EXPERIMENTAL E. COLI ENDOTOXEMIA IN NEONATAL HOLSTEIN CALVES AND THE CHANGES IN ARTERIAL BLOOD GASES, PH, SELECTED ELECTROLYTES AND PROTEINS AND THEIR EFFECT ON ACID-BASE BALANCE

by

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INTRODUCTION

Colibacillosis is a systemic and/or enteric disease which occurs in the neonatal calf of all breeds of dairy and beef cattle. It causes an estimated annual loss of 150-250 million dollars to the cattle raiser (2). It is most common where calves are raised in a confinement situation. The calf is most susceptible during its immediate postnatal life and under conditions that alter the animal's susceptibility. The clinical term colibacillosis is derived from the bacterium Escherichia coli which is often isolated from the organs of animals that have died with signs of septicemia and enteritis. The disease also occurs in young pigs and lambs.

Clinical and experimental investigations of colibacillosis in calves have been made in the following areas: (1) environmental conditions conducive to animal's susceptibility; (2) bacterial and other suspected pathogens; (3) endotoxins produced by E. coli organisms; (4) the physiological and clinical response by the animal and (5) histological findings.

The results of these investigations are often difficult to evaluate and correlate due to a lack of normal physiological data on the neonatal calf. A further difficulty of interpreting the research in this area arises because experimental calves are usually of different ages and originate from different environmental and nutritional backgrounds.

There will be an attempt in this experimental project to serially determine values for whole blood gases, pH, serum proteins and selected electrolytes in a uniform group of neonatal calves beginning at birth and continuing for a period of ten days. There will be two other groups of calves; one challenged with E. coli endotoxin given intravenously and one challenged with E. coli endotoxin given orally. The results and clinical observations will then be evaluated.

REVIEW OF LITERATURE

Historical Review

In the 1920's (2, 3, 5) Smith reported on calves suffering from diarrhea, confirming the association of the disease with E. coli.

In 1922 Smith and Little (5) stated, "It is well established that immunity of the calf to septicemic infections by strains of E. coli is conferred by the ingestion of colostral antibodies against the strains concerned in relation to neonatal enteritis." Nutritional and dietetic causes were postulated along with avitaminoses A. Their findings clearly demonstrated that in cases of neonatal enteritis or diarrhea there were substantial losses of water, increased loss of dry matter, and nondigestion of fats with subsequent fecal loss at greatly increased rates.

Lovell (2, 3) in 1937 was able to distinguish differences in the various strains of the organism serologically by precipitation tests. Further refinement of serological techniques was made by Kaufman, Knipschildt and Tohlne. The latest refinements commonly used were done by Ewing and Orskov; this made world classification and identification techniques uniform.

Blaxter and Wood (5) in 1953 concluded: (1) that scouring is associated with high intestinal tract failure, indicating fermentation and absence of digestion, and (2) that bacteria play a secondary role by multiplying in the anterior part of the intestinal tract during this digestive disturbance favorable for their rapid growth. In diarrhea associated with certain systemic infections this sequence does not occur; this being during helminth or coccidial invasion; but does occur for a wide range of scouring conditions where calves are given rations of milk or rations closely simulating milk. It

appears the central feature is the abnormal presence of large amounts of fermented materials in the lower third of the intestinal tract. If strains of Coliform organisms against which the calf has no immunity multiply in the lower part of the gut, then ascend higher and higher, tissue invasion follows and death results. It is possible that the survival of calves given no colostrum is due to the absence of favorable conditions for bacterial growth in the lower intestinal tract rather than to some unknown and rapidly acquired natural resistance. Bacteria not met by resistance spread higher and advance to a more and more anterior location in the small intestine when natural resistance is lacking. The products of their metabolism are in part absorbed and in part diluted by an inflow of water. The consequent loss of unabsorbed food materials in the feces is undoubtedly severe, but more severe is the depletion of electrolytes, which may result in dehydration and death. In many instances, however, additional amounts of the same food always serve to make matters worse. Starvation of the calf leads, however, to very severe losses of body constituents, much more than in the adult, and this lack of resistance of the calf must be taken into account. The salient role played by sodium and potassium loss during dehydration and by calcium in promoting clot formation should not be ignored in any veterinary treatment (5).

Colibacillosis may occur in one of three clinical syndromes (2, 3, 5, 6): (1) the septicemic form; (2) the enterotoxemic form; or (3) the enteric form. Clinical signs of these three forms are generally separable.

The acute septicemic form is frequently observed in the first 24 to 36 hours of life. Calves most frequently will not exhibit diarrhea. There will be a transient fever, depression and weakness. The condition may or may not be noticed by the owner until extreme toxemia has developed; death may follow

in a matter of hours. The septicemic or toxic form is generally considered to be most common in calves deprived of colostrum immediately following birth. It is considered to be precipitated by an E. coli infection of the gastro-intestinal tract producing an overwhelming degree of toxin formation by the organism. The organism may be cultured from such organs as the spleen, liver, kidney, joint cavities, and central nervous system. This form of the disease is usually not amenable to treatment for the overwhelming toxemia and infection usually is so extensive that treatment is of little value. Initially these calves usually have little or no degree of clinically observable dehydration. Should the infection and toxemia be of a lesser degree, such that the calf is amenable to treatment or a degree of spontaneous recovery, systemic infections are a very common sequel; polyarthritis, omphalophlebitis, meningitis or meningioencephalitis being very common. Such calves usually die in the course of prolonged treatment or are so chronically affected that it is economically unwise to consider further maintenance.

The enterotoxemic form is seen to occur with almost as rapid an onset and may early in the course of the disease very well resemble the septicemic form; however, there is an early pronounced observable enteritis, some depression, mild toxemia, and a febrile reaction is clearly demonstrable for various lengths of time. Death may ensue but is less rapid than in the septicemic form; however, dehydration here is usually pronounced but the calves are somewhat more responsive to treatment. The sequel of polyarthritis, omphalophylioitis and encephalomyelitis or meningitis, however, can occur without early and proper treatment.

The third form generally considered is the enteric colibacillosis. This is characterized by a profuse, prolonged diarrhea. The animals have a state

of febrile reaction early and there is usually mild to marked dehydration. The appetite may be markedly affected and weight losses are rapid. Depression and weakness very often follow prolonged (several days) enteritis in this particular form. With early and proper treatment these calves usually will survive without subsequent complications of polyarthritis and central nervous system involvement. However, they very often are retarded in growth and a prolonged period of recovery is evident. The morbidity rate varies from one affected premise to another, depending usually on husbandry practices and specific therapy.

On some premises only an occasional calf develops the disease; most of these affected calves survive. On other premises, most calves born during an enzootic develop the disease in spite of intensive care and a variety of therapeutic measures, sanitation and environmental control being probably the most suitable means of prevention and control. The enteric form is not considered to have a bacteremia present and death is presumably due to mild chronic toxemia, debility, dehydration and electrolyte imbalance; this truly resembling a malabsorption syndrome and secondary infection.

It is generally considered that neonatal calves have absolutely no resistance to E. coli, septicemia and bacterial invasion when deprived of colostrum (2, 3, 5). This fact has been conclusively demonstrated by many series of experiments where deprivation of colostrum has been carried out and the calves then challenged to virulent E. coli strains. These immune factors are believed to be and have been relatively conclusively shown to be the antigen or antibody production by the dam against the "K" antigens or capsular antigen, and the "O" antigen or somatic antigens of the E. coli organism. There is a considerable fall of the serum immunoglobulins of the dam during the

period just prior to parturition and this fall coincides with the time at which the protein content can be shown to be increasing in the udder secretion (12, 3, 48). This fall in serum proteins is due to a loss of beta-2 and gamma-1 globulins, there being no loss of gamma-2 globulins from the blood. The increase in protein content of the colostrum is primarily due to a tremendous increase in beta-2 and gamma-1 globulins, and this gain is quantitatively equivalent to the loss from the blood serum. The direct transfer of immunity from the colostrum of the dam is carried out by the absorption of the gamma globulins and beta-1 globulins contained in the colostrum through the intestinal mucosa, thus contributing directly to the serum proteins of a calf.

There has been much work on the time limitations affecting the efficient and greatest degree of absorption of the colostrum from the gut of the calf, the site of absorption of the immune proteins from the small intestine. This is believed to be achieved by passage through the epithelial cells to reach the lymphatics. They may be detected in the thoracic duct one to two hours after the introduction of the protein into the duodenum (13). The absorption of antibodies through the intestinal wall in ruminants is limited to a 24-36 hour span following birth. This statement, however, gives a false impression for it has been shown that, in terms of absorption of antibodies to a somatic antigen of E. coli, this function is reduced to almost 50% at 16 hours after birth. In some calves, this function may be lost as early as 6 to 8 hours after birth.

The factors involved in this cessation of intestinal permeability are unknown but digestive degradation of the protein does not appear to play a part as originally was thought. The absorption of protein from the intestine of newborn herbivores is not as selective as it is for some other animal species because proteins of low molecular weight such as beta-lacto-globulins are

absorbed along with the immune lacto-globulins (2, 6, 8, 17, 18). The former are cleared from the blood by the kidneys. This results in a proteinuria which lasts for approximately the same period of time that the intestine is permeable (49). The immune lacto-globulins are largely retained, very little, if any, being filtered out in the urine. The principal constituents of the proteinuria are beta-lacto-globulins. The half-life of these immune globulins is considered to be about sixteen days. However, the antibody levels to different antigens do not necessarily decrease uniformly.

The factors associated with resistance to the septicemic form of colibacillosis in the colostrum fed calf are not fully understood. Resistance does not appear to be associated with agglutinating antibodies since many calves in the field are devoid of demonstrable agglutinins against E. coli (3) strains associated with colibacillosis. Those calves that do possess agglutinins against these E. coli strains generally only possess agglutinins against the somatic or "O" antigens. Few receive agglutinins against the "K" antigens of these bacteria. Furthermore, many E. coli strains which produce colisepticemia when fed to colostrum-deprived calves do not produce colisepticemia when fed to colostrum-fed calves regardless of the presence or absence of "O" and "K" agglutinins in the calf's sera. In light of the recent findings of the Nebraska team in relation to virus-associated with E. coli enteritis, a statement made by Gay (3) in 1965 seems in order: "In one or the other of several strains of mucoid E. coli, the clinical course of disease is very short. Death occurs within a few hours of initial symptoms and appears to be associated with a massive proliferation of these strains in the small intestine. It is not unlikely that this syndrome is a result of absorbed endotoxin, as it resembles in several features that seen when purified endotoxin is given

intravenously to calves. This syndrome has not been reproduced by oral feeding of these strains to calves. They may form part of the intestinal flora without ill effects. The factor which allows or initiates their sudden multiplication in cases of colibacillosis is unknown. Undoubtedly there are many causes, both known and unknown, of scouring calves of which E. coli is only one."

Thus, with the same basic factors in mind, Barnum, Glance and Moon suggested (2) "Colostrum may fail to protect calves from E. colibacillosis for the following reasons: (a) there may be a delay in the ingestion of colostrum until the ability of the small intestine to absorb the protein has been lost or reduced; (b) a calf may be agammaglobulinemic in spite of consuming colostrum within the required period for absorption; (c) the newborn calf may have ingested a pathogenic sera-type prior to colostrum; (d) absence in the colostrum of specific "K" antibody against virulent sera-types; (e) lack of presently unknown protective factors in the colostrum.

In the early 1950's, the attention of calf septicemias and calf enteritis began to focus around the effects of the disease on the electrolyte and pH values in affected calves. This work was primarily begun by such workers as McSherry and Grinyer (8, 9) and was tailored to follow some of the patterns used by Darrow and his co-workers in the field of human pediatrics. In McSherry's work, he determined that many calves may be complicated in the course of the disease by the development of an uncompensated acidosis which, in its terminal stages, could variously affect the other related electrolytes such as chlorides and potassium. It was his feeling at this time that the acidotic stages could effect the transfer of potassium from intracellular to extracellular fluids, thus effecting a rise in potassium and concommitant stupor and weakness that was observed in many cases. However, this was an inconsistent finding.

The chlorides he considered were a compensating factor for the decrease in bicarbonate. Thus he attributed low chloride findings to excessive loss due to the condition of diarrhea. The low calcium levels were also attributed to excessive loss of this ion in the feces. His findings with the electrolyte sodium were that they were not uniformly altered but they increased greatly in some places and decreased considerably in others. The loss of sodium is to be expected if this element is lost in quantity from body during the course of the disease. But the increase, he stated, is more difficult to explain. Thus, with these facts in mind, he made the statement, "It is shown by the use of balanced electrolyte solutions, many of the abnormalities can be corrected. In many instances, the early use of antibiotics and chemotherapeutic agents by controlling the diarrhea, prevents electrolyte changes from becoming extensive."

Concurrent with the uncompensated acidosis, there is considered to be a leaching or transfer of the potassium ion from the intracellular space, and in particular the myocardium, thus effecting a hyperkalemia decreased cardiac output and progressively increasing acidosis, this sequence of events effecting the death of the calf.

J. G. Watt (6) wrote: John Mills writing in 1776 quoted the Romans, Vegeteas and Columilla as once advising "a dry bed with good drainage and a supply of clean food and water for oxen and their young;" thus, diarrhea has been recognized as an important disorder of cattle for at least 2,000 years. White, in 1825, attempted to be rational when he suggested that the condition is a symptom of digestive upset. In 1859, Dadd remarked on the fact that diarrhea was accompanied by a loss of condition with the skin and the ribs entered into permanent relationship. This undoubtedly was one of the first statements of dehydration or recognition of dehydration and extreme weight loss

in diarrhea. Indeed, he went further and suggested that indigestion and improper feeding is the cause of most such disorders of calves. Over the next period of 140 years, the bacterial organism was being studied with greater intensity and was being incriminated with higher and higher degrees of frequency (1, 2, 5); this organism being escherichia coli.

Thus, as time went on, the thoughts of extermination of the disease by the use of antibacterial drugs was thought to be the torch of success. In the prevention, treatment and eventual elimination of calf scours as a disease entity in cattle, this, however, as all well know, was met with very limited success. As time progressed and animal husbandry became a more specific science in the hands of professionals, educators and qualified farmers, it became apparent that the disease was nearly as familiar to areas of good animal husbandry as it was in areas of poor animal husbandry. Thus, the etiological factor of nutrition was considered to be, to a greater degree, less important as an initial or etiological agent. Its considerations as a contributory factor, however, still are not eliminated (3, 8, 40).

Electrolytes

Serious and exacting work in the fields of serum electrolytes and pH was reported in 1954 by McSherry and Grinyer (8, 9). These studies were patterned along the lines of human research in the field of physiological chemistry. This a field of medicine just beginning to blossom forth, and its role in calf septicemia was being investigated. Their initial work (8) was a concerted effort to establish normal values for serum electrolytes: sodium, potassium, calcium, chloride, organic phosphorus, carbon dioxide and pH. Their studies involved normal cattle in the age groups of 4-10 days, 4-10 months and 2-13

years. They investigated clinical cases that entered into their hospital with varying nutritional backgrounds, stage of disease and treatment. They reported normal values as follows:

pH	7.3 to 7.54
Bicarbonate	31.03 ± 1.9 mEq/L
Chlorides	103 mEq/L
Sodium	142 mEq/L
Potassium	5.2 mEq/L
Calcium	5 mEq/L

These values were derived from calves that were from 4 days to 70 days of age, with no p.c.v. evaluated at this time.

McSherry and Grinyer's (9) subsequent work was in relation to the disturbances in acid-base balance in electrolytes and the treatment of eighteen cases. Their findings indicated that, in most cases, a moderate to severe metabolic acidosis was present. Concomitant with the acidosis, variations were observed in the serum chloride, sodium, calcium and potassium levels. It must also be emphasized that these evaluations were usually obtained from cases that were in the advanced stages of diarrhea. They also made the statement that by the use of balanced electrolyte solutions many of the abnormalities were readily corrected. It was also their determination that the use of intracellular, as well as extracellular electrolytes were of extreme importance in the regulation; control; and balancing of the serum values. Early treatment of diarrhea with antibiotics had a tendency to prevent any disturbances in the electrolyte imbalances; but antibiotics used alone were most apt to give disappointing results. Overhydration, however, is a factor that must be

strongly considered in the application of fluids and electrolytes in neonatal diarrhea.

In 1965, E. W. Fisher (10) in the study of "Death in Neonatal Calf Diarrhea," examined the effects of cardiac activity as a result of supposed electrolyte disturbances. This was done by the use of electrocardiography during which time evaluations of pH, sodium, potassium and bicarbonate were determined and recorded. The findings of the study at that time were that there was no significant difference between the plasma concentrations of surviving and dying calves. However, he did state that there were significantly lower plasma concentrations of sodium in his two groups of calves than of normal calves. In reference to potassium, there was no significant difference between plasma potassium concentrations of normal calves and calves that survived diarrhea, the values for which were determined previously by Fisher. The plasma potassium concentrations of dying calves were significantly higher than those of both normal calves and calves that survived diarrhea. The serum chloride concentrations of diarrhea surviving and dying diarrhea calves were significantly lower than normal calves. Table 1 gives the relative values for serum sodium, potassium and chlorides as found by Fisher (10) in diarrhea surviving, dying and normal calves:

Table 1.

	Diarrheic Calves				
	Surviving		Dying		
	No.	Mean	No.	Mean	Normal Calves
Na, mEq/L	31	129.4 ± 4.0	25	128.9 ± 6	141.8 ± 3.5
K, mEq/L	31	5.12 ± 0.4	25	6.11 ± 1.5	5.1 ± 0.4
Cl, mEq/L	31	92.3 ± 4.0	21	94.0 ± 5.4	100.3 ± 3.5

Fisher stated that there was a significant difference between the plasma pH of normal and diarrhea calves and between the pH of diarrhea surviving and diarrhea dying calves, as indicated by the following figures in Table 2 (10):

Table 2. pH and plasma bicarbonate of calves.

Calves	No.	pH	HCO_3^- mmol/L
Normal	9	7.38 ± 0.04	28.8 ± 2.4
		p 0.001	p 0.001
Diarrheic recovery	9	7.29 ± 0.07	21.6 ± 2.5
		p 0.001	p 0.001
Diarrheic dying	5	6.85 ± 0.14	8.9 ± 2.7

The plasma bicarbonate concentrations were significantly different between normal diarrheic-surviving, and diarrheic-dying calves. Cardiac arrythemias were observed in many of the calves and the arrythemias were related to high plasma potassium concentrations but evidence was obtained of high plasma potassium concentrations with no accompanying arrythemias (above 6.5 mEq/L). Thus, in conclusion of his discussion, Fisher makes the statement that "death in most diseases is due to circulatory failure and death in calf diarrhea can be considered to be no exception to this." Of the three components of circulation, the heart, the containing vessels and the circulating fluid, it was concluded that in these experiments the primary failure was of the heart and that the terminal hyperkalemia may have been brought about by secondary renal failure preventing renal excretion of this ion. The initial potassium elevation was effected by a kidney tubule exchange of potassium for the hydrogen ion. No post-mortem evidence of an increase in capacitance of blood

vessels in calf diarrhea was found while plasma volume; plasma sodium; although below normal, were not different in dying and surviving diarrhea calves. Thus, neither blood vessel capacity nor circulating volume was the critical deficiency. "Evidence was obtained of a primary interference with the function of the conducting tissue of the heart which appeared to cause death. This interference was apparently brought about by the electrolyte disturbance in the severe metabolic acidosis. Hyperkalemia was not always implicated." It must also be emphasized that the stages of diarrhea at which these calves were being studied was not indicated.

A very interesting study was reported by Dalton, Fisher and McIntyre (11) in 1965. In this study, attempts were made to determine the changes of blood chemistry; body weight; and hematocrit of calves affected with neonatal diarrhea. These studies were made on calves whose fluid and electrolyte intake was maintained at the same level when the calves were affected with diarrhea, as when they were healthy, so the effects of diarrhea would not be complicated by the effects of withholding milk. It was their concern to try to evaluate on a time basis the changes observed in these particular perimeters of blood chemistries. In this work, their findings were evaluated on the basis of the number of consecutive days of diarrhea. The first group included 31 calves with 2-3 days of consecutive diarrhea. In this group, sodium was found to be depressed in one-fourth of the group. In potassium, there was no significant depression or hypokalemia or hyperkalemia. The chlorides were not significantly changed. The second group consisted of 18 calves with 4-5 consecutive days of diarrhea; nine calves were hyponatremic, one was hyperkalemic, and one hypokalemic. Thus, there was questionable significance in any respect to potassium. Chlorides were not significantly changed. The third group included

12 calves affected for 6-7 consecutive days. Six calves had hyponatremia; and four had hypokalemia of questionable significance; there were no significant changes in chlorides. The fourth group was 7 calves affected for 8-9 consecutive days of which 7 showed significant hyponatremia. No significant changes in potassium, one showed hypokalemic, and one showed hyperkalemic. Three showed significant changes of hypochloremia. In these studies, 140 ± 5 mEq/L was the normal mean for sodium; 4.9 ± 0.4 potassium milliequivalents; 98.0 ± 3.0 chloride milliequivalents. In these four groups of calves, results from 40 of the 60 calves were suitable for selection into these particular categories.

Further consideration on these groups of calves was made in respect to the differences in hematocrits on the consecutive days of diarrhea. Also body weight differences were studied. In the calves that had 2-3 days consecutive diarrhea, there was a minus 2 ± 2 pounds of body weight lost for this group, ranging up to a minus 12 ± 5 pounds for the calves affected 9-10 consecutive days. Hematocrits in all of these groups showed no significant changes. In the calves that had diarrhea for 2-3 consecutive days, the sodium evaluations showed a hyponatremia in approximately 50% of the calves only. Thus (11), the statement is made that 54% of the sodium concentrations were within the normal range. In conclusion, Dalton et al. expresses the opinion that hyperelectrolytemia was not observed in the least significant extent in the present study and, in those few cases in which raised potassium and chloride concentrations were observed, the sodium concentrations were within or below the normal range. It would, therefore, appear that hypertonic dehydration did not occur in the diarrhea calves described in the present study. The raised potassium concentrations were probably not significantly elevated to have any serious effect on cardiac function. "Bergman and Sellers," he states, "in 1953 and

1954, showed that in calves, experimental hyperkalemia caused cardiac signs when the plasma concentration was raised to 8 milliequivalents per liter and cardiac arrest occurred when the concentration reached 12.7 milliequivalents per liter. However, a strict comparison with their results is not possible since their calves had only one electrolyte disturbance, whereas in diarrhea there are multiple disturbances. Correct cardiac function is dependent on specific concentrations of many electrolytes." Dalton et al. also state that in the present studies, the milk intake was maintained when the calves were affected with diarrhea and, consequently, they became isotonically and hypotonically dehydrated. However, there appears to be no significant differences in his hematocrit percentage changes. The lack of detection of increased hematocrits was unexpected in that it was assumed that the dehydration which obviously occurred in the diarrheal calf would lead to a reduction in plasma volume and a rise in hematocrit. "It was possible," he states, "that the plasma volume was maintained despite the dehydration or, alternatively, that the erythrocytes were either destroyed as part of the catabolic process to diarrhea or moved out of the general circulation."

As a follow-up to Fisher's (10) report in 1965 in the study of cardiac arrythemias and potassium toxicities in calves, Fisher et al. (12) (1967) studied the role of oxygen and potassium in relation to arrythemias. They state, "It is noted that the mucosas of dying diarrhea calves have a bluish coloration, presumably from desaturation of capillary blood. And when blood has been removed from such calves, it has been observed by us to be very dark in color. The dissociation curve of hemoglobin indicates that as pH falls the ability to carry oxygen decreases, particularly when the pH falls to about 7.0." The summary of their work indicated that there was no significant

depletion of body potassium, except when it is associated with severe protein deficiency, results in a loss of skeletal muscle potassium. The fall in cardiac muscle potassium level is comparatively small. In their study, dietary potassium deficiency produced a considerable fall in the plasma potassium content and in the potassium content of skeletal muscle. The fall in plasma potassium content was less as potassium depletion became more severe. The loss of cardiac muscle potassium is considerably less than that of skeletal muscle potassium. However, the rise in the potassium ion concentration gradient in cardiac muscle was twice that of skeletal muscle. Hill (1955) and Hodgkin (1951) (13) found that the resting membrane potential of muscle was a function of a logarithm of the concentration gradient of potassium across the muscle cell membrane. Hence, a change in gradient is likely to be of greater importance than a change in content. Potassium depletion associated with sodium lowering causes a fall in the intracellular pH of skeletal muscle despite the development of extracellular alkalosis (Gardner et al., 1952; Irvin et al., 1961; Grantham and Schloerb, 1965; Sands, Malone and Muntwiler, 1966; Wilson and Simons, 1967). However, none of these workers observed any significant relationship between the intracellular pH and potassium content of cardiac muscle or between the intracellular pH of cardiac muscle and potassium content of skeletal muscle. The most important change in cardiac muscle and potassium depletion is the rise in potassium ion gradient; this rise, which is seen in both skeletal and cardiac muscles, is accompanied in both cases by a fall in intracellular pH and a rise in the hydrogen ion gradient. They suggest the most serious consequences of potassium depletion relate to the heart, and, particularly, to disturbances of cardiac rhythm caused by potassium depletion in association with digitalis intoxication (Welt et al., 1960). They also

suggest that the changes in potassium ion gradient with accompanying changes in the hydrogen ion gradient play a more important part in changes in potassium content than causing disturbances of cardiac rhythm. Little is known about the factors controlling the transfer of potassium or hydrogen ions across the cell membrane. If both ions move passively and the magnitude and direction of their movement is controlled by the Donnan equilibrium, then the transmembrane potential would be equal. The potassium ion ratio is consistently approximately ten times the hydrogen ion ratio, indicating that overriding forces are in operation. It is suggested that there is active and continuous extrusion of hydrogen ions from the cell (Irvin et al., 1961; Woodbury, 1965). They found also that the intracellular bicarbonate concentration of cardiac muscle rose with increasing potassium deficiency which would be consistent with attempts to compensate for increased numbers of hydrogen ions leaving rather than entering the cell. The major determinant of the Donnan equilibrium across the muscle cell membrane is the excessive anionic charge associated with the nondiffusible cell proteins at physiological pH. As cell pH is lowered, the pK of the cellular proteins is approached and the excessive anionic charge is neutralized. The distribution of diffusible ions across the membrane will tend to be equalized. In metabolic acidosis, when the fall in pH inside the cell is less than the fall in pH in the extracellular medium, these protein buffers play an important role in the maintenance of cellular acid-base stability. Fewer cations are required to preserve electrical neutrality and potassium ions move out of the cell. The opposite effect would occur in metabolic alkalosis. This movement of potassium ions in response to acid-base changes probably accounts for the linear relationship between potassium and hydrogen ion gradients found in metabolic acidosis and alkalosis. Changes in plasma potassium content are

used frequently as an indication of disturbances in total body potassium and the plasma potassium content is of considerable importance in clinical medicine. Irvine et al. found that the plasma potassium content was significantly related to the extracellular pH and hydrogen ion gradient of skeletal muscle but not to the intracellular pH of skeletal or cardiac muscle or the hydrogen ion gradient of cardiac muscle. Excess potassium in extracellular fluids causes the heart to become extremely dilated and flaccid and slows the heart rate. Very large quantities can also cause atrial ventricular block. Two or three times the normal value will cause such weakness of the heart that death will ensue. All these effects of potassium excess are believed to be caused by decreased resting membrane potentials which result from high potassium concentration in the extracellular fluids. As the membrane potential decreases, the intensity of the action potential also decreases which makes contraction of the heart become progressively weaker. The strength of the action potential determines, to a great extent, the strength of contraction.

In respect to calcium ion concentrations, Guyton (41) stated, "It is doubtful that the calcium ion concentration ever changes sufficiently during life to alter cardiac function greatly, for greatly diminished calcium ion concentrations will kill a person because of tetany before it can significantly affect the heart; an elevation of the calcium ion concentration to a point that will materially affect the heart almost never occurs because calcium ions are precipitated in the body's tissues as insoluble calcium salts before such a level can be reached." Excess sodium depresses cardiac function similarly to that of potassium ions but for an entirely different reason. Sodium ions compete with calcium ions at some yet unexplained point in the contractile process of muscle in such a way that the greater the sodium ion concentration

in the extracellular fluid, the less the effectiveness of calcium ion in effecting contraction by an action potential curve. Conversely, decreased sodium ion concentration increases the strength of cardiac muscle contraction, for then the calcium ions have less competition. However, he stated, "From a practical point of view, the sodium ion concentration in extracellular fluids probably never becomes abnormal enough, even in serious pathological conditions, to cause significant changes in the cardiac function."

Proteins

In the review of literature on protein studies including electrophoretic patterns of serum proteins in calves, there is little work done in calves of extremely early age in the evaluation of serum proteins. Some of the earliest work was done in 1946 by Hogueness et al. (27), in which they gave the evaluations of 38% albumin, 8% alpha-1, 12% alpha -2, 7% beta-1, 9% beta-2, and 25% gamma. These studies are in relation to Carroll and Kaneko (14), who stated that the bovine has a normal total protein of 7.1 grams per 100 milliliters which is composed of 45% albumin, 14.5% alpha-1, 13.5% beta-1, and 27% gamma-2. This was determined on the adult animal. Work done by Weber (18) in 1963 gave the following average percentage of these components and the albumin-globulin ratios in 6 calves as determined by vertical- and horizontal-type paper electrophoresis in animals ranging in age from 2 weeks to 12 months of age. His findings were as follows: 51.2 % albumin; 48.8% globulins; with a break-down of alpha-1 3.9%; alpha-2 10.1%; beta-1 11.6%; beta-2 8.1%; and gamma 15.1%. The average total protein content of the serums of these cattle was 7.9 grams per 100 milliliters. Sex or age differences were not observed.

Summaries and studies on serum proteins of calves have been done by Marsh et al. (20) in which they state that loss of serum proteins via the intestinal tract in normal calves and in calves with diarrhea was determined by immuno-electrophoresis and polyacrilamide disc electrophoresis. Calves with diarrhea lost more serum protein and unabsorbed milk proteins than did normal calves. Normal calves excreted more serum protein in the urine than did calves with diarrhea. However, in this study, there was no reference made to any normal serum protein values. Considerable work has been done by Leland et al. (19) in the study of serum changes in protein in parasitized states of animals. However, these were in calves of considerably older age.

A rather complete study of neonatal alterations in serum gamma globulin levels was reported by Tennant et al. (17). In this study, the concentrations of albumin and alpha, beta and gamma globulins in the serum of Jersey and Holstein-Friesen calves from birth until 8 months of age were made with the following results in 2 groups of calves 1-10 days of age (Table 3). In summary, he stated, "Total protein concentration in normal Jersey and Holstein calves was measured from the time of their birth to 16 weeks of age. Mean plasma protein concentration increased rapidly in calves of both breeds after their ingested colostrum but was significantly greater in Jersey calves than in Holstein calves. Plasma protein concentration decreased gradually in Jersey calves between the second and sixth weeks and then remained constant. The value did not change significantly in the Holstein calves between the second and sixteen weeks of age. The increase in the serum protein concentration after calves were born was due primarily to gamma globulin. The mean concentration of gamma globulin of serum of one-day-old Jersey calves was more than two times that of one-day-old Holstein calves. When the initial increase

Table 3. Concentrations of albumin and alpha, beta, and gamma globulin in serum of Jersey and Holstein-Friesian calves from birth until 8 months of age (17).

Calves			Serum Protein Fraction				
Age (Days)	No.	No. of Samples	Total Serum Protein (Gm/100 ml) Mean ±	Albumin (Gm/100 ml) Mean ±	Alpha Globulin (Gm/100 ml) Mean ±	Beta Globulin (Gm/100 ml) Mean ±	Gamma Globulin (Gm/100 ml) Mean ±
Jersey Calves							
Precolostrum	4	4	4.3 ± 0.3	2.0 ± 0.1	1.4 ± 0.2	0.6 ± 0.1	0.3 ± 0.1
1-5	12	22	7.8 ± 1.2	2.1 ± 0.2	1.3 ± 0.2	1.4 ± 0.3	3.0 ± 1.1
6-10	12	19	7.5 ± 0.9	2.3 ± 0.2	1.1 ± 0.1	1.5 ± 0.3	2.6 ± 0.8
11-15	8	8	6.9 ± 0.6	2.3 ± 0.2	1.0 ± 0.1	1.2 ± 0.3	2.4 ± 0.6
Holstein-Friesian Calves							
Precolostrum	15	19	4.4 ± 0.3	2.3 ± 0.2	1.4 ± 0.2	0.6 ± 0.1	0.2 ± 0.1
1-5	22	51	5.7 ± 1.0	2.2 ± 0.3	1.3 ± 0.2	1.0 ± 0.3	1.3 ± 0.7
6-10	10	16	5.4 ± 0.9	2.3 ± 0.2	1.1 ± 0.1	1.1 ± 0.2	1.0 ± 0.6
11-15	7	9	5.1 ± 0.7	2.4 ± 0.2	1.0 ± 0.2	0.9 ± 0.2	0.8 ± 0.5

Table adaptation by permission of Tennant et al. (17).

occurred after calves ingested colostrum, the concentration of gamma globulin in the serum of Holstein calves remained relatively constant, whereas in Jersey calves, the concentration of gamma globulin decreased gradually during the first forty-five days. The concentration of beta globulin in serum of calves of both breeds increased after ingestion of colostrum and then decreased to normal levels during the second week of life. The concentration of beta globulin in the serum was significantly greater in Jersey calves during the first fifteen days of life. There were no significant differences between breeds and concentration of alpha globulin in the serum. The mean concentration decreased in calves of both breeds during the first fifteen days of life and, thereafter, was constant. The mean concentration of albumin in serum increased progressively with aging calves of both breeds, the greatest concentrations being observed in calves between four and eight months of age." In contrast to beta and gamma globulin concentrations, the concentration of alpha globulin in serum decreased after calves ingested colostrum and a difference between breeds was not observed. In discussing the difference between the Jersey and Holstein values, he states that these may be explained on the basis of a greater ability to absorb colostrum and protein elements in the Jersey calf in relation to the Holstein calf. Also, the generally considered possibility is that the Jersey colostrum has a higher or larger concentration of the gamma globulin constituents, thus, a higher elevation, initially, of serum gamma globulin components in the serum of Jersey calves, which later regresses to that of normal and Holstein calves. This subsequent depression of the gamma globulins was considered possibly due to differences in turn-over rate of gamma globulins. The urinary loss could, basically, be eliminated as a possibility as the large gamma globulin molecules do not pass the glomerulus and, therefore, are not

lost in the urine. The protein loss in the urine by the neonatal animal is almost entirely albumin and lacked beta macroglobulins.

Logan and Penhale (55, 56, 57, 58, 59) studied the effect of the various E. coli immune globulins from colostral whey. They identified IgA, IgG and IgM by gel diffusion. The whey prevented the development of colibacillosis in newborn unsuckled calves.

Initial finding with high doses of pooled globulins given intraperitoneally gave varied results when the calves were challenged by pathogenic E. coli. There was a definite delay in onset and development of disease, and some increase in survival rate. IgG and IgM were thought to confer protection. However, all calves developed colibacillosis to some degree in a second trial. They used a more purified IgM fraction in the third study and calves were protected with: (1) oral whey, (2) intravenous and oral whey, and (3) intravenous IgM. They interpreted these results to mean that IgM was conclusively related to immunity against E. coli.

It was their hypothesis that a local protective function took place within the gastrointestinal tract; thus giving a local immune type of protection as well as the circulating antibody protection. The antibodies were found to be adsorbed in varying quantities; some are thought to be digested in varying amounts and passed in the feces, depending on the degree of diarrhea.

Jack and Glantz (60) in 1970 isolated the 7S and 19S fractions of bovine, calf and dam serum and the dams' whey. These fractions were found by indirect hemagglutination to be antigenically active against the O antigens of four recognized E. coli serotypes pathogenic to the bovine.

The serum of the dam contained 19S macroglobulins and these appeared to be IgM immunoglobulins. Colostrum and calf serum contained both 7S and 19S

globulins and believed to be IgG and IgA.

In their final work (59) Logan and Penhale appear to have achieved a separation of the septicemic and enteritis syndromes. There was some evidence of this separation in the work of Mebus (39). Agammaglobulinemic calves (by electrophoresis) were challenged with pathogenic strains of E. coli after intravenous protection with IgG and IgM fractions (1.5 gm/30 gm IgG and 0.26 g IgM); survivors were given a second immune dose at 4 days of age (post-challenge). Feces was collected and checked for IgA, IgM, IgG classes of immunoglobulins. All were present after 48 hours thus they considered IgA was produced by the intestinal epithelium. Sodium, potassium and chloride values were determined by flame photometry. BUN, PCV and pH values were determined on prechallenge, and dying calves.

All calves developed severe diarrhea; all challenged prior to 24 hours of age died; two of five died when challenged between 39 and 48 hours of age. All blood cultures and post-mortem organ cultures were negative. Therefore, they grouped then as shown in Table 4. Fecal dry matter from dying calves decreased rapidly from 10 to 50 per cent as they voided 2 kg of feces daily. Dying calves became dehydrated (PCV up to 50%) with sunken eyes. Unlike septicemic calves of previous experiments, early muscle tone loss was not observed. There was marked oliguria and terminal anuria. PCV was elevated early in the course of the disease (40 + 12 hrs post challenge).

