibacterial agent administered the day prior to the positive clinical response was continued for 48 hours post-response. Clinical response to treatment was reviewed daily and the treatment regime was changed for all calves similiarly on day 0 through day 2 to establish a standard to evaluate clinical response. Antibacterial agents were continued until the day of discharge from the trial.

The need for supportive therapy was evaluated daily on an individual animal basis. The clinical signs of anorexia and refusal of water were used to determine the treatment, in addition to the antibacterial agents, an animal would receive daily. 10 cc of B-complex vitamins[r] administered intravenously and/or .454 kg of a nutritional supplement[s] administered per os were used to combat nutritional deficits. 4-8 liters of water administered via a stomach tube per os were used to combat dehydration.

Rectal temperatures and clinical observations were recorded daily for each calf throughout the test period. Clinical observations were grouped for classification of Severity of Illness. Severity of Illness was measured by giving each calf a daily numerical score. One point was assessed for each of the following subjective signs typical of bronchopneumonia: depression, dyspnea, cough, epiphora,

---

r Multibex C, Eli Lilly & Co., Indianapolis, In.
s Proleen T^{20} powder, Diamond Laboratories, Des Moines, Ia.

serous nasal discharge, mucopurulent nasal discharge, and ptyalism.

Statistical evaluation was obtained by comparing values of the subjective "Degree of Illness," the objective Severity of Illness, and rectal temperatures in the test group to those values in the control group. Daily values for the arterial blood gases were statistically analyzed on the test group and compared to the control group. Statistical comparison of the control and test group on day 0 and day 3 of the trial were made for hematocrit, hemoglobin content, total plasma protein, plasma fibrinogen, and total white cell levels.

RESULTS

Tracheal catheterization of the animals selected for the test group was accomplished on the day of arrival at the trial location. The time required for the catheterization procedure on each calf was approximately five minutes. Slight difficulty was noted in the passage of the catheter through the 8 gauge trochar. Passing the catheter through the trochar several times prior to the procedure, or removing 5 mm of the proximal portion of the catheter facilitated the actual placement of the catheter into the trachea. Complications following this procedure were minimal throughout the course of the trial in most of the recipients. Calves 1 through 4 experienced minor tracheal irritation as demonstrated by slight coughing for approximately 60 minutes following placement of the catheter into the trachea. A small area of subcutaneous emphysema developed near the area of catheter exit from the trachea in calf 8. The catheter placed in calf 1 was partially collapsed at the cutaneous exit point on the day of removal. All catheters were covered with mucous at the time of removal.

The transtracheal aspiration technique was performed on day 0 of the trial on calves 1 and 12. Both aspirates contained an abundant growth of Pasteurella hemolytica. The results of the sensitivity tests (Table 2) were obtained on day 3 of the trial, and thus were of little value in the selection of an appropriate antibacterial agent(s) to be used in the trial. The organism isolated was found to be resistant

in vitro to four of the antibiotics generally administered for the treatment of bovine bronchopneumonia. The isolate from calf 12 was found to be resistant to tetracycline and sulfadimethoxine, whereas tetracycline was found to be resistant in calf 1. The organism was found to be sensitive to kanamycin in both isolates. Oxytetracycline and sulfadimethoxine were the primary antibacterial agents administered from day 0 through day 3 of the trial.

Rectal temperatures were obtained daily on each animal throughout the trial (Table 3), except for calf 16 where a temperature was not recorded on day 4. The mean daily temperatures for the test and control groups were statistically evaluated (Table 4). The test group exhibited a significantly ($P>.05$) lower rectal temperature on day 2 of the trial with a mean of 39.18 versus a mean of 39.71 for the control group. As a group, the test animals maintained a mean rectal temperature of less than 39.5^{o} C from day 1 through the remainder of the trial, whereas, the control group mean temperature was greater than 39.5^{o} C throughout the course of the trial.

Temperature declines of greater than 1.2^{o} C or to values less than 39.5^{o} C were interpreted as an indication of positive response to treatment. Based on this classification of response, calves 1, 2, 3, and 6 responded to treatment on day 1 of the trial and calves 5 and 8 on day 2. Calf 4 had a temperature decline of $.6^{o}$ C from day 0 to day 1 and stabilized for the duration of the trial at values of 39.5^{o} C to 39.6^{o} C. Calf 7 maintained temperatures of greater than 39.5^{o} C throughout

the duration of the trial. Calves 13 and 15 responded favorably on day 1 of the trial, however, the rectal temperatures rose to greater than 39.5° C on day 2 and remained elevated until day 4 when a decline to less than 39.5° C occurred in calf 13. A positive temperature decline occurred on day 2 of the trial in calf 16 and 20, however, the temperature of calf 20 rose to 39.5° C on day 3. Calves 18 and 19 rectal temperatures remained elevated throughout the course of the trial.

Rectal temperature values on the day of discharge for the test group would classify calves 1, 2, 3, 5, 6, and 8 as having responded to treatment, and calves 4 and 7 as nonresponsive to treatment. Values for the control group would classify calves 12, 13, 16, and 20 as responsive to treatment by the day of discharge and calves 15, 18, and 19 as nonresponsive.

"Degree of Illness," the subjective measurement of illness in each individual, was recorded daily, and is tabulated in Table 5. The test and control groups were compared statistically using the daily mean scores and are evaluated in Table 6. The mean daily values of the control group were maintained at a level of moderately ill, e.g. greater than 2, until the day of discharge from the trial. The daily means of the test group remained less than the moderately ill level throughout the course of the trial with a range of 1.375 to 1.750. Statistical evaluation of the daily mean "Degree of Illness" indicated two days where significant differences ($P>.05$) were noted, day 1 and day 2.

The "Degree of Illness" was used as an indicator of response to treatment. A decrease in numerical score was interpreted as a positive response, whereas, no change in score or an increase was interpreted as no response unless the value was 1. Positive responses to treatment in the test group were obtained in calf 3 on day 1, calves 6 and 8 on day 2, and calf 5 on day 4. Positive responses in the control group were seen in calves 19 and 20 on day 2, calf 16 on day 3 and calves 12, 13, and 15 on day 4. No response as indicated by an increased value was determined for control group calves 12, 15, and 18 on day 1, and test group calf 4 on day 4 of the trial. Calves considered slightly ill at the day of discharge in the test group were numbers 1, 2, 3, 5, 6, and 8. Those considered slightly ill in the control group were numbers 12, 13, 15, and 16. Calves considered moderately ill at discharge were test group number 7 and control group numbers 19 and 20. Those severely ill at discharge were numbers 4 and 18 in the test and control group, respectively.

The observation of clinical signs, excluding temperature, of bronchopneumonia were collectively evaluated as Severity of Illness. This allowed for a daily objective assessment of the clinical signs based on a numerical score in each animal (Table 7). Depression and serous nasal discharge were the most frequently observed signs, however, a daily variation occurred throughout the course of the trial. A distinct pattern of alleviation of clinical signs could not be determined in either group based upon the parameters of depression, dyspnea, cough,

epiphora, serous nasal discharge, mucopurulent nasal discharge, or ptyalism. However, by day 3 of the trial the calves in the test group responding favorably to treatment as indicated by temperature or "Degree of Illness" generally expressed a lower numerical score than did the calves classified as nonresponsive. This pattern could not be established for the control group. The daily mean values established for each group were variable and no significant differences were found during the course of the trial (Table 8). Mean daily values were less for the test group than for the control group with the exception of day 0 of the trial.

EDTA samples for hematological studies were drawn on day 0 and the day of discharge from the trial. Samples obtained from calves 4 and 19 on the day of discharge clotted prior to evaluation. The collected samples were analyzed for the blood parameters of packed cell volume, hemoglobin content, total plasma protein, fibrinogen, and total white blood cells (Tables 9 and 10). Statistical comparisons were performed on the data for the test group day 0 versus the control group day 0, test group day of discharge versus control group day of discharge, control and treatment group day 0 versus test group day 3, and control and treatment group day 0 versus control group day 3 (Tables 11, 12, 13, and 14, respectively).