Surviving calves showed no decrease of urine output and fecal regulation was soon recovered. PCV and blood urea nitrogen elevation was transient. During the acute phase of the disease hyperkalemia (7.4 mEq/L) was "severe" in the dying calves. They state that spontaneous diarrhea always developed even in the absence of challenge. They also felt there was some local immune

Table 4. Changes in blood chemistry of diarrhoeic calves.

			Na+ mEq/L	K+ mEq/L	Cl- mEq/L	Urea nitrogen mg/100ml	pH	Weight (kg)
Dying calves	Pre-challenge	Mean	140	4.8	108	14	7.42	38.3
		Range	132-150	4.3-5.7	97-114	10-17	7.36-7.53	
	At death	Mean	133	7.4	106	61	7.29 (6 calves)	32.7
		Range	127-147	4.8-9.8	90-129	37-94	7.21-7.36	
Surviving calf	Pre-challenge	Range during illness	140 128-144	5.2 5.2-7.2	106 95-106	16 16-36		
Surviving calf	Pre-challenge	Range during illness	136 120-136	5 4.0-6.75	103 100-108	12 12-25		

Table adaptation by permission of Logan and Penhale (59).

globulins produced by the intestinal epithelium, especially IgA. The diarrhea calves "did not" develop acidosis as did older calves as observed by Dalton, Fisher 1965; Friden 1965 and Watt 1967, "nor had they" significantly higher plasma potassium levels; as detected by Fisher 1965; than surviving calves.

"In the present study, it was considered that the most significant difference between surviving and dying calves was the marked increase in PCV seen in dying calves. Although there were only two survivors, this difference has been observed also in earlier studies (Logan, Penhale 1971) and it is possible that during the course of scouring this "factor" is absorbed into the circulation where it causes hemodynamic changes leading to the circulatory and renal failure observed. Under normal circumstances intestinal immunoglobulins may have the ability either to neutralize or block this factor." (59).

Endotoxins

The study of bacterial endotoxins (23) has been greatly expanded in recent years. Endotoxin producing bacteria contain the toxin and it is released on destruction of the bacteria while exotoxin bacteria actively excrete their toxin. The metabolic byproducts of the gram-negative bacteria are endotoxins. These toxins, confined within the bacterial cell, are present in nonpathogenic and pathogenic gram-negative bacteria. When E. coli rapidly increases in numbers, there is a corresponding increase in endotoxin that can overwhelm the host animal. In newborn animals, endotoxin toxemia may result from toxin absorption via a nasopharyngeal route or directly through the gut (2). Destruction of bacteria by antibiotic therapy may release greater amounts of endotoxin, abruptly intensifying the toxemia. Many bacteria produce bactericidal substances active upon other related and unrelated bacteria with a degree

of specificity but without the capacity to rapidly reproduce themselves. These characteristics occur among the E. coli organisms and are called colicines. Thus, many strains of E. coli are colicinogenic. This bactericidal activity has been used as a prophylactic regimen in recent years; whereby it has been suspected that the ratio of antagonistic bacteria to the pathogenic bacteria has been disturbed; thus, the digestive tract has been treated by organisms that are supposedly colicinogenic to the E. coli pathogen. This method of treatment, however, has little degree of reliability. Hemolysins are another byproduct of E. coli organisms that have been recognized and have the ability to lyse mammalian red blood cells. However, hemolysins are not considered an outstanding attribute of the virulence of the E. coli organism. How they act on the body is the subject of much current study. The former type, or the excreted toxin, is thus called an exotoxin bacteria. Among the diseases caused by exotoxins are diphtheria, tetanus, gas gangrene, botulism, and scarlet fever. The endotoxin diseases include cerebrospinal meningitis, dysentery, typhoid fever, undulant fever, gonococcal arthritis, various kidney infections and tularemia. The exotoxins have to a large degree been controlled in the field of medical research by the development of antitoxins. This type of success has been met with considerable failure in relation to the control of the endotoxin diseases, their mode of action being largely a mystery. Endotoxins were first isolated some thirty years ago by Andre Boivin of the Pasteur Institute in Paris. In extracting them from bacteria, Boivin made a remarkable discovery. The bacterias that produced endotoxins were all of the gram-negative type and it later developed that almost all gram-positive bacteria produced exotoxins.

It was also discovered by Braude and his co-workers (23) that even non-pathogenic, gram-negative organisms contain endotoxins, these bacteria being

saphrophytic in nature. Their toxins were as potent as those produced by any infectious bacteria. Another remarkable aspect of the exotoxin produced by gram-positive organisms is that each exotoxin disease has its own specific symptoms and is generally easily distinguishable from the others. In contrast, the endotoxins all produce the same general symptoms in experimentally exposed animals regardless of what bacteria may have furnished the toxin.

One of the distinctive features of the endotoxins is their fast action. Intravenous injection can produce within very few minutes in an experimental animal a rapid loss of white cells from the blood stream. Radioactive experiments of the endotoxin indicate that the endotoxin almost instantly "enters" the white cells and acts to drive them out of the circulation. First to go are the granulocytes; during the next few hours, the lymphocytes gradually decline in number and platelets also drop out of circulation. As the white cells disappear from the blood, they turn up in increasing numbers in the tissues of the lung and other organs. Then, some four hours after endotoxin injection, granulocytes suddenly flood into the blood stream, raising the number of white cells to abnormally high levels. Then comes a rush of immature red cells. The influx of white and red cells probably represents a general outpouring of the reserve centers of blood cell formation, in storage and bone marrow. The second response to intravenous injection of endotoxin, following the initial disappearing of granulocytes from the blood by about one-half hour, is a rise in the body temperature. This is believed to be due to a reduction of the normal rate of radiation of body heat from surface tissues due to slowing of the circulation through the skin. However, some effect on the thermostatic center in the hypothalmus of the brain, is believed also to occur in some way. This may be by the release of pyrogenic products from the damaged white cells or that the

endotoxin itself acts on the hypothalmus, reaping it from the blood stream by way of the cerebrospinal fluid that circulates around the brain. It has been found that fever can be induced by amazingly small intravenous doses of endotoxin, as little as one-billionth of a gram or mg in rabbits and comparably small amounts in other animals including man. A dose one hundred thousand times larger than the minimum for fever will cause a collapse of blood circulation amounting to shock (23). Here the collapse of circulation stems not from depletion of the body blood volume but from the shutdown of blood to the heart so that the heart is no longer able to pump the normal amount of blood into the arteries. In the dog the shutdown has been found to be in the liver. Where the blockage occurs in the vessels is not yet known.

Gregory Swartzman (23) found that when a sublethal dose was given in rabbits and followed 12-24 hours later with another dose, the second dose led to a massive destruction of kidney tissues. His conclusion was that the endotoxin caused fibrin to collect in the capillaries of the glomeruli; as a result, the glomeruli gradually became clogged and kidney tissue then dies for lack of blood circulation. This also was his conclusion on second endotoxin injections in tissue sites, thus causing the well-known Swartzman reaction. This damage, however, could be forestalled by giving the animals heparin, which prevented the collection and clotting of fibrin. Other experiences have also shown the action of endotoxin in stopping blood flow can produce other kinds of tissue damage. For example, in an animal with a rapid growing tumor, an injection of endotoxin in the blood stream will lead in a few hours to hemorrhage in the tumor and death of its cells. Endotoxin will also kill the fetuses in a pregnant mouse. Thus, due to the variety of reactions and actions to endotoxins, workers have postulated it is made up of several constituents

that act in independent ways. There has been little success, however, in the separation of toxins and the identification of various toxic components. Thus, the available evidence indicates that all its toxic properties are in a single molecule.

The physical and chemical properties of endotoxins have been determined as follows: it has a protein, a lipid, and a polysaccharide or sugar fraction. It then was determined that the lipid fraction was the toxic fraction and the polysaccharide fraction was non-toxic. Walter Goble (23) separated the fractions with alkaline alcohol and found that the polysaccharide portion also is toxic. This ambiguity and other evidence make it seem most likely that the entire molecule is essential for the action of the endotoxin in producing specific diseases.

With this advanced study into the reactions of endotoxins, the question of an allergic reaction or anaphylaxis became a subject of primary interest and much investigation on this was done by workers such as Chandler Stetson, Jennie Siemienski, Sal Braude, and later by Wheel and Spink (23). The results of their works showed that there is a tremendous histamine release in the tissues of most animals. In the dog, it causes muscle fibers in the walls of the veins in the liver to contract, thereby narrowing the veins. In the guinea pig, it tightens muscles around the airways of the lungs so that in anaphylactic shock the animal is suffocated. The injection of histamines produced shock with many of the characteristics of both anaphylactic and endotoxic shock. The details of these events varied considerably in different animals. In a monkey, a shock-producing dose of histamine or endotoxin does not affect the large veins and the fall in blood pressure is gradual. The rat has considerable resistance to histamine, endotoxin, and anaphylactic shock, but a large dose of endotoxin

or an anaphylactic substance will overcome this resistance. In endotoxic shock, the small veins in the rat's intestinal tract are constricted with the result that blood accumulates here and hemorrhages occur throughout the intestinal tract and the adjacent lymph glands.

Thus, the very crucial question arose. Do antibodies play a part in the effects of endotoxin? Endotoxin, however, produces the same kinds of reaction regardless of whether or not the animal knowingly has previously been infected by bacteria. This suggests that the body may posses a natural antibody to endotoxin. If so, what stimulated its formation? The symbiotic bacteria that live in the intestinal tract of mammals are known to contain endotoxins. Considerable study has been made of these bacteria in attempts to determine whether or not the natural antibody could be produced by sensitization to these symbiotic bacteria. Irwin Nader (23) found natural antibodies to endotoxin in the blood of virtually all mammals he examined. With this in mind, Gilbert and Braude looked for evidence that these antibodies actually combined with endotoxin in the bloodstream of animals during their responses to an endotoxin injection. Their findings were conclusive in that there was a definite and marked sharp decrease of the natural antibodies almost to the point of non-detectability. Along with the disappearance of the antibodies, the "protein-complex complement" also disappeared from the rabbit's blood.

Spink and Veik (23) have found that in dogs, endotoxin shock can be prevented by removing complement from the animal's blood plasma before the injection of endotoxin. However, in further experiments on antibody reactions, Braude et al. discovered that if non-lethal doses of endotoxin were used, the smaller doses had the opposite effect of the removal of antibody, and the amount of antibody in the blood actually would gradually increase by as much as a

thousand-fold rise within a week. With this type of reaction with a non-lethal dose of endotoxin, one would expect a multiplication of antibodies would intensify the endotoxin damages as described by Swartzman, However, this is not the case and furthermore, this line of thinking would run counter to the whole concept of antibodies as the body's defense against foreign substances. It is now believed that antibodies sometimes increase resistance to endotoxins and sometimes lower the resistance. This paradox, at the moment, is completely unexplained.

The "Arthus phenomenon" has clearly shown that "antibody" levels of the serum directly affect the reaction to endotoxins given subcutaneously. On initial injection in the rabbit, for instance, small and slow reactions are detectable. Subsequent reactions to subsequent injections, however, show a marked increase in the rate of skin reaction, similar to the initial injection in man. This discrepancy has been explained by the fact that rabbits have a much smaller population of gram-negative intestinal bacterial than does man. Thus, the additional endotoxin injection steps up the serum "antibody" levels, effecting a much higher serum antibody level prior to the second endotoxin injection which then produced a marked skin reaction similar to that in man. This fact was further proven to be conclusive by the taking of the so-called hyperimmunized serum of the first rabbit and injecting it into an unsensitized second rabbit followed by a subcutaneous endotoxin injection which resulted in the accelerated type of reaction, "arthus phenomenon" as seen in man on the initial injection. However, investigators Dubois and Schaedler, of the Rockefeller Institute, and Douglas and Braude (23) injected only the antibody containing serum into animals instead of a sensitizing dose of endotoxin itself, it did not lower their resistance to large doses.

When Dubois et al. (23) injected only antibody into the serum of the animals instead of the sensitizing dose of endotoxin itself, it did not lower their resistance to large doses. Their conclusion was "one or more vaccinating doses of endotoxin will elevate, not lower, resistance to the toxin." When the rabbit is given small injections of endotoxin, about one-tenth of a microgram on successive days, the height and duration of its fever responses diminish from day to day. Diesen concluded that the increased resistance was due to a heightened ability of the animal's liver and spleen to remove endotoxin from the blood stream. Radioactive studies by Braude et al. at the Pasteur Institute where the endotoxin was labeled, has shown similarly that the liver cleared the toxin out of the blood stream much faster if the animal had been pre-treated with small doses of the substance. Thus, the paradox that antibodies sometimes heighten resistance and sometimes lower resistance, still needs to be clarified and explained.

One possible answer projected is that the issue is decided by the relative proportions to endotoxin to antibody. If the amount of antibody exceeds the amount of toxin, it protects. If it does not, it may add to the toxicity. The other explanation is that substances other than antibody are involved. Skarnes and Chedid of the Pasteur Institute (23) have been some of the leaders in this field of investigation. They have found that a blood constituent that is definitely not antibody can detoxify endotoxins, apparently by breaking down the endotoxin molecule into smaller units. They have observed that animals become almost incredibly sensitive to endotoxins by the removal of the adrenal glands. Thus, they theorized that the adrenal hormone, cortisone, aided in the elimination of the endotoxin; however, work by Braude et al. appears to nullify this theory but, in some way, it gives the animal greater resistance to the

toxin. The hormone, adrenalin, in contrast to cortisone, can greatly accentuate the toxic effects of endotoxin. It is possible that the endotoxin sensitizes blood vessels in such a way that they over-react to adrenalin and remain contracted long enough to cause a damaging interruption of circulation.

These previous findings that have been detailed have been carried out with endotoxin extracted from bacteria, not with the toxin producing bacteria themselves. In some work done by Jones, Douglas and Braude (23), where E. coli bacillus was injected into the knee of a rabbit, the typical fever response took place and endotoxin was demonstrable in the blood. Subsequently, the fever disappeared and the antibody level increased and the fever eventually disappeared. However, at the local site of injection, infection persisted and endotoxin was demonstrable for a considerable time, many weeks after all bacteria were eliminated. Other investigators have also noted a similar persistance of endotoxin in other organs. Considerable work is now underway to purify endotoxins so that its toxic effect can be correlated to the features of its chemical structure. When this is achieved, many of the puzzling and seemingly contradictory aspects of endotoxin's biological behavior may become understandable.

Mebus, Underdahl, Rhodes and Twiehaus (39) have brought to light the strong probability of an accompanying virus in colibacillosis. This virus alone did not produce the devastating effects usually associated with colibacillosis but repeatedly produced a disease of definite similarity. Thus it has been postulated that the virus is a contributing etiological factor in colibacillosis.

Raven et al. (23), using E. coli 011184, demonstrated that intestinal absorption of bacteria from the intestine occurred in the rabbit subjected to hemorrhagic shock but not in the normal rabbit. They concluded that the

bacterial endotoxin moved across the intestinal membrane primarily by passive diffusion. And their findings also were in agreement with Braude and others that intravascular coagulation with thromboembolism widespread in the microvasculature was considered the primary fundamental lesion, in that the clotting forces were initiated by the effect of the endotoxin on platelet factors.

Hemodynamic and Vascular Responses

J. Clark Osborne (24) studied the oral route of inoculation in 18 calves with 5 known serotypes of E. coli and concluded that the most common lesions were vascular stasis, edema, hemorrhage, and thromboemboli that were especially prominent in the microvasculature. Acute and chronic gastroenteritis characterized the disease clinically and, in many of the calves the generalized Schwartzman reaction such as fibrin thrombi in the glomeruli and generalized vascular stasis mentioned previously were very common. In a subsequent paper by Osborne et al., using E. coli serotypes intravenously (25), it was found that the calves were naturally hypersensitive to E. coli. Multiple inoculations produced tolerance. In this experiment, Osborne et al. used whole cultures of E. coli organisms that were injected intravenously. Clinical manifestations included chills; biphasic fever spikes; hyperpnea; tachyhypnea; dyspnea; coughing; expiratory grunting; cold clammy extremities; retching and diarrhea; marked depression; bloating and anorexia. They state that the shock syndrome produced by E. coli whole cell cultures was only slightly more severe than that produced by E. coli free supernatant fluid. And, he stated that this is probably related to retention of part of the endotoxin in the bacterial cell wall. He also stated that neonatal calves deprived of colostrum and those that suckle their dams were both hypersensitive to intravenous inoculations of E. coli

whole culture and cell free supernatant fluids. Classic and irreversible anaphylactoid endotoxin shock followed single inoculations in 6 calves. Two intravenous inoculations, two or three days apart, produced a fatal reaction in two calves. Other calves, obviously naturally hyporeactive, were given up to 18 inoculations at 1-7 day-day intervals without fatal reaction. The shock reaction was diminished and tolerance was increased after the third and each subsequent inoculation.

In a subsequent review of the pathological findings of his work, Osborne (28) made the following statement, "Hyperemia; stasis; emboli; thrombi: hemorrhagic diathesis, and edema were regularly seen and altered reology in the microvasculature of the thoracic and abdominal viscera was a most striking finding." These observations, he states, were by no means new for numerous previous studies, though not working with these serotypes in these animal species have provided good descriptions of the lesions of E. coli endotoxin shock. Coronary thrombosis was demonstrated microscopically in one calf as an unusual finding in fatal E. coli anaphylactoid shock under the conditions of these experiments. The clinical features and laboratory findings indicated a chain-reaction-like occurrence of the physiological, pathologic and hemeostatic events following intravenous inoculation of endotoxin. The brain barrier, he states, was obviously penetrated as indicated by the hemorrhages into the Virchow-Robin spaces of the brain in a colostrum-deprived calf that was given E. coli endotoxin intravenously.

The hemorrhagic brain lesions were not noted in calves that received colostrum. The statement here is also made that endotoxin also apparently releases the lysosomal contents of leukocytes and these directly, or through mediators, influence the progression to the irreversible state in endotoxemia.

This conclusion was described by Davis and Horowitz in a study of the liberation of serotonin after the injection of bacterial endotoxins.

In a paper by Tennant et al. (29) in the study of hypoglycemia in neonatal calves, 11 cases of hypoglycemia in neonatal calves were reported. All calves had diarrhea and were either extremely lethargic or comatose when hypoglycemia was demonstrated. Varying degrees of oligemic shock were present when hypoglycemia was demonstrated and it is suggested that hypoglycemia was related to alterations in tissue oxygenation and metabolism which were the direct results of decreased blood flow to peripheral tissues.

Several recent reports on the hemodynamic effects of endotoxins in animals have attempted to clarify or more clearly define some of the physiological effects on the vasculature and vascular regulatory mechanisms in animals.

Kuida et al. (30), in the "Study of pulmonary vascular response to acute hypoxia in normal unanesthetized animals," made the following observations in the process of trying to determine the effect of acutely induced hypoxia on pulmonary-vascular tone, this being considered in direct relation to a disease, that is, enzootic in cattle in high mountain ranges. This disease occurs in the United States in Colorado and in Utah and has been reported in the Peruvian Andes. This study was undertaken to examine the hypothesis that the disease results from excessive pulmonary vasoconstriction due to hypoxia. In this study the methods used to determine the perimeters examined were: (1) collection of expired air; (2) the administration of hypoxic gas mixtures; (3) venous cardiac catheterization; (4) carotid artery cannulation and in some instances (5) left ventricular catheterization. Kuida et al. discuss many aspects that may affect the variability of the outcome of the perimeters in the process of handling the experimental animal. The conclusions which Kuida et al. came to

were that hypoxic vasoconstriction in certain animals provides a possible mechanism for the development of pulmonary hypertensive heart disease in a significant percentage of calves after prolonged exposure to mild hypoxia. Evidence to support such a mechanism has been convincingly demonstrated by the recent study by Will et al. (30). Thus, the physiological significance of hypoxic vasoconstriction in the bovine cannot be said to be as doubtful as some workers believe.

Tikoff et al. (22) studied the use of E. coli endotoxin in calves ranging in age from 2 to 4 weeks of age. He used doses of purified E. coli endotoxin either 0.25 or 0.50 mg/kg with most animals receiving the latter dose. This was injected either into the pulmonary artery or the right atrium within a 30-second period. A lethal dose in dogs, they state, was often as low as 1.0 mg/kg. It was their conclusion that pulmonary vascular hypertension is the most prominent feature of the hemodynamic response to endotoxin in calves since left heart filling pressures were essentially unchanged and blood flow was usually decreased; such a response could only be secondary to pulmonary vasoconstriction. These conclusions were drawn from the following findings: pulmonary arterial pressures; although control pressures vary considerably; had a consistently striking increase, the maximum averaged 33 ± 14.6 mm Hg. Thus, the hypertensive response did not begin with the first circulation of the endotoxin through the pulmonary circulation where control cardiac outputs were much lower; the increase in pulmonary arterial pressure was more gradual and tended to occur later.

Tikoff (22) found that systemic arterial pressures generally dropped. The time of the fall in pressure, however, was quite variable. All animals, however, showed a systemic hypertension one hour after endotoxin was given.

Left ventricular and diastolic pressure did not increase significantly. Pulmonary artery wedge pressures all were considered to be markedly elevated. As a rule, the rate of increase of the pulmonary arterial wedge pressure was slower initially compared to the pulmonary arterial pressure and the decline following peak response was sometimes more rapid. It must be understood that all calves in these studies were anesthetized with phenobarbital given intravenously. In the discussion of their findings, Tikoff et al. state that "we interpret these variable changes in pulmonary arterial wedge pressure to indicate that pulmonary-venoconstriction, although variable in degree, occurs in the calf in response to endotoxin as it was previously described to occur in the dog. The hemodynamic changes suggest that the pulmonary vascular constrictive response to endotoxin may occur at both arterial and venous loci, and in varying proportions from animal to animal, or at different intervals following endotoxin in the same animal. The consistent delay of at least several seconds (up to 30) which occurred after injection was more than enough time for the endotoxin to circulate through the systemic circulation as judged by time components of indicator dilution curves. This effectively rules out a pulmonary vasoconstrictive response to the effect of an injection of a colloidal suspension or to the direct effect of endotoxin molecules alone on the pulmonary vascular tree." Thus, Tikoff et al. (22) suggests that a blood and/or tissue reaction is necessary, and that endotoxin effects involved vasoactive intermediaries. Cardiac output response in calves contrasted to that seen in dogs; but the fall was neither as precipitous nor as persistent as that seen in dogs. Not infrequently, there was a tendency for cardiac output to return toward control levels even while systemic arterial pressure continued to fall. In all studies, the calculated total systemic resistance was below control levels by one hour

following endotoxin administration and remained so. These findings may be interpreted to indicate peripheral vasodilation since the expected mechanical response to a decrease in both flow and pressure is an increase in calculated resistance. This finding of a decreased total systemic resistance; late in the course of endotoxin challenge; is consistent with the findings in eviscerated profused dogs. There is no evidence in the results of the present study to justify an interpretation of vasoconstriction in endotoxin shock, at least in the calf.

A transient modest and early relative bradycardia was commonly seen following endotoxin administration by Tikoff et al. (22). The absence of bradycardia 30 minutes following endotoxin, at a time when both systemic arterial pressure and total systemic resistance were falling, however, mitigates against the mechanism of carotid sinus resetting at a lower level, as an important mechanism, as postulated by Trank and Visscher in the canine species. The increase in the mesenteric venous pressure following endotoxin in three of the four studies where it was measured, suggests the possibility that hepatic and/or mesenteric venoconstriction may occur in calves. However, the absence of progressive hemoconcentration, as well as the presence of only minimal hepato-splenic congestion without necrosis, provides evidence that this phenomenon does not appear to play a vital role in the hemadynamics of shock in calves. This is comparable to that described in the cat, the rabbit, and the monkey and is significantly different from that which is characteristic for the dog. The characteristic and usually abrupt fall in arterial oxygen saturation in the face of an unchanged arterial carbon dioxide tension can be explained on the basis of increased venous admixture. While detailed evaluation of pulmonary function was not carried out during these studies, it was obvious that the animals breathed with great difficulty following endotoxin. This they attached

to the fact that bronchoconstriction which has been observed in cats and sheep may also occur in the calf. Since overall alveolar ventilation must have remained adequate, the marked arterial oxyhemoglobin desaturation must have been due to either a diffusion abnormality or abnormal ventilation perfusion relationships. "Our limited data, however, does not permit a precise delineation as to what extent either of these possible mechanisms played a role in the production of arterial oxyhemoglobin desaturation." Metabolic acidosis was mild, although severe acidosis was present in the three calves in which arterial blood samples were obtained just prior to death. There was also a definite increase in arterial carbon dioxide. Thus, in these animals a large component of the terminal acidosis can be explained on a respiratory basis.

The response described above is similar to that described in cats and sheep in that the lung appears to be the major target organ, thus effecting vasoconstriction of the thick muscular coat prominent in the pulmonary vasculature of calves when appropriate stimuli such as endotoxins or hypoxia is applied.

Three calves that were secondarily challenged one to two weeks subsequent to the initial study showed no apparent acquired tolerance to the endotoxin. These findings are in contrast to Kuida et al. (30) who felt that the pulmonary vasculature of calves is incapable of vasoconstriction.

Dedichen et al. (26), in studying the hemodynamics of endotoxin shock in dogs, made the following conclusions. The typical response to intravenous endotoxin was a sharp fall in blood pressure; cardiac output; and regional blood flows. This was seen within a few seconds after the injection and was followed by a slow partial recovery in these functions, only to decrease slowly again during the following hours. Blood flows in the superior mesenteric,

renal and femoral arteries decreased to approximately the same degree as cardiac output. No significant redistribution of cardiac output was therefore observed in this shock model. Total peripheral vascular resistance increased slowly and to a moderate degree (30%). Vascular resistance in the mesenteric, renal and femoral vessels increased slightly more than total peripheral resistance. This moderate increase in vascular resistance is due mainly to decreased vascular filling and to increased viscosity rather than to active vasoconstriction. These observations, Dedichen et al. state, "do not support the hypothesis that vasodilating drugs will be useful in the treatment of endotoxin shock." Blood gas analyses showed a slight decrease in arterial oxygen saturation and a marked decrease in mixed venous oxygen saturation. The widening of arterio-venous oxygen difference did not compensate for the reduced flow and a decreased oxygen consumption and acidosis were observed.

In some work done by Silove and Grover (31), they attempted to investigate the mechanism by which hypoxia increases pulmonary vascular resistance. They state that it had been suggested that catecholamines were involved in this response. However, subsequent investigations have been inconclusive in either supporting or refuting this hypothesis. Several investigators concluded that blockade of the sympathetic nervous system reduces or abolishes the pulmonary repressor response to hypoxia. There is equally strong evidence to dispute this. To explore the problem, Silove and Grover selected the newborn calf as a model with a highly reactive pulmonary vascular bed that would yield pressure changes at larger magnitude than seen in any other experimental animals in which studies of this nature have been performed. They approached the problem by using the intact pulmonary circulation of the newborn calf to compare the effects of hypoxia and norepinephrine; and to determine the influence of either

alpha-adrenergic blockade or of catecholamine depletion on the hypoxia-pulmonary repressor response. Hypoxia produced large increases in pulmonary arterial pressure. During the early phase of the response to hypoxia, the first minute pulmonary blood flow remained relatively constant but later the blood flow decreased. Consequently, calculated pulmonary vascular resistance increased primarily as a result of the rise in pressure during the early phase of the response with a further increase resulting from the subsequent decrease in blood flow. This secondary increase in resistance could represent simply a "delayed response of pulmonary blood vessels after the decrease in blood flow. On the other hand, the earlier increase in resistance in the absence of a change in pulmonary blood flow is more likely to indicate active vasoconstriction." "Therefore," Silove et al. state, "we will confine our argument to those changes in resistance which were associated with only minor changes in flow." During the first minute of hypoxia, the pulmonary vascular resistance increased by 62% of control values before alpha-adrenergic blockade, with phenoxybenzamine with a further increment in resistance and no diminution in flow in three of the five animals. Since the increment in resistance in response to hypoxia after phenoxybenzamine was 106%, it is apparent that this vasoconstrictor response was not changed by blockade.

The methods used in this research involved the anesthetization with pentobarbital and the changes in arterial blood gases were analyzed and changes in pulmonary vascular resistance were determined in response to ventilation with 10% O_2 and 100% O_2. The systemic arterial blood PO_2 ranged from 44.5 to 55.0 mm Hg during ventilation with room air. These values are considered within the range observed in normal awake calves of the same age in Denver, the area in which this research was done. Ventilation with 10% oxygen and nitrogen

reduced the systemic arterial blood PO_2 to 18-24 mm Hg. In a few animals in which pulmonary venous blood was also obtained simultaneously, its PO_2 was higher than that of arterial blood which indicated that varying degrees of right to left shunting through the foremen ovale were present. Therefore, the arterial blood PO_2 was not a reliable index of either pulmonary arterial alveolar or pulmonary venous PO_2 levels. For this reason, they did not attempt to correlate systemic PO_2 levels with changes in pulmonary vascular resistance.

The pulmonary pressor response to hypoxia in awake calves, in the Silove (31) study after catecholamine depletion by the use of reserpine (91% increment in the pressure), was clearly not reduced when compared with normal awake animals (51% increment). When the reserpinized animals were anesthetized, the low cardiac output resulted in an increased calculated pulmonary vascular resistance. Consequently, the percentile increment in resistance during hypoxia was less than that observed in normal anesthetized animals, although in absolute units, the increase in calculated resistance was at least as great. When the problem of diminished flow was resolved by perfusing a portion of the pulmonary vascular bed at a constant normal flow rate, both the absolute and percentile increments in resistance varying hypoxia were identical with comparable observations in normal animals. Consideration of these three sets of observations in the reserpinized animals indicates that catecholamine depletion with reserpine did not diminish the pulmonary vascular resistance to hypoxia. Many investigators, both in the clinical and experimental fields, have reported that the hypoxic pulmonary pressor response was reduced or abolished by pharmacological or surgical sympathectomy. However, other work was cited in which the pulmonary vascular response to hypoxia persisted following such procedures. A review of the responses indicate that in most species there were usually of

small magnitude and often difficult to interpret. Silove and others state that the large changes in pulmonary arterial pressures and resistances which they had obtained in the newborn calf have helped to resolve this uncertainty after finding strong evidence that neither alpha-adrenergic blockade. . .nor tissue catecholamine depletion prevents or diminishes the pulmonary vascular response to hypoxia.

Norepinephrine produced a significant increase in the pulmonary-vascular resistance with little change in the pulmonary blood flow in all animals before alpha-adrenergic blockade which implied pulmonary-vasoconstriction (31). This effect was qualitatively similar to the early response to hypoxia. However, after the administration of phenoxybenzamine, norepinephrine failed to increase the pulmonary-vascular resistance, whereas the pulmonary-vascular response to hypoxia persisted. This selective blocking of the effects or norepinephrine but not of hypoxia suggests that they acted through different mechanisms. When norepinephrine was injected during hypoxia, or both before and after alpha-adrenergic blockade, it caused a decrease in the calculated pulmonary-vascular resistance. This was due almost entirely to an increase in pulmonary blood flow which may have opened passively some segments of the vascular bed that had been closed. However, this effect was more pronounced after blockade than before, an observation that suggests that alpha-adrenergic blockade may have unmasked the beta-receptor stimulating properties of norepinephrine. Norepinephrine is known to have a vaso-depressor effect on systemic circulation when administered during vasoconstriction, probably by a peripheral action and it is conceivable that a similar mechanism operates in the pulmonary circulation.

A further argument favoring a vasodilator effect of norepinephrine is Silove et al.'s (31) observation that in the presence of constant flow profusion

of a portion of the pulmonary vasculature, the drug lowered the pulmonary vascular resistance in the presence of pulmonary vasoconstriction induced by a combination of hypoxia and acidosis. Similarly, isoproterenol is known to produce pulmonary-vaso dilitation and it is of interest that during hypoxic pulmonary vasoconstriction, its effects resembled those of norepinephrine, namely, a decrease in calculated pulmonary resistance. Again, however, it is possible that in these studies, the decrease in resistance caused by isoproterenol was in part due to its constant effect in increasing blood flow by increasing cardiac output. The results of their study conclude that neither alpha-adrenergic blockade with phenoxybenzamine nor depletion of tissue catecholamine stores with reserpine, prevents the hypoxic pulmonary propressor response. Moreover, this study has indicated that the pulmonary vaso constrictor effect of hypoxia and norepinephrine are mediated differently. Thus, this pharmacologic approach in a suitable experimental model implies that hypoxic pulmonary vasoconstriction is not mediated through adrenergic receptor stimulation or release of endogenous catecholamines.

Work done by Robert L. Hauman (32) on "The effects of celiac blockade on intestinal arterial resistance and critical closing pressure during endotoxin shock" states: "It is irreversible shock in dogs, whether caused by hemorrhagic endotoxin, epinephrine or superior mesenteric artery inclusion, and it is marked by an acute hemorrhagic necrosis of the intestine. This lesion in fact reflects the intense and prolonged mesenteric vasospasm elicited by compensatory sympathetic activity which, during endotoxin shock decreases capillary flow to the mucosa, submucos, and muscularus by 60%." His studies, he states, were carried out to determine if celiac blockade during endotoxin shock would decrease intestinal arterial resistance and, thereby, restore integrity of

mucosal capillary flow. These studies were done in dogs anesthetized with sodium pentobarbital. In those dogs, subjected to lethal endotoxin shock, it is suggested that the changes observed in mucosal blood flow are directly related to the development of arterial tensions in excess of mean available blood pressure as an expression of compensatory sympathetic hyperactivity. The degree to which the functional and structural integrity of the adjacent tissue is impaired is related to the duration and magnitude of this response. In all experiments, celiac blockade tempered the increase in arterial tension and if instituted before the arteriole had become unresponsive, effective mucosal blood flow was restored and maintained. Preservation of effective mucosal blood flow aborted the development of hemorrhagic necrosis of the intestinal mucosa. This contributed to survival from an otherwise lethal dose of endotoxin. His findings indicated that when celiac blockade was performed 60 minutes and progressively up to 120 minutes following endotoxin injection, active flow was restored in the intestinal mucosa. Periods including and greater than 180 minutes showed that the microcirculation became progressively stagnant in a manner similar to the endotoxin control animals. Celiac blockage in this experiment was obtained by the injection of 15 cc of lidocaine in oil injected into the ciliac plexus. Endotoxin dosage was 5 mg/kg of Difco E. coli endotoxin given intravenously.

Whole Blood Acid Base Balance

In reviewing the literature to determine some normal values on serial sampling of the neonatal calf in a relation to blood gases (PO_2, PCO_2), buffer base excess, and total bicarbonate, a paper by Donawick (33) reports the following normal values in Holstein-Freisen calves of approximately 3 weeks of

age and weighing 47-65 kg that had been cannulated via the saphenous artery and the femoral artery with the cannula tip end being in the abdominal aorta. This work was done in unanesthetized resting calves. His findings were as follows: (1) arterial oxygen tension (P_aCO_2 93.6 ± 6.78 mm Hg); (2) arterial carbon dioxide (P_aCO_2 42.8 ± 3.28 mm Hg); (3) pH 7.37 ± 0.02; (4) standard bicarbonate 23.9 ± 1.42 mEq/L, and (5) base excess (BE 0.0 ± 1.78 mEq/L).

The mean alveolar-arterial difference ($A\text{-}aDo_2$) (33) which they considered to be the quantitative measurement of the efficiency of ventilation was 11.7 ± 7.3 mm Hg; and in this study; he considered that to be the difference between the saturation of arterial blood in complete equilibrium with alveolar oxygen. The difference between the saturation of arterial blood in complete equilibrium with alveolar oxygen and mixed venous blood was assumed to have been 25%; therefore, the $A\text{-}aDo_2$ would indicate a shunt of 5.2% of the cardiac output which is not oxygenated as it passed through or is shunted around the pulmonary circulation. In this work (33), acid-base determinations were done by the method of Astrup; the nomographs of Siggard-Anderson and Engel were used for the determinations of pH, CO_2, standard bicarbonate, actual bicarbonate, total carbon dioxide, and base excess. In discussing the venous admixture contribution, Donawick states that all contributing factors were considered collectively. It is realized that the result is only an approximation of all these factors, including direct pulmonary-arteriovenous communication, blood profusing unventilated alveoli and other factors of "lesser magnitude, such as shunting of some bronchial and coronary arterial blood flow."

A brief summarization of the causes of venous admixtures to pulmonary circulation by Said et al. (34) would include the following: at any given time, the alveolar arterial oxygen partial pressure difference (AaDo) may be due to

one or more of the three following mechanisms: (1) failure of pulmonary capillary blood to come to complete equilibrium with alveolar gas; (2) uneven ventilation perfusion ratios; and (3) admixture of venous blood by direct shunting. The first mechanism causes the diffusion component of the AaD relating to diffusion across the alveolar-capillary membrane as well as chemical reaction rates of oxygen with hemoglobin. The second mechanism accounts for the "distribution component" and the third, is spoken of as the true or pure anatomical shunt, or the "direct venous admixture component."