Mean packed cell volume (PCV) expressed as a percentage were highest on day 0 averaging 34.5 for the test group and 35.857 for the control group. The range for day 0 being 27-41 for the test group and 26-40 for the control group. These

values declined 5.143 for the test group to a level of 29.357 on the day of discharge as compared to a decline of 5.357 in the control group to a level of 30.5 on the day of discharge. The range was 22.5 to 34.0 and 20 to 38.0 for the test and control groups, respectively, on the day of discharge. All animals exhibited a decline in PCV during the course of the trial except calves 13 and 16 which remained constant at 26 and 38, respectively. No significant differences were found on the comparisons of the test and control groups on day 0 or on the test and control groups on the day of discharge (Tables 11 and 12).

Hemoglobin content expressed in grams % was higher in the control group on day 0 with a mean of 11.87 as compared to a mean of 11.23 in the test group (Table 11). Comparison on the day 0 values to the day of discharge values on an individual animal basis obtained variable results with some animals increasing slightly while others declined (Tables 9 and 10).

Mean total plasma protein levels expressed in grams % decreased from 7.13 to 6.86 from day 0 to the day of discharge in the test group, and 6.83 to 6.75 over the same time span in the control group (Tables 11 and 12). Individual variance did occur and a definite trend could not be established.

Mean fibrinogen levels expressed in milligram % were greater for the test group on day 0 than for the control group. However, the levels were not of statistical significance. Fibrinogen levels on day 0 ranged from 100 to 800 in the test

group with a mean of 487, whereas, the range of the control group was 200 to 800 with a mean of 400. Four animals (numbers 3, 4, 5, and 8) in the test group and only calf 20 in the control group were found to have fibrinogen levels greater than 600 on day 0 of the trial. The mean fibrinogen levels were elevated by the day of discharge and were comparable with a mean of 1000 for test group and 1017 for the control group. Significant differences were not obtained on either day 0 or the day of discharge in the comparison of test to control for each day.

Total white blood cells expressed as cells per cubic millimeter rose slightly from a mean of 8887 to 9529 from day 0 to the day of discharge in the test group. No significant differences were found between groups on day 0 or on the day of discharge.

The data obtained from the hematological studies for day 0 was statistically compared to the data obtained on the day of discharge (Tables 13 and 14). The test and control groups were combined on day 0 to provide a larger data base to evaluate changes in hematological parameters. The test group PCV and hemoglobin content had significantly decreased ($P>.05$) from a mean of 35.13% to 29.36% and 11.55 gm% to 10.2 gm%, respectively. The fibrinogen levels were elevated significantly ($P>.05$) in both the test and control groups. The parameters of PCV and hemoglobin content for the control group, and total plasma protein and total white blood cell count for both test and control groups were not statistically

significant when day 0 and day of discharge were compared.

The statistical analysis of the blood gas data is shown on Tables 15-21. Comparisons are made only from day 0 through day 3 of the trial due to damage to the PO_2 membrane on the blood gas analyzer. PO_2 and PCO_2 values are expressed as millimeters of Mercury (mmHg). HCO_3 and Total CO_2 values are expressed as millimoles per liter. Base Excess values are expressed as millequivalents per liter. Arterial samples were not obtained on calves 3, 4, 7, and 8 on day 0; calf 19 on day 1; calf 6 on day 2; and calves 3, 6, 7, 8, 19, and 20 on day 3 of the trial due to failure to accurately locate the coccygeal artery. Repeated sampling of the coccygeal artery resulted in either a subcutaneous hematoma or thrombosis of the coccygeal artery. The ability to obtain reliable arterial blood samples, e.g. samples that were not mixed venous-arterial samples, decreased as multiple arterial invasions progressed throughout the trial.

The mean arterial pH values (Table 15) were comparable in both the test and control groups during the course of the trial. The range of the means for the test group was 7.468-7.510, whereas, the control group range was 7.466-7.509. Significant differences were not found.

PO_2 values were found to flucuate daily in the individual calf and a pattern of response to either treatment could not be established (Table 15). Samples for calf 4 day 1 (PO_2 119.2), calf 8 day 2 (PO_2 110.2), calf 20 day 2 (PO_2 107.4), calf 12 day 3 (PO_2 107.3), calf 8 day 3 (PO_2 112.1) were not utilized

in the statistical evaluation due to aerobic collection of the sample. The mean arterial PO_2 value for the test group rose significantly ($P>.05$) by day 2 of the trial (Table 17, Figure 1) while the PO_2 values of the control group remained basically stable with a range of 62.583 to 68.467.

The comparison of the daily mean PCO_2, HCO_3, total CO_2, and base excess are shown on Tables 18-20 and Figures 2-5. On day 0 of the trial, the mean values for each parameter were comparable, in both the test and control groups. Day 1 through day 3 of the trial revealed mean levels that were greater in the test group than in the control group for all parameters measured. Significant differences ($P>.05$) existed for the blood gas parameters of HCO_3 and Total CO_2 between the test and control groups on day 2 of the trial. The mean values for the parameters of PCO_2, HCO_3, Total CO_2, and Base Excess decreased from the peak values found on day 1 for both the test and control groups.

DISCUSSION

Pasteurella spp. are commonly incriminated as a causal agent in bacterial bronchopneumonia in the bovine in the first 45 days postshipment (Jensen et al. 1976, Thomson et al. 1969). Pasteurella hemolytica produces a fibrinous bronchopneumonia and pleuritis with prominent interlobular septa and evident hemorrhage into the alveoli giving extensive and confluent ventral consolidation of the pulmonary tissue (Collier, 1968). Histopathological findings of the bronchi and bronchioles demonstrate lumens filled with exudate composed of mucus, bacteria, neutrophils, macrophages, and blood (Jensen et al. 1976).

Pasteurella organisms are not associated with apparently healthy tissue of the lower respiratory tract in cattle (Collier and Rossow 1964, and Lillie 1974). The association of clinical bronchopneumonia in the calves on this trial and isolation of Pasteurella hemolytica from the bronchial airways would indicate that this organism was the primary bacterial etiological agent. The use of transtracheal aspiration technique provided a convenient method to obtain bacterial cultures from the lower airways in cattle. The practicality of using such a technique, however, is of limited value due to the time interval between collection and receipt of the culture and sensitivity data. Its use as a screening procedure to catalog sensitivity data for future use has merit.

The selection of therapeutic antibacterial agents used in this trial may have limited the response to treatment in both

the test and control groups. Based on the in vitro sensitivity results, oxytetracycline was of questionable value and sulfadimethoxine may have been beneficial in some of the cases. The addition of kanamycin sulfate to the aerosol solution widened the spectrum of the therapeutic regime since both isolates were sensitive.

Rectal temperatures were used as a direct and convenient method to evaluate the response of the animals to treatment. The rectal temperature maximum was based at a level of 39.5° C with temperatures greater than this value considered as an elevation above normal body temperature. The majority of maximum temperatures were found on day 0 of the trial and subsequent temperatures were variable throughout the remainder of the trial. Thomson et al. (1975) found that by day 3 of illness the rectal temperatures were significantly higher in animals with pneumonic pasteurellosis than those of normal animals. The rectal temperatures of the test group declined at a more rapid rate and were significantly lower ($P>.05$) by day 2 of the trial than the temperatures in the control group. Rectal temperatures on the day of discharge would indicate that 75% of the test group and 57.1% of the control group met the qualifications as responding to treatment.

The use of "Degree of Illness" provides a subjective means to evaluate the clinical response of an animal to treatment. It provides the observer a method to numerically score an animal's progress and to evaluate the changes in severity of the clinical condition. The test group calves, as a group,

improved significantly (P>.05) in attitude and clinical appearance by days 1 and 2 of the trial. On the day of discharge 75% of the test group were classified as slightly ill or well, 12.5% moderately ill, and 12.5% as severely ill, whereas, values of 57.1, 28.6, and 14.3, respectively were classified in the control group.

The clinical signs used to evaluate Severity of Illness were depression, dyspnea, cough, epiphora, serous nasal discharge, mucopurulent nasal discharge, and ptyalism. These parameters varied in frequency and duration throughout the course of the trial in all calves. Collier (1968) experimentally induced pasteurella pneumonia in calves and evaluated the clinical signs of anorexia, depressed attitude, cough, and increased respiratory rate. Anorexia was found to persist for an average of 3 days, depression for an average of 2.75 days, and cough for an average of 2.5 days in clinically responsive calves. Due to the limitations placed on the clinical signs in this trial the use of Severity of Illness as a method to evaluate response to treatment was of limited value.

Hematological studies indicated no significant differences between the test and control groups on the day of discharge. Significant difference (P>.05) was noted between the combined test and control group on day 0 and the test group on day of discharge for the parameters of PCV, Hg%, and fibrinogen and the combined group on day 0 and the control group on day of discharge for the parameter of fibrinogen.

Packed cell volume and hemoglobin content decreased from

levels of 35.1 and 11.6, respectively, on day 0 of the trial to levels of 29.3 and 10.2 in the test group and 30.5 and 10.7 in the control group on day of discharge. Kumar et al. (1970) states that hematocrits increase during the course of pneumonia due to a hypodynamic circulatory response and then abate in convalescence because of expansion of blood volume. Weiss (1977) found that following respiratory disease in cattle the PCV decreases until approximately two weeks post-recovery then returns to normal levels because of rehydration and improvement of the nutrient state of the animal.

Total plasma protein did not decrease significantly from levels of 7.00 gm% on day 0 to levels of 6.85 and 6.75 in the test and control groups, respectively. These levels are greater than the ranges of 6.3 gm% found by Vestweber et al. (1977) on calves with chronic bronchopneumonia and 6.5 gm% found by Weiss (1977) in acutely ill feedlot steers. Wohler (1972) reported a progressive depression of serum protein levels for 1 week post-shipment. The levels found in this trial might reflect a state of rehydration.

McSherry et al. (1970) reports that elevated fibrinogen is a nonspecific indication of illness in cattle. During the inflammatory response to pasteurella pneumonia fibrinogen is coagulated into fibrin (Smith and Jones, 1972). Fibrinogen levels rose significantly in both the test and control groups from a level of 447 mg% to approximately 1000 mg% by the day of discharge. Thomson (1975) reports the normal bovine plasma fibrinogen levels as 400-800 mg%. Thomson (1975) states that

plasma fibrinogen levels occur within 72 hours of a temperature level of 40.0° C and are significantly higher than normal animals by day 3-4 of illness with mean values of 1000-1100 mg%. Thomson et al. (1969) suggests the use of plasma fibrinogen in conjunction with body temperature to detect illness and to identify animals with bacterial pneumonia.

White blood cell counts elevated slightly by the day of discharge from levels of 8813/cmm to levels of 9529/cmm and 8950/cmm in the test and control groups, respectively. This slight elevation is comparable to the changes found by Weiss (1977) and Thomson et al. (1975). Both test and control group levels are higher than the level of 8292/cmm found in calves with chronic pneumonia by Vestweber et al. (1977).

The arterial blood gas evaluation was designed to determine if differences exist between the test and control groups during the course of the trial. Value ranges as determined by other researchers are listed in Table 22. The pH values were found to be consistently greater in both the test and control animals than the values established as normal. The PO_2 levels increased daily until day 3 in the test animals and were significant ($P>.05$) on day 2 (82.1 mmHg) of the trial. The control group PO_2 levels tended to remain depressed (<70 mmHg). Base excess levels remained lower through the course of the trial in the control group. Blood HCO_3 and total CO_2 levels were found to be significantly ($P>.05$) elevated on day 2 of the trial. Vestweber et al. (1977) reported

significant decreases in levels of blood PO_2, HCO_3, and total CO_2 in calves with chronic bronchopneumonia compared to normal calves.

The collection of arterial blood in the bovine to evaluate daily clinical progress presents a technical problem. The repeated daily coccygeal arterial puncture in this study increased in difficulty as the time on trial lengthened. Subcutaneous hematoma and failure to obtain samples limits the usefulness of this technique as a diagnostic tool to evaluate daily clinical progress in a group of pneumonia animals. However, practical alternatives are few.

Pasteurella colonize in the bronchi, bronchioles, and alveoli of infected animals (Jensen et al, 1976; Lillie, 1974; and Thomson, 1974). In pasteurellosis the number of bacteria increase markedly as does mucus production (Lillie, 1974). Nebulization techniques provide an alternate method with which to adminster antibacterial agents in bacterial bronchopneumonia in cattle. The installation of antibacterial agents directly to the area of greatest benefit, e.g. bronchi and bronchiolar airways, could decrease the population of organisms to a level sufficient to decrease the severity of the disease. Recent work by Bemis and Appel (1977) has shown that bacterial numbers were reduced significantly in the respiratory tract when antibacterials were administered by aerosols. The benefits of increased oxygen values to the alveolar macrophage system has been reviewed by Veit (1976). The use of mucolytic agents to liquefy bronchial secretions

could further benefit the response of a compromised respiratory system.

Clinical signs attributable to bronchospasm e.g. inspiratory and expiratory dyspnea, apprehension, flared nares, and cyanosis, were not observed during the course of nebulization treatment in this trial. The use of bronchodilators at this time, in conjunction with nebulization therapy, appears to be unnecessary.

The use of nebulization therapy in the bovine provides an alternate method to approach the treatment of acute bacterial bronchopneumonia. A positive response to therapy was observed during the course of the trial in the nebulized animals. However, practical limitations do exist, such as the time involved in placement of the indwelling tracheal catheter, medication costs, and repeated handling of clinically sick animals. The surgical procedure could be eliminated by the introduction of a larger diameter catheter through the nostrils with the medication deposited in the retropharyngeal area. This could accomplish the same results as with the tracheal catheter in that the turbinate are by-passed thus depositing a larger volume of medication into the tracheal airways.

CONCLUSION

Nebulization therapy provides an alternate method for the treatment of acute bacterial bronchopneumonia in cattle. Disadvantages to the technique include the time involved in the surgical placement of an indwelling tracheal catheter, labor costs, medication costs, and the repeated handling of clinically sick animals. Clinical cases of early acute bronchopneumonia generally respond favorably to conventional antibacterial and supportive therapy. A general recommendation would be to reserve nebulization therapy to animals that fail to respond to conventional treatment by the second or third day of clinical signs.

REFERENCES

1. Ayres, S. M., Griesbach, J., and Giannelli, S.: A Study of Bronchial Irritation and Systemic Absorption of Aerosolized Kanamycin. Curr. Ther. Res., Vol. 14, No. 4, p. 153 (1972).

2. Bemis, D. A., Appel, M. J. G.: Aerosol, Parenteral, and Oral Antibiotic Treatment of Bordetella Bronchiseptica Infections in Dogs. J.A.V.M.A., Vol. 170, No. 10(1), p. 1082 (1977).

3. Bernstein, L. I., Ausdenmore, R. W.: Iatrogenic Bronchospasm Occurring During Clinical Trials of a New Mucolytic Agent, Acetylcysteine. Dis. Chest, 46, p. 469 (1964).

4. Bilodeau, M., Roy, J.: Aerosol Therapy with Kanamycin in 200 Cases of Broncho-Pulmonary Suppurations. Can. Med. Assoc. J., 89, p. 537 (1963).

5. Bilodeau, M., Roy, J. C., and Giroux, M.: Studies of Absorption of Kanamycin by Aerosolization, Ann. N.Y. Acad. Sci., 132, p. 870 (1966).

6. Bisgard, G. E., Ruiz, A. V., Grover, R. F., Will, J. A.: Ventilatory Acclimatization to 3400 Meters Altitude in the Hereford Calf. Respir. Physiol., 21, p. 561 (1969).

7. Bolton, G. R.: Aerosol Therapy; In Kirk, R. W. and Scott, F. W. (ed.), Current Vet. Therapy VI. W. B. Saunders Co., Philadelphia, PA., p. 12 (1977).

8. Collier, J. R., and Rossow, C. F.: Microflora of Apparently Healthy Lung Tissue of Cattle. Am. J. Vet. Res., 25, p. 391 (1964).

9. Collier, J. R.: Pasteurellae in Bovine Respiratory Disease. J.A.V.M.A., Vol. 152, No. 6, p. 824 (1968).

10. Dalton, R. G., Phillips, G. D.: Renal Function in Neonatal Calves: Response to Acidosis. Br. Vet. J., Vol. 125, No. 8, p. 367 (1969).

11. Dickie, K. J., deGroot, W. J.: Ventilatory Effects of Aerosolized Kanamycin and Polymyxin. Chest, 63, p. 694 (1973).

12. Donawick, W. J., Baue, A. E.: Blood Gases, Acid-Base Balance, and Alveolar-Arterial O_2 Gradient in Calves. Am. J. Vet. Res., 29, p. 561 (1969).