Phillips and Knox in 1969 (35) discussed acidosis due to diarrhea in calves. They state: "Diarrhea calves have a partially compensated metabolic acidosis with decreased PCO_2, a negative base excess, a decreased buffer base and a lowered blood pH. As diarrhea progresses, they appear to lose their ability to compensate and die. Some hypotheses are suggested to explain this loss of compensation." Their experimental procedure was such that normal and diarrhea calves were obtained from a local sales yard and maintained in individual metabolism stalls. Milk, or a milk substitute, was used as a primary food as well as water and pelleted alfalfa and libitum. Jugular blood was removed anaerobically by venipuncture or from an indwelling catheter. Blood gas content and pH were determined with a radiometer blood gas analyzer. Values from 9 normal calves with 57 determinations were cited as follows: pH 7.41 ± 0.02; PCO_2 45.5 ± 3.1; PO_2 27.5 ± 4.1; buffer base 48.7 ± 2.6; base excess 3.2 ± 2.2. In 5 calves with diarrhea, 26 determinations were made with the following results: pH was 7.23 ± 0.05; PCO_2 37.4 ± 5.7; PO_2 29.0 ± 5.7; buffer base 36.8 ± 4.0; base excess -9.2 ± 4.9. The data indicate, according to Phillips et al., that calves are capable even at a very young age of respiratory compensation in response to a metabolic acidosis. "In severe cases, it seems

that the ability to compensate is lost and the animals die shortly thereafter. The important question of what causes the loss of the ability to compensate remains unanswered. Several possibilities exist. Perhaps the dehydration alone was sufficiently severe to cause death although the cause of death in dehydration is not well established." No figures on hematocrit and so forth were included in this paper. "It is also possible that the increasing hydrogen ion might have had a directly detrimental effect on the heart. To use a more plausible explanation of this sequence of events, is that the continual loss of body fluids results in both intracellular and extracellular dehydration. As sodium and extracellular fluids are lost, water and potassium are drawn from the intracellular spaces. It has been reported that considerable potassium is lost through the intestinal mucosa but a hyperkalemia may still exist although potassium concentration varies during the early stages of diarrhea. The potassium ion is known to be cardioinhibitory. Thus, as its concentration increases in the blood, cardiac function decreases. If this occurred, as cardiac output declined, there would be a decrease in the ability of the calf to continue its respiratory compensation and the PCO_2 and hydrogen ion concentration would increase." "The preceding sequence of events, even if true, only describes secondary changes. The primary occurrence may well be the failure of the intestinal ion transport systems causing the initial electrolyte and water losses. Unfortunately, intestinal transport mechanisms have not been investigated in the calf and limited information is available concerning intestinal volume changes during diarrhea."

Work done by Snell and Ramsey (36) in the study of pulmonary edema as a result of endotoxemia indicate that no observable signs of change in physical condition were noted in dogs following intravenous injection of saline.

However, when endotoxin (.5 mg/kg) was injected, tachypnea, cyanosis of the buccal mucosa and hypotension occurred within 5 minutes. Perivascular lung water content increased considerably and by 30 minutes much of the excess edema fluid had been removed. This, he states, correlates well with the histological picture at 30 min which shows lymphatics containing fluid. The left arterial pressure did not rise sufficiently in open chested dogs to produce pulmonary edema, confirming what has been reported previously by Kuida et al. (30), Border et al. (62). Mean pulmonary artery pressure was changed very little by endotoxemia while cardiac output was extremely depressed, indicating that pulmonary vascular resistance was increased. Kuida et al. state that they believe this increase is due to capillary hydrostatic pressure increase. It is also possible that chemical mediators are released by the endotoxin and cause contraction of vascular smooth muscle in pulmonary venules and arterioles. It is also possible that the pulmonary edema results from altered permeability of the pulmonary capillary membrane and the edema increases interstitial pressure on pulmonary veins and arteries to give increased vascular resistance. Snell et al. state that the pulmonary edema caused in these dogs by endotoxin is not sufficient to cause the syndrome of endotoxin shock. It may, however, represent a significant complication of endotoxemia which is capable of influencing the prognosis in animals more severely affected.

Pandeli et al. studied the relationship of oxygen consumption to hemodynamic changes in experimental endotoxin shock in dogs with an initial intravenous dosage of 2 mg/kg under general anesthesia (60). His findings were an early increase in oxygen consumption that did not parallel the circulatory perimeter. Then a short period of oxygen consumption decrease that was reversed. This initial decrease was thought to be due to an immediate negative

cellular response in metabolism. Then a second gradual decrease in oxygen consumption occurred effecting cellular hypoxia and lactic acid buildup. It was probably believed a latent effect of the original cellular hypoxia and large oxygen debt that occurred then that effected the later O_2 uptake. Thus an irreversible histotoxicity occurred in spite of restored oxygen tensions in circulating fluids, and a progressive decrease in pH considered to be due to reduced PCO_2, catecholamine actions and marked corticoid increases.

Plasma proteins reduced significantly in the latter period (4 hrs) and hemoglobin markedly increased.

There was the usual hyperventilation as seen in dogs following endotoxin administration which accounted for the reduced PCO_2 and early increased PO_2. Some state that lactate excess is inversely proportioned to the endotoxin dose (60).

The following is a graphic compilation of oxyhemoglobin dissociation curves; that will be used to determine hemoglobin oxygen saturation percentage for the calves in this experimental project (44).

THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE.

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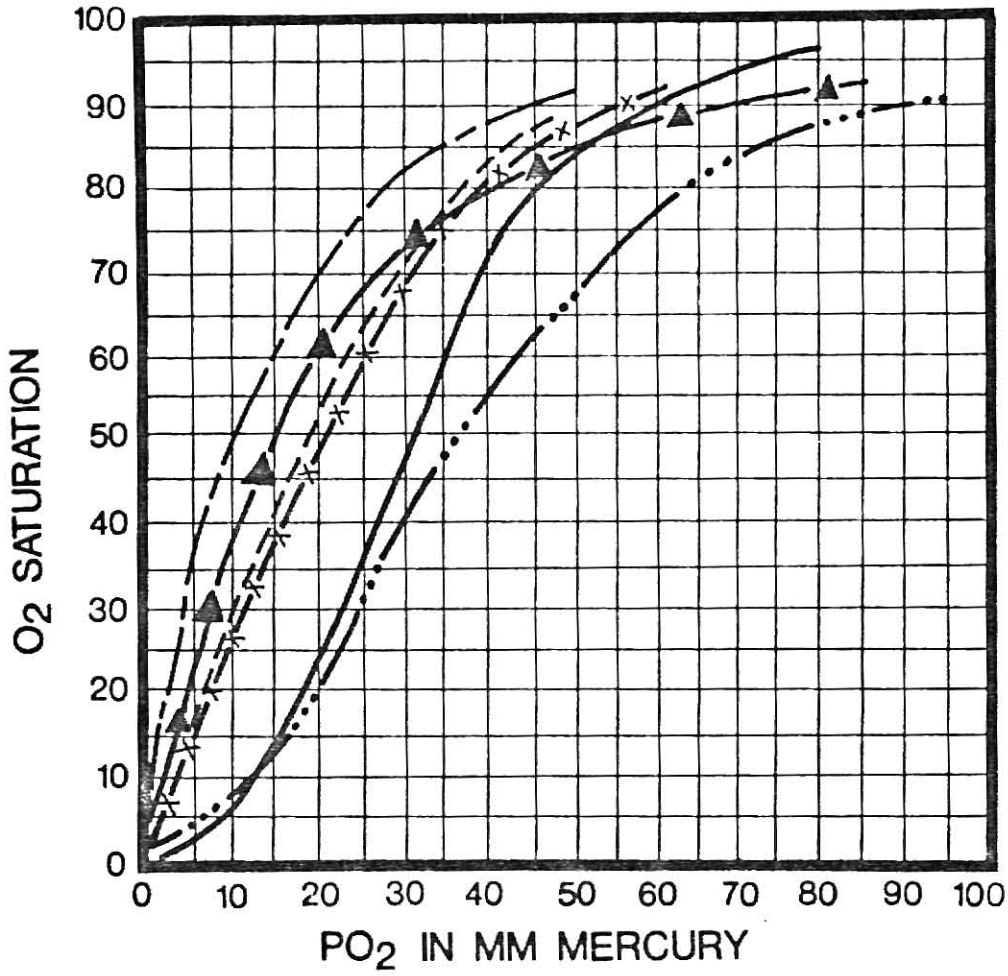

Figure 1. OXYHEMOGLOBIN DISSOCIATION CURVES

——— Adult Bovine: Blood and other body fluids, Bartels, Heinze, et.al. (42)

— — — Normal	calf	Hb.	9.5 gm%	PH, 7.45	9.57 Vol.% oxygen capacity
—▲— Newborn	calf	Hb.	11.8 gm%	PH, 7.38	19.5 Vol.% oxygen capacity
— — — 7-Day	calf	Hb.	8.0 gm%	PH, 7.39	9.50 Vol.% oxygen capacity
—X— Newborn	calf	Hb.	10.7 gm%	PH, 7.41	12.3 Vol.% oxygen capacity
—•••— Normal	calf	Hb.	7.0 gm%	PH, 7.01	12.75 Vol.% oxygen capacity

All calf values: Wass PhD 1961 (44)

MATERIALS AND METHODS

This study of experimental endotoxemia in the newborn calf was made to provide background information for the study of spontaneous colibacillosis in calves. The following observations and evaluations were made on 15 newborn Holstein-Freisian calves: (1) clinical response to a quantitative dose of endotoxin; (2) arterial blood pH, P_aO_2, and P_aCO_2; (3) base excess; (4) total bicarbonate; (5) total carbon dioxide; (6) quantitative and qualitative serum proteins; (7) selected electrolytes; and (8) hemoglobin and packed cell volume.

Calves were taken in consecutive order of birth except when limited by laboratory space. Seven calves were repeatedly studied over the first 10 days of life, control calves (Group I); while 4 calves were given E. coli endotoxin by the intravenous route (Group II); and 4 calves were given E. coli endotoxin by the oral route (Group III). In each instance, endotoxin was given in split dosages to all but three oral challenge calves; at 48 + hours after birth.

The selection of calves for Groups II and III; the two toxin groups; was done by random assignment. Data collected on these two groups during the pretoxin period (48 hours immediately postnatal); was also used as control data for this time period and combined with the Group I data for this time period.

The fifteen male Holstein-Freisian calves were obtained from the Kansas State University dairy herd. They ranged in weight from 36 to 48 kg. Colostrum was hand-fed at the rate of 4% of their body weight immediately following birth. Subsequent feedings were of whole milk fed at the rate of 8% of their birth weight per day, divided into two equal feedings. The calves were housed in individual metabolism stalls.

The method of obtaining arterial blood for long-term serial studies as outlined by Donawick and Braude (33) was utilized with minor modifications.

Pilot cannulations of the abdominal aorta via the saphenous and femoral artery were carried out on anesthetized dogs with the recommended intramedic Polyethylene-lure end catheter (PE-190) with no difficulty. Calves used in this study were cannulated immediately following birth, usually after the feeding of colostrum. They were restrained in left lateral recumbancy on the surgery table, the entire medial aspect of the thigh was clipped and prepared in the usual manner for aseptic surgery. Aseptic surgical approach was made to the saphenous artery of the left leg.

It was quite apparent on catheterization of the first three calves that considerable difficulty was being experienced by attempting to use the PE-190 (Bolab, Inc., Reading, Mass.) catheter. The PE-901C 15" catheter was then used with a little or no problem of cannulation. Blood gas and related analyses on these three calves were not included in this experiment due to problems with the initial blood gas analyzer that was used. A three-way stopcock (Pharmaceal-K75) was cemented with plastic cement into the distal end of the catheter. This was then affixed to the skin by continuation of the nonabsorbable suture used to close the site of cutdown to the artery. This prevented the catheter from slipping out of the saphenous-femoral artery and aorta. The three-way stopcock facilitated the drawing of samples with little or no disturbance of the calf.

Ammonium heparin distilled water was used (1 mg/10 ml H_2O) to maintain patency of the catheter when not in use. The catheter lengths were reduced to 27-32 cm in length depending on the size of the calf.

Blood collections were made as follows: the three-way stopcock was opened and blood allowed to flow freely for 18-25 drops or more. The EDTA sample for CBC was taken first; then either the sample for serum determination or the

blood gas analysis was drawn. Blood gas analysis samples were taken in heparinized glass syringe; analyses of blood gases and pH was begun within 15 seconds of the anaerobic collection; these values were determined at 39°C. Where short periods existed between sample drawing, no heparin solution was injected into the catheter. Initial blood gas analysis was run no sooner than one hour following catheterization.

Initial whole blood and serum samples were taken by jugular venopuncture prior to colostrum feedings and arterial cannulation.

Blood gas analyses during the first 48 hours of life were run at approximately 12-hour intervals. For the remainder of the experiment the control or Group I calves were sampled at 24-hour intervals. The calves; following endotoxin challenge (Groups II and III); were sampled as often as time allowed and clinical conditions indicated. Blood gas and pH determinations were run on the ultra-micro pH/blood gas analyzer model 113-S1 (Instrumentation Laboratory, Inc., 9 Galen St., Watertown, Mass.).

Duplicate determinations were made on each sample of whole blood. The pH meter was standardized prior to all series of determinations using commercially prepared solutions. P_aO_2 was standardized immediately prior to determination of the unknown by use of atmospheric air. P_aCO_2 was also standaridized immediately prior to determinations by the use of standard calibrated P_aCO_2 gases. Standardizing checks of blood gases and pH meter was carried out frequently during intensive sampling periods.

Line charts for temperature and pH correction of blood gas tension were used (39, 42, 45). Oxyhemoglobin dissociation curve graphs in relation to pH were used to determine percent of hemoglobin oxygen saturations (45, 43). The blood acid-base alignment nomogram, according to Siggard-Anderson (42), was

used for determination of plasma bicarbonate, total Co_2 content and base excess. Rosenthal's (42) factor of 0.0147 pH units per degree of difference in temperature was used to adjust pH to body temperature as measured with a clinical rectal thermometer. Respiratory and heart rates were recorded immediately following or during the blood sample collection period. Packed cell volume (PCV) was determined by the microhematocrit method and hemoglobin was determined by the cyanmethemoglobin spectrophotometer method, both being run from the CBC sample.

Serum electrolyte determinations were made by use of the flame photometer Model 4-7006 (National Instrument Laboratories, Inc., Rockville, Md.); the initial 32 samples were run on Coleman Flame Photometer Model 21*. Total serum protein determinations were made by the method of Biuret and the quantitative, qualitative determinations were done by strip electrophoresis using Gelman Procedures Techniques and Apparatus with the power unit Model 8321; Sepraphore III, cellulose polyacetate electrophoresis strips (Catalog No. 5100) were used; the buffer solution had ionic strength of 0.05 and a pH of 8.6. Voltage was adjusted at 275 and the time interval was 60 minutes with the amperage running at 1.0 milliamp per strip.

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*Appendix, page 222.

Dosage chart for E. coli endotoxin challenge calves.

Group	Calf	Route of Administration	Time (Age In Hours) Dose	Total Dosage	mg/Kg Per Initial Wt
II	207	Intravenous	T^1-48.0-35mg		1.5
			T^2-50.0-35mg	70mg	
	209	Intravenous	T^1-48.2-15mg		
			T^2-48.9-15mg		
			T^3-50.9-15mg		
			T^4-52.1-15mg	60mg	1.5
	210	Intravenous	T^1-48.1-20.1mg		
			T^2-49.8-20.1mg		
			T^3-50.2-20.1mg		
			T^4-52.0-48.8mg	109.1mg	1.5
	216	Intravenous	T^1-48.0-15.0mg		
			T^2-49.8-15.0mg	30.0mg	0.81
III	313	Per os	T^1-48.0-70.0mg		
			T^2-96.2-218.0mg	288.2mg	9.0
	314	Per os	T^1-48.0-180.0mg	180.0mg	3.42
	315	Per os	T^1-48.0-260.0mg	260.0mg	5.7
	317	Per os	T^1-48.1-225.0mg	225.0mg	6.8

RESULTS

The results of this experimental work will be presented as follows:

Group I Control Calves

Group II Intravenous Endotoxin Challenge Calves

Group III Oral Endotoxin Challenge Calves

Group I Control Calves

Figures 2-6
Tables 5-12, Pages 156-163

Mean P_aO_2 at 1 hr was 75.9 mmHg; the mean value rose the first 12 hours of age to 78.2 mmHg and decreased the second 12 hour period to 71.4 mmHg. This was followed by an increase to 82.7 mmHg between 36 and 96 hours of age. From then till 240 hours of age P_aO_2 stabilized at 77.8 $\pm$ 3.0 mmHg.

P_aCO_2 had a mean 1 hour value of 43.04 mmHg; at 12 hours of age it was 39.6 mmHg and peaked at 18 hours of age at 48.52 mmHg. It decreased and stabilized at 48 hours of age at 40.1 $\pm$ 3.0 mmHg; with a high of 43.94 mmHg at 144 hours of age for the 48 to 240 hour time period.

Control calves 1 hour mean pH was 7.37 and there was an abrupt rise to 7.46 at 18 hours of age. It stabilized at 18 hours of age at 7.46 $\pm$ 0.02.

Base excess; total bicarbonate and total carbon dioxide mean values at 1 hour of age were: 0.94 mEq/L; 23.7 mEq/L; and 24.7 mm/L respectively. There was a sharp rise in all three to peaks at 24 hours of base excess 5.37 mEq/L; HCO_3^- 30.1 mEq/L and total Co_2 31.28 mm/L. At 72 hours of age there were lows of base excess 2.94 mEq/L, HCO_3^- 25.84 mEq/L and total Co_2 26.94 mm/L; this was followed by a monophasic curve with a peak at 144 hours of age. At 192 hours of

age they stabilized at: base excess 2.7 ± 0.4 mEq/L; HCO_3^- 26.3 ± 0.3 mEq/L and total Co_2 27.3 ± 0.3 mm/L.

Hemoglobin oxygen saturation (42, 44) 1 hour mean value was 92.0%. It decreased to 90.0% and 91.0% at 18 and 24 hours of age respectively. It rose to highs of 93% and 94% at 48 and 72 hours respectively and then stabilized at 91.5 ± 1.5% through 240 hours of age.

Temperature mean values were 38.6 ± 0.4°C between 1 and 36 hours of age and 39.4 ± 0.2°C between 48 and 240 hours of age.

Hemoglobin and packed cell volume in control calves at 1 hour of age were 10.4 Gms/100 ml and 33.3 volumes % respectively. Both showed a fluctuating decline: Hb to a value of 8.8 Gms/100 ml and P.C.V. value of 27.4 volumes % at 96 hours of age. From 96 hours of age until 240 hours they stabilized at a Hb value of 8.1 ± 0.2 Gms/100 ml and a P.C.V. value of 26.5 ± volumes %.

Serum sodium and potassium mean values* at 1 hour of age were 136.9 mEq/L and 6.9 mEq/L, respectively. Sodium abruptly rose to peaks of 146.1 mEq/L and 143.3 mEq/L at 6 and 18 hours of age, respectively. It then stabilized at 135.5 ± 1.6 mEq/L between 24 and 240 hours of age. Potassium fluctuated with values of 6.9 mEq/L at 1 hour, 7.28 mEq/L at 96 hours and 8.4 mEq/L at 168 hours of age. All other values were within the mean range of 6.3 ± .5 mEq/L.

Heart rate showed a gradual decrease from a 6 hour mean of 138/min to 121/min at 86 hours of age and stabilized at a rate of 100 to 120/min. Respiratory rate had a 6 hour mean value of 57/min that stabilized at a rate between 52 and 46/min thereafter.

Serum protein mean values showed very early rapid changes. Total protein

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*Appendix, page 222.

showed an immediate decline from a 1 hour value of 6.05 Gms/100 ml to a 6 hour value of 5.43 Gms/100 ml. This rose to 6.67 Gms/100 ml at 12 hours and 8.86 Gms/100 ml at 18 hours. This 3.43 Gms/100 ml increase can be divided as such: albumin 1.06 Gm; alpha 1 0.0 Gm; alpha 2 0.49 Gm; beta 1 0.5 Gm; beta 2 0.8 Gm and gamma 1.9 Gm. After 18 hours of age there was considerable instability in total protein until 168 hours of age when it stabilized at 8.2 $\pm$ 0.2 Gms/100 ml. Albumin elevations and depressions were identical to total protein changes in quantity and time. Gamma globulins exhibited a more stable rise and showed more stability throughout the 240 hour period then did total proteins. They increased from 1 hour level of 1.07 Gms/100 ml to a 36 hour peak of 2.73 Gms/100 ml with a slight decline at 24 hours of age. They stabilized at 2.2 $\pm$ 0.15 Gms/100 ml at 120 hours of age, with a slightly higher value of 2.48 Gms/100 ml at 144 hours of age.

Individual alpha and beta fractions showed considerable changes. Alpha 1 decreased abruptly from a 1.0 hour mean value of 0.38 Gms/100 ml to 0.05 Gms/100 ml at 48 hours of age. After 48 hours it markedly increased to 0.21 Gms/100 ml at 120 hours of life and stabilized between 0.11 and 0.19 Gms/100 ml through 240 hours of age. Alpha 2 showed a fluctuating rise to a peak of 1.28 Gms/100 ml at 240 hours of age. Beta 1 showed an identical pattern in proportion and time to alpha 2 with 1 hour and 240 hour values of 0.6 Gms/100 ml and 0.9 Gms/100 ml, respectively. Beta 2 value changes were .2 to .4 Gms/100 ml higher than beta 1 during the first 24 hours. After 24 hours the gram difference between beta 1 and beta 2 increased to 0.5 Gms/100 ml and persisted.

THIS BOOK CONTAINS NUMEROUS PAGES WITH ILLEGIBLE PAGE NUMBERS THAT ARE CUT OFF, MISSING OR OF POOR QUALITY TEXT.

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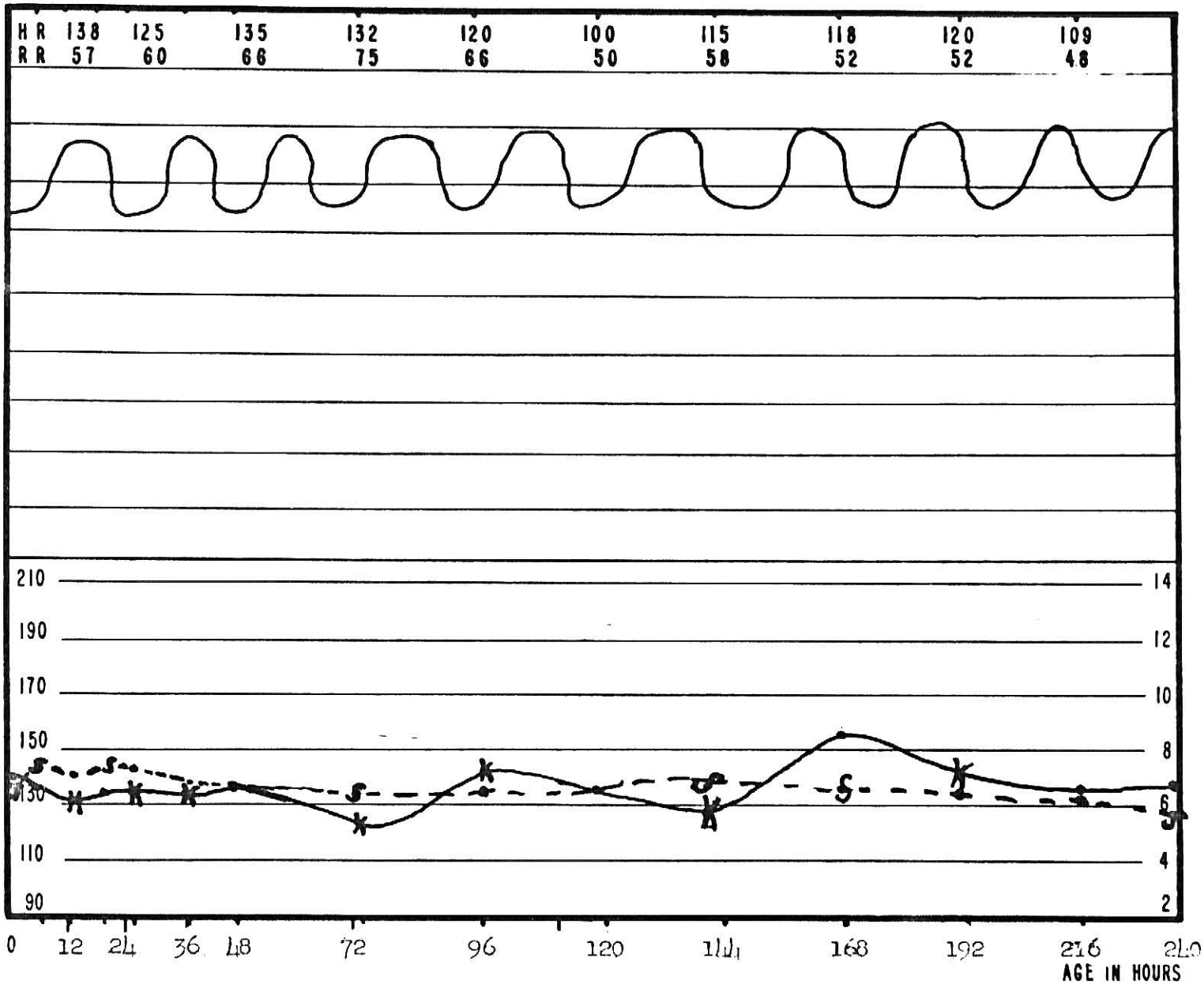

FIG. 2. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP I, CONTROLS SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 9, page 160 and Table 12, page 163.)

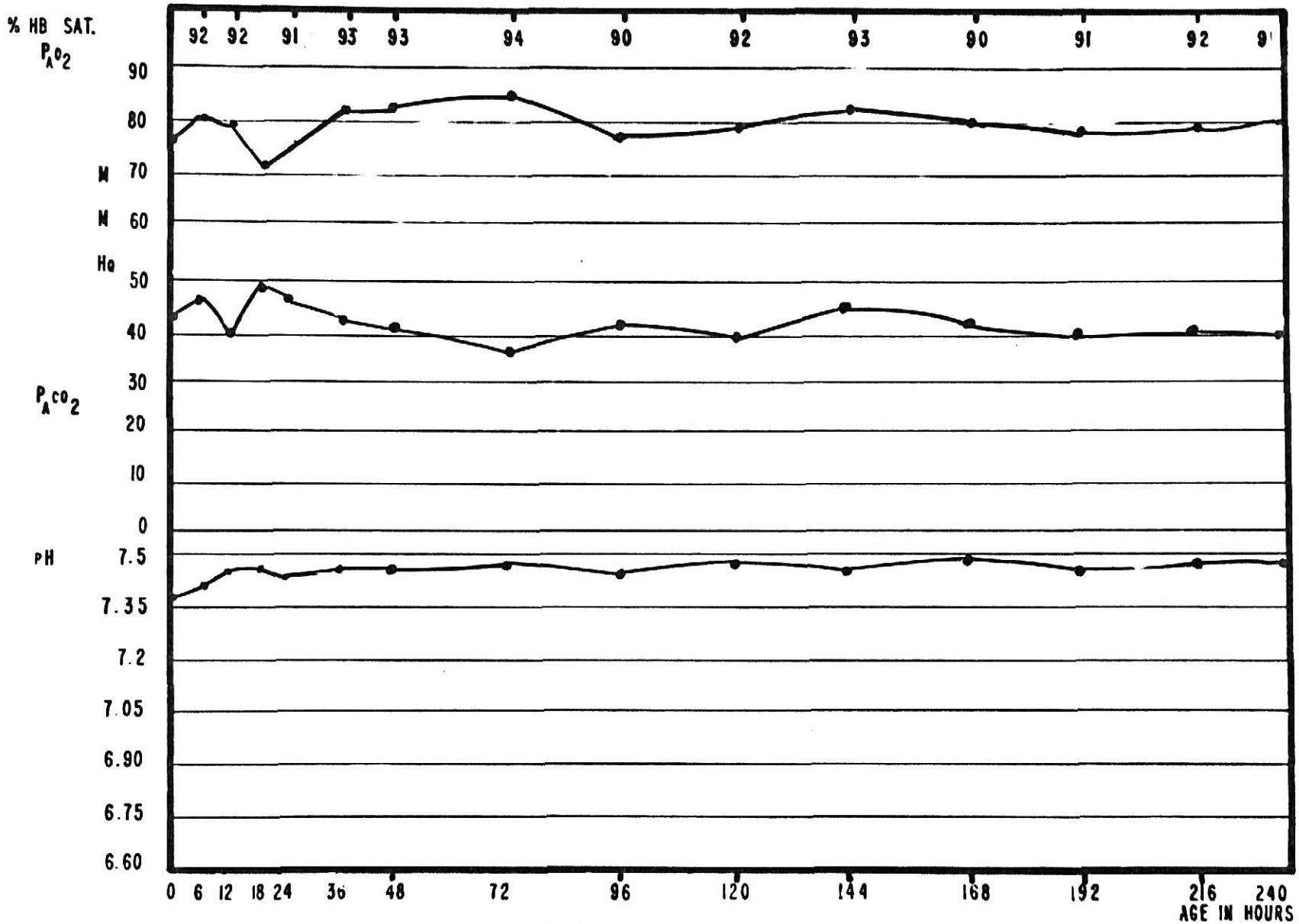

FIG. 3. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP I , CONTROLS WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 5, page 156 and Table 7, page 158.)

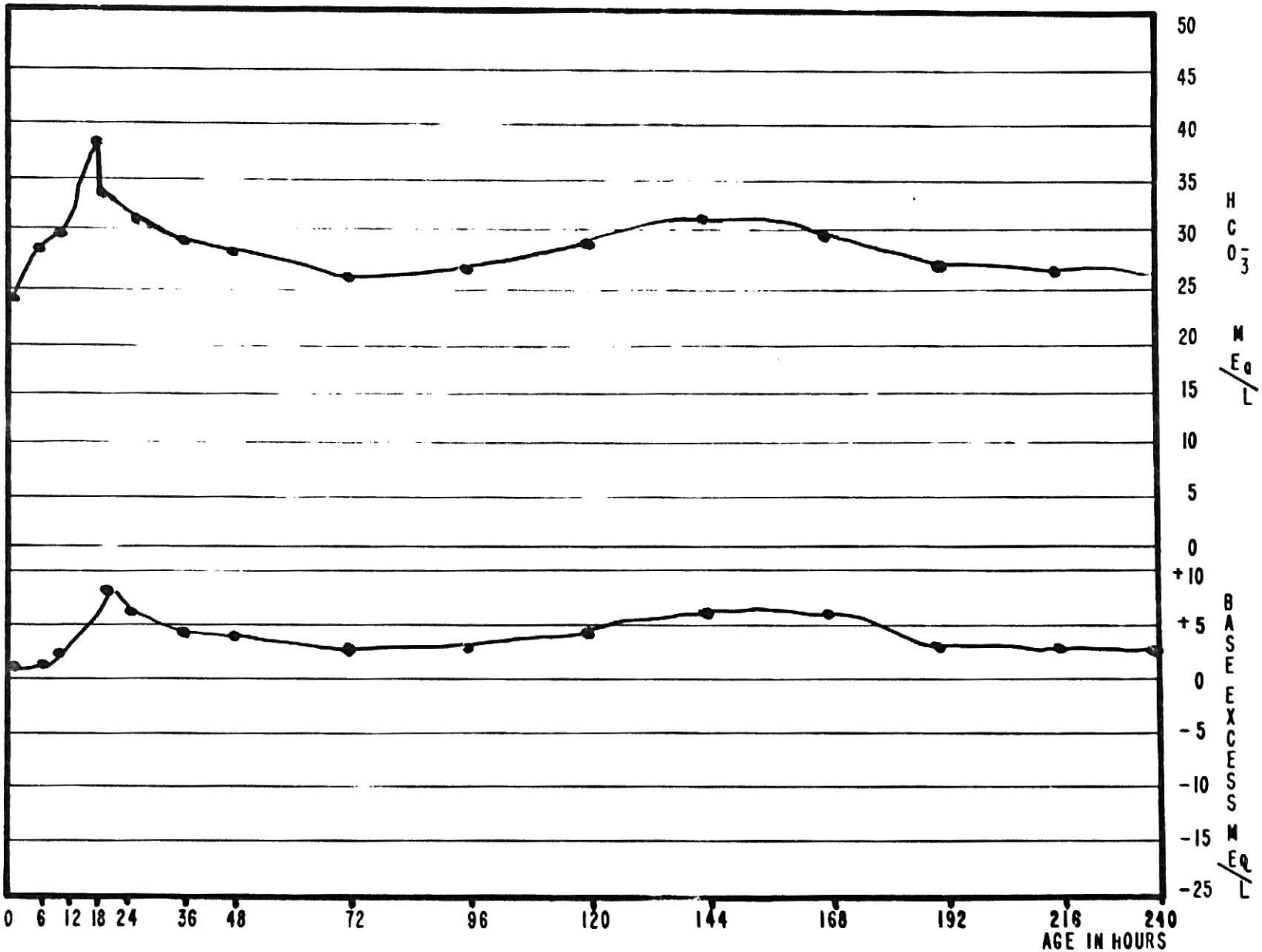

FIG. 4. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP I, CONTROLS
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 6, page 157.)

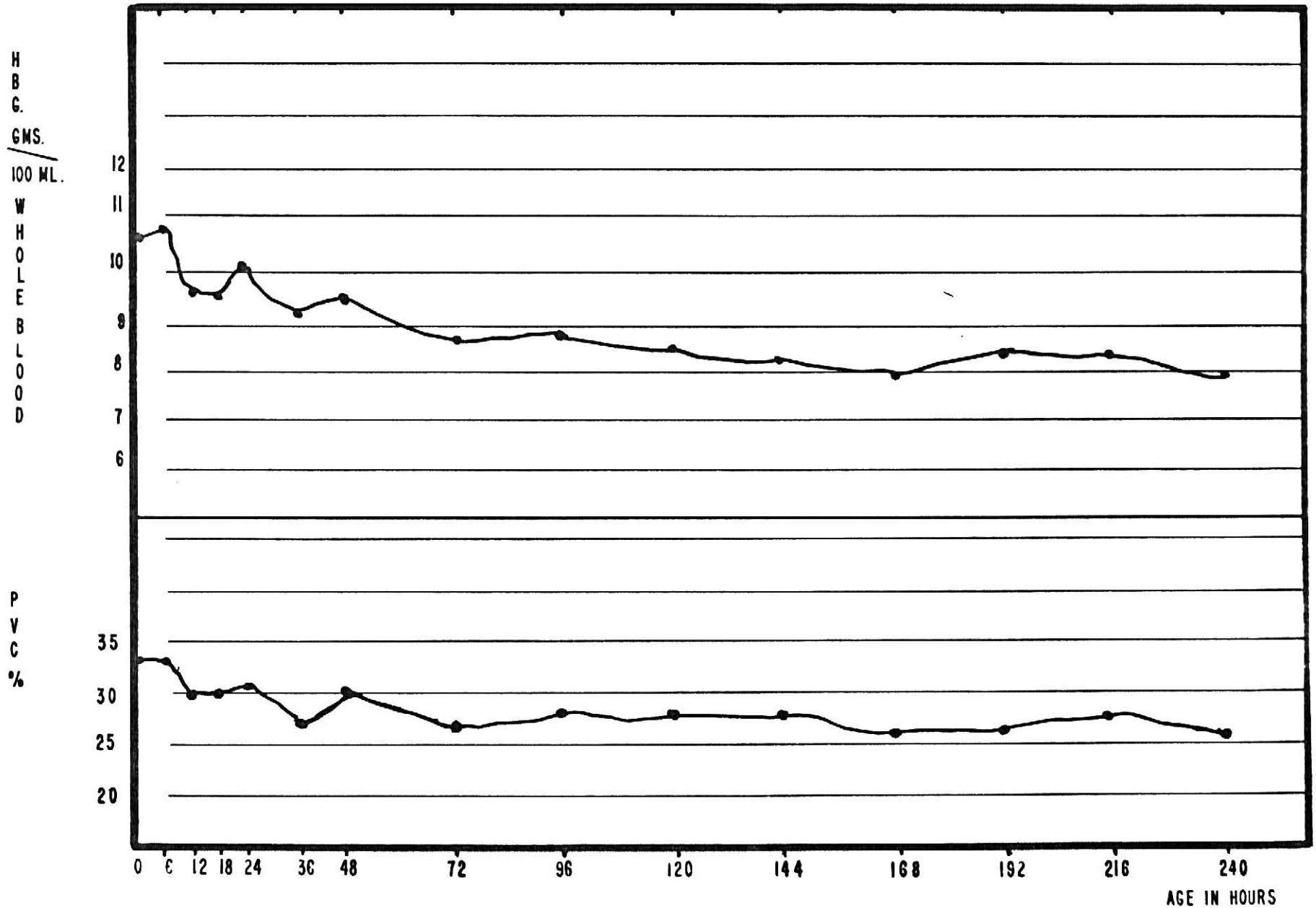

FIG. 5. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP I, CONTROLS HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 8, page 159.)

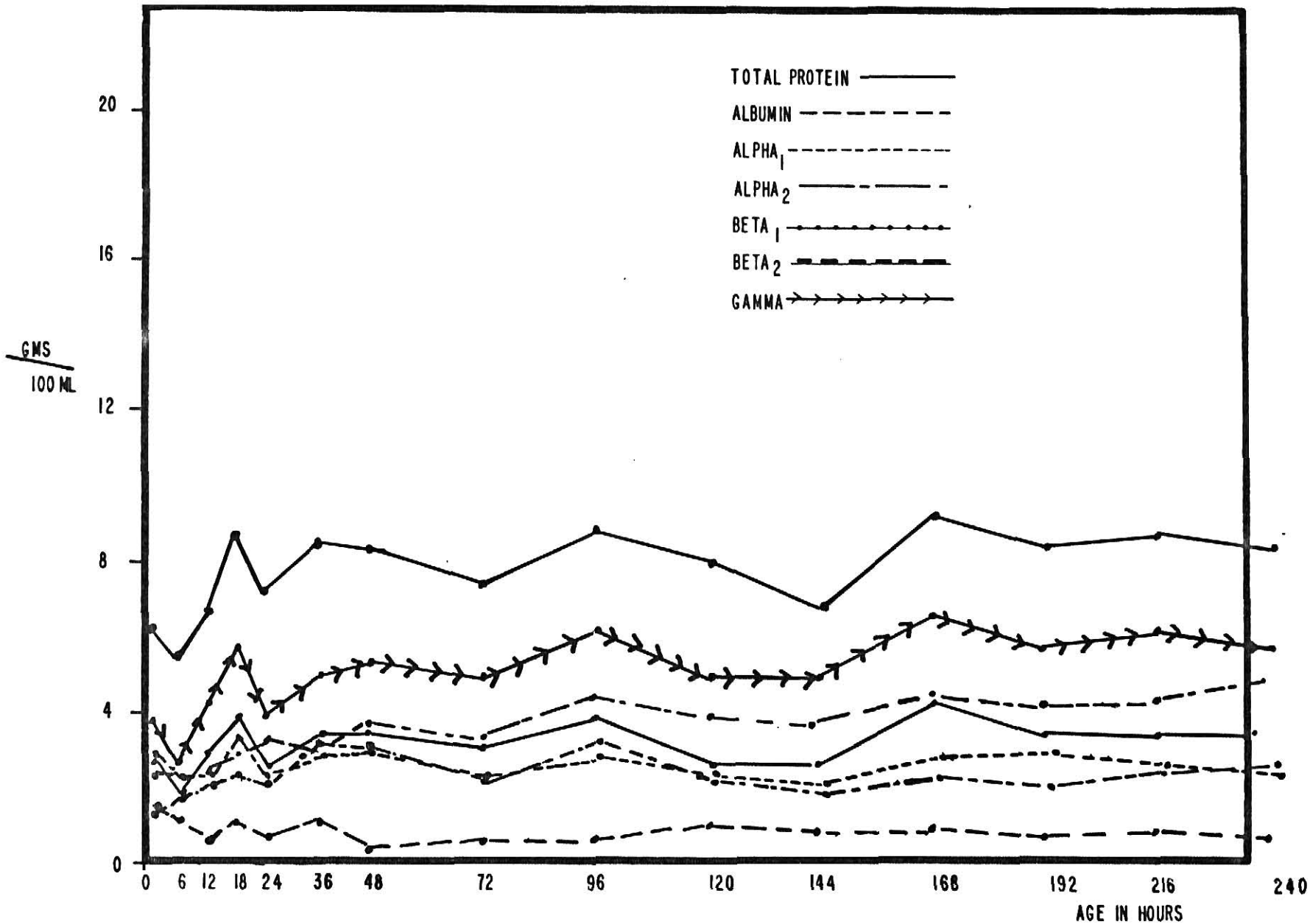

FIG. 6. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP I , CONTROLS . (See Table 10-11, pages 161-162).

Group II Intravenous Endotoxin Challenge Calves

Figures 7-26
Tables 13-36, Pages 164-197

Intravenous endotoxin challenge calves were calves 207, 209, 210 and 216. Their results will be presented individually.

Calf No. 207

Figures 7-11
Tables 13-18, Pages 164-169

Blood gases and respiratory pattern in calf 207 rose to 97.0 mmHg at 48 hours of age. Following endotoxin challenge (T^1) at 48 hours of age P_aO_2 decreased to 41.8 mmHg in 12 minutes (T^1 + 12 min). This accompanied a rise in P_aCO_2 from a prechallenge value of 37.1 mmHg to 53.8 mmHg at T^1 + 12 min. The calf was recumbent within 5 minutes. Respiratory depression was evident in that there was a reduced tidal volume and a reduction of respiratory rate. P_aO_2 continued to decline: T^1 + 30 min 28.2 mmHg; T^1 + 72 min 16.2 mmHg. P_aCO_2 rose sharply during this period: T^1 + 20 min 69.5 mmHg; T^1 + 30 min 69.5 mmHg; T^1 + 72 min 71.1 mmHg. There were three periods of hyperventilation; 5 and 6 cycles each of expiration and inspiration; between 49 and 50 hours of age. This series of respirations corresponded with an increase in P_aO_2: T^1 + 102 min 28.1 mmHg; T^1 + 108 min 43.4 mmHg. At 50.0 hours of age (T^1 + 120 min) the second endotoxin challenge (T^2) was administered.

The calf became markedly depressed and a very shallow panting type of respiration occurred post T^2. P_aO_2 declined to 20.5 mmHg (T^2 + 12 min) and 17.5 mmHg (T^2 + 30 min). During this time interval P_aCO_2 rose to 62.7 mmHg (T^2 + 12 min) and 74.8 mmHg (T^2 + 20 min).

The pH values of calf 207 declined gradually post challenge (T^1); stabilized then rose slightly during the hyperventilatory period and declined rapidly post T^2 to a value of 6.78 just prior to death at 50.5 hours of age.

Base excess, bicarbonate and total carbon dioxide in calf 207 were 56 mEq/L, 38.0 mEq/L and 29 mm/L at prechallenge (48.0 hours). There was an exact paralleling of pH decline, base excess reduction and total bicarbonate reduction following endotoxin challenge, with one exception; when P_aO_2 rose, P_aCO_2 declined and pH rose slightly prior to T^2; the bicarbonate and base excess showed a slight delayed elevation. At T^1 + 12 min base excess was -0.6 mEq/L. Prior to death at 50.5 hours of age base excess was -25.0 mEq/L, total HCO_3^- 10.0 mEq/L and total Co_2 was 11.5 mm/L (T^1 + 2.5 hours, T^2 + 0.5 hours).

The calf's temperature was very stable through the experimental period, showing only a 0.1°C decrease between 48.5 and 49.7 hours. Hemoglobin oxygen saturation remained above 50% except following T^2; and between the hours of T^1 + 30 min and T^1 + 112 min when lows of 32.0, 20.0 and 15.0% were determined.

Hemoglobin and packed cell volume showed no changes from prechallenge values of 9.0 Gms/100 ml and 26 volumes %, respectively.

Sodium and potassium prechallenge (48.0 hour) values were similar to control means. Following challenge T^1 serum sodium declined to 103.2 mEq/L (T^1 + 12 min) from 143.6 mEq/L at 36 hours of age. At T^1 + 72 min it was 119.8 mEq/L and 129.2 mEq/L at T^1 + 102 min. Following the second endotoxin challenge (T^2) it was 137.5 mEq/L. Potassium values showed a fluctuating pattern post challenge.

Changes in heart rate and respiratory rate and clinical observations in calf 207 were marked following endotoxin challenge, at T^1 + 3.0 min there was an abrupt reduction in respiratory rate to 10/min and heart rate reduced to 40/min. Muscle tone was severely reduced, with ears dropped and head lowered. Minute

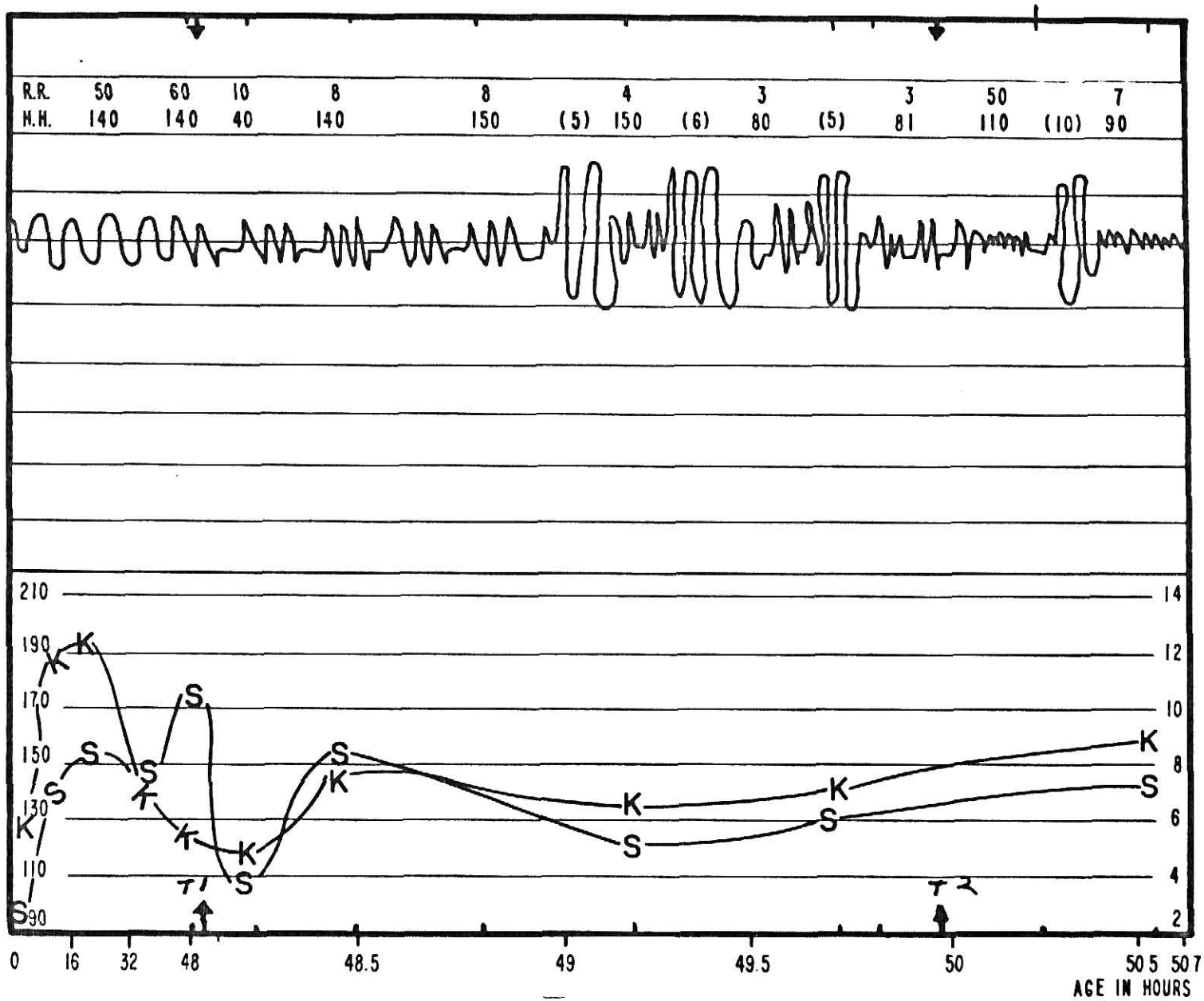

FIG. 7. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 207
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 17, page 168.)

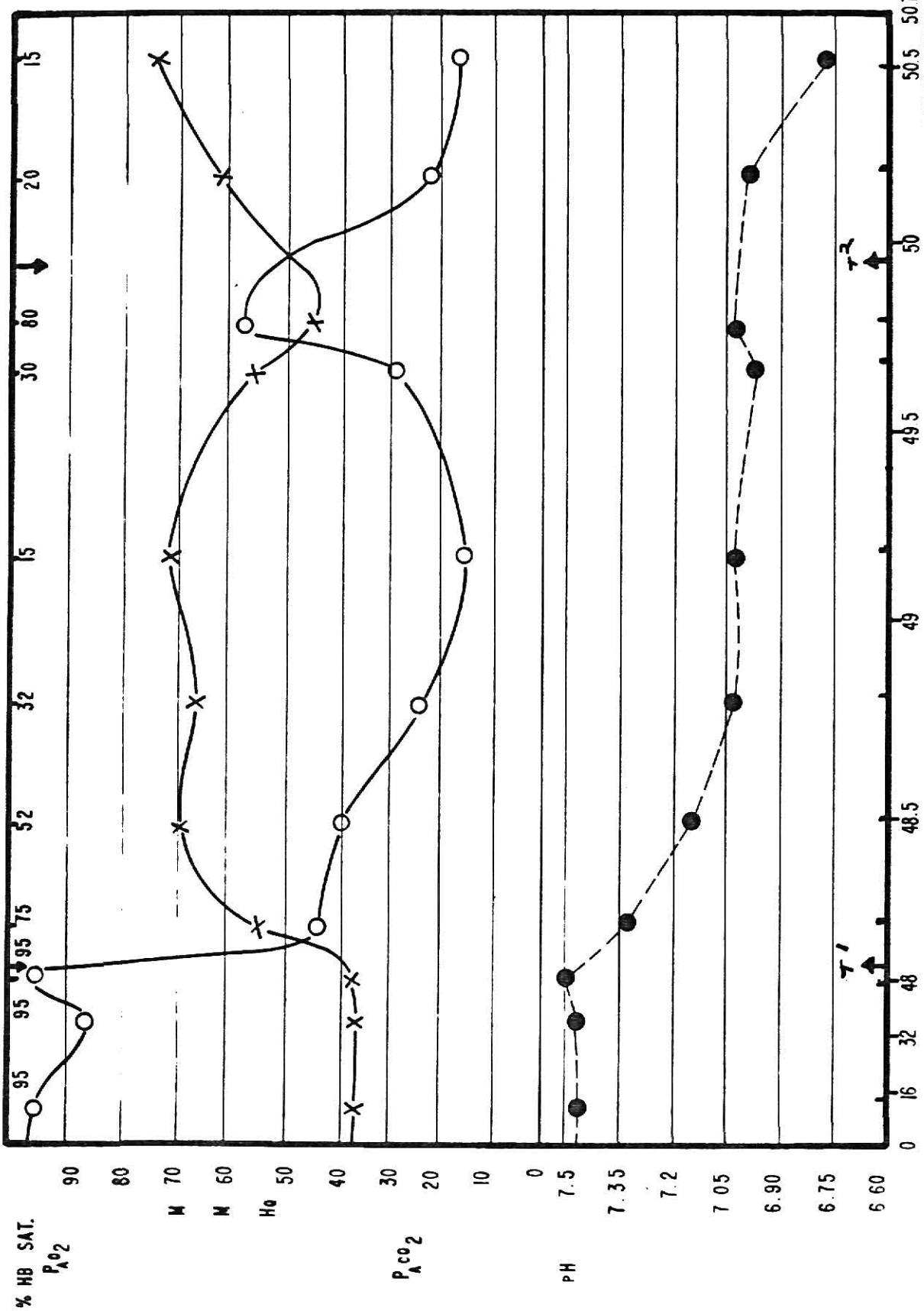

FIG. 8. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 207
WHOLE BLOOD $P_A O_2$, $P_A CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 13, page 164 and Table 14, page 166.)

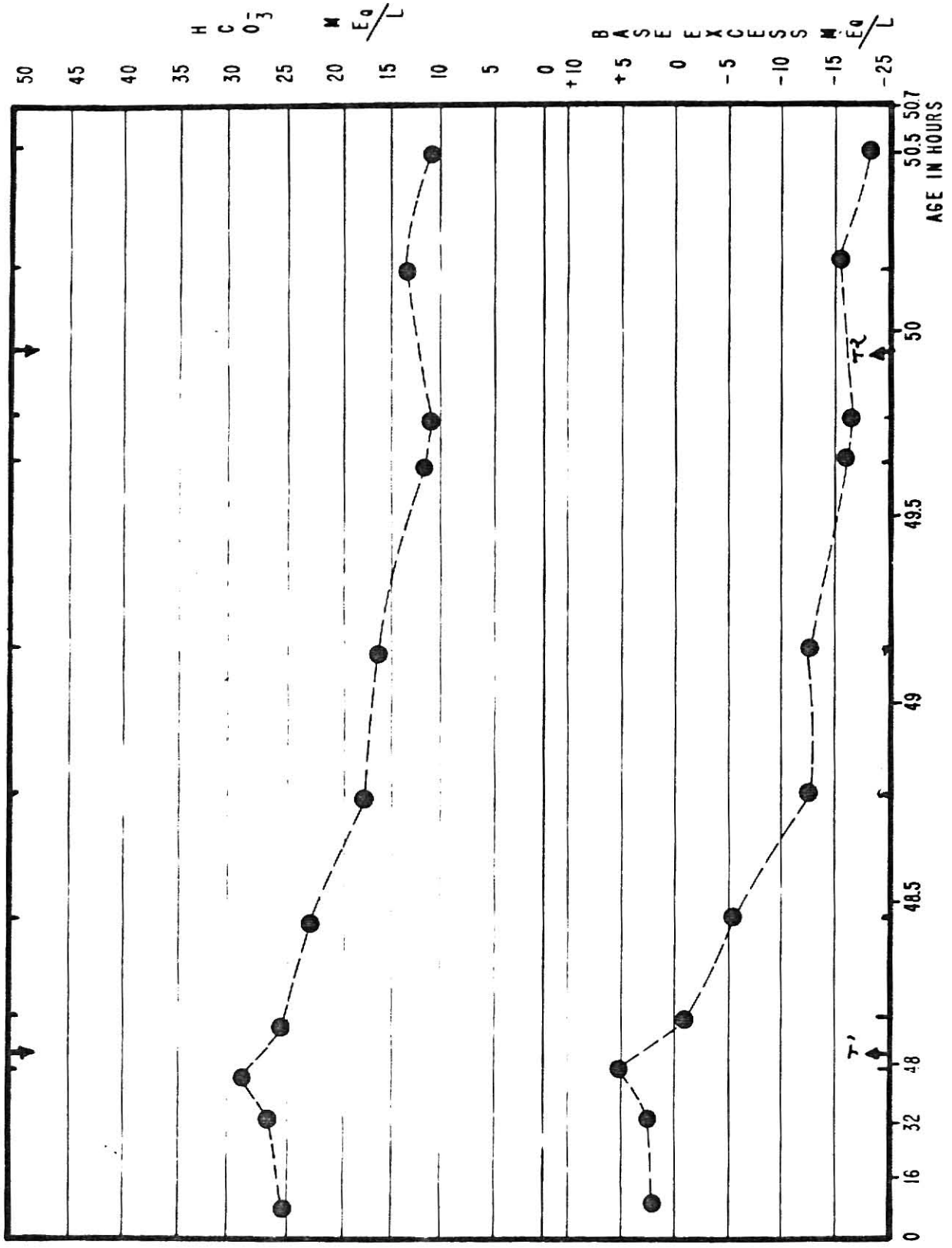

FIG. 9. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 207
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 11, page 165.)

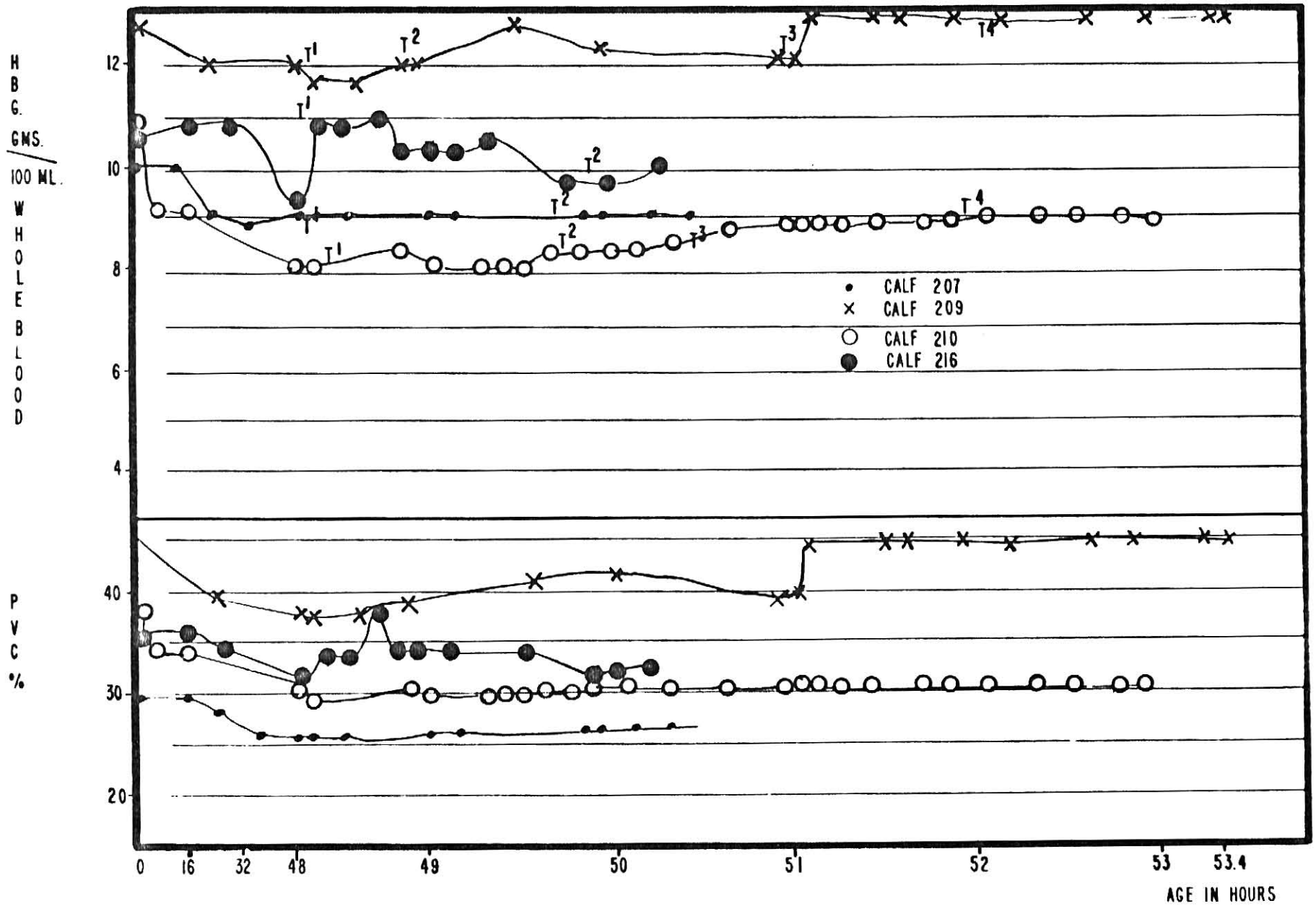

FIG. 10. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 207,209,210,216
GROUP II HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 16, page 167.)

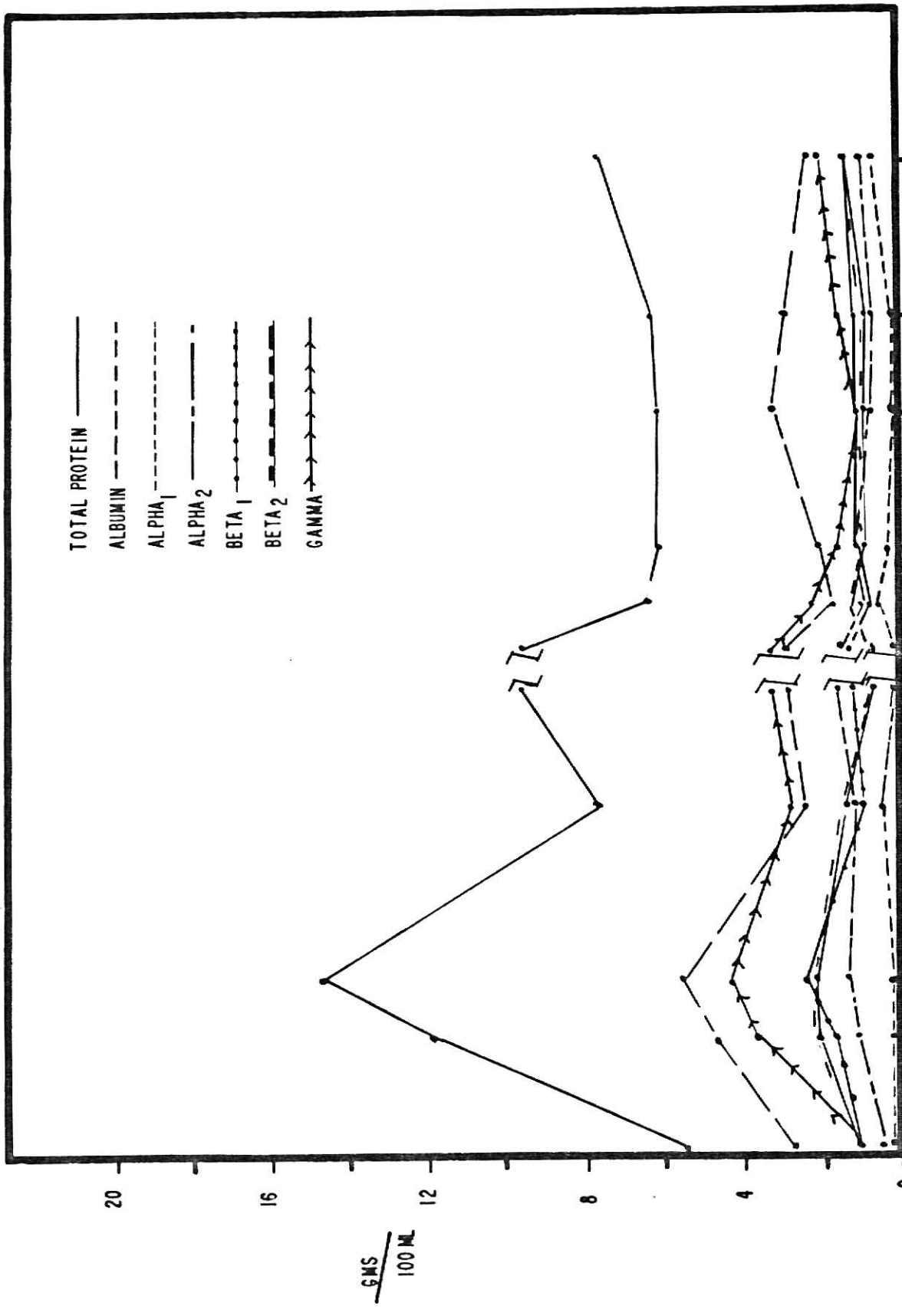

FIG. 11. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP II, CALF 207.(SEE TABLE 18, page 169.)

volume certainly was reduced as a result of the reduced rate and depth of respirations. Heart sounds appeared strong but were infrequent at 48.2 hours (T^1 + 12 min) this quickly recovered and at 48.5 hours was 150/min. Following T^2 the respiratory pattern changed to a more rapid, shallow panting type. There was then a reduced respiratory rate but a continued shallow pattern persisted.

At 36 and 48 hours of age, all serum proteins were in close approximation to control mean values. Total protein post challenge showed a decline from a prechallenge value of 9.6 Gms/100 ml to 6.2 Gms/100 ml at T^1 + 12 min and remained at this level until post T^2 when it rose to 7.5 Gms/100 ml. All fractions rose and fell in proportion to the total protein changes. Packed cell volume showed no appreciable changes throughout the experimental period.

Calf No. 209

Figures 12-16
Tables 19-24, Pages 170-180

Blood gases and pH prechallenge blood gas values closely correlated with the control group mean values while pH was slightly higher. Following endotoxin challenge (T^1) there was an immediate decrease in P_aO_2 to 52.0 mmHg at 48.5 hours (T^1 + 18 min) with very little effect on P_aCO_2 (38.5 mmHg). There was a mild elevation in pH (7.52). The respiratory pattern was effected with markedly reduced tidal volume and an extreme increased rate but a partial recovery to normal soon occurred. Hyperventilation occurred at 48.6 hours and at 48.8 hours (T^1 + 26 min), P_aO_2 was 62.9 mmHg, while P_aCO_2 was still unaffected (38.9 mmHg) and pH showed a slight decline to 7.50. Following endotoxin challenge (T^2) P_aO_2 declined to 42.6 mmHg and P_aCO_2 rose to 48.9 mmHg

and pH declined to 7.29 at T^1 + 102 min or T^2 + 42 min. At 50.0 hours hyperventilation occurred and P_aO_2 rose to 55.1 mmHg and P_aCO_2 declined to 35.5 mmHg and pH rose slightly to 7.39.

T^3 was administered at 50.9 hours of age. P_aO_2 declined sharply to 29.7 mmHg at 51.0 hours (T^3 + 6 min) and continued to decline--21.7 mmHg at T^3 + 30 min. P_aCO_2 was stable at 34.7 mmHg until 51.1 hours when it decreased to 25.1 mmHg; this being during a period of hyperventilation and P_aO_2 began to rise to a level of 43.6 at 51.8 hours. P_aCO_2 rose slightly to 31.5 mmHg at 51.8 hours but was still below prechallenge levels; pH had rapidly declined to 7.22 at 52.0 hours of age (T^1 + 3.8 hours, T^3 + 1.1 hours).

Endotoxin challenge (T^4) given at 52.1 hours affected an abrupt decline in P_aO_2; elevation in P_aCO_2 and decline in pH; this during a concurrent period of hyperventilation. These trends continued unabated and at T^4 + 78 min (53.4 hours) P_aO_2 was 23.3 mmHg, P_aCO_2 was 81.5 mmHg and pH was 6.51 and death occurred.

Prechallenge bicarbonate, base excess and total carbon dioxide values in calf 209 were slightly higher than control mean values. Following endotoxin challenge (T^1) these values were all increased as was pH at post T^1 + 18 min and 36 min. Following T^2 a declining trend occurred but stabilized at T^2 + 60 min (49.9 hours) when base excess was -1.1 mEq/L. pH also stabilized at this time. There was a period of fluctuating stability that continued post T^3 for an elapsed time of 42 min. Base excess then declined sharply and at 52.0 hours was -13.9 mEq/L. Following endotoxin challenge T^4 plasma values declined to lows of base excess: -32.2 mEq/L, HCO_3^- 6.5 mEq/L and total Co_2 7.5 mEq/L at 53.4 hours of age.

Temperature values in calf 209 showed a total increase of 0.5°C following challenge T^1. Temperature declined a total of 1.5°C after challenge T^2 over

the next 2 hours.

Hemoglobin oxygen saturation remained at 50% and above until post T^4 when it declined sharply.

Prechallenge hemoglobin and packed cell volume values in calf 209 were higher than control mean values. Following endotoxin challenge there was a 10% increase in PCV at 51.5 hours (Post T^3). Hemoglobin was increased accordingly.

Serum sodium and potassium values in calf 209 were approximately equal to control mean values for the prechallenge period. Some potassium values for this calf were discarded for evaluation due to hemolysis*. Post challenge values for potassium were lower than mean control values except the value just prior to death. Post challenge serum sodium declined at 48.8 hours of age (T^1 + 36 min) to 124.4 mEq/L and at 53.4 hours (T^4 + 78 min) it rose to 151.6 mEq/L.

Calf 209 showed a slight increase in serum proteins following intravenous endotoxin challenge at 48.2 hours (T^1). The fractions increasing were albumin, gamma globulin and beta 2. All other fractions declined slightly. At 49.2 all values were generally equivalent to prechallenge levels.

Calf No. 210

Figures 12-16
Tables 25-30, Pages 181-191

At 48 hours of age P_aO_2 was equal to control mean values while P_aCO_2 was slightly lower (34.2 mmHg). Following endotoxin challenge (T^1) P_aO_2 dropped sharply from 77.2 mmHg to 46.6 mmHg at T^1 + 36 min, this was coupled with a pH drop to 7.38 from 7.48 at 48.0 hours of age, while P_aCO_2 rose to 46.5 mmHg.

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*Appendix, page 222.

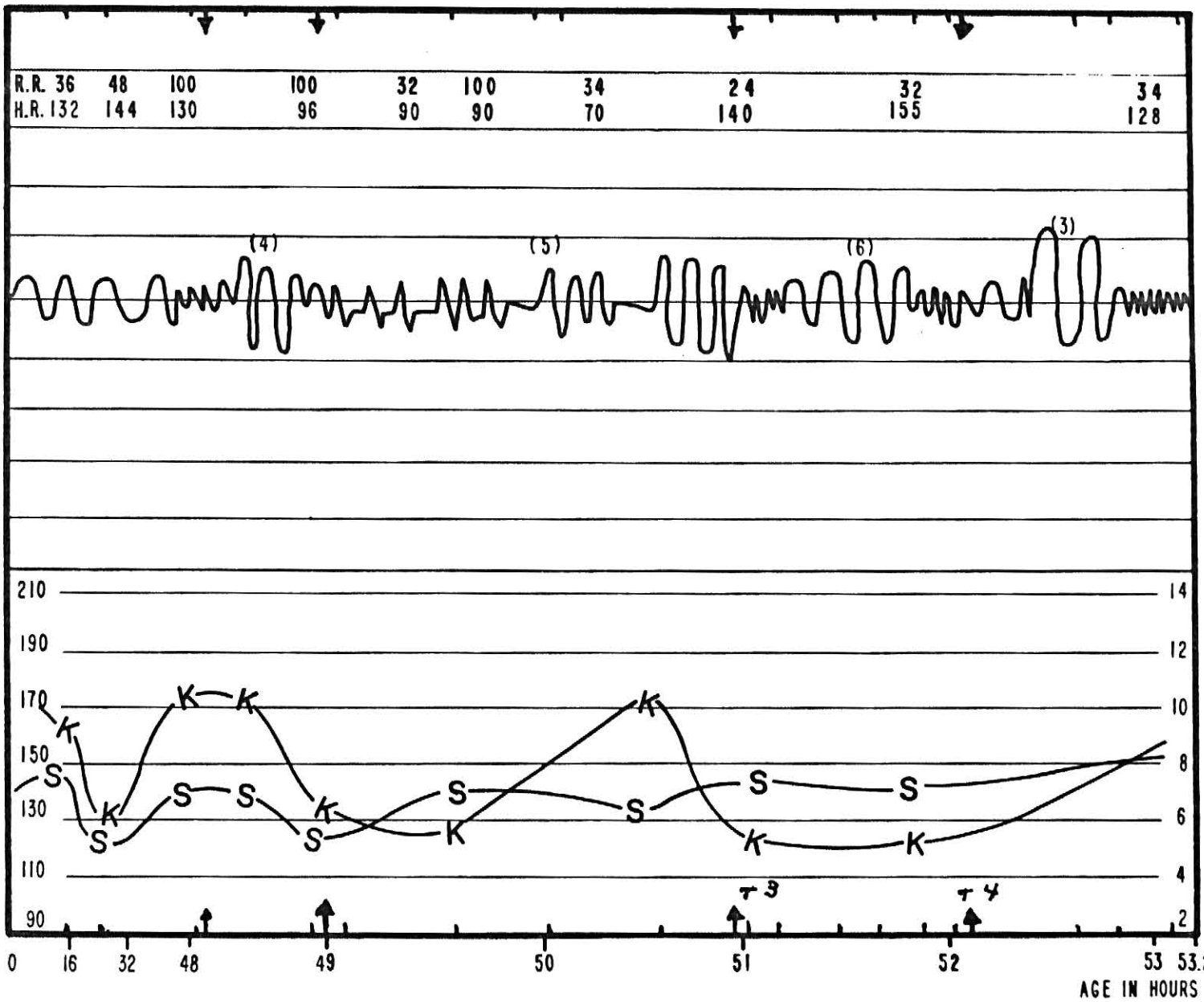

FIG. 12. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 209
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 23, page 178.)