13. Dulfano, M. J.: Sputum, Fundamentals and Clinical Pathology. C. C. Thomas, Springfield, IL. (1973).

14. Feeley, T. W., duMoulin, G. C., Hedley-Whyte, J., Bushnell, L. S., Gilbert, J. P., and Feungold, D. S.: Aerosol Polymixin and Pneumonia in Seriously Ill Patients. N. Engl. J. Med., 293, p. 471 (1975).

15. Goldhamer, R. E., Carson, S., Vogin, E. F., Posner, S., Drobeck, H. P.: Effects of a Mucoevacuant on Mucus and Respiratory Tract Fluid. Arch. Environ. Health, Vol. 20, No. 5, p. 586 (1970).

16. Hales, J. R. S., Fendlay, J. D.: Respiration of the Ox: Normal Values and the Effects of Exposure to Hot Environment. Resp. Phys., 4, p. 333 (1968).

17. High, R. H., Sarria, A., Huang, N. N.: Kanamycin in the Treatment of Infections in Infants and Children. Ann. N.Y. Acad. Sci., 76, p. 289 (1958).

18. Hjerpe, C.: "Treat the Bacteria, Not the Disease." Feedlot Management, p. 22 (Aug., 1975).

19. Huang, N. N., Sarria, A., High, R. H.: A Limited Study on the Use of Kanamycin in Patients with Fibrocystic Disease of the Pancreas: in Welch, H., and Marti-Ibanez, F. (ed.), Antibiotics Annual, 1958-1959, Interscience Publishers, Inc., New York, p. 687 (1959).

20. Hurst, G. A., Shaw, P. B., LeMaistre, C. A.: Laboratory and Clinical Evaluation of the Mucolytic Properties of Acetylcysteine. Am. Rev. Respir. Dis., Vol. 92, No. 2, p. 962 (1967).

21. Jenkins, C. H., van Ovost, J. M.: Intermittent Positive-Pressure Therapy in Treatment of Viral Pneumonia in a Horse. Vet. Med./Sm. An. Cl., Vol. 69, No. 11, p. 1388 (1974).

22. Jensen, R.; Pierson, R. E.; Braddy, P. M.; Saari, D. A.; Lauerman, L. H.; England, J. J.; Keyvanfar, H.; Collier, J. R.; Horton, D. P.; McChesney, A. E.; Benitez, A.; Christie, R. M.: Shipping Fever Pneumonia in Yearling Feedlot Cattle. J.A.V.M.A., Vol. 9, No. 5, p. 500 (1976).

23. Klastersky, J., Huysmans, E., Weerts, D., Hensgens, C., Daneau, D.: Endotracheally Administered Gentamicin for the Prevention of Infections of the Respiratory Tract in Patients with Tracheostomy: A Double Blind Study. Chest, 65, p. 650 (1974).

24. Kory, R. C., Hirsch, S. R.: Nebulization of N-Acetyl-cysteine Combined with a Bronchodilator in Patients with Chronic Bronchitis. Dis. Chest, 54, p. 18 (1968).

25. Kuida, H., Brown, A. M., Lange, R. L. Hecht, H. H.: Cardiovascular Studies in Normal Calves. Am. J. Physiol., 200, p. 247 (1961).

26. Kumar, R., Wallace, W. A., Ramirez, A., Benson, H., Abelmann, W. H.: Hemodynamic Effects of Pneumonia: II Expansion of Plasma Volume. J. Clin. Invest., Vol. 149, p. 799 (1970).

27. Leak, E. S.: Enzymatic Differences Between Normal Alveolar Macrophages and Oil-induced Peritoneal Macrophages Obtained From Rabbits. Exp. Cell. Res. 33: p. 553 (1964).

28. Lebedev, L. A., Goloviznin, Yu. V., Omarov, R. Sh.: Aerosols of Therapeutic Substances for Broncho-pneumonia (in calves and piglets). Veterinariya, Moscow, USSR, No. 10, p. 67 (1976).

29. Leipold, H. W.: personal communication, 1977.

30. Lieberman, J.: The Appropriate Use of Mucolytic Agents. Am. J. Med., No. 49, Vol. 1, p. 1 (1970).

31. Lifschitz, M. I., Denning, C. R.: Safety of Kanamycin Aerosol. Clin. Pharm. Ther., 12, p. 91 (1971).

32. Lillie, L. E.: The Bovine Respiratory Disease Complex. Can. Vet. J., Vol. 15, No. 9, p. 233 (1974).

33. Lourenco, R. V.: Aerosol Therapy. Am. Rev. Respir. Dis., Vol. 110, No. 6 (part 2 of 2 parts), p. 85 (1974).

34. Matthews, L. W., Doershuk, C. R., Wise, M., Eddy, G., Nudelman, H., and Spector, S.: A Therapeutic Regimen for Patients with Cystic Fibrosis. J. Pediat., 65, p. 558 (1964).

35. McSherry, B. J., Horney, F. D., deGroot, J. J.: Plasma Fibrinogen Levels in Normal and Sick Cows. Can. J. Comp. Med., 34, p. 191 (1970).

36. Miller, W. F.: Aerosol Therapy in Acute and Chronic Respiratory Disease. Arch. Intern. Med., 131(1), p. 148 (1973).

37. Miller, W. F.: Antibiotic Aerosols; in Kagan, B. M. (ed.): Antimicrobial Therapy, (2nd ed.). W. B. Saunders Co., Philadelphia, PA., p. 403 (1974).

38. Morel, G.: Treatment of Respiratory Infections of Domestic Animals with Aerosols Based on Essential Oils. Trial of Two Proprietary Drugs Based on Essential Oils. These, Ecole Nationale Veterinaire deLyon, p. 1-94 (1971).

39. Morrow, P. E.: Aerosol Characterization and Deposition. Am. Rev. of Respir. Dis., Vol. 110, No. 6 (part 2 of 2 parts), p. 88 (1974).

40. Peters, J. L., Hess, T. O., Leach, C. S., Imby, T., Gardner, R. O., Donovan, F. M., Van Krimpen, K. R.: Hemic and Spirometric Profiles in Calves Used for Cardiovascular Research. Am. J. Vet. Res., 34, p. 1595 (1973).

41. Pines, A., Raafat, H., Siddigui, G. M., Greenfield, J. S. B.: Treatment of Severe Pseudomonas Infections of the Bronchi. Br. Med. J., 1, p. 663 (1970).

42. Potter, J. L., Matthews, L. W., Spector, S., Lemin, J.: Complex Formation Between Basic Antibiotics and Deoxyribonucleic Acid in Human Pulmonary Secretions. Pediatrics, 36, p. 714 (1965).

43. Prisgal, S. J.: Aerosol Therapy in the Practice of Allergy. New York J. Med., 59, p. 910 (1956).

44. Prokhorova II: Absorbability of Kanamycin Upon Inhalation of the Aerosol. Antibiotiki, 13, p. 351 (1968).

45. Reas, H. W.: The Effect of N-Aceolylcysteine on the Viscosity of Tracheobronchial Secretions in Cystic Fibrosis of the Pancreas. J. of Pediatrics, 62, p. 31 (1963).

46. Rose, H. D., Pendharker, M. G., Snider, G. L., Kory, R. C.: Evaluation of Sodium Colistimethate Aerosol in Gram-Negative Infections of the Respiratory Tract. J. Clin. Pharmacol., 10, p. 274 (1970).

47. Schotman, A. J. H.: The Acid-Base Balance in Clinically Healthy and Diseased Cattle. Neth. J. Vet. Sci., Vol. 4, No. 1, p. 5 (1971).

48. Sheffner, A. L.: The Reduction in In Vitro Viscosity of Mucoprotein Solutions by a New Mucolytic Agent, N-Acetyl-L-Cysteine. Ann. N.Y. Acad. Sci., 106, p. 298 (1963).

49. Sheffner, A. L.: The Mucolytic Activity, Mechanisms of Action and Metabolism of Acetylcysteine. Pharmakotherapia, 1, p. 47 (1965).