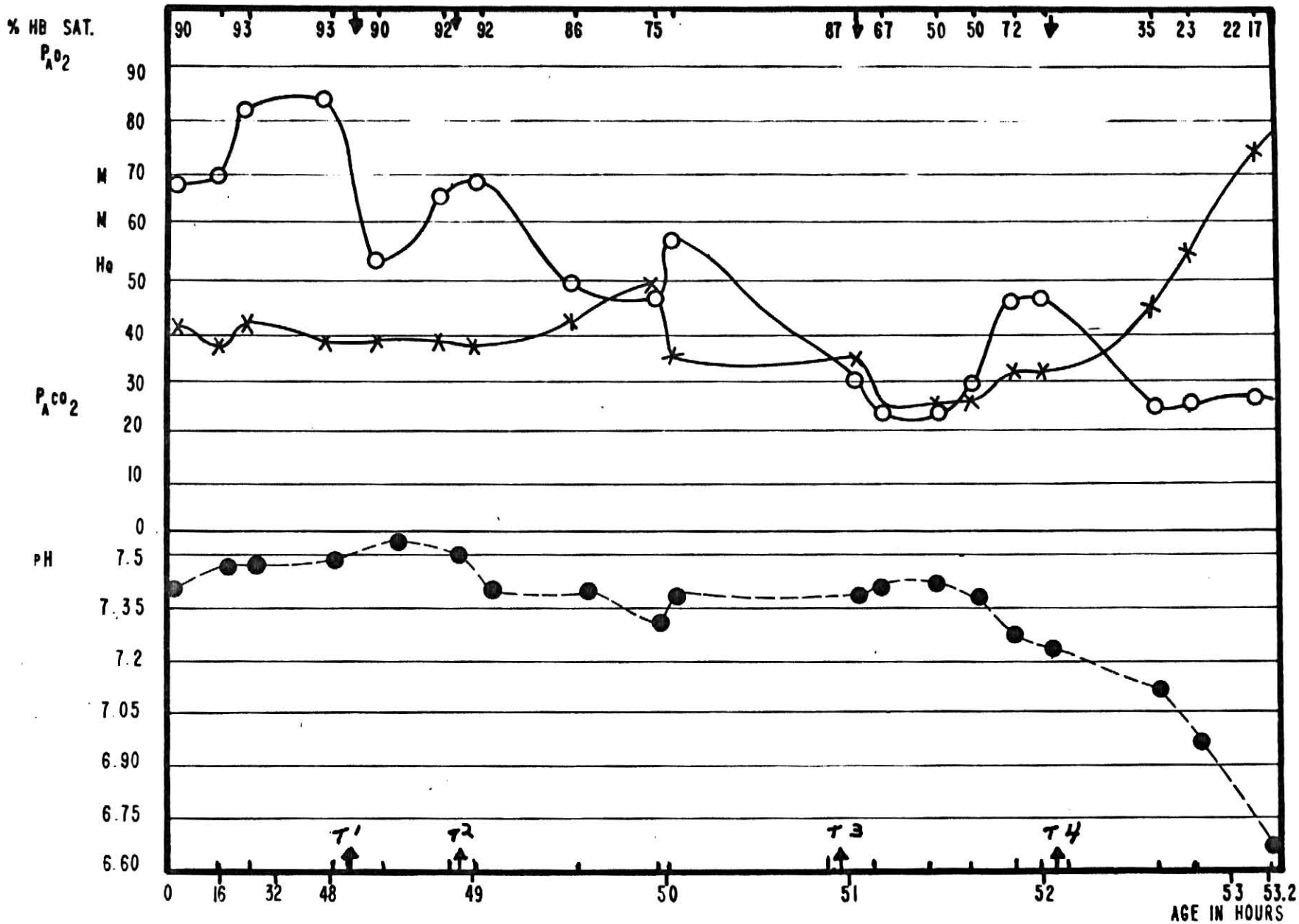

FIG. 13. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 209
WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 19, page 170 and Table 21, page 174.)

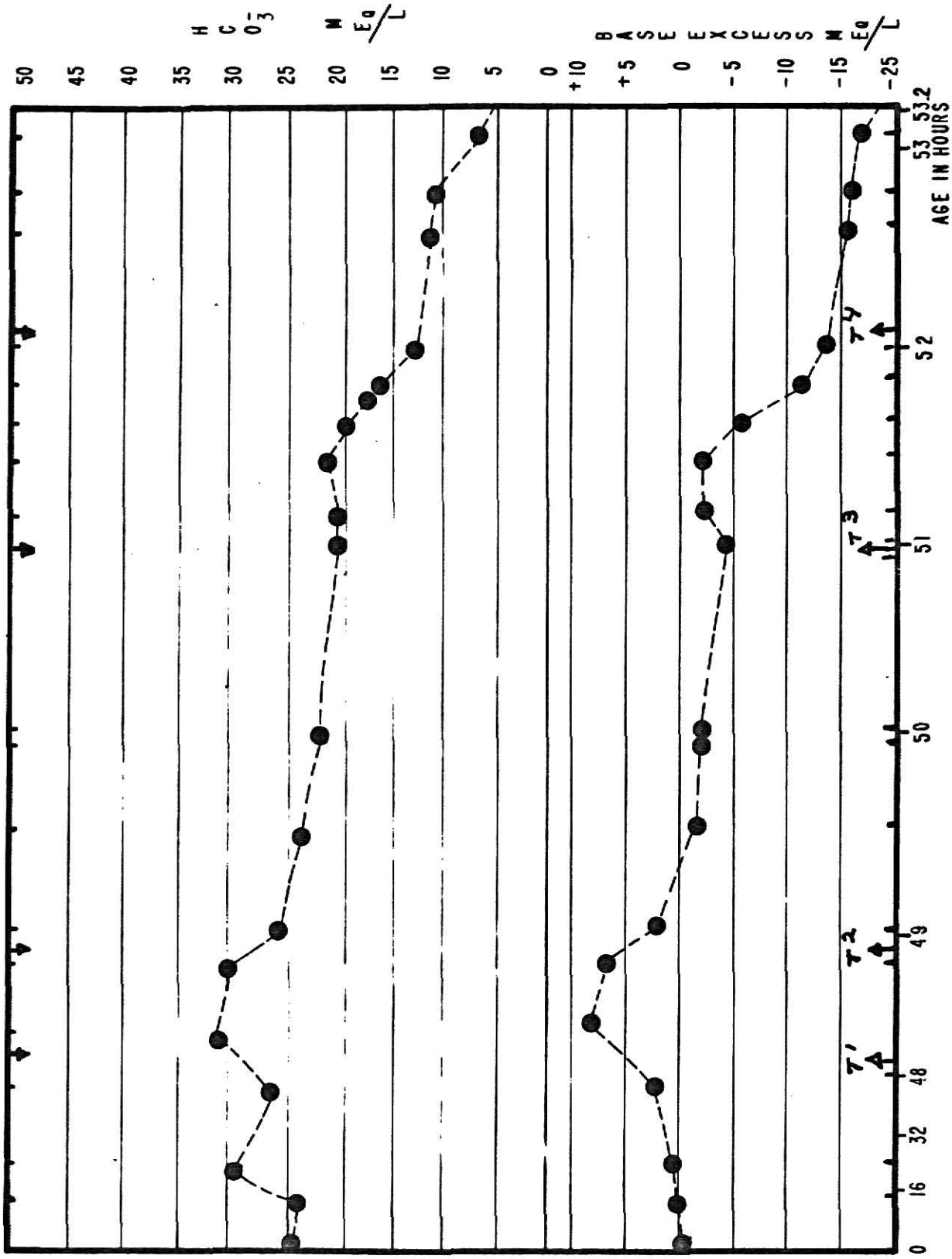

FIG. 11. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 209
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 20, page 172.)

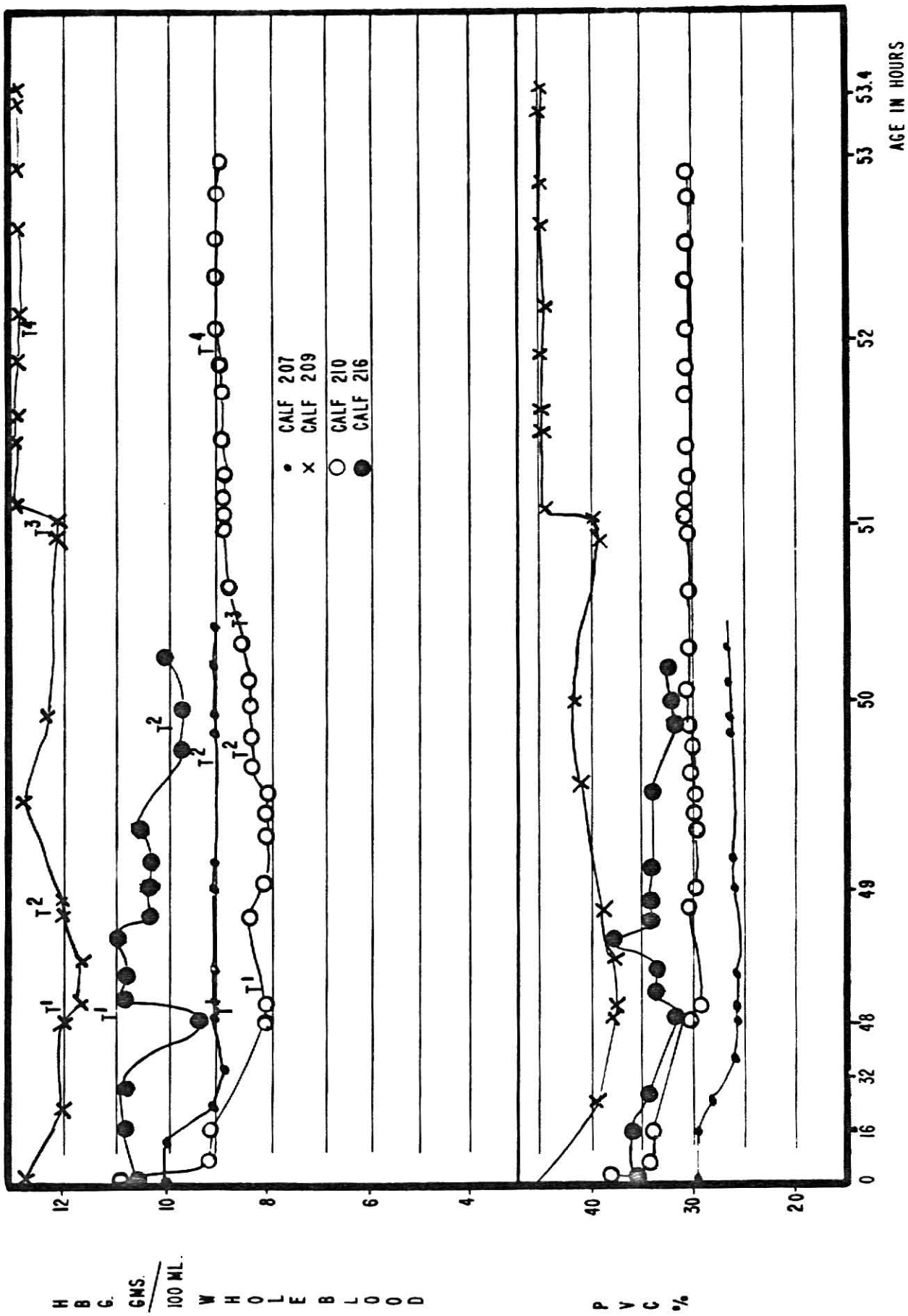

FIG. 15. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 207,209,210,216
GROUP II HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 22, page 176.)

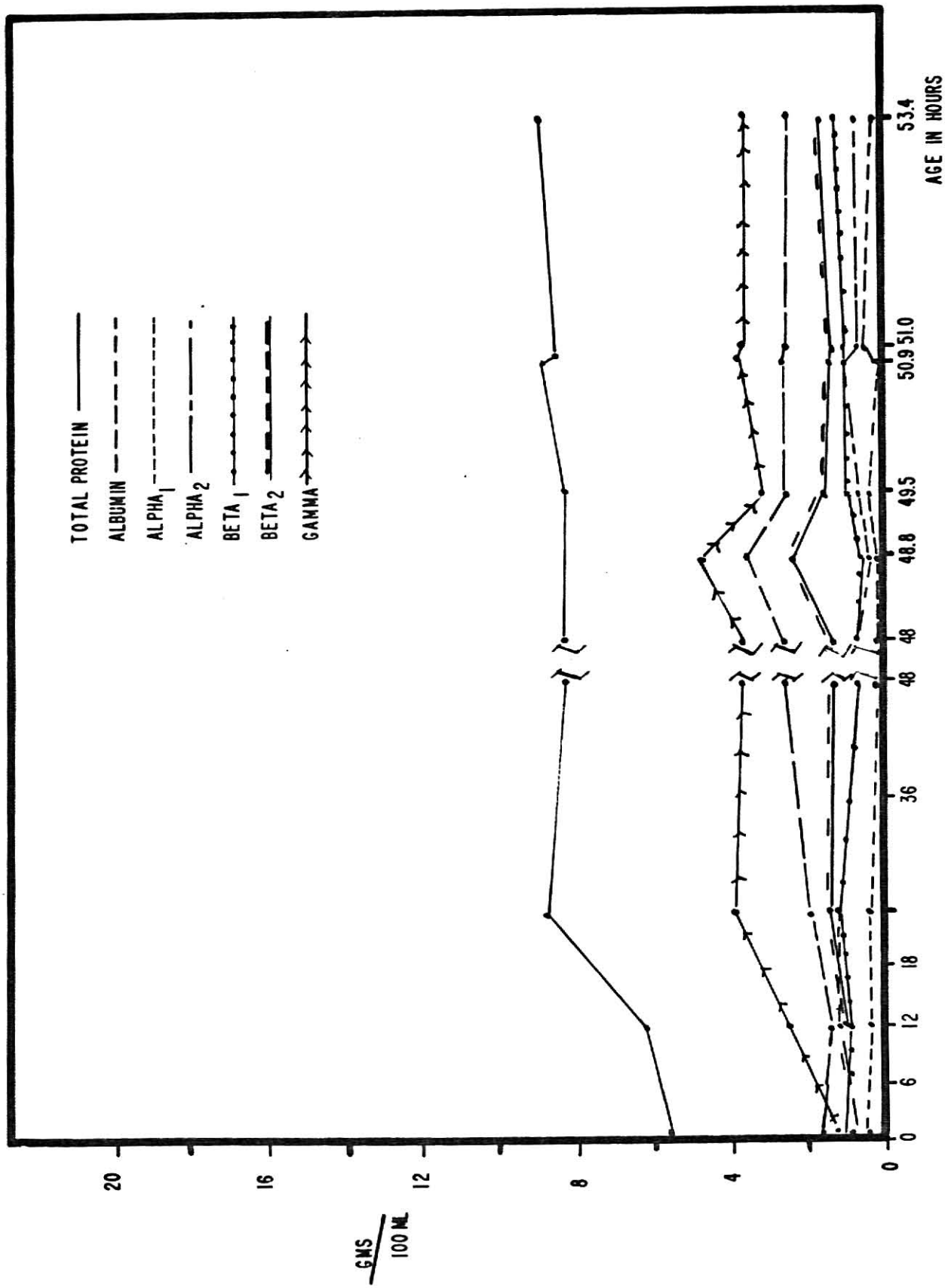

FIG. 16. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP II, CALF 209 (SEE TABLE 21, page 180.)

There was a gradual P_aO_2 recovery for the next 42-45 min (46.6 to 64.4 mmHg) coupled with an increase in depth of respiration resulting in an increased tidal volume. P_aCO_2 remained stable--between 39.7 and 41.0 mmHg and pH increased slightly (7.40). At 49.5 hours of age (T^1 + 84 min) P_aO_2 decreased to 48.7 mmHg and pH began to drop, this coupled with a decreasing respiratory rate (60 to 40 to 28 and 24 per min). pH continued to drop to 7.33.

Prior to 49.7 hours of age the tidal volume appeared to improve markedly as the respiratory pattern changed and P_aO_2 rose to 55.4 mmHg and pH showed a slight rise to 7.36. The second endotoxin challenge (T^2) was given at 49.8 hours, after which blood gases continued to improve as the respiratory rate increased and the improved respiratory pattern continued and heart rate rose slightly. P_aO_2 rose from 55.4 mmHg to 59.1 mmHg (T^2 + 6 min), to 63.7 mmHg (T^2 + 18 min). This was coupled with a slight decrease and stability of P_aCO_2 values at this time, ranging between 40.2 and 43.1 mmHg; pH had stabilized at 7.31. T^3 was given at 50.7 hours of age. Within 12 min P_aO_2 declined to 29.7 mmHg, P_aCO_2 rose to 48.3 mmHg and pH decreased to 7.26. At this time respirations were irregular and depth of respiration decreased. At 51.1 hours (T^3 + 30 min) P_aO_2 was 32.6 mmHg and began to rise slowly but P_aCO_2 continued to rise also and pH dropped to 7.13 in spite of a period of hyperventilation. P_aO_2 continued to rise until 51.8 hours (T^3 + 66 min) at which time P_aCO_2 had declined to 49.5 mmHg. At 51.8 hours the respiratory pattern degenerated and coupled with the administration of T^4 at 52.0 hours of age, P_aO_2 declined to new successive lows of 27.8, 30.5, 29.0 and 30.6 mmHg. P_aCO_2 showed a mild elevation and stabilized between 51.0 mmHg and 54.8 mmHg. During this time pH declined to 7.11 at 52.9 hours of age. The experiment was terminated at T^1 + 288 min and T^4 + 54 min.

Prechallenge base excess was 2.3 mEq/L (average of two 48.0 hour values). Following T^1 there was a fluctuating stability between 2.6 and 1.2 mEq/L for the next 78 min; followed by a decline to 0.7 mEq/L just prior to T^2 (49.7 hours). Following T^2 at 49.8 hours of age there was a marked decline of base excess value to -4.7 mEq/L at T^2 + 6 min. It remained at a stable -3.7 mEq/L between T^2 and T^3. After challenge T^3 (50.7 hours) base excess became more deficient, to new lows of -9.4 and -7.5 mEq/L at T^3 + 78 min and T^3 + 9 min, respectively. The final dose of endotoxin (T^4) given at 52.1 hours of age affected an additional marked decline in base excess, bicarbonate and total carbon dioxide at 52.9 hours.

Temperature values for calf 210 were comparable to control calf values at 48.0 hours. Following T^3 temperatures gradually declined from 38.0°C (50.6 hours) to 35.0°C (52.1 hours) post T^4 challenge.

Hemoglobin oxygen saturation remained high, 84% and above, until the rapid pH decrease occurred at 50.8 hours of age.

Hemoglobin and packed cell volume remained very stable and unchanged throughout the experimental period.

Sodium and potassium values for calf 210 were lower than control calf mean values prior to the 48.0 hour endotoxin challenge. Following endotoxin challenge (T^1) there was a small decline in sodium at T^1 + 54 min and a return to normal 42 min later. Potassium showed no discernable effects.

Prechallenge protein values in calf 210 were lower than control means. All protein increased immediately following the initial endotoxin challenge (T^1 + 36 min) and then regressed to values below the prechallenge level at T^1 + 20 min. At 52.6 hours all proteins were equal to prechallenge levels except Alpha 1.

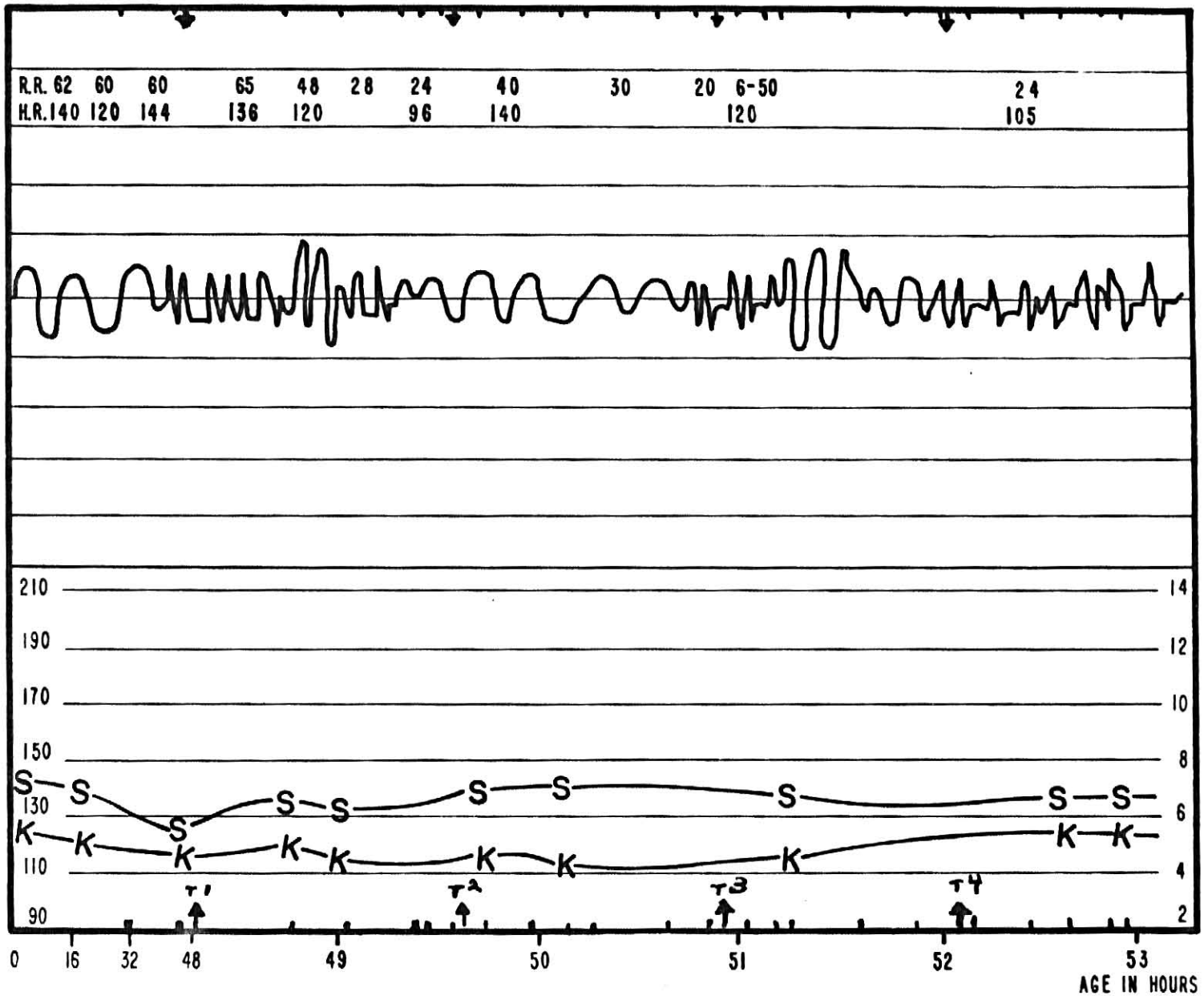

FIG. 17. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 210
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 29, page 189.)

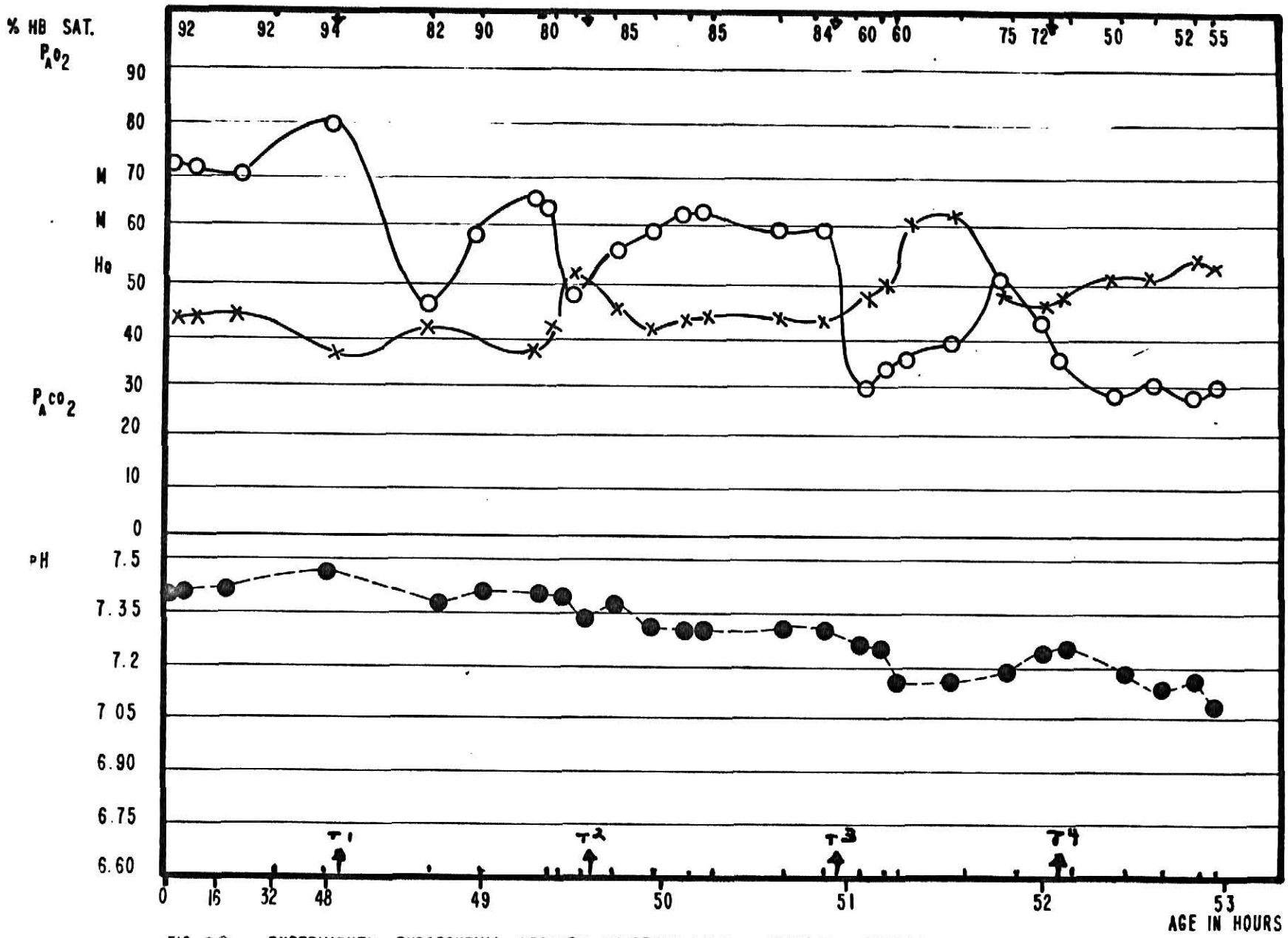

FIG. 18. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II , CALF 210
WHOLE BLOOD $P_{A}o_2$, $P_{A}co_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 25, page 181 and Table 27, page 185.)

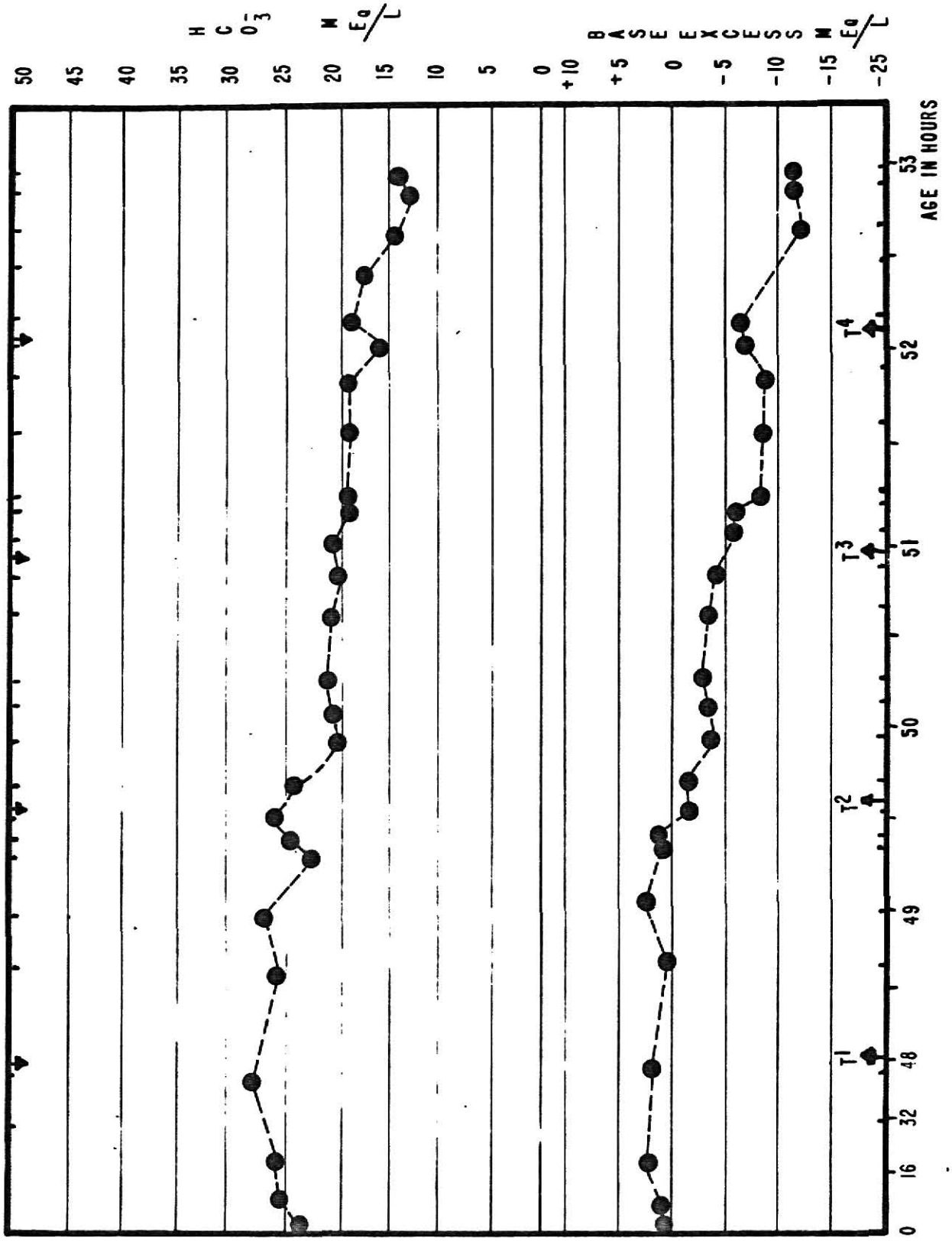

FIG. 19. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 210
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 26, page 183.)

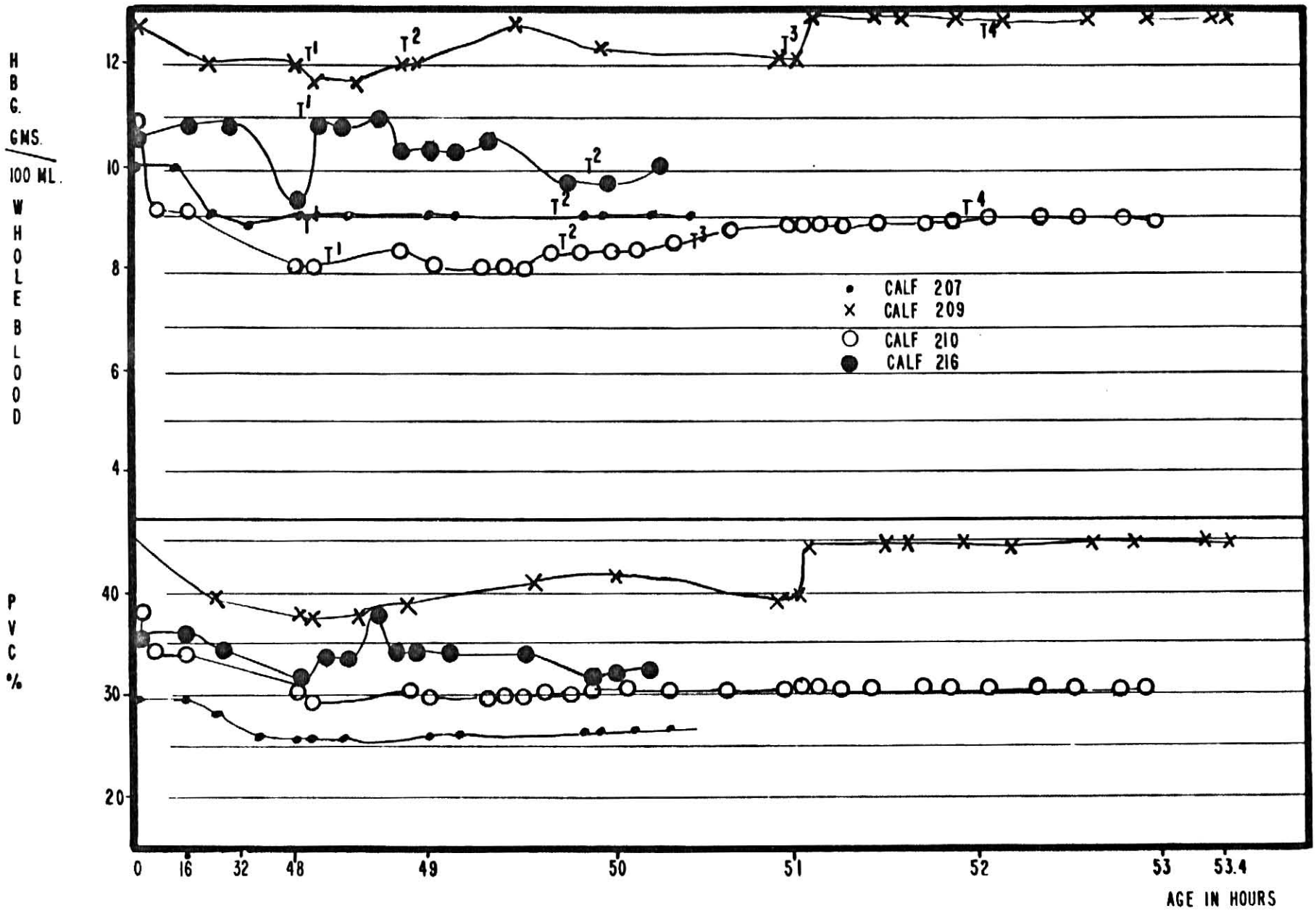

FIG. 20. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 207,209,210,216
GROUP II HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 28, page 187.)

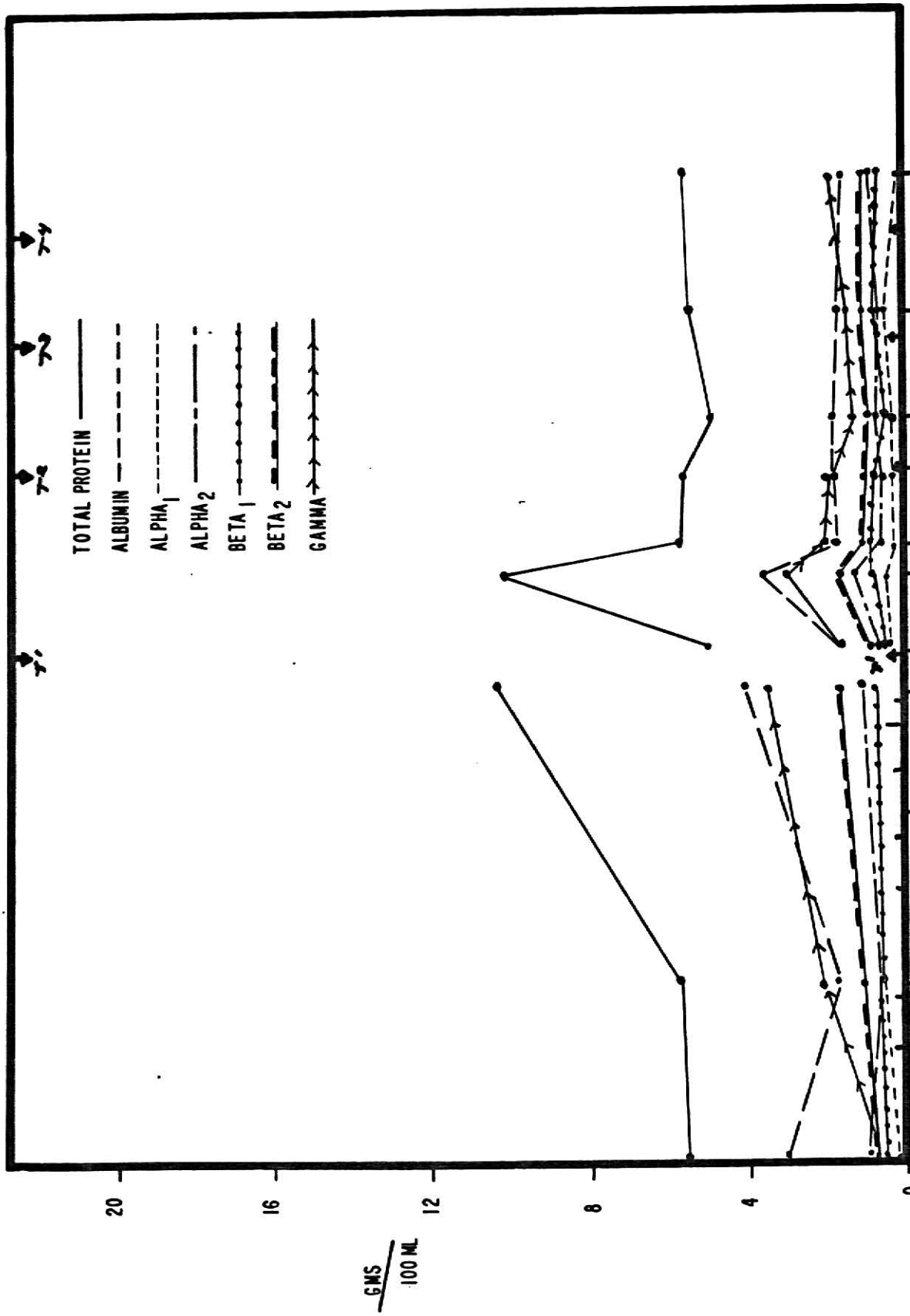

FIG. 21. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP II, CALF 210. (SEE TABLE 30, page 191.)

Calf No. 216

Figures 22-26
Tables 31-36, Pages 192-197

Calf 216 developed a very mild case of diarrhea just prior to endotoxin challenge.

Blood gases and pH prior to endotoxin challenge were slightly elevated in P_aCO_2 (45.9 mmHg) and pH (7.49). Following endotoxin challenge there was an abrupt decrease in P_aO_2 and continued gradual increase in P_aCO_2 and pH declined while the respiratory pattern was markedly effected. At 48.6 hours (T^1 + 36 min) P_aO_2 was 31.7 mmHg, P_aCO_2 was 59.8 and pH was 7.28. These changes continued unabated and at 49.7 hours (T^1 + 102 min) P_aO_2 was 27.3 mmHg, P_aCO_2 84.0 mmHg and pH 6.92. Following endotoxin challenge (T^2) at 49.9 hours they dropped to terminal values of P_aO_2 8.6 mmHg, P_aCO_2 99.9 mmHg and pH 6.12 at T^2 + 24 min or 50.2 hours when death occurred. This calf exhibited periods of cessation of respiration in the inspiratory phase (apneusis) and a dramatically reduced respiratory rate.

Base excess, total bicarbonate and total carbon dioxide values during the prechallenge period in calf 216 were much higher than control mean values--48.0 hour values. Following endotoxin challenge (T^1) there was a continual decline to values of: base excess -18.0 mEq/L, total bicarbonate 16.3 mEq/L and total carbon dioxide 18.0 mm/L at 49.7 hours (T^1 + 102 min). Following challenge T^2 at 49.8 hours base excess decreased to a -32.3 mEq/L and death occurred.

Temperature declined a total of 0.8°C throughout the experimental period of 2.1 hours.

Percent hemoglobin oxygen saturation showed a continual, uninterrupted decline to values of 25.0 and 15.0 % prior to death.

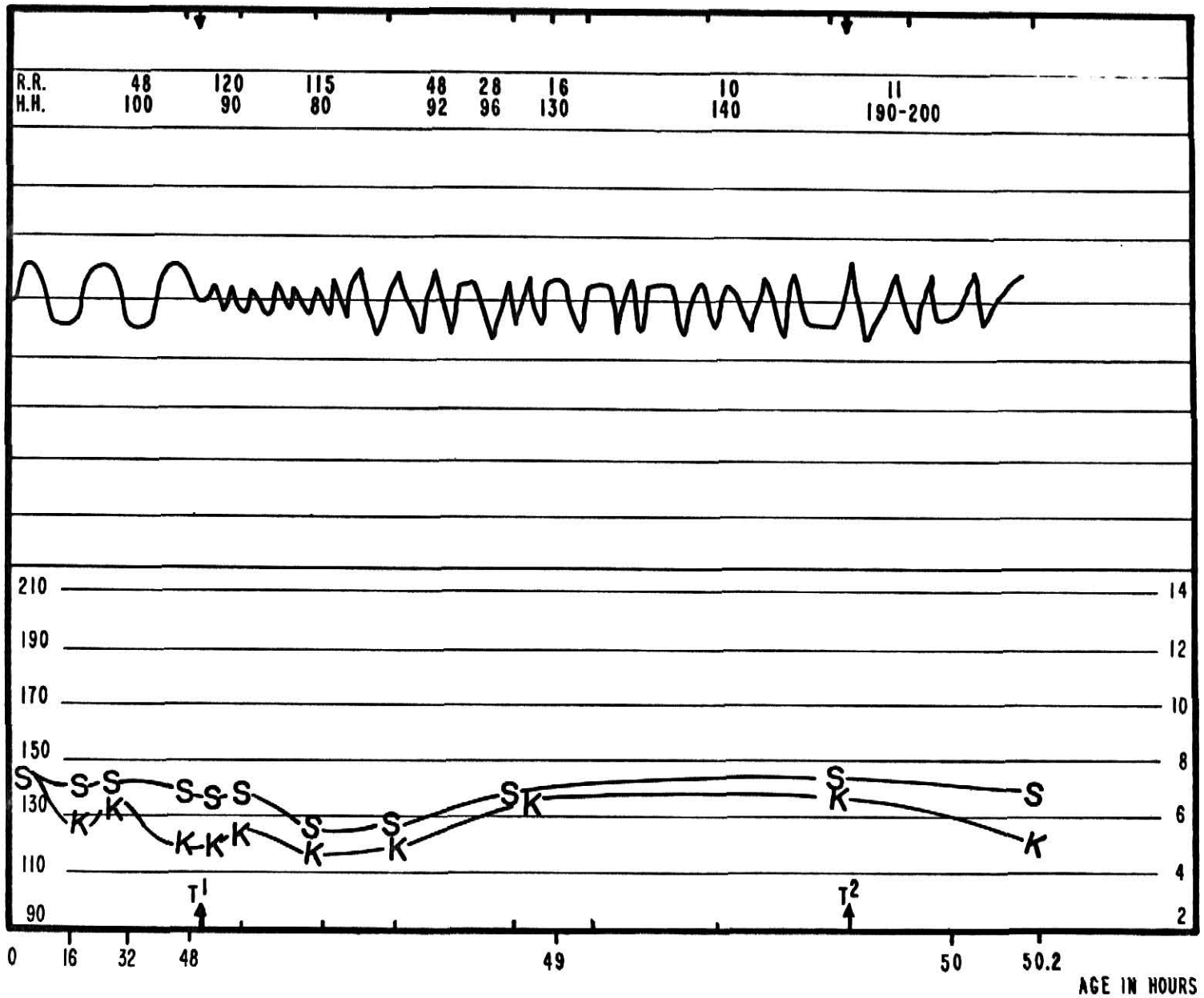

FIG. 22. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II. CALF 216
SERUM SODIUM. POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 35, page 196.)

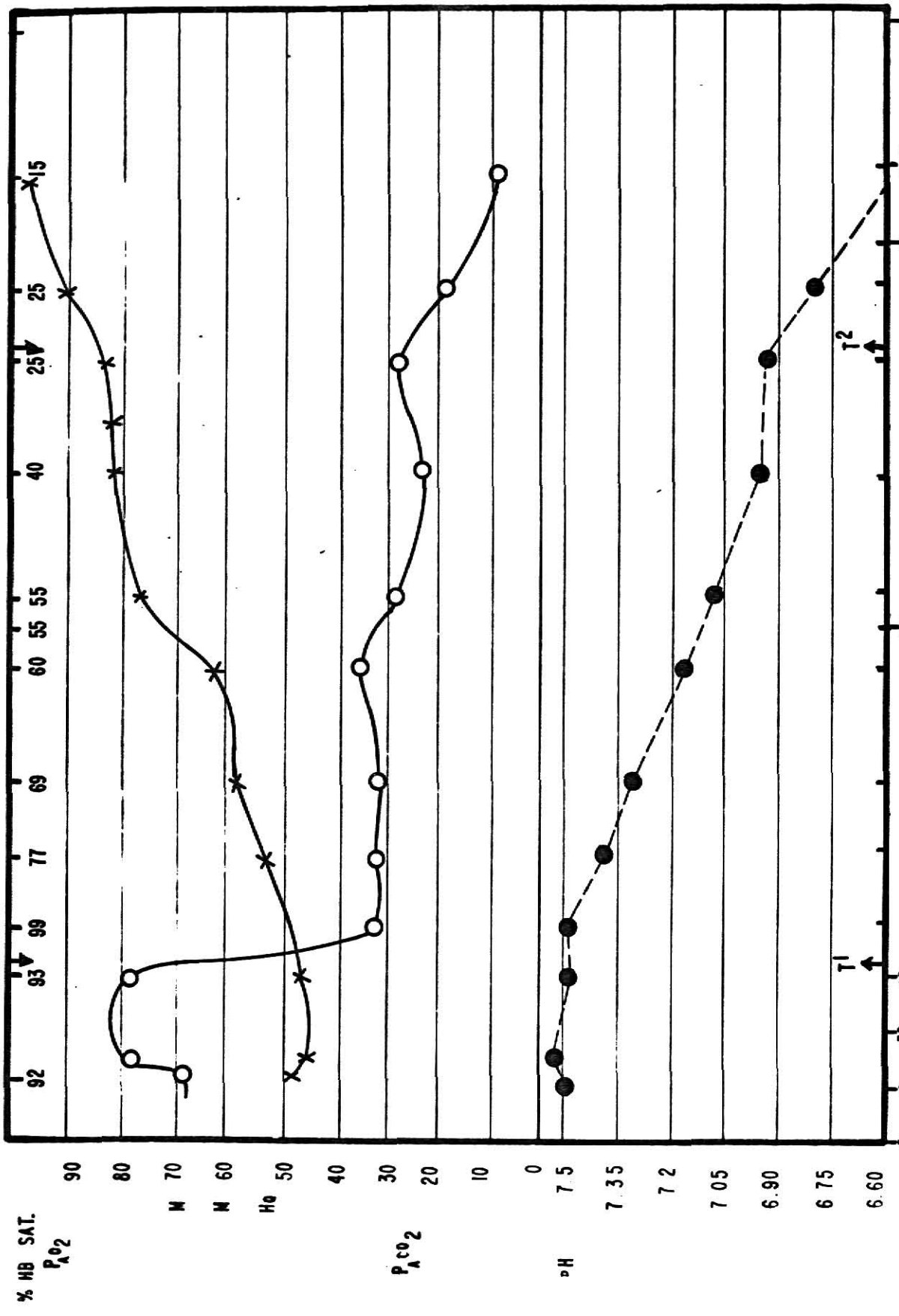

FIG. 23. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 216
WHOLE BLOOD P_AO_2, P_ACO_2, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 31, page 192 and Table 33, page 194.)

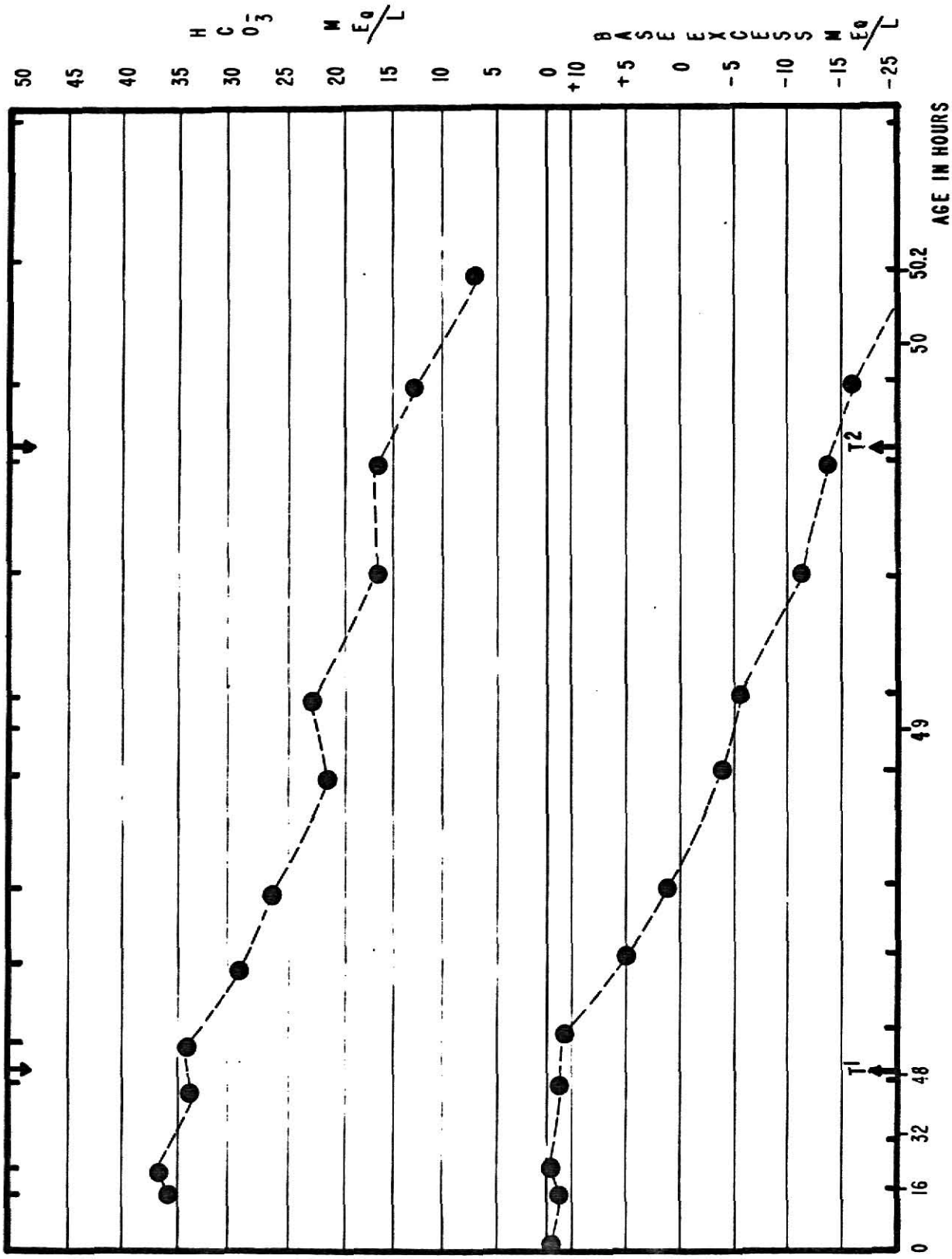

FIG. 24. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP II, CALF 216
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 32, page 193.)

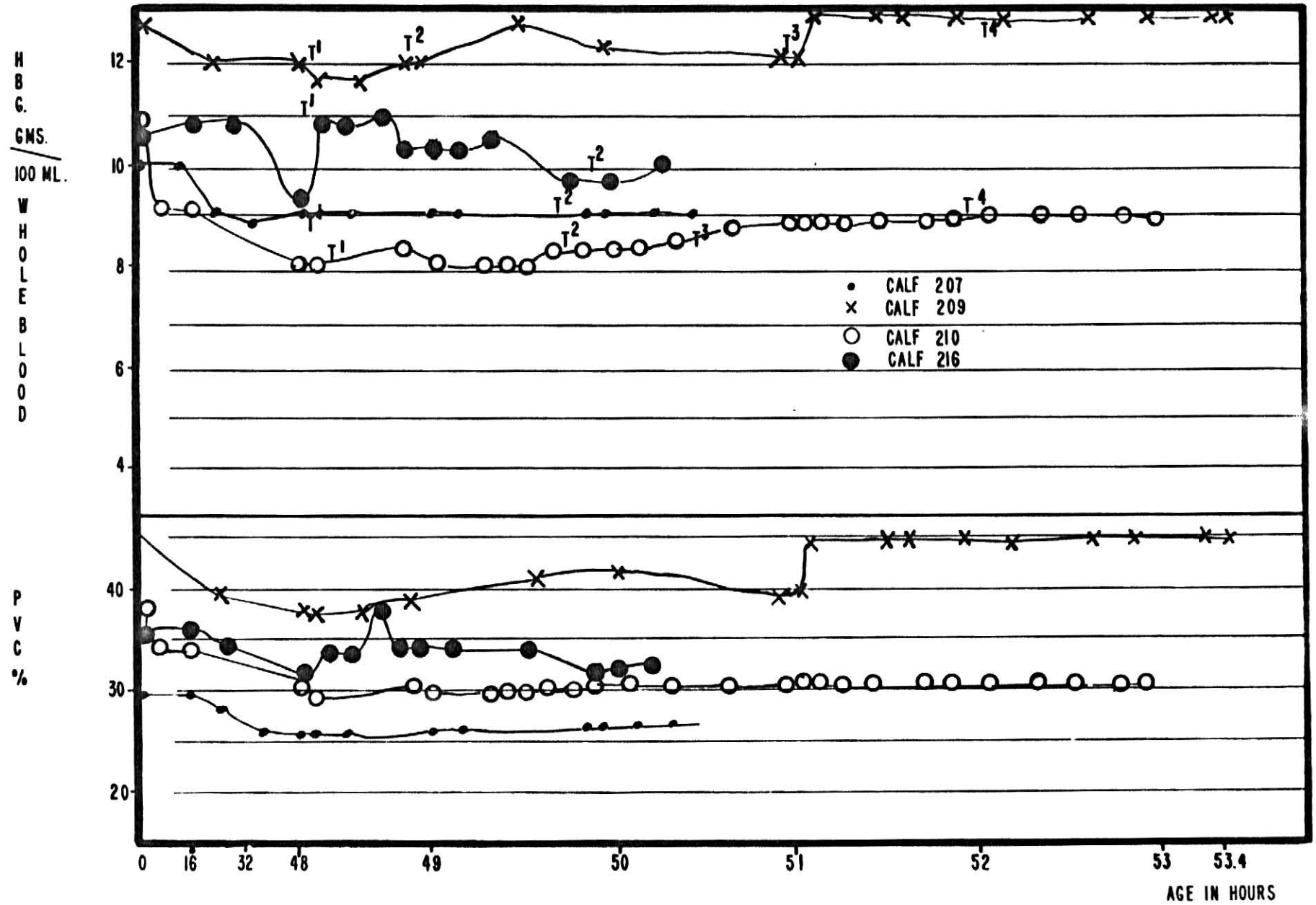

FIG. 25. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 207, 209, 210, 216
GROUP II HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 34, page 195.)

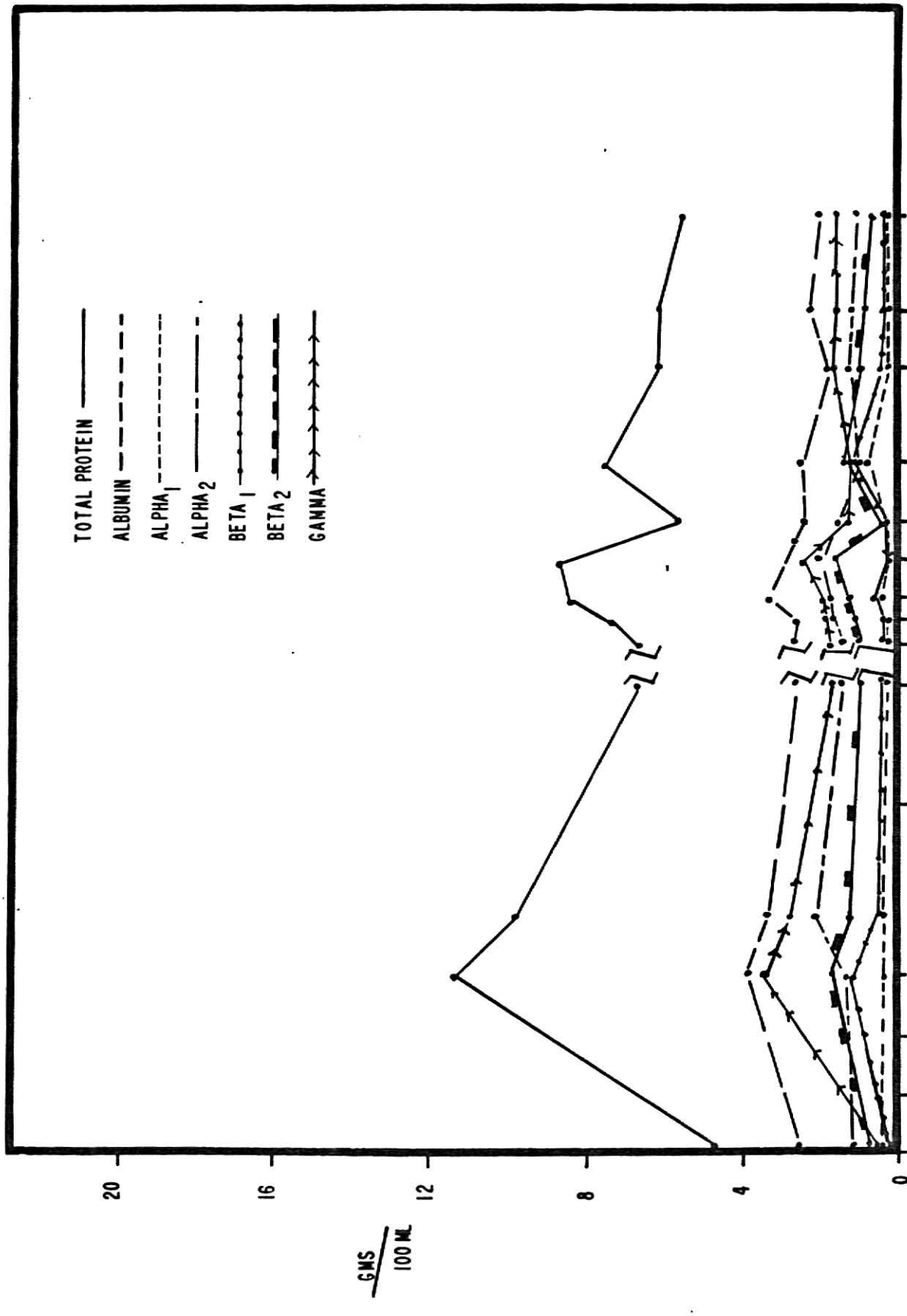

FIG. 26. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP II, CALF 216. (SEE TABLE 36, page 197.)

Packed cell volume and hemoglobin in calf 216 was persistently higher than control calves and remained so through the test period.

Sodium prechallenge values were equal to mean control values (139.0 mEq/L). Post T^1 sodium was 125.0 mEq/L at T^1 + 24 min and T^1 + 30 min. At 49.7 hours it was 141.0 mEq/L. Post T^2 there was no significant change. Potassium values showed no evidence of significant change at any time.

Serum protein values were all lower than control mean values and over 50% of all protein was albumin. Following endotoxin challenge all proteins rose, except alpha 1, and then returned to prechallenge levels. Following T^2 there was no change.

Group III Oral Endotoxin Challenge Calves

Calves Nos. 313, 314, 315, 317

Figures 27-46
Tables 37-60, Pages 198-221

Two calves in this group (313 and 315) had episodes of diarrhea just prior to T^1 at 48.0 hours of age. Calf 314 and 315 showed evidence of pulmonary complication at birth and were given antibiotics at 1 hour of age.

Calf No. 313

Figures 27-31
Tables 37-42, Pages 198-203

This calf showed slightly higher P_aO_2 prechallenge values but equal P_aCO_2 values in relation to control calves. Following oral endotoxin challenge P_aO_2 was not affected. P_aCO_2 rose to 49.1 mmHg (prechallenge 42.9 mmHg) at

T^1 + 60 min; but returned to 42.4 mmHg at T^1 + 12 hours and remained at this approximate value. pH rose gradually following T^1 to 7.47 (prechallenge 7.42) at 96.0 hours of age (T^1 48.0 hours); after T^2 it rose to 7.48 and remained at this value.

Base excess, bicarbonate and total carbon dioxide values were equal to control means at 48 hours of age. Following T^1, base excess was 6.0, 4.5 and 7.2 mEq/L at T^1 + 1, T^1 + 24 and T^1 + 48 hours, respectively (prechallenge base excess 3.0 mEq/L). Following T^2 base excess rose to 9.0 mEq/L at T^2 + 3.7 hours and at 120.0 hours or T^2 + 23.8 hours it was 6.0 mEq/L.

Temperature values in calf 313 rose 0.6°C at T^1 + 1 hour; declined to 38.9°C (0.5°C below prechallenge temperature) at T^1 + 48 hours. Following T^2 it rose 0.8°C in 3.7 hours. Hemoglobin oxygen saturation remained in excess of 95% at all times except at 120 hours of age.

Sodium and potassium prechallenge values were slightly above mean control values (K 0.7 mEq/L, Na 169.8 mEq/L). Sodium was 134.6 mEq/L and potassium 7.8 mEq/L at T^1 + 1 hour. Sodium returned to 144.4 mEq/L at T^1 + 12.0 hours and remained at this level except for a 99.5 hour value of 125.0 mEq/L. Potassium fluctuated considerably post challenge.

Hemoglobin and packed cell volume were stable throughout the entire experimental period but both were at all times higher than control means.

All serum proteins increased following T^1 challenge except alpha 1 which decreased at T^1 + 114 min; other proteins had returned to prechallenge levels. Following T^2 proteins again rose (T^2 + 18 min) and again returned to pre T^2 values (T^2 + 3.7 hours).

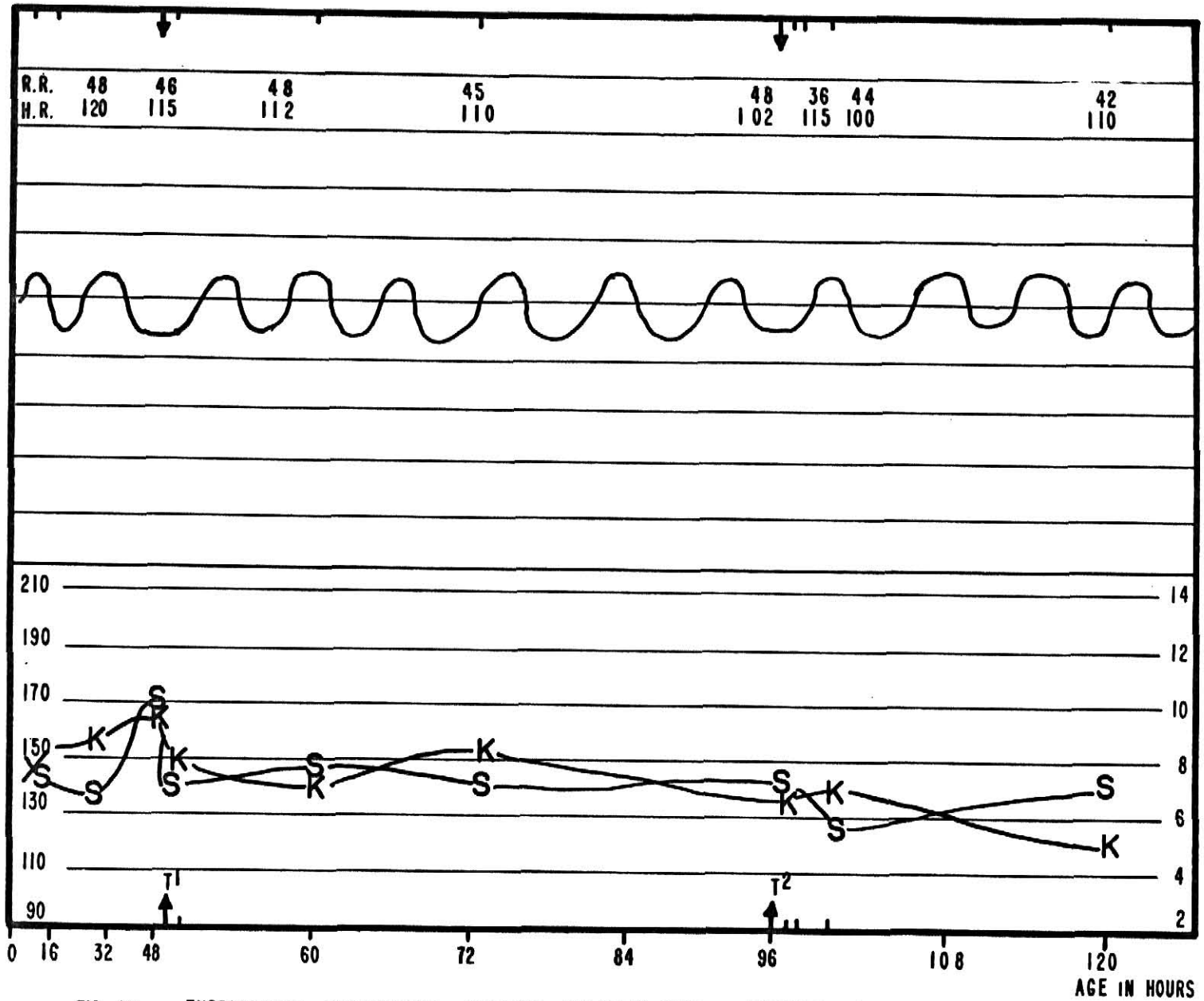

FIG. 21. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 313
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 41, page 202.)

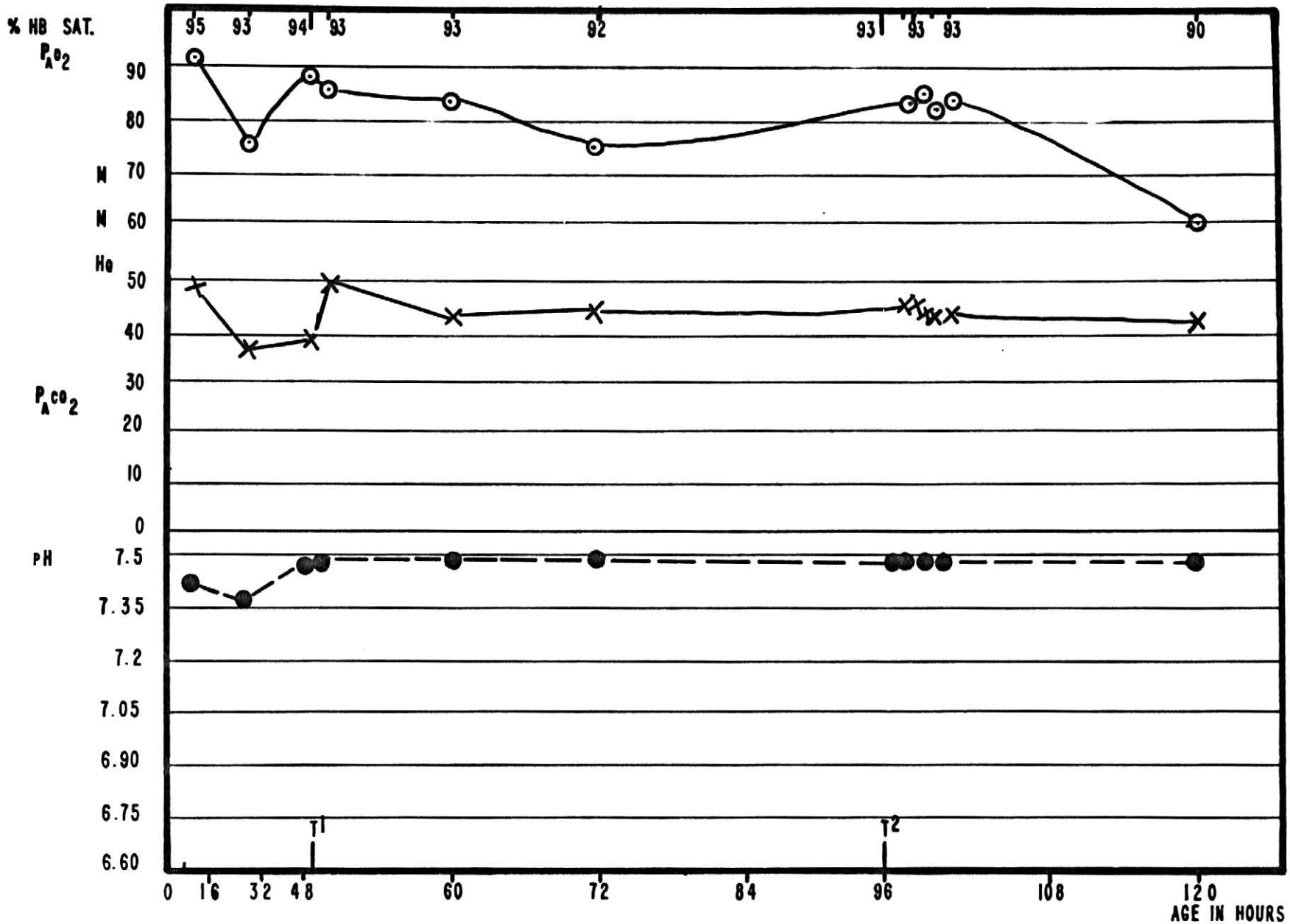

FIG. 28. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 313 WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 37, page 198 and Table 39, page 200.)

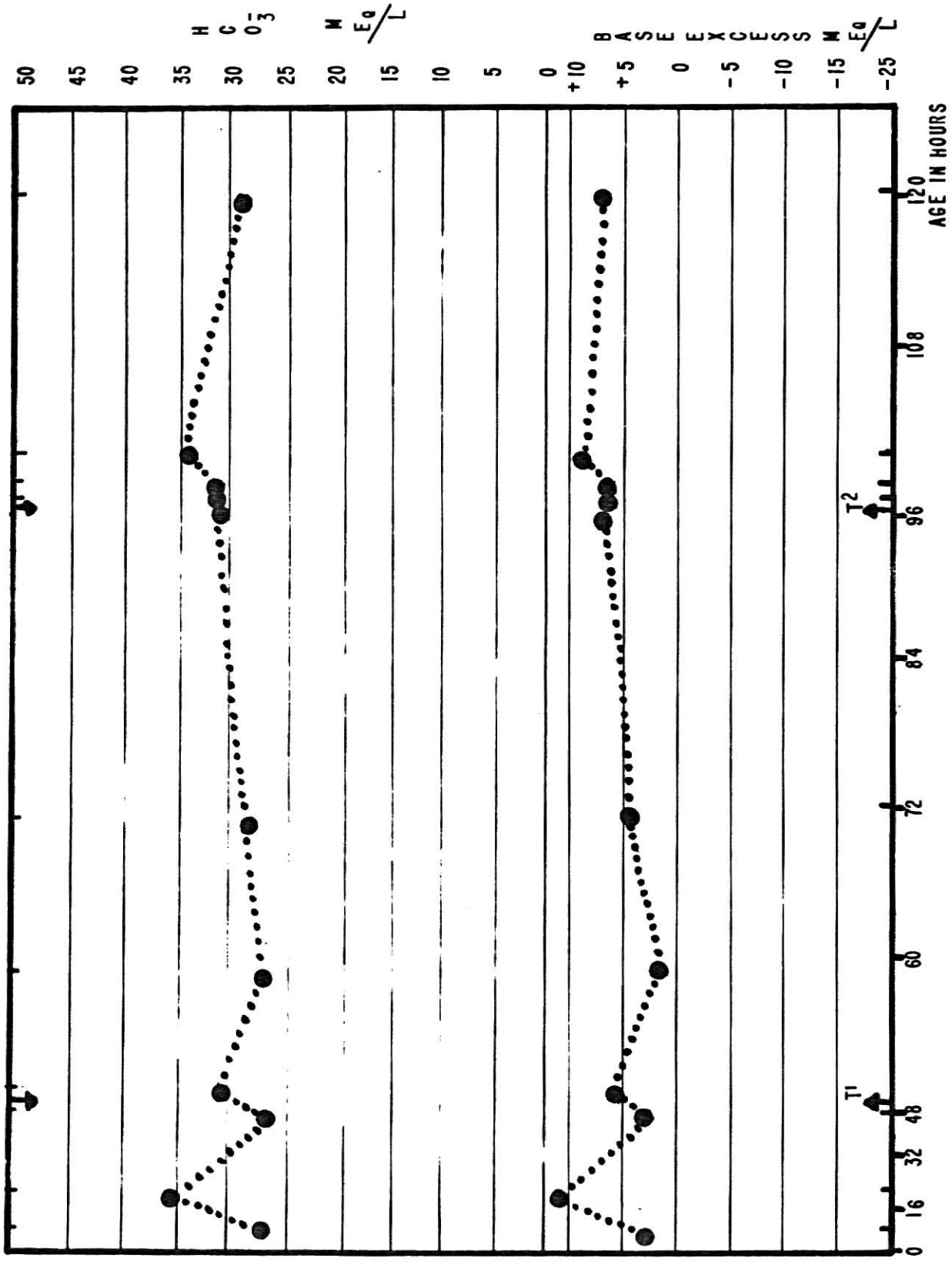

FIG. 29. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 313
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 38, page 199.)

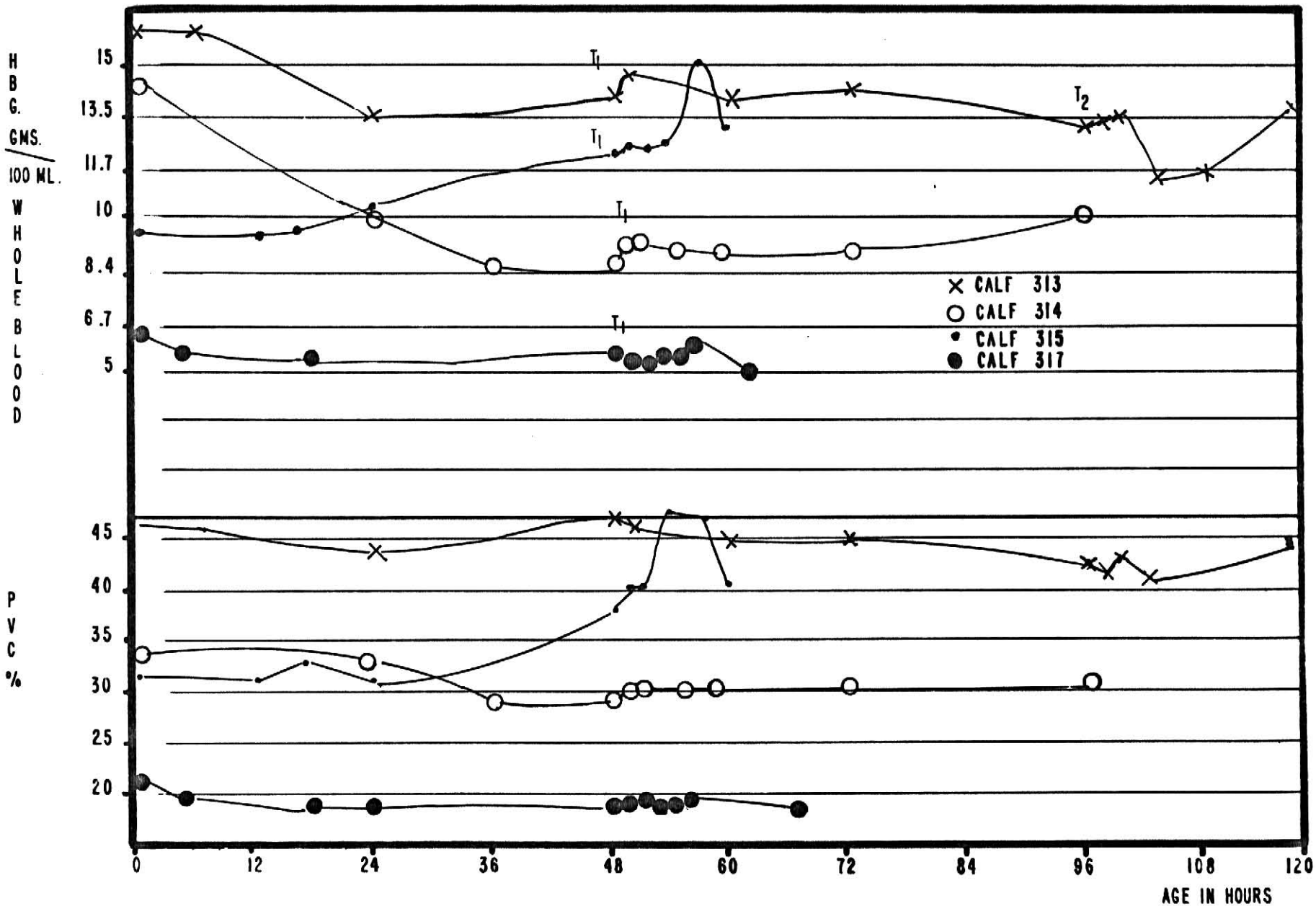

FIG. 30. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 313, 314, 315, 317, GROUP III HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 40, page 201.)