50. Smith, H. A., Jones, T. C., Hunt, R. D.: Veterinary Pathology (4th ed.). Lea and Febiger, Philadelphia, PA. (1972).

51. Spier, R., Witebsky, E., Baine, J. R.: Aerosolized Pancreatic Dornase and Antibiotics in Pulmonary Infections. J.A.M.A., 178, p. 878 (1961).

52. Stossel, T. P.: Phagocytosis (Part I, II, III). N. Engl. J. Med., 290:No. 13, 14, 15, p. 717, 774, 833 (1974).

53. Thomas, P. A., Treasure, R. L.: Effect of N-Acetyl-L-Cysteine on Pulmonary Surface Activity. Am. Rev. Respir. Dis., 94(2), p. 175 (1966).

54. Thomson, R. G., Benson, M. L., Savan, M.: Pneumonic Pasteurellosis of Cattle: Microbiology and Immunology. Can. J. Comp. Med., Vol. 33, p. 194 (1969).

55. Thomson, R. G.: Pathology and Pathogenesis of the Common Diseases of the Respiratory Tract of Cattle. Can. Vet. J., Vol. 15, No. 9, p. 249 (1974).

56. Thomson, R. G., Chander, S., Savan, M., Fox, M. L.: Investigation of Factors of Probably Significance in the Pathogenesis of Pneumonic Pasteurellosis in Cattle. Can. J. Comp. Med., Vol. 39, p. 194-207 (1975).

57. Utkin, V. V., Marga, O. Ya., Magalif, N. I., Ginters, Ya. Ya., Balynya, N. A., Bernshteum, B. A.: Assessment of Clinical Use of N-Acetylcysteine in Chronic Inflammatory Diseases of the Lung. Klinicheskaya Meditsina (Moscow), Vol. 50, No. 12, p. 95 (1972).

58. Vagher, J. P., Pearson B., Blott, S., Kaye, M.: Biochemical and Hematologic Values in Male Holstein-Friesian Calves. Am. J. Vet. Res., 34, p. 273 (1973).

59. Veit, H.: The Anatomy of the Lung and Relationship to Disease: American Association of Bovine Practioners, District 4 Conference, (August, 1976).

60. Vestweber, G. E., Guffy, M., Kelly, B., Leipold, H. W.: Chronic Bronchopneumonia in Cattle. The Bovine Practitioner, No. 12, p. 55 (1977).

61. Walker, J. S., Stephen, E. L.: Aerosol Therapy and Vaccination. In Kirk, R. W. and Scott, F. W. (ed.), Current Vet. Therapy VI. W. B. Saunders Co., Philadelphia, PA., p. 1345 (1977).

62. Weiss, D. J.: Biochemical and Cellular Profiles in Feedlot Cattle as They Progress Through Feeding Trials and During Transport and Respiratory Disease. Master's Thesis, Kansas State University, (1977).

63. Williams, M. H.: Steroids and Antibiotic Aerosols. Am. Rev. Respir. Dis., Vol. 110, No. 6 (part 2 of 2 parts), p. 122 (1974).

64. Wohler, W. H.: Shipping Stress in Cattle: Blood Chemistry. Mod. Vet. Pract., 53, No. 1, p. 39-40 (1972).

APPENDIX

TABLE 1

Therapeutic Regime Established for Control and Test Groups

Calf	Day of trial 0	1	2	3	4
Test					
1	AEX	AEFX	ABCX	AX	N.T.
2	AEX	AEFX	ABCX	AX	N.T.
3	AEX	AEFX	ABCX	DX	DX
4	AEX	AEFX	ABCX	DX	DX
5	AEX	AEFX	ABCX	AX	N.T.
6	AEFX	ABCX	AGX	N.T.	N.T.
7	AEFX	ABCX	ACX	DX	DX
8	AEFX	ABCX	ACX	N.T.	N.T.
Control					
12	AE	AEF	ABC	CF	N.T.
13	AE	AEF	ABC	A	N.T.
15	AE	AEF	ABC	A	C
16	AE	AEF	ABC	A	N.T.
18	AE	AEF	ABC	A	D
19	AEF	ABCEFG	ACEFG	D	D
20	AEF	ABCE	ACEFG	D	D

A - oxytetracycline
B - sulfadimethoxine bolus
C - sulfadimethoxine solution
D - tylosin
E - B-complex vitamins
F - nutritional supplement
G - water
X - aerosol therapy B.I.D.
N.T. - no treatment

TABLE 2

The Results of the Kirby-Bauer Susceptibility Tests on Calf 1 and 12 Obtained from Transtracheal Aspirates

Antibacterial Agent	Calf 1	Calf 2
Ampicillin	--	+
Cephalothin	+	+
Chloramphenicol	+	+
Erythromycin	Int	Int
Furazolidone (Furoxone)	+	+
Gentamicin	+	+
Kanamycin	+	+
Neomycin	+	+
Nitrofurazone (Furacin)	+	+
Penicillin	--	+
Polymyxin B	Int	+
*Spectinomycin	Int	Int
Streptomycin	--	--
*Sulfadimethoxine	+	--
Tetracycline	--	--
Triple Sulfa	--	--
Trimethoprim/sulfamethoxazole	+	+

+ = sensitive
Int = intermediate
- = resistant
*Not measured by Kirby-Bauer Method

TABLE 3

Rectal Temperatures (°C) of Steers with Bronchopneumonia Taken at 24-Hour Intervals

Calf No.	Day of trial 0	1	2	3	4
Test					
1	39.7	39.0	39.2	39.2	38.7
2	39.9	39.0	38.9	39.1	39.2
3	40.8	39.2	39.1	38.8	38.7
4	40.2	39.6	39.5	39.6	39.5
5	40.3	39.6	39.1	39.1	38.9
6	39.5	39.1	38.8		
7	41.2	40.0	39.6	40,9	39.8
8	40.1	39.9	39.2	28.9	
Control					
12	41.1	40.4	40.5	40.1	38.6
13	40.0	38.9	39,7	39.7	39,2
15	39.8	39.1	39.8	39.8	39.5
16	40.1	39.9	39,2	38.9	N.E.
18	40.1	39.6	40.1	40.2	39.5
19	41.6	41.8	39.9	40.0	41.3
20	40.2	41.0	38.8	39,5	39.2

Calf 3 discharged on Day 2
Calf 8 discharged on Day 3
N.E. = not evaluated

TABLE 4

Statistical Comparison of the Daily Mean Rectal Temperatures of Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	8	40.21	0.562	0.199	39.7-40.3	0.20	0.637	N.S.
C[6]	0	7	40.41	0.667	0.252	39.8-41.1			
T	1	8	39.42	0.403	0.142	39.0-40.0	0.68	1.700	N.S.
C	1	7	40.10	1.043	0.394	38.9-41.8			
T	2	8	39.18	0.271	0.096	38.8-39.6	0.53	2.413	Sig.
C	2	7	39.71	0.564	0.213	38.8-40.5			
T	3	7	39.37	0.720	0.272	38.8-40.9	0.37	1.162	N.S.
C	3	7	39.74	0.443	0.167	38.9-40.2			
T	4	6	39.13	0.450	0.184	38.7-39.8	0.42	0.998	N.S.
C	4	6	39.55	0.918	0.375	38.6-39.5			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 T = test group

6 C = control group

TABLE 5

"Degree of Illness" in Steers with Bronchopneumonia Assessed at 24-Hour Intervals During the Trial

Calf No.	Day of trial 0	1	2	3	4
Test					
1	1	1	1	1	1
2	1	1	1	1	1
3	2	1	1	1	1
4	2	2	2	2	3
5	2	2	2	2	1
6	2	2	1	X	X
7	2	2	2	2	2
8	2	2	1	1	X
Control					
12	1	2	2	2	1
13	2	2	2	2	1
15	1	2	2	2	1
16	2	2	2	1	N.E.
18	2	3	3	3	3
19	3	3	2	2	2
20	3	3	2	2	2

Calf 6 discharged Day 2
Calf 8 discharged Day 3
N.E. = not evaluated

TABLE 6

Statistical Comparison of "Degree of Illness"[ABC] in Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	8	1.750	0.463	0.164	1-2	.250	.743	N.S.
C[6]	0	7	2.000	0.816	0.309	1-3			
T	1	8	1.625	0.518	0.183	1-2	.804	2.955	Sig.
C	1	7	2.429	0.535	0.202	2-3			
T	2	8	1.375	0.518	0.183	1-2	.768	3.236	Sig.
C	2	7	2.143	0.378	0.143	2-3			
T	3	7	1.429	0.535	0.202	1-2	.571	1.922	N.S.
C	3	7	2.000	0.577	0.218	1-3			
T	4	6	1.500	0.837	0.342	1-3	.167	.349	N.S.
C	4	6	1.667	0.816	0.333	1-3			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 T = test group

6 C = control group

A = severely ill (weak, very depressed, labored breathing) score 3

B = moderately ill (moderately depressed, gaunt, rough hair coat) score 2

C = slightly ill or well score 1

TABLE 7

Severity of Illness[1] in Steers with Bronchopneumonia Assessed at 24-Hour Intervals

Calf No.	Day of trial 0	1	2	3	4
Test					
1	2	2	1	1	N.A.[2]
2	2	3	2	1	1
3	2	2	1	1	N.A.
4	3	3	3	3	2
5	1	2	1	2	1
6	1	1	1	--	--
7	2	2	4	4	N.A.
8	3	1	1	1	--
Control					
12	2	2	2	2	2
13	2	2	3	2	1
15	2	3	4	5	1
16	1	1	1		1
18	2	2	2	1	2
19	2	3	3	3	N.A.
20	2	2	1	1	N.A.

Calf 6 discharged Day 2

Calf 8 discharged Day 3

1 Severity of Illness = the objective evaluation of clinical signs based on a numerical value. One point was assessed for each of the following clinical signs: depression, dyspnea, cough, epiphora, serous nasal discharge, muco-purulent nasal discharge, or ptyalism.

2 N.A. = no assessment

TABLE 8

Severity of Illness[1] - Statistical Comparison of Test and Control Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[2]	SDM[3]	SEM[4]	Range	Absolute diff. of means	t-value	Significance[5]
T[6]	0	8	2.000	.756	.267	1-3	.143	0.452	N.S.
C[7]	0	7	1.857	.378	.143	1-2			
T	1	8	2.000	.756	.267	1-3	.143	0.380	N.S.
C	1	7	2.143	.690	.261	1-3			
T	2	8	1.750	1.165	.412	1-4	.679	1.212	N.S.
C	2	7	2.429	.976	.369	1-4			
T	3	7	1.857	1.215	.459	1-4	.643	0.849	N.S.
C	3	6	2.500	1.517	.619	1-5			
T	4	3	1.333	.577	.333	1-2	0.067	0.164	N.S.
C	4	5	1.400	.548	.245	1-2			

1 Severity of Illness = the objective evaluation of clinical signs based on a numerical score. One point was assessed for each of the following clinical signs: depression, dyspnea, cough, epiphora, serous nasal discharge, mucopurulent nasal discharge, or ptyalism.

2 $\bar{x}$ = mean

3 SDM = standard deviation mean

4 SEM = standard error mean

5 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

6 T = test group

7 C = control group

TABLE 9

Hematological Values for the Test and Control Groups on Day 0 of the Trial

Calf No.	PCV (%)	Hemoglobin Content (grams%)	Total Plasma Protein (grams%)	Fibrinogen (milligram%)	Total White Blood Cells (cells/cubic millimeter)
Test					
1	27.0	9.5	6.5	100	11,100
2	31.0	11.0	7.2	300	6,200
3	41.0	11.0	6.8	800	9,800
4	32.0	12.4	7.6	600	7,000
5	39.0	12.8	6.9	800	11,600
6	32.0	10.3	7.0	400	7,300
7	38.0	12.0	7.8	300	12,500
8	36.0	11.2	7.2	600	5,600
Control					
12	40.0	14.5	7.1	400	8,000
13	26.0	9.1	6.6	200	9,700
15	38.0	12.0	7.2	200	8,600
16	38.0	13.2	7.1	500	7,900
18	30.0	9.8	6.3	300	10,400
19	39.0	12.5	6.7	400	6,100
20	40.0	12.0	7.1	800	10,400

TABLE 10

Hematological Values for the Test and Control Groups on Day 3 of the Trial

Calf No.	PCV (%)	Hemoglobin Content (grams%)	Total Plasma Protein (grams%)	Fibrinogen (milligrams%)	Total White Blood Cells (cells/cubic millimeter)
Test					
1	25.0	9.8	7.0	800	8,200
2	28.0	9.5	6.9	700	8,900
3	34.0	11.0	6.5	1200	7,600
4	----	----	---	---	----
5	32.0	10.4	6.9	1100	14,300
6	22.5	8.2	6.5	900	7,100
7	32.0	11.3	7.2	1100	10,300
8	32.0	11.3	7.0	1200	10,300
Control					
12	30.0	10.4	6.6	1100	6,700
13	26.0	9.0	6.6	900	13,900
15	32.0	11.0	6.5	900	7,800
16	38.0	14.3	7.1	900	10,400
18	20.0	7.0	6.3	900	6,500
19	----	----	---	---	----
20	37.0	12.5	7.4	1400	8,400

TABLE 11

Statistical Evaluation of the Test and Control Groups on Day 0 for the Values of Packed Cell Volume (PCV), Hemoglobin Content (Hg%), Total Plasma Protein (TPP), Fibrinogen, and Total White Blood Cell Count (WBC)

Group	Parameter	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	PCV(%)	8	34.500	4.751	1.680	27 - 41	1.357	0.511	N.S.
C[6]	PCV(%)	7	35.857	5.551	2.098	26 - 40			
T	Hg%(gm%)	8	11.275	1.094	0.387	9.5- 12.8	.596	0.766	N.S.
C	Hg%(gm%)	7	11.871	1.874	0.708	9.1- 14.5			
T	TPP(gm%)	8	7.125	0.423	0.150	6.5- 7.8	0.254	1.265	N.S.
C	TPP(gm%)	7	6.871	0.340	0.129	6.3- 7.2			
T	Fibrinogen (mg%)	8	487.0	253.0	90.0	100.0- 800.0	87.0	0.724	N.S.
C	Fibrinogen (mg%)	7	400.0	208.0	79.0	200.0- 800.0			
T	WBC(cells/cmm)	8	8887.0	2679.0	947.0	5600.0-12500.0	158.0	0.137	N.S.
C	WBC(cell/cmm)	7	8729.0	1564.0	591.0	6100.0-10400.0			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM - standard error mean

4 significance N.S. = not significant at 0.05 level

5 T = test group

6 C = control group

TABLE 12

Statistical Evaluation of the Test and Control Groups on Day of Discharge for the Values of Packed Cell Volume (PCV), Hemoglobin Content (Hg%), Total Plasma Protein (TPP), Fibrinogen, and Total White Blood Cell Count (WBC)

Group	Parameter	No.	$\bar{x}$[1]	SDM[2]	SEM[4]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	PCV(%)	7	29.357	4.289	1.621	22.5- 34	1.143	0.368	N.S.
C[6]	PCV(%)	6	30.5	6.804	2.778	20 - 37			
T	Hg%(gm%)	7	10.214	1.136	0.430	8.2- 11.3	0.486	0.454	N.S.
C	Hg%(gm%)	6	10.700	2.567	1.048	7.0- 14.3			
T	TPP(gm%)	7	6.857	0.264	0.100	6.5- 7.2	0.107	0.566	N.S.
C	TPP(gm%)	6	6.750	0.414	0.169	6.3- 7.4			
T	Fibrinogen (mg%)	7	1000.0	200.0	76.0	700.0- 1200.0	17.0	0.148	N.S.
C	Fibrinogen (mg%)	6	1017.0	204.0	83.0	900.0- 1400.0			
T	WBC(cells/ cmm)	7	9529.0	2440.0	922.0	7100.0-14300.0	579.0	0.398	N.S.
C	WBC(cells/ cmm)	6	8950.0	2803.0	1144.0	6500 -13900.0			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level

5 T = test group

6 C = control group

TABLE 13

Statistical Evaluation of the Test, Control Group Day 0 and the Test Group Day of Discharge for the Values of Packed Cell Volume (PCV), Hemoglobin Content (Hg%), Total Plasma Protein (TPP), Fibrinogen, and Total White Blood Cell Count (WBC)