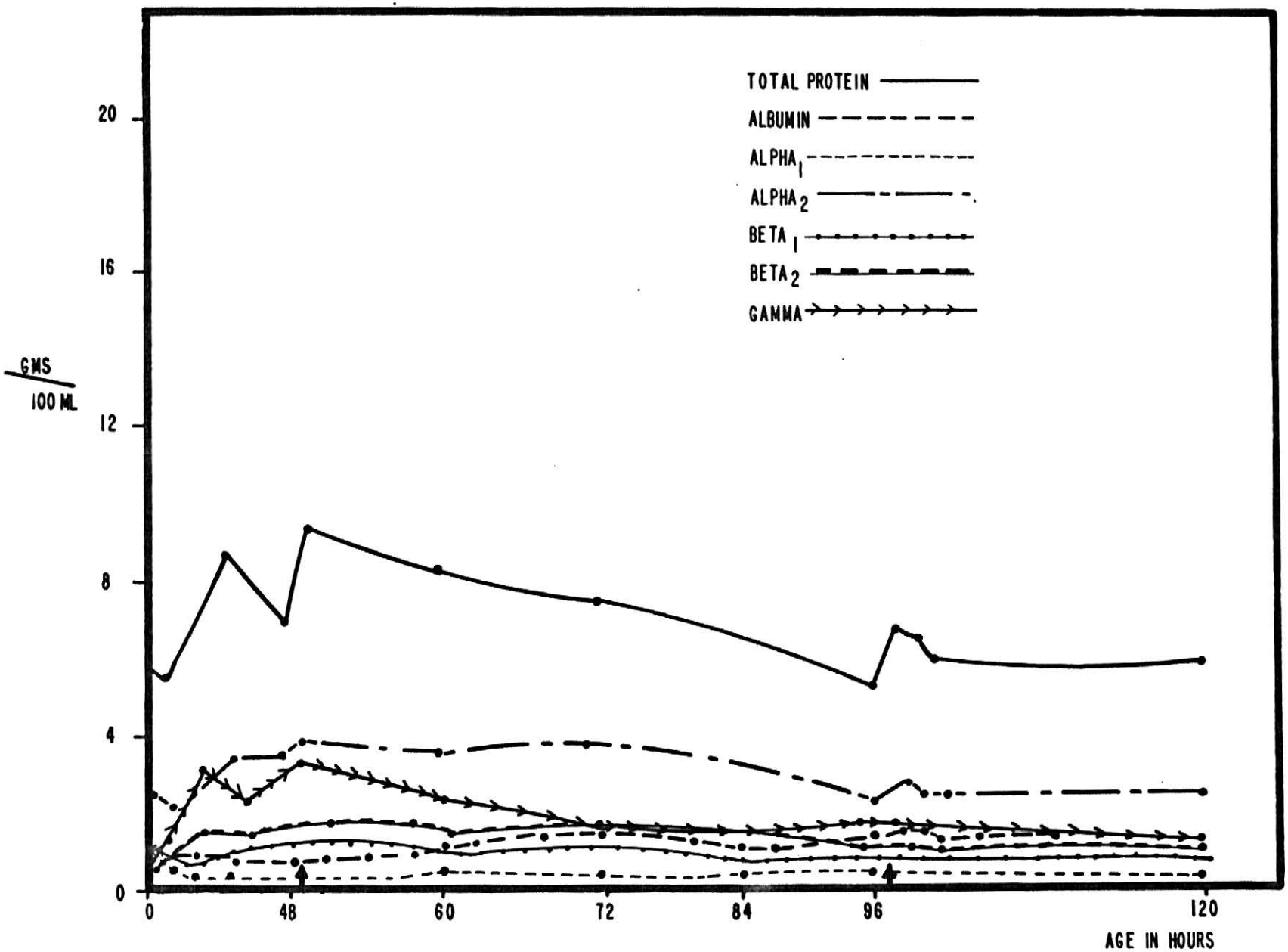

FIG. 31. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF 313 GROUP , CALF . (SEE TABLE L2, page 203.)

Calf No. 314

Figures 32-36
Tables 43-48, Pages 204-209

One to 24 hour blood gas values showed early deviation from control means. Prechallenge (48 hr) values were equal to controls (P_aO_2 86.2 mmHg, P_aCO_2 43.0 mmHg). Following T^1 P_aO_2 reduced to 78.6 and 76.0 mmHg at T^1 + 6 min and T^1 + 3.6 hours, respectively; P_aCO_2 rose to 52.3 mmHg at T^1 + 3.6 hours. During this interval pH remained stable at 7.48 ± .01. There was little change through the next 36 hours. Following endotoxin challenge (48.3 hrs) the calf appeared depressed; respiratory rate increased slightly as did heart rate but returned to prechallenge values in 45 min.

Prechallenge base excess was higher than control means (7.2 mEq/L) and rose to 8.7, 10.8, 11.0 and 13.0 mEq/L at T^1 + 6, 36, 216 and 1440 min, respectively; then declined to 7.0 mEq/L at T^1 + 48 hours.

Temperature and hemoglobin oxygen saturation values were unchanged following endotoxin challenge; as were hemoglobin and packed cell volume values.

Sodium showed a pre and post endotoxin value of 125 mEq/L. T^1 + 2.6 hours and T^1 + 8.6 hours values were 119.0 and 167.6 mEq/L, respectively.

Serum proteins showed a marked reduction following endotoxin challenge and this reduction persisted through 96.0 hours of age. At 51.7 hours (T^1 + 3.6 hours) there was a partial recovery.

Calf No. 315

Figures 37-41
Tables 49-54, Pages 210-215

Calf 315 showed early (1 hr) respiratory complication evidenced by an

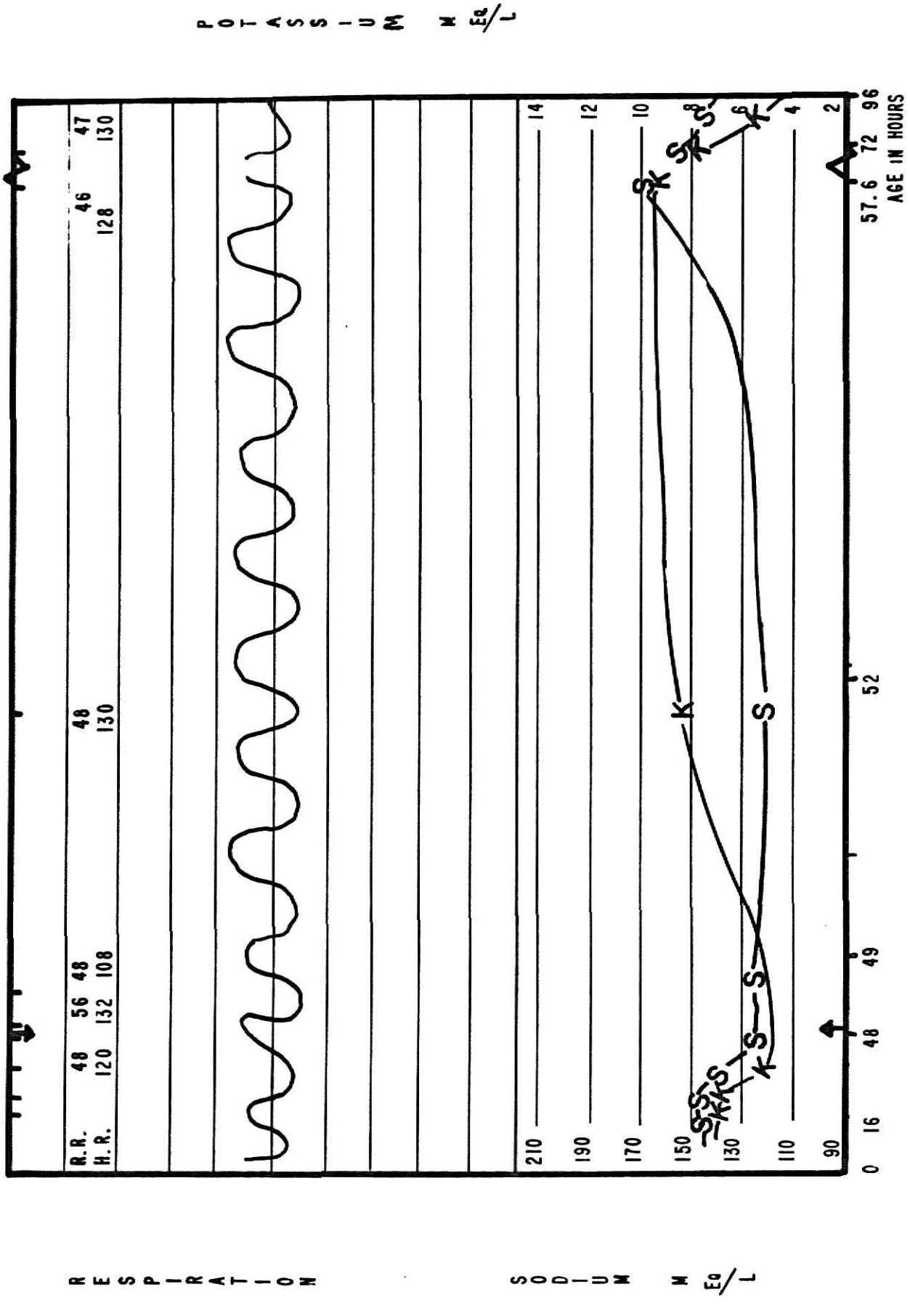

FIG. 32. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF, GROUP III, CALF 314
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 47, page 208.)

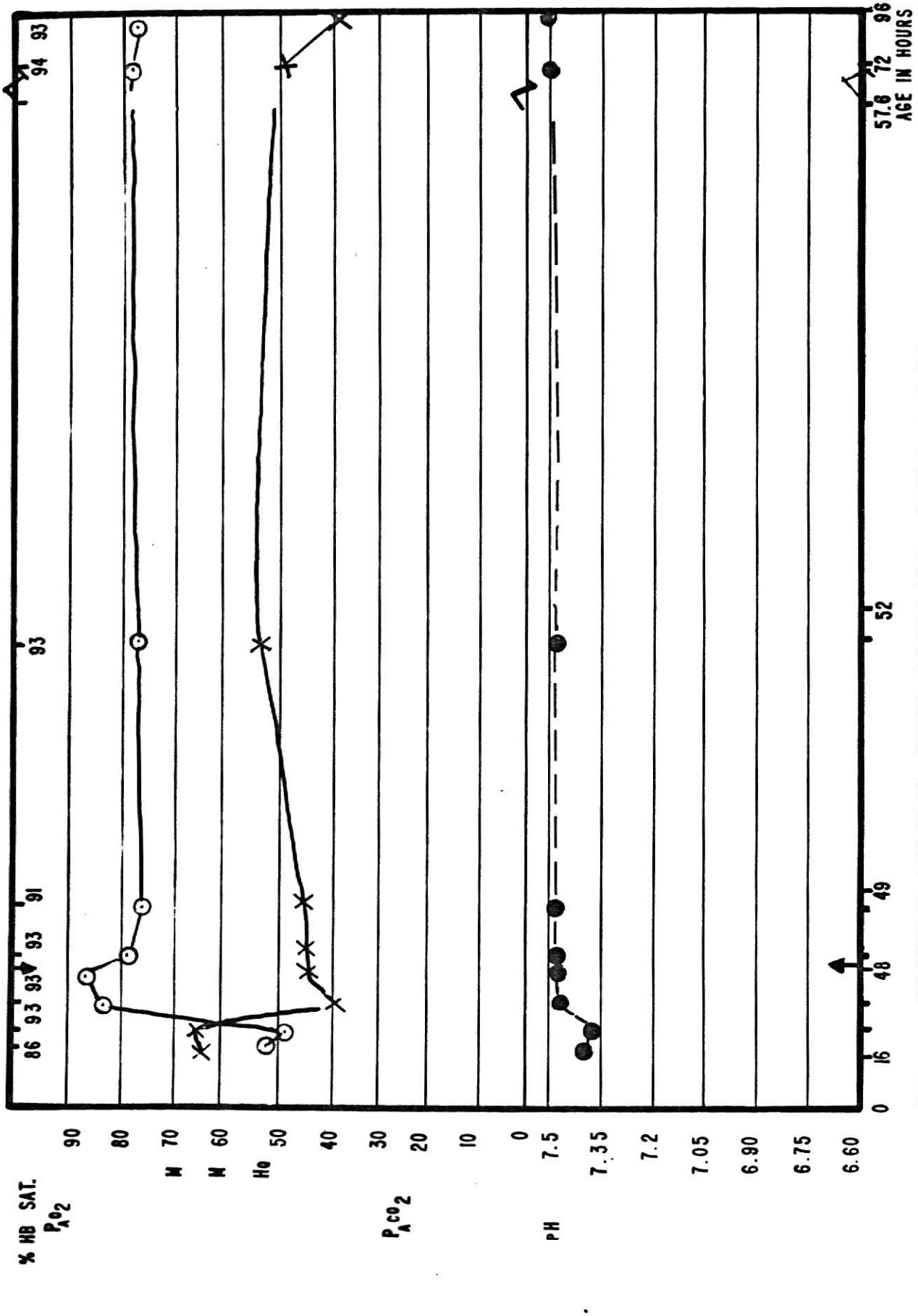

FIG. 33. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 314
WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 43, page 204 and Table 45, page 206.)

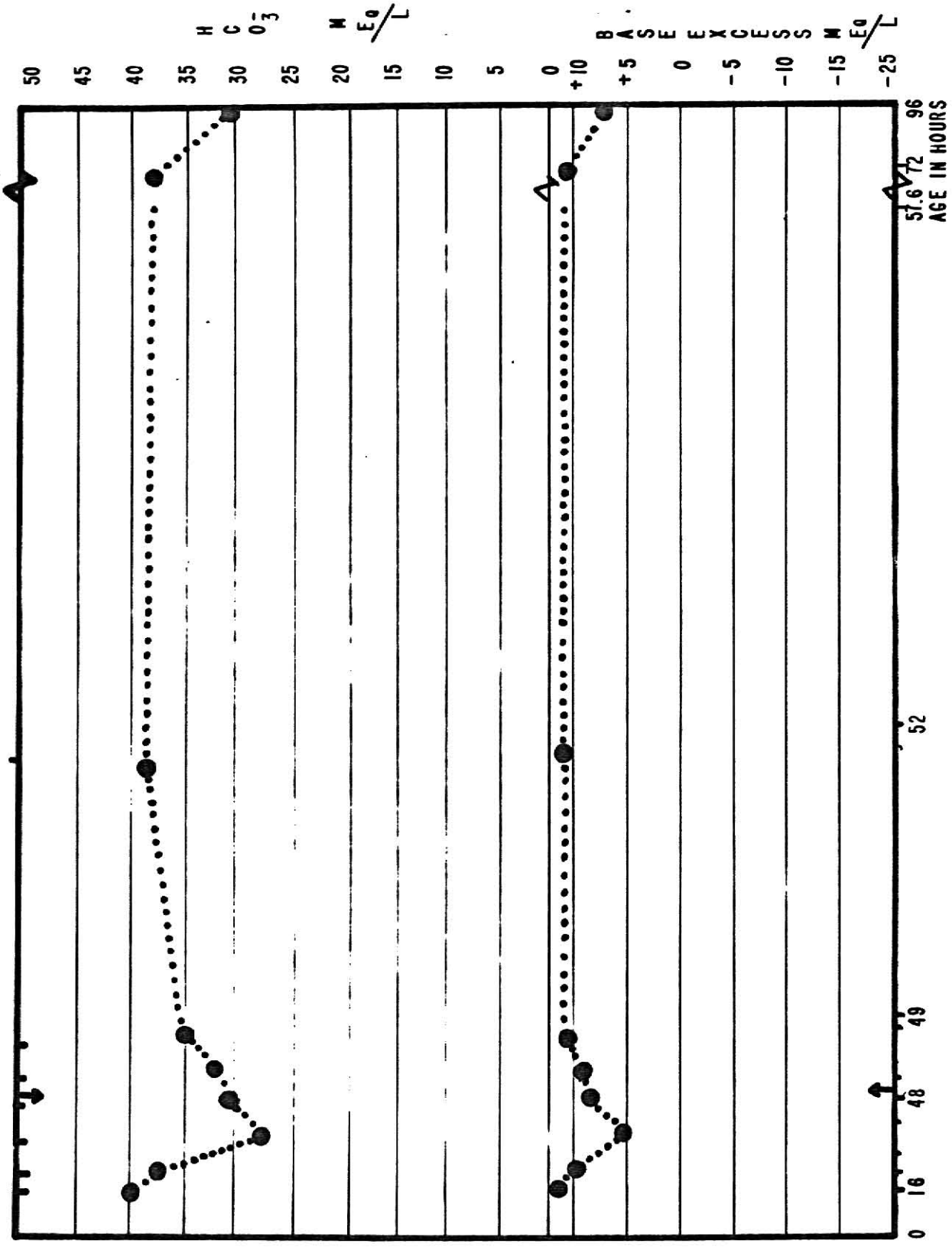

FIG. 34. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 314
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 44, page 205.)

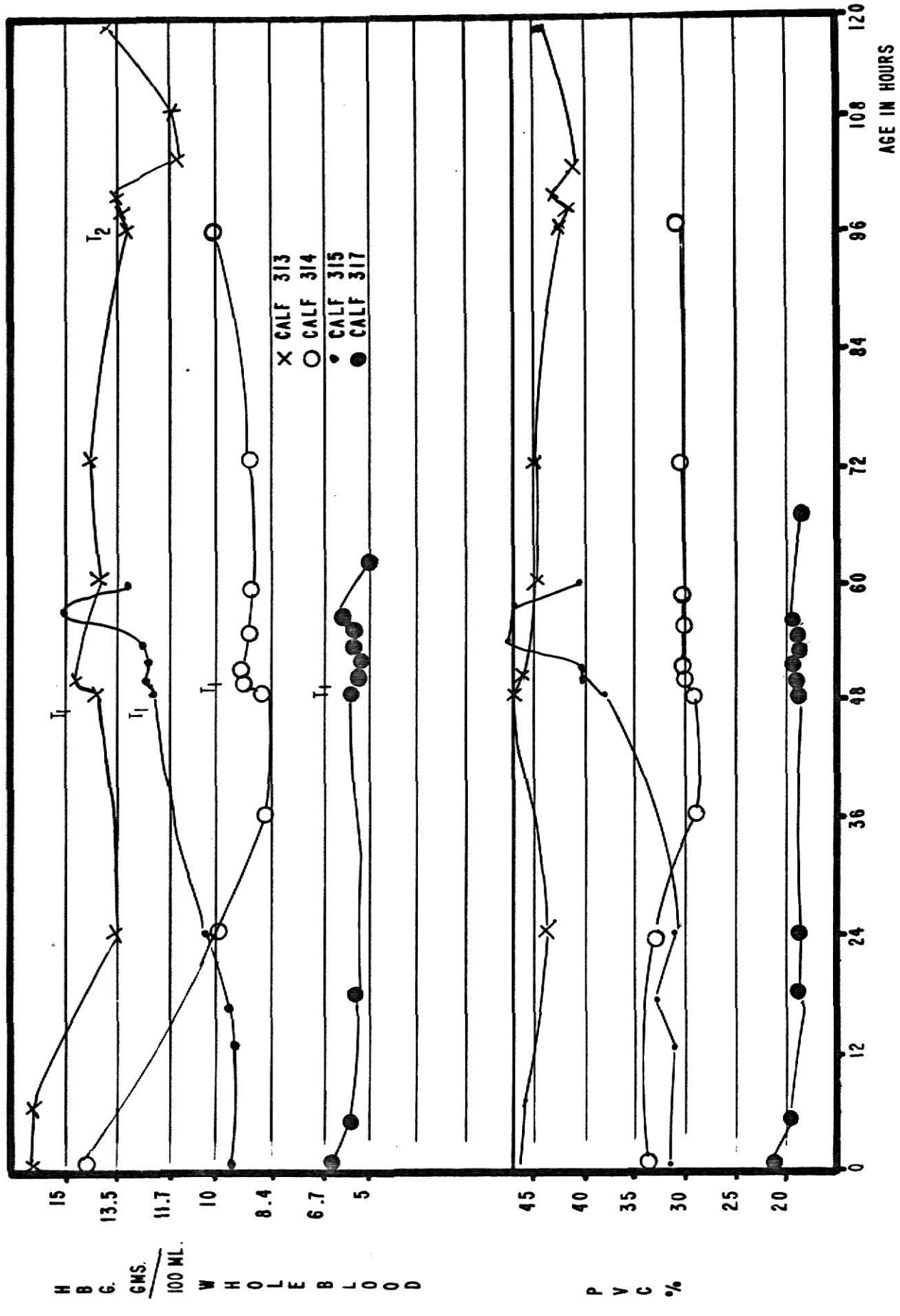

FIG. 35. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 313, 314, 315, 317, GROUP III HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 16, page 207.)

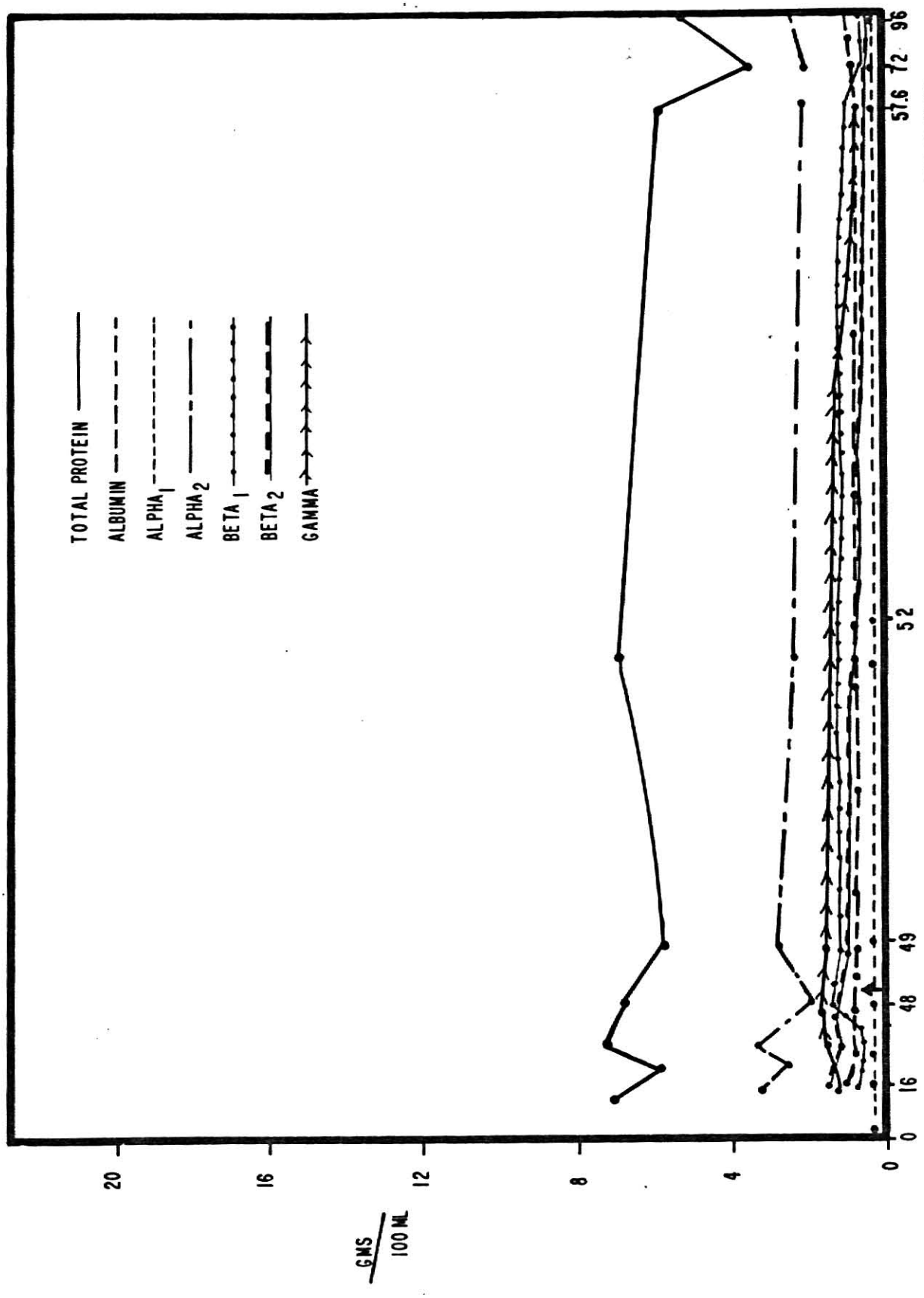

FIG. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP III, CALF 3LL (SEE TABLE 1B, page 209.)

abnormal respiratory pattern; this was not evident at 24 hours of age. At 48 hours (prechallenge) a severe case of diarrhea was evident; rectal temperature was normal and there were no clinical signs of dehydration.

Prechallenge blood gases and pH were comparable to control calves. Following oral challenge P_aO_2 and P_aCO_2 slowly but persistently changed: P_aO_2 T^1 + 30 min 76.6 mmHg; T^1 + 11.1 hours 21.7 mmHg; P_aCO_2 35.8 mmHg and 68.0 mmHg at these respective hours. pH declined from 7.42 to 6.34 and death occurred.

Respiratory pattern changes were similar to those of intravenous challenge calves but with a slower rate of onset.

Base excess, total Co_2 and bicarbonate followed pH decline precisely, with the following base excess values per time interval: 48.0 hours -1.0; T^1 + 5.6 hours -5.0; T^1 + 11.1 hours -30.0 mEq/L.

The temperature of calf 315 showed slight decrease (0.3°C) until T^1 + 10.1 hours when it declined to 37.8°C. Hemoglobin oxygen saturation was maintained at 80+% until T^1 + 10.1 hours when it was 73.0%.

Packed cell volume rose from 37.5 volumes % prechallenge to 40.02 volumes % at T^1 + 11.0 hours. Hemoglobin showed one significant period of elevation; at T^1 + 10.1 hours with a value of 14.7 Gms/100 ml.

Serum sodium and potassium values for calf 315 post challenge showed marked deviation from expected values*. At T^1 + 1.4 hours sodium was 205 mEq/L and potassium was 12.7 mEq/L; at T^1 + 11.0 hours sodium was 56.0 mEq/L and potassium was 14.8 mEq/L.

Serum proteins at 48.0 hours were uniformly lower than control mean values. Following endotoxin challenge (T^1 + 5.6 hours) total protein increased from

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*Appendix, page 222.

4.6 Gms/100 ml to 6.3 Gms/100 ml.

Calf No. 317

Figures 42-46
Tables 55-60, Pages 216-221

Prechallenge blood gases and pH were equal to mean control values. Following endotoxin challenge P_aO_2 rose: T^1 + 30 min 85.1 mmHg to 92.9 mmHg at T^1 + 3.6 hours. P_aCO_2 did likewise: T^1 + 1.8 hours 51.0 mmHg; then declined to a T^1 + 19.3 hours value of 40.6 mmHg. pH was stable at 7.53 and 7.54 post challenge.

The respiratory pattern and heart rate appeared uneffected.

Base excess rose sharply--48.0 hours 2.5; 48.2 hours (T^1 + 6 min) 8.5 and remained at 8.5 mEq/L and 9.5 mEq/L thereafter.

Hemoglobin and packed cell volume were unaffected post challenge as was hemoglobin oxygen saturation and tempurature.

Sodium and potassium values were extremely variable*.

Serum proteins increased post challenge at T^1 + 24 min; and T^1 + 48 min with values of 13.6 and 14.8 Gms/100 ml, respectively. All fractions were increased proportionally.

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*Appendix, page 222.

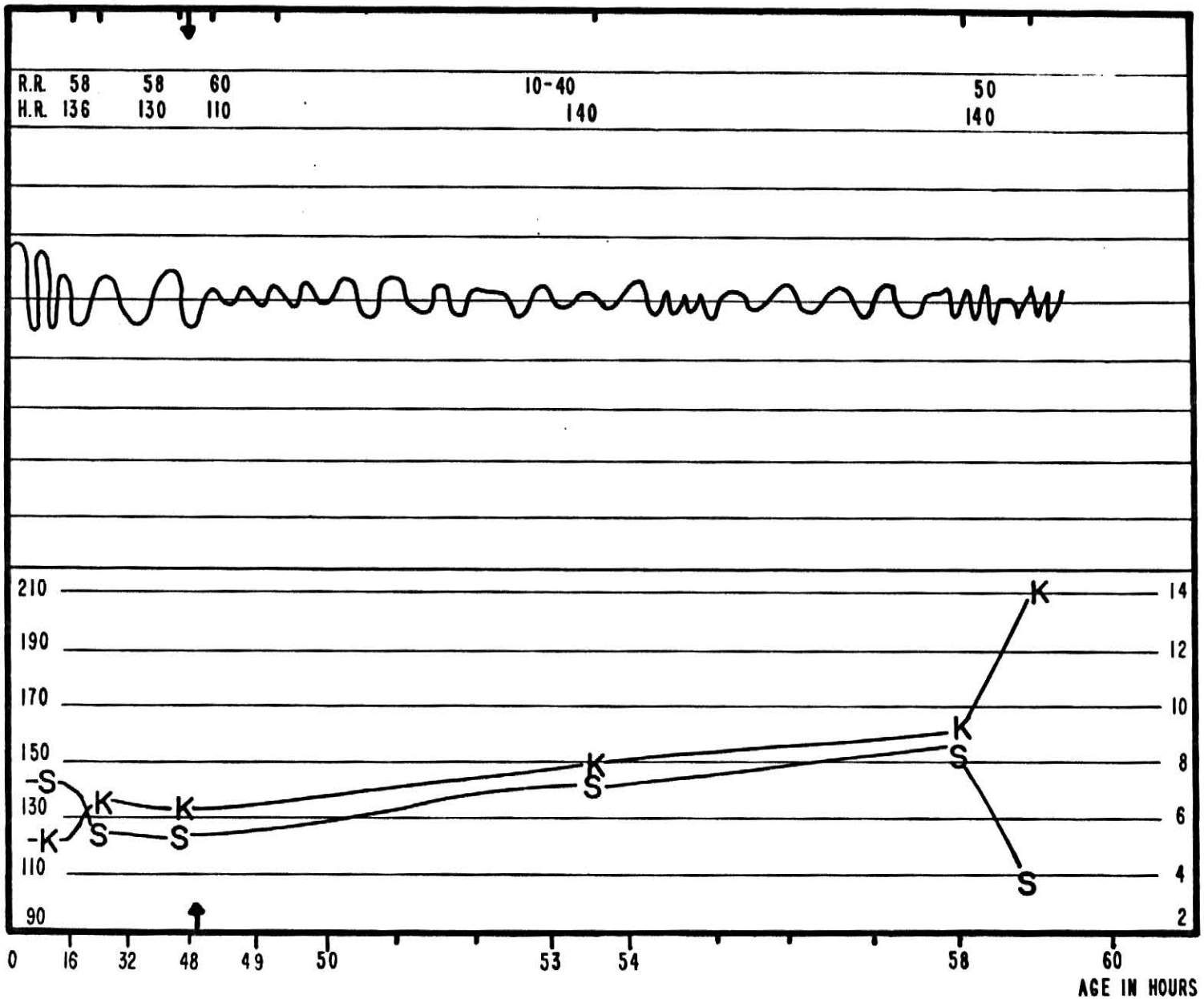

FIG. 37. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 315
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 53, page 214.)

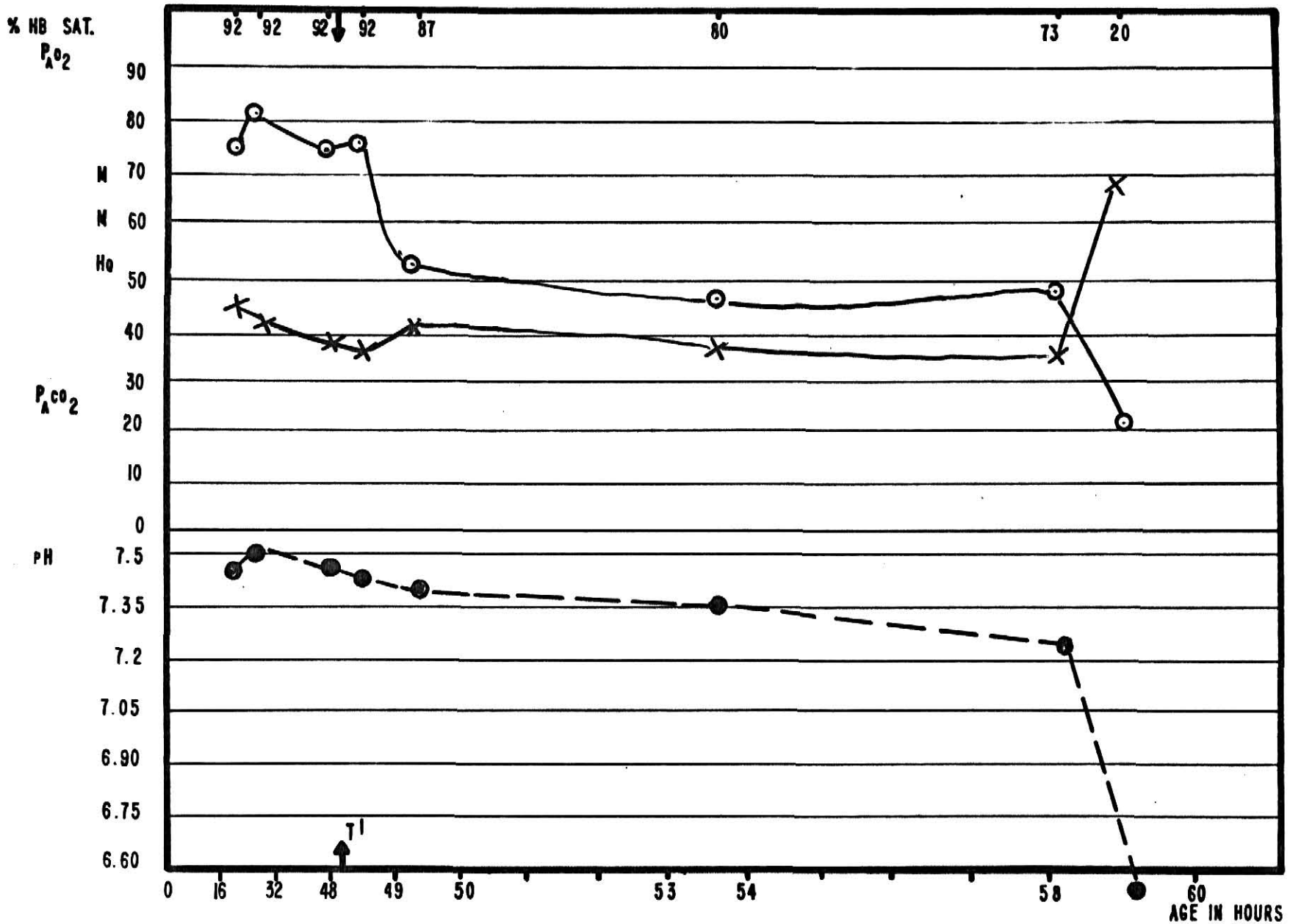

FIG. 38. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 315
WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 49, page 210 and Table 51, page 212.)