Group	Parameter	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
TC[5]	PCV(%)	15	35.133	4.998	1.291	26.0- 41.0	5.776	2.631	sig.
T[6]	PCV(%)	7	29.357	4.289	1.621	22.5- 34.0			
TC	Hg%(gm%)	15	11.553	1.483	0.383	9.1- 13.2	1.339	2.108	sig.
T	Hg%(gm%)	7	10.214	1.136	0.430	8.2- 11.3			
TC	TPP(gm%)	15	7.007	0.395	0.102	6.3- 7.8	0.150	0.905	N.S.
T	TPP(gm%)	7	6.857	0.264	0.100	6.5- 7.2			
TC	Fibrinogen (mg%)	15	447.0	229.0	59.0	100.0- 800.0	553.0	5.468	sig.
T	Fibrinogen (mg%)	7	1000.0	200.0	76.0	800.0- 1200.0			
TC	WBC(cells/ cmm)	15	8813.0	2155.0	556.0	5600.0-12500	716.0	0.696	N.S.
T	WBC(cells/ cmm)	7	9529.0	2440.0	922.0	7100.0-14300.0			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 TC = test, control group

6 T = test group

TABLE 14

Statistical Evaluation of the Test, Control Group Day 0 and the Control Group Day of Discharge for the Values of Packed Cell Volume (PCV), Hemoglobin Content (Hg%), Total Plasma Protein (TPP), Fibrinogen, and Total White Blood Cell Count (WBC)

Group	Parameter	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
TC[5]	PCV(%)	15	35.133	4.998	1.291	26.0- 41.0	4.633	1.734	N.S.
C[6]	PCV(%)	6	30.500	6.804	2.778	20.0- 38.0			
TC	Hg%(gm%)	15	11.553	1.483	0.383	9.1- 13.2	0.853	0.965	N.S.
C	Hg%(gm%)	6	10.700	2.567	1.048	7.0- 14.3			
TC	TPP(gm%)	15	7.007	0.395	0.102	6.3- 7.8	0.257	1.327	N.S.
C	TPP(gm%)	6	6.750	0.414	0.169	6.3- 7.4			
TC	Fibrinogen (mg%)	15	447.0	229.0	59.0	100.0- 800.0	570.0	5.289	sig.
C	Fibrinogen (mg%)	6	1017.0	204.0	83.0	900.0- 1400.0			
TC	WBC(cells/ cmm)	15	8813.0	2155.0	556.0	5600.0-12500.0	137.0	0.121	N.S.
C	WBC(cells/ cmm)	6	8950.0	2803.0	1144.0	6500.0-13900.0			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. - significant at 0.05 level

5 TC = test control group

6 C = control group

TABLE 15

Daily Statistical Evaluation of Arterial pH for Test and Control Groups of Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	7.468	0.025	0.013	7.446-7.504	0.002	0.058	N.S.
C[6]	0	7	7.466	0.068	0.026	7.372-7.561			
T	1	8	7.505	0.039	0.014	7.437-7.547	0.011	0.666	N.S.
C	1	6	7.494	0.015	0.006	7.481-7.524			
T	2	7	7.510	0.009	0.004	7.495-7.524	0.001	0.052	N.S.
C	2	7	7.509	0.043	0.016	7.464-7.582			
T	3	4	7.492	0.026	0.013	7.471-7.525	0.015	0.869	N.S.
C	3	5	7.477	0.027	0.012	7.440-7.502			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level

5 T = test group

6 C = control group

TABLE 16

Daily PO_2 (mmHg) Values of Arterial Blood Samples from the Test and Control Groups of Steers with Bronchopneumonia

Calf No.	Day of Trial 0	1	2	3
Test				
1	64.5	75.9	84.4	72.0
2	60.7	66.6	95.6	53.5
3	N.S.	84.3	73.9	N.S.
4	N.S.	A.S.	85.5	N.S.
5	61.5	84.1	79.6	74.8
6	52.3	46.0	N.S.	N.S.
7	N.S.	78.8	73.4	N.S.
8	N.S.	60.1	A.S.	N.S.
Control				
12	76.0	62.0	59.1	A.S.
13	57.3	78.4	75.1	67.7
15	87.1	84.2	67.9	69.2
16	58.8	68.4	58.9	63.1
18	62.4	58.7	61.2	A.S.
19	49.1	N.S.	53.3	N.S.
20	63.3	59.1	A.S.	N.S.

N.S. = No sample

A.S. = Aerobic sample collection

TABLE 17

Daily Statistical Evaluation of Arterial PO_2 (mmHg) for Test and Control Groups of Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	59.750	5.229	2.615	52.3-64.5	5.107	0.754	N.S.
C[6]	0	7	64.857	12.711	4.804	49.1-87.1			
T	1	7	70.543	13.951	5.273	46.0-84.3	2.076	0.297	N.S.
C	1	6	68.467	10.688	4.363	58.7-84.2			
T	2	6	82.067	8.346	3.407	73.4-95.6	19.484	4.197	sig.
C	2	6	62.583	7.730	3.156	53.3-75.1			
T	3	3	66.767	11.574	6.682	53.5-74.8	0.100	0.014	N.S.
C	3	3	66.667	3.179	1.835	63.1-69.2			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 T = test group

6 C = control group

TABLE 18

Daily Statistical Evaluation of Arterial PCO_2 (mmHg) for Test and Control Group Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	30.875	3.094	1.547	26.8-34.3	0.175	0.065	N.S.
C[6]	0	7	30.700	4.805	1.816	23.0-38.2			
T	1	8	35.125	4.422	1.564	28.3-41.3	1.725	0.827	N.S.
C	1	6	33.400	2.905	1.186	29.8-37.3			
T	2	7	34.029	1.585	0.599	32.6-36.5	2.400	1.561	N.S.
C	2	7	31.629	3.746	1.416	27.7-37.0			
T	3	4	32.925	2.752	1.376	28.9-35.0	2.545	1.300	N.S.
C	3	5	30.380	3.036	1.358	25.9-33.8			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level

5 T = test group

6 C = control group

TABLE 19

Daily Statistical Evaluation of Arterial HCO_3 (mM/L) for Test and Control Group Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	22.100	2.968	1.484	18.1-24.5	0.186	0.063	N.S.
C[6]	0	7	22.286	5.330	2.015	13.2-27.2			
T	1	8	27.312	3.347	1.183	23.4-34.4	1.929	1.295	N.S.
C	1	6	25.383	1.606	0.655	22.8-27.3			
T	2	7	26.657	1.219	0.461	25.3-28.5	1.771	2.259	sig.
C	2	7	24.886	1.679	0.634	23.0-27.3			
T	3	4	24.875	3.123	1.562	20.8-28.3	2.815	1.563	N.S.
C	3	5	22.060	2.303	1.030	19.7-25.1			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 T = test group

6 C = control group

TABLE 20

Daily Statistical Evaluation of Arterial Total CO_2 (mM/L) for Test and Control Group Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	23.075	3.051	1.526	18.9-25.4	.025	0.008	N.S.
C[6]	0	7	23.100	5.399	2.041	13.9-28.4			
T	1	8	28.200	3.077	1.088	24.4-34.4	1.367	1.015	N.S.
C	1	6	26.833	1.288	0.526	25.0-28.4			
T	2	7	27.486	1.173	0.443	26.2-29.6	1.900	2.307	sig.
C	2	7	25.586	1.836	0.694	23.0-28.4			
T	3	4	25.850	3.247	1.624	21.6-29.4	2.870	1.538	N.S.
C	3	5	22.980	2.372	1.061	20.5-26.1			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level
sig. = significant at 0.05 level

5 T = test group

6 C = control group

TABLE 21

Daily Statistical Evaluation of Arterial Base Excess (mEq/L) for Test and Control Group Steers with Bronchopneumonia

Group	Day	No.	$\bar{x}$[1]	SDM[2]	SEM[3]	Range	Absolute diff. of means	t-value	Significance[4]
T[5]	0	4	0.525	2.855	1.427	-3.2- 3.3	0.068	0.022	N.S.
C[6]	0	7	0.457	5.775	2.183	-9.0- 5.1			
T	1	8	5.375	2.733	0.966	1.5-10.9	1.742	1.443	N.S.
C	1	6	3.633	1.239	0.506	1.5- 4.9			
T	2	7	5.000	1.000	0.378	3.8- 6.5	1.471	1.869	N.S.
C	2	7	3.529	1.827	0.691	1.0- 6.2			
T	3	4	3.275	3.021	1.511	-0.4- 6.8	2.615	1.527	N.S.
C	3	5	0.660	2.136	0.955	-0.6- 3.3			

1 $\bar{x}$ = mean

2 SDM = standard deviation mean

3 SEM = standard error mean

4 significance N.S. = not significant at 0.05 level

5 T = test group

6 C = control group

TABLE 22

Values of Arterial Blood Gas as Determined from Previous Studies

Arterial Parameter	Vestweber[60] (normal)	Vestweber[60] (pneumonia)	Schotman[47] (pneumonia)	Hales[16]	Donawick[12]	Bisgard[6]	Kuida[25]	Dalton[10]	Vagher[58]	Peters[40]
pH	7.45	7.41	7.3-7.45	7.41	7.37	7.34	----	7.403	----	7.42
pO_2 (mmHg)	77.02	52.33	-----	91.9	93.6	85.7	----	----	----	----
pCO_2 (mmHg)	37.69	36.07	35-50	47.3	42.8	38.7	34.2	----	----	----
HCO_3 mM/L	26.35	23.06	21-31	----	23.6	20.6	----	25.4	30.7	----
Total CO_2 mM/L	27.67	24.50	-----	----	----	----	----	----	----	----
Base Excess mEg/L	3.82	0.22	-2-+8	----	----	----	----	----	----	----

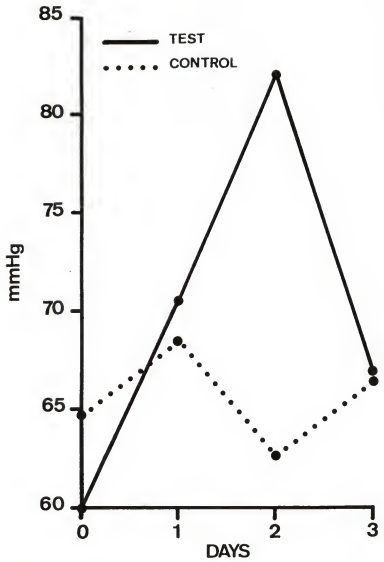

FIG. 1 ARTERIAL PO_2 VALUES FOR TEST AND CONTROL STEERS WITH BRONCHOPNEUMONIA

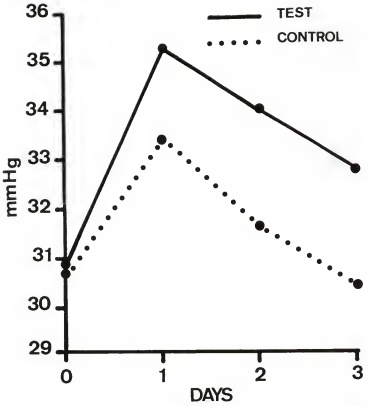

FIG. 2 ARTERIAL PCO_2 VALUES FOR TEST AND CONTROL STEERS WITH BRONCHOPNEUMONIA

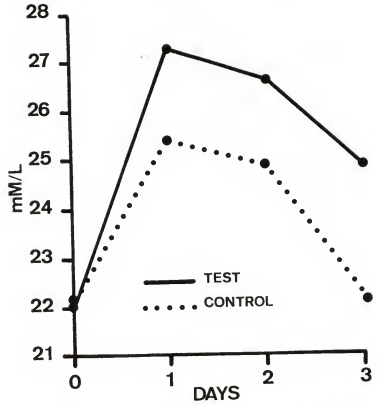

FIG. 3 ARTERIAL HCO_3 VALUE FOR TEST AND CONTROL STEERS WITH BRONCHOPNEUMONIA

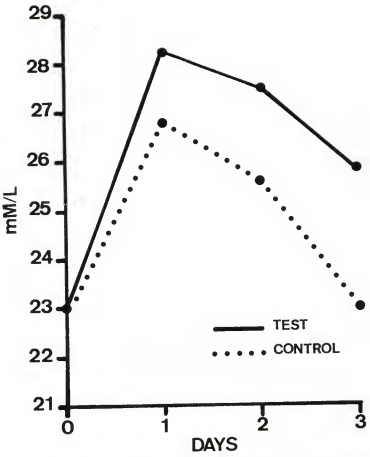

FIG. 4 ARTERIAL TOTAL CO_2 FOR TEST AND CONTROL STEERS WITH BRONCHOPNEUMONIA

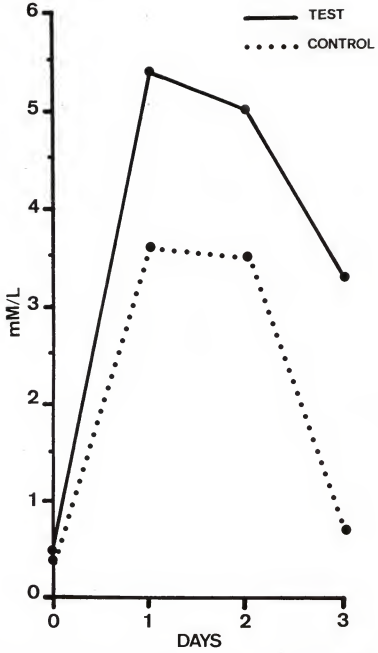

FIG. 5 ARTERIAL BASE EXCESS FOR TEST AND CONTROL STEERS WITH BRONCHOPNEUMONIA

NEBULIZATION THERAPY AS ADJUNCT TO CONVENTIONAL TREATMENT OF BOVINE RESPIRATORY DISEASE

by

MARK F. SPIRE

B. S., West Texas State University, 1971
D.V.M., Texas A & M University, 1974

AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1978

Fifteen mixed breed castrated male calves averaging 213 kg were utilized in this trial. The calves were part of a group of 105 calves shipped from central Texas to central Kansas. Clinical cases were selected as signs of bronchopneumonia developed over a two day period. Fifteen cases were randomly selected into an eight animal nebulized (test) group and a seven animal control group.

Transtracheal aspirations demonstrated Pasteurella hemolytica from the lower tracheal airways. Both groups were treated with oxytetracycline and/or sulfadimethoxine. The test group, in addition to parental therapy, were nebulized for five minutes duration B.I.D. The nebulization solution used was 20% N-acetyl-L-cysteine and 200 mg/cc kanamycin sulfate administered with a small commercial nebulizer through an indwelling tracheal catheter.

Response to treatment was determined by using rectal temperatures and scoring as to "Degree of Illness." A positive response to treatment was considered when the rectal temperature declined by 1.2^{o} C or to a level less than 39.5^{o} C. "Degree of Illness" was based upon a classification of 1-slightly ill or well, 2-moderately ill, or 3-severely ill. A decline to a lower numerical classification was interpreted to be a positive response to treatment unless the value was 1.

Rectal temperatures of the test group declined significantly ($P>.05$) by day 2 of the trial to a mean level of 39.18^{o} C compared to a mean level of 36.76^{o} C for the control group. By the day of discharge 75% of the test group and 56.1% of the

control group were classified as responding to treatment.

Statistical evaluation of the daily mean "Degree of Illness" indicated days 1 and 2 were significantly ($P>.05$) lower in the test group. Mean values were 1.625 on day 1 and 1.375 on day 2 in the test group, whereas, mean values of 2.429 and 2.143 were found in the control group on day 1 and 2, respectively.

Blood samples drawn from the external jugular vein mixed with EDTA and used for hematological studies. Samples were obtained on day 0 and the day of discharge from the trial. On the day of discharge significant ($P>.05$) decreases in PCV and hemoglobin content existed in the test group when compared to day 0 values. Significant ($P>.05$) increases in fibrinogen levels had occurred in both the test and control groups by the day of discharge.

Heparinized arterial samples were obtained daily from the coccygeal artery. The blood gas parameters of pH, PO_2, PCO_2, HCO_3, total CO_2, and base excess were evaluated on each sample. Significant difference ($P>.05$) existed between the test and control groups on day 2 of the trial for the values of PO_2, HCO_3, and total CO_2.

The nebulized calves appeared to respond more rapidly to the treatment of acute bacterial bronchopneumonia than did the control group calves. Nebulization therapy provides an alternate approach to the treatment of acute bronchopneumonia in cattle.