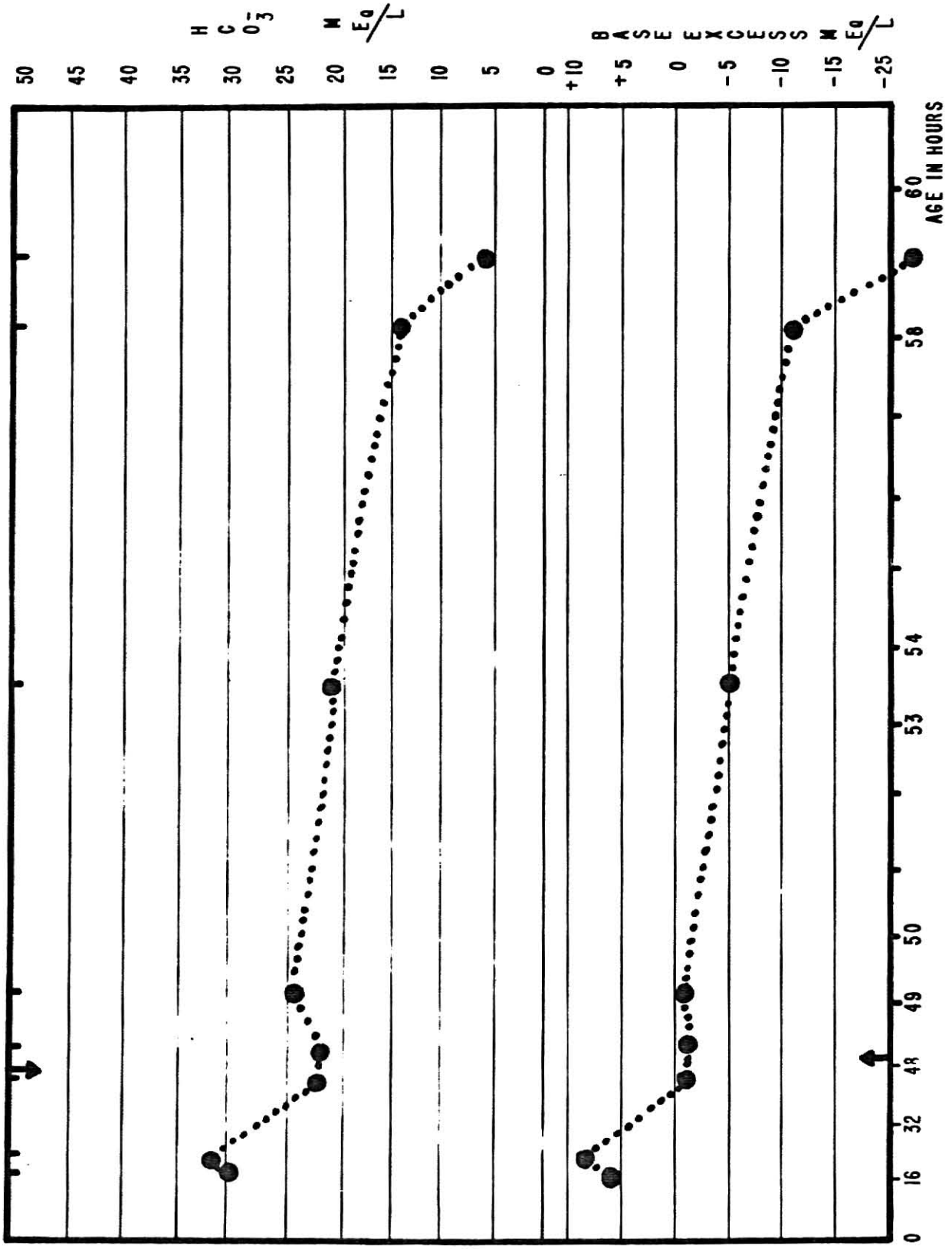

FIG. 39. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF, GROUP III, CALF 315
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 50, page 211.)

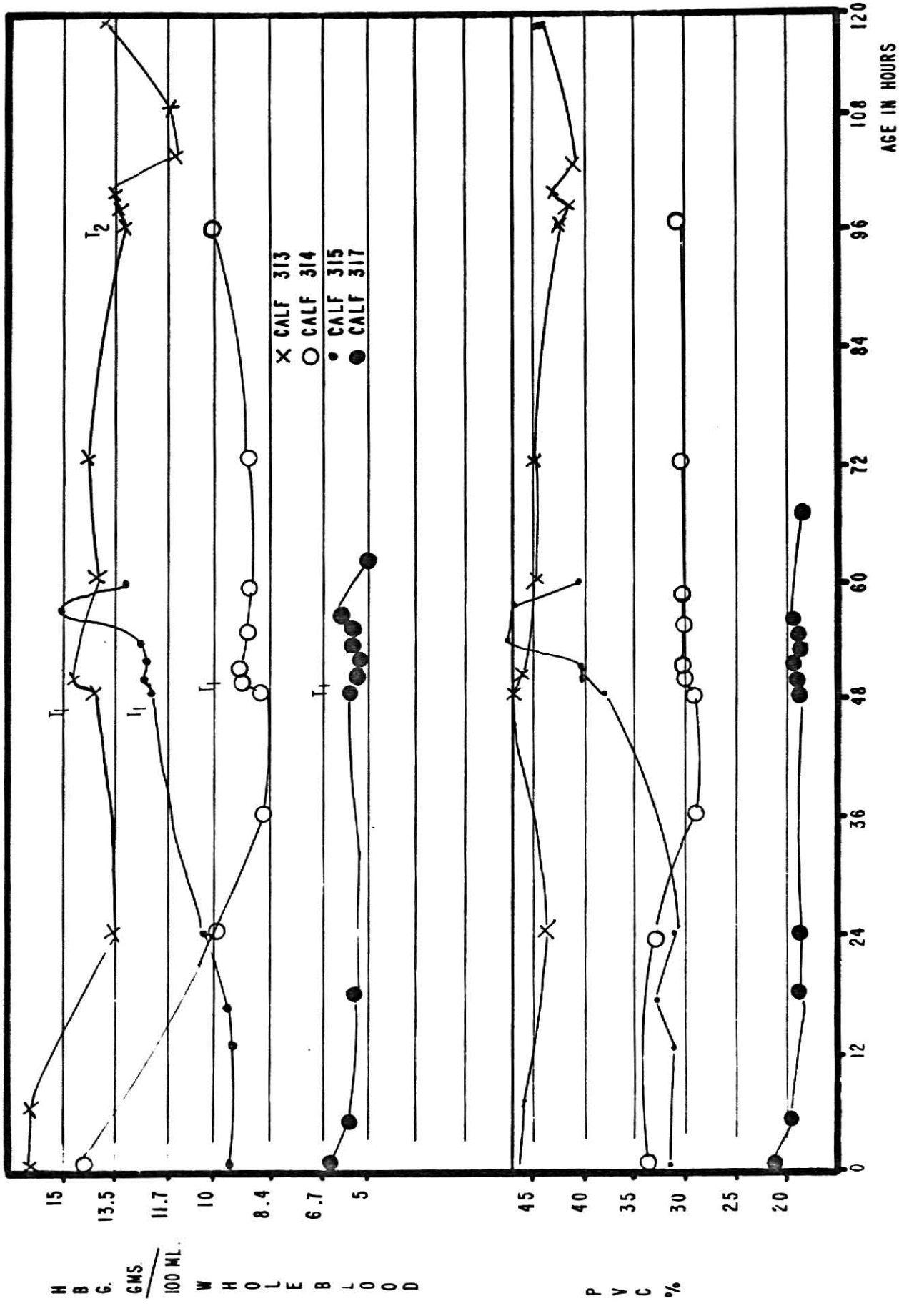

FIG. 40. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 313, 314, 315, 317, GROUP III HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 52, page 213.)

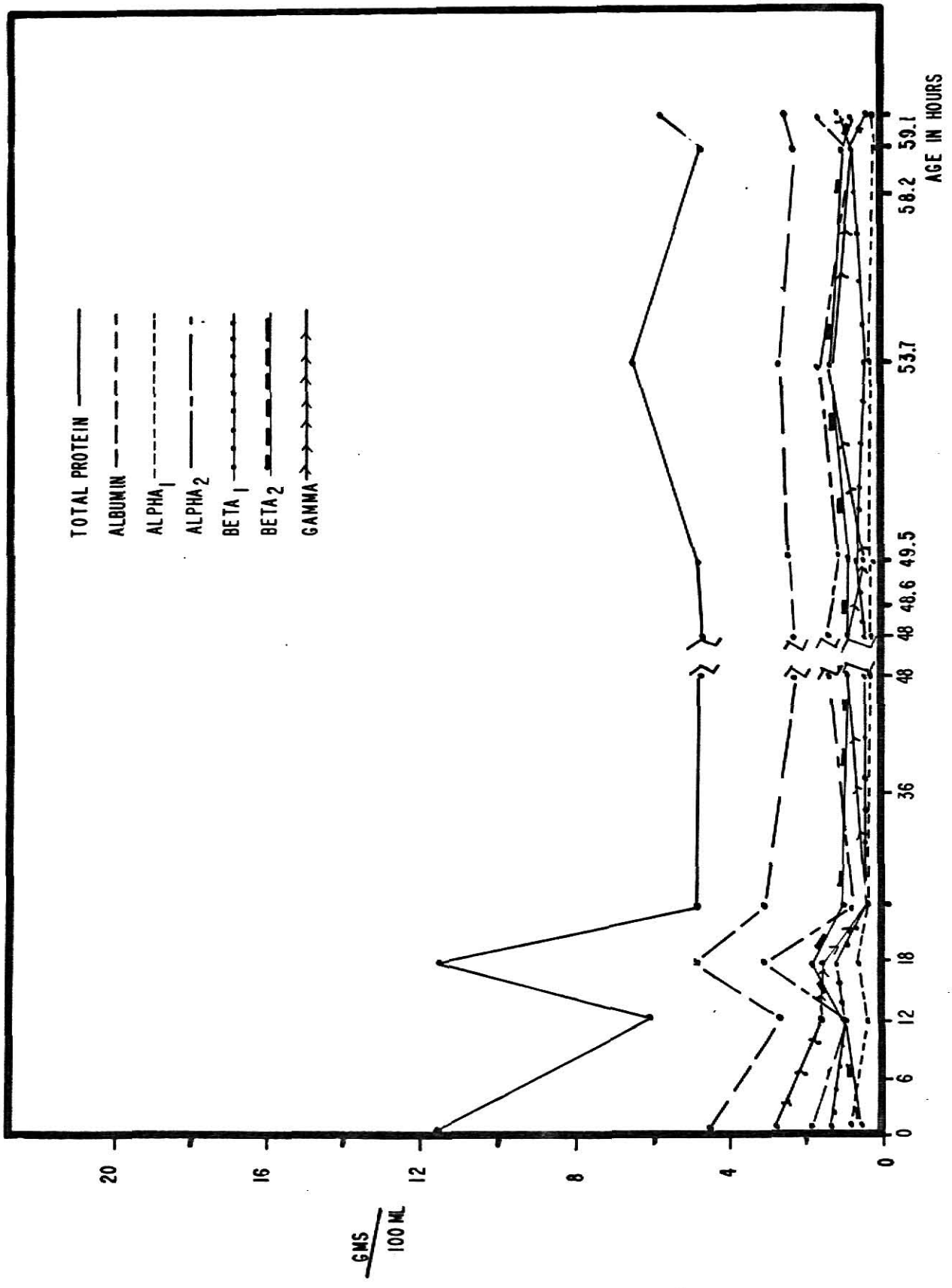

FIG. 11. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP III, CALF 315. (SEE TABLE 5b, page 215.)

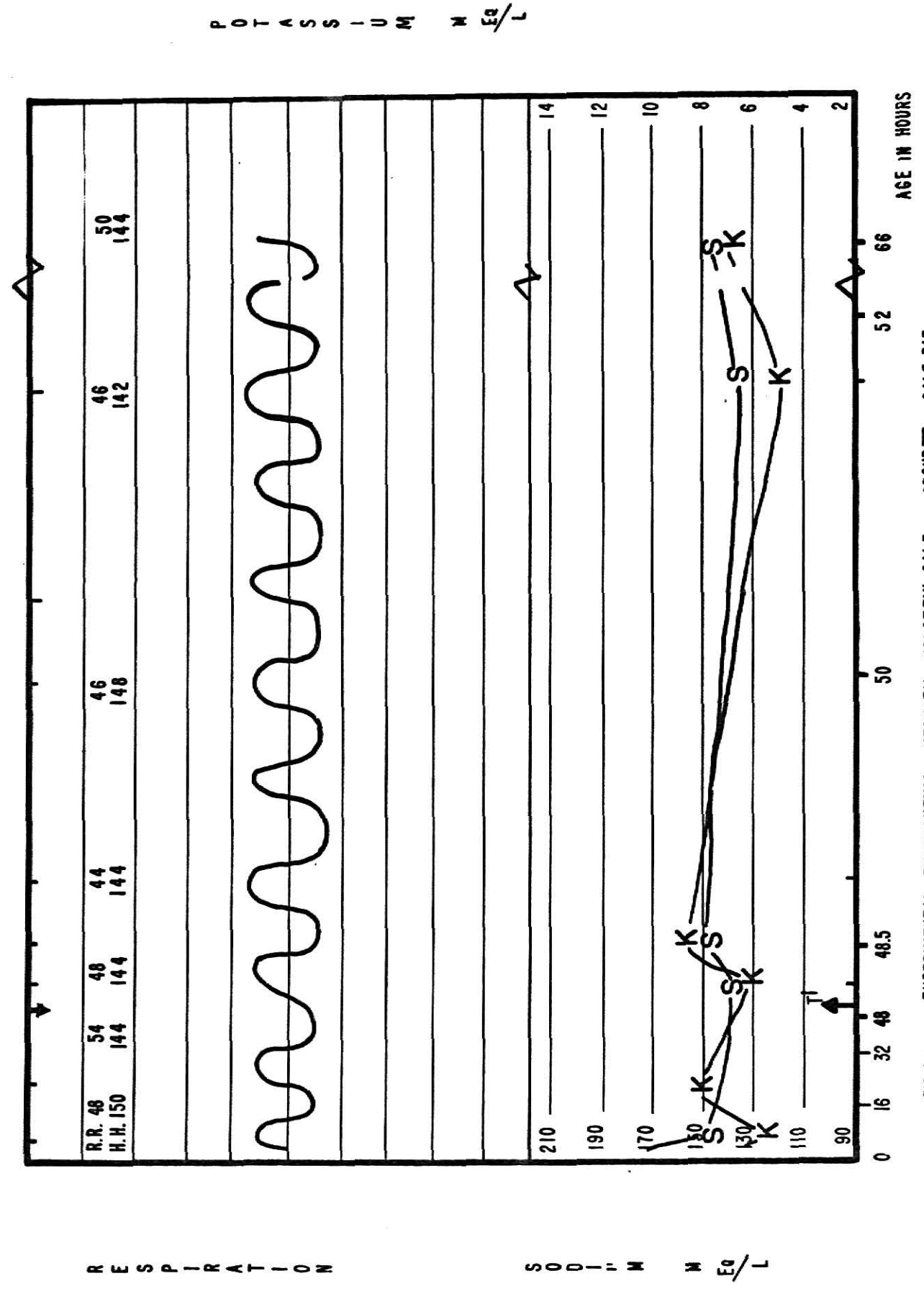

FIG. 12. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF, GROUP III, CALF 317
SERUM SODIUM, POTASSIUM AND RESPIRATORY PATTERN. (SEE TABLE 59, page 220.)

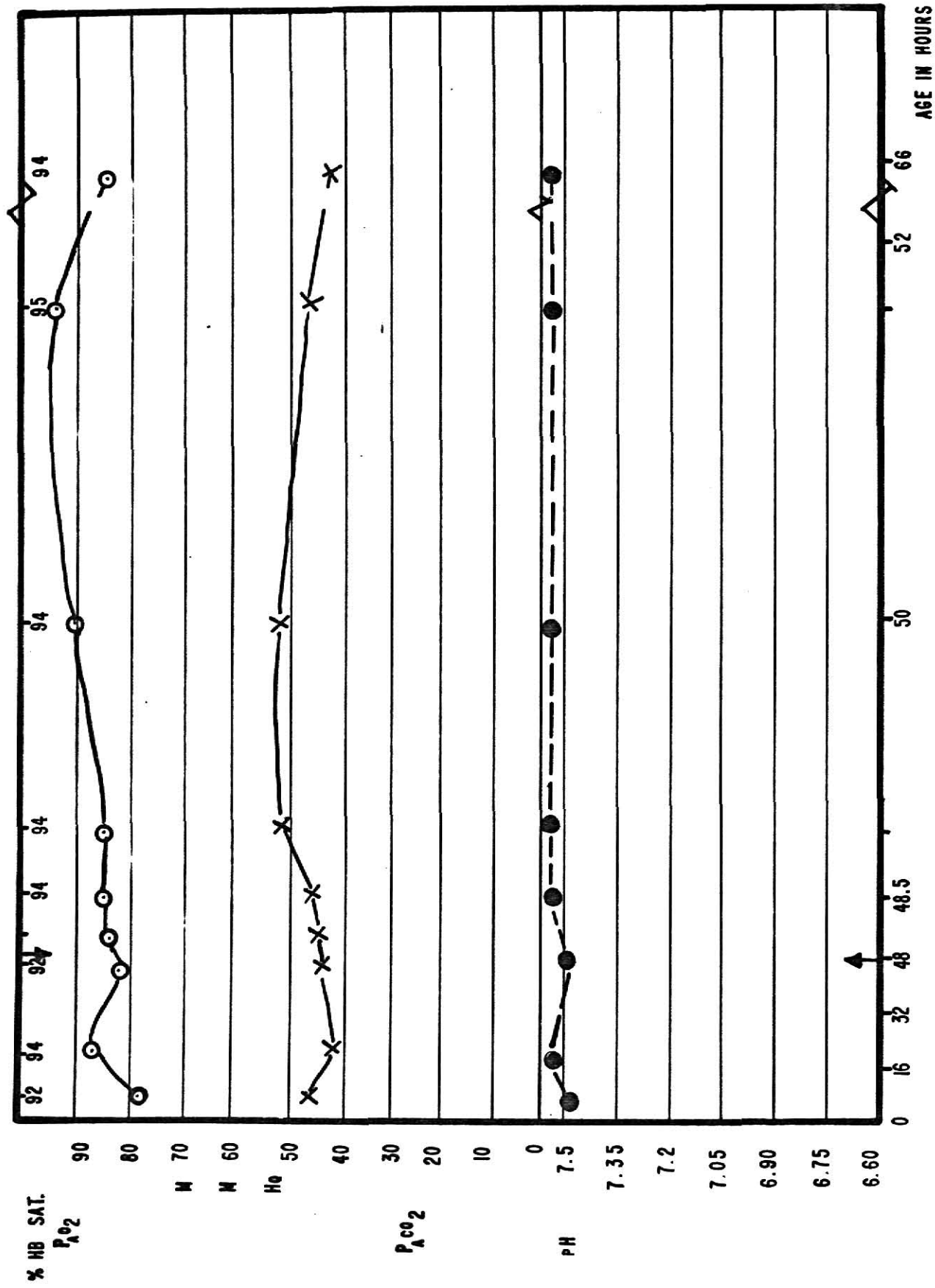

FIG. 13. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 317
WHOLE BLOOD $P_{A}O_2$, $P_{A}CO_2$, pH, AND HEMOGLOBIN PERCENT SATURATION. (SEE TABLE 55, page 216 and Table 57, page 218.)

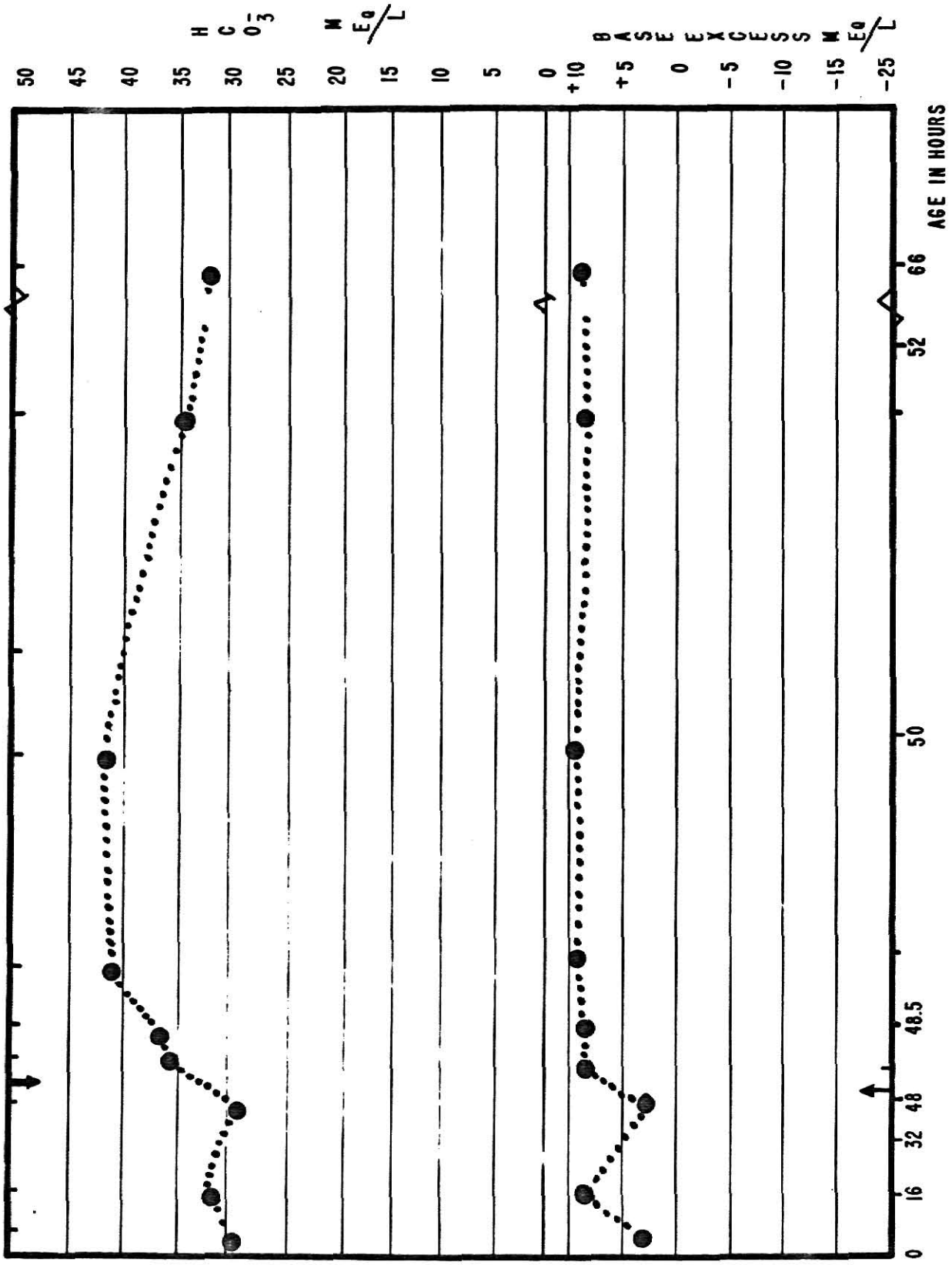

FIG. 44. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALF. GROUP III, CALF 317
PLASMA TOTAL BICARBONATE AND BASE EXCESS. (SEE TABLE 55, page 217.)

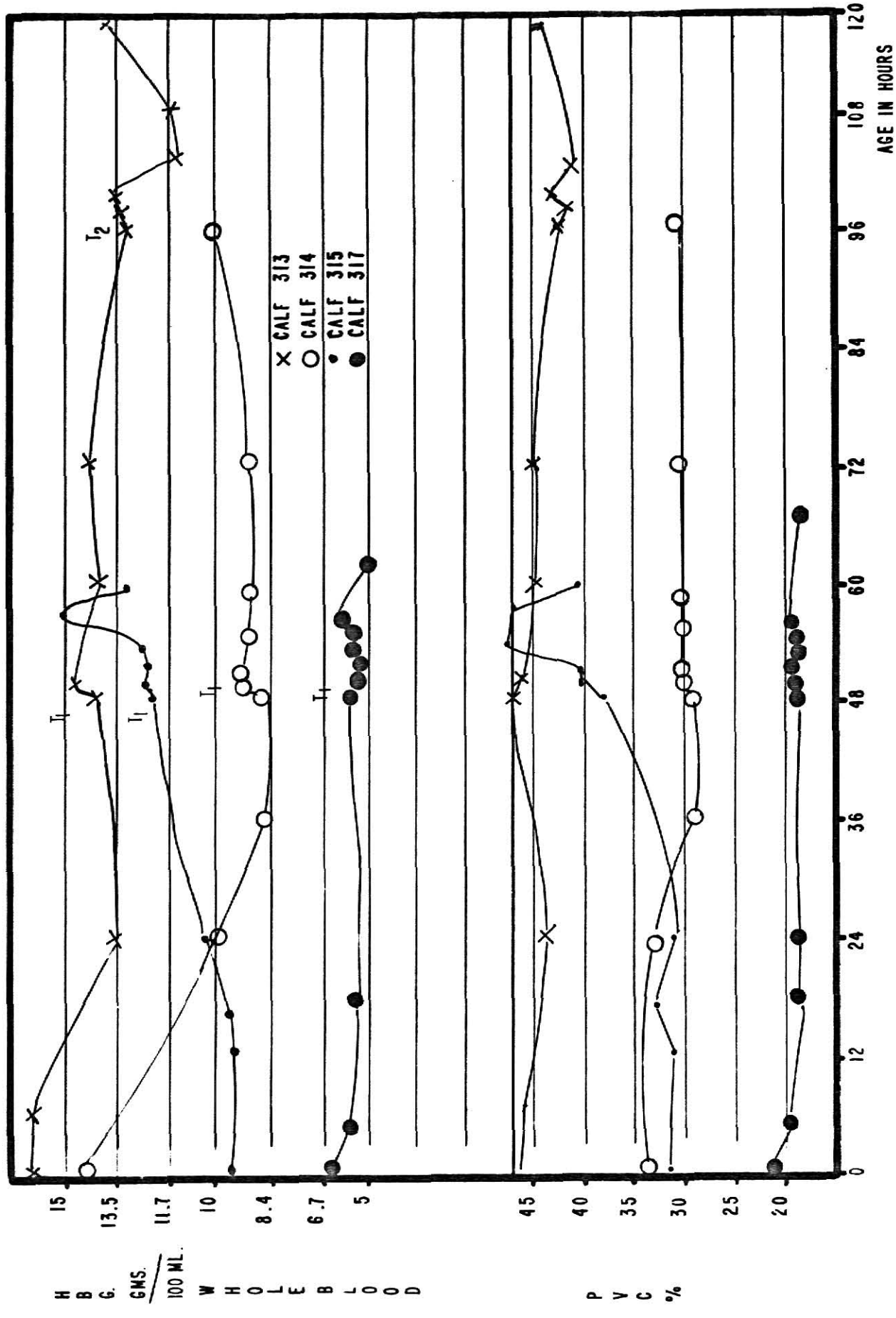

FIG. 45. EXPERIMENTAL ENDOTOXEMIA, NEONATAL HOLSTEIN CALVES 313, 314, 315, 317, GROUP III HEMOGLOBIN; PACKED CELL VOLUME. (SEE TABLE 58, page 219.)

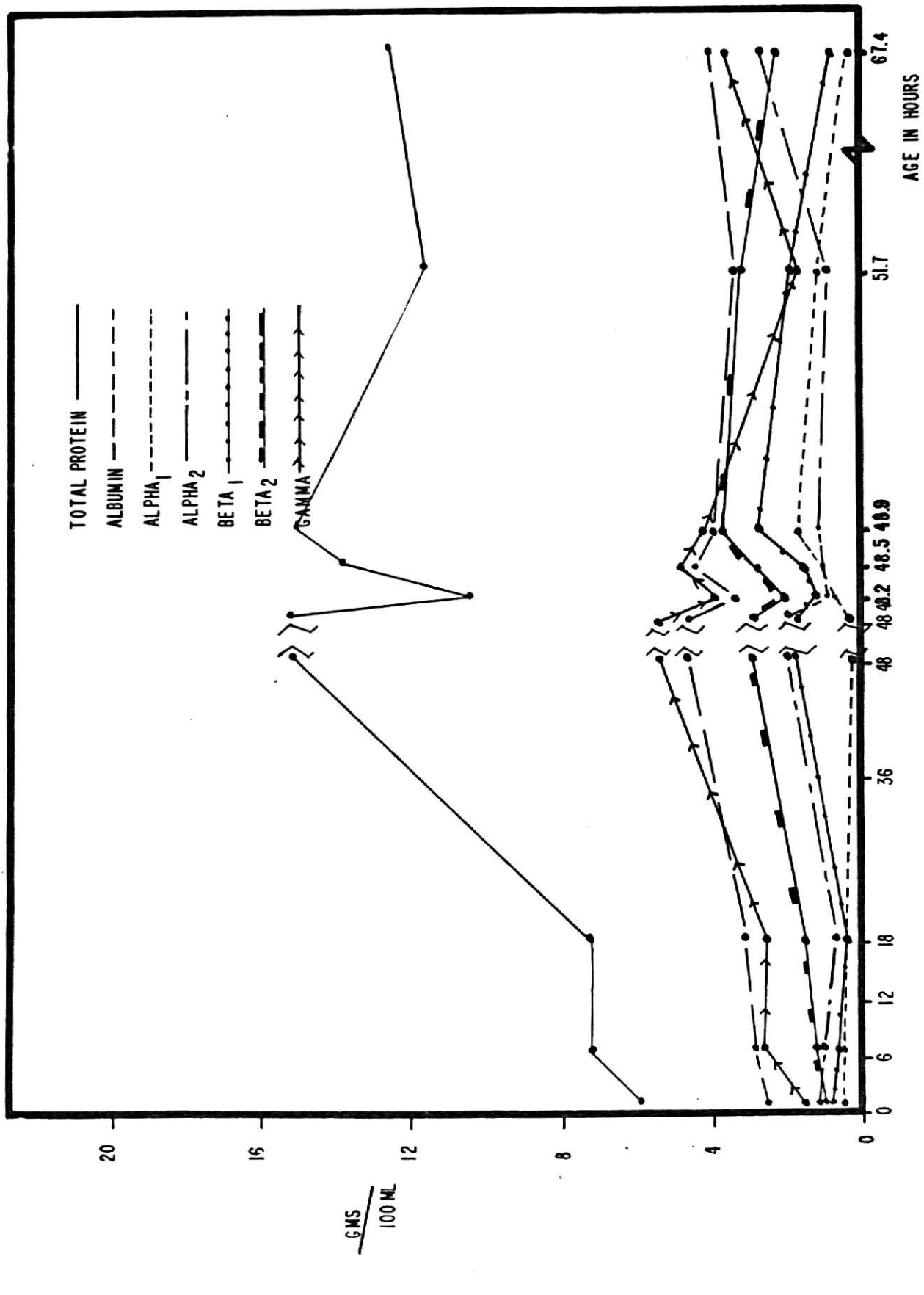

FIG. 46. TOTAL SERUM PROTEIN AND SERUM ELECTROPHORESIS VALUE IN NEWBORN HOLSTEIN CALF GROUP III, CALF 317. (SEE TABLE 6b, page 221.)

DISCUSSION

The discussion will be carried out in relation to the group response and observations within the group but with some cross references.

Group I Control Calves

Group II Intravenous Endotoxin Challenge Calves

Group III Oral Endotoxin Challenge Calves

Group I

Control Calves

Control calves showed an early instability in all parameters studied.

The initial sustained rise in pH was a direct effect of (1) P_aCO_2 elevation, effected by increased and more complete metabolic activity; probable increased and/or maintained right to left shunting; these effecting a right shift in the carbonic acid-bicarbonate mechanism of acid-base balance; (2) higher P_aO_2 values aiding in an increased rate of metabolism and (3) high levels of kidney function thus rapidly eliminating accumulated metabolic acids present at high levels post partum. Concurrent with this kidney acid elimination there is a very high level of bicarbonate and sodium conservation and tubular phosphate buffering occurring in the proximal middle and distal collecting tubules. These actions being coupled with increasing heart and respiratory rates.

Thus at this time there is the initiating period of respiratory function; CNS and peripheral respiratory center activation; working in concert with the vascular chemoreceptors (carotid and ortic bodies, etc.). These effecting a very complex exchange and balancing of acids, bases, gases and vascular

pressures, only partially active prior to birth. Superimposed upon the above described activities is a sudden influx of new proteins obtained from colostrum feeding and giving some aid to acid base control both by way of their bivalent activity; introduction into the metabolic cycles and red blood cell protein (hemoglobin) conversion. The end result being, sustained acid-base balance in relation to blood gases, kidney function and metabolic activity.

Therefore P_aO_2 rose from 75.9 mmHg at 1 hour of age to 78.0 and 79.0 mmHg at 12 hours of age. P_aCO_2 rose from 43.0 mmHg at 1 hour to 48.5 mmHg at 18 hours. This in spite of a more evident ventilating process taking place by way of pulmonary perfusion (heart rate increase); if it may be assumed cardiac output, etc. is sustained; maintained high level of respiratory rate (60/min and above) and normal breathing pattern.

Concurrent with this initial 18 hours phase of life as discussed above was a rapid increase in base excess from 0.94 mEq/L at 1 hour of age to 7.96 mEq/L at 18 hours of age. This being directly related to the above discussed kidney, respiratory and metabolic changes and pH elevation. Total plasma bicarbonate rose from a 1 hour value of 23.7 mEq/L to an 18 hour value of 32.9 mEq/L. This bicarbonate increase which may seem to be overresponsive is probably directly proportional to the degree of metabolic acidosis post partum. However, it is evidenced as a lag phenomenon in acid base response.

After 18 hours of age pH remained very stable at 7.44 ± 0.01; with two highs of 7.46 and 7.47 at 36 and 120 hours, respectively. These highs correlate with a beginning decline in base excess and sodium adjustment.

P_aO_2 showed a significant 18 hour decline to 70.34 mmHg then rose to a new high of 82.68 mmHg at 72 hours of age and are undoubtedly related to improvements in fetal circulating changes as effected by foramen ovale and ductus

closure and improved pulmonary gaseous exchange.

P_aCO_2 regressed slowly from the 18 hour high of 48.52 mmHg to a consistent 40.1 ± 3 mmHg at 48 hours of age while P_aO_2 stabilized at 77.8 ± 3 mmHg between 96 and 21 hours of age. Thus one might speculate there is still some lingering evidence of continued immaturity of the adjustment and balancing actions between the vascular, CNS, kidney and respiratory systems as discussed earlier. For it was at these approximate hours (79-96), that heart rate and respiratory rate reduced and stabilized (Table 12).

A slight peaking of base excess at 144 hours is also reflected in a high pH, P_aO_2 and P_aCO_2.

What may be considered high base excess values, as compared to man, may also be an indication of incomplete pulmonary perfusion, and/or improper alveolar-vascular gaseous transfer and/or unbalanced kidney function and/or a greater degree of right to left cardiac or aortic shunting. These may be normal for calves to varying degrees and these base excess values may be normal for these calves or the calf showing none of these complications.

Mean temperature values in control calves progressively elevated from a 1 hour value of 100.6°F (38.8°C), to 102.5°F (39.3°C) at 48 hours of age and 103.0°F (39.5°C) at 144 hours of age and remained stable through 240 hours.

Mean arterial blood hemoglobin values for the Group I control calves showed a very gradual decline from 1.0 hour and 6.0 hour mean values of 10.4 Gms/100 ml, to a stable mean value range of 8.8 Gms/100 ml at 72 hours and 7.9 Gms/100 ml at 240 hours of age. These declines are undoubtedly related to fetal changes, and the probable 6 hour period of neonatal hydration (see proteins) and rapidly elevating plasma proteins.

Hemoglobin oxygen saturation in control calves showed two high peak periods.

These being at 6 hours (92.4%) and 26-72 hours (93.4-94.1%). The initial period correlating to the very low pH period. This is also the period of high levels of fetal hemoglobin. The second peak is during a period when both pH and P_aO_2 are at high levels; this combination effecting high levels of hemoglobin oxygen association. Following the 72 hour high of hemoglobin oxygen saturation there is a persistent decline to a stable value of 91.0 + 1.0% at 168.0 hours of age. These values may be effected by shifting from one Hb oxygen dissociation curve to another as per pH change (Figure 1) and animal age (44).

Heart rates and the respiratory rate and patterns were determined by: (1) auscultation of the heart and (2) visual observation, respectively. Heart rate showed a gradual and regular decrease from the 6 hour rate of 138 per minute to 121 per minute at 86 hours of age; at this time there was a fluctuating stability of 100 and 120 beats per minute throughout the remainder of the experimental period. The respiratory rate showed an initial increase from a 6 hour rate of 57 to a rate of 75 at 72 hours. This was followed by a gradual decrease for the next 72 hours, after which it stabilized between 52 and 46 cycles per minute. The pattern of respiration was very stable unless the animal was physically handled, in which case the heart rate had a tendency to become elevated.

Potassium was considered to be very stable throughout the 240 hours experimental control period for it began at 6.87 mEq/L at 1 hour and declined to 6.22 at 6 and 12 hours then ranged from 6.34 to 7.28 mEq/L throughout the rest of the experimental period except at 168 hours of age when it was 8.43 mEq/L; percentage wise this could be considered a fairly wide range of mean values. There seemed to be a substantial lowering of potassium during the 216 and 240 hour period of life to 6.59 and 6.8 mEq/L. These mean values are higher than

those previously reported (8, 9, 10, 11, 12); however, they were all in older animals except possibly one (12). These values, except for two, were under those values considered high enough to cause cardiac irregularties (8, 9, 10, 11, 12)*.

Mean serum sodium values in Group I control calves showed considerable instability during the first 48 hours of life. There was a rapid increase from 1 hour mean value of 136.9 mEq/L to 146.1 mEq/L at 6 hours of age; then a decrease to 140.6 mEq/L at 12 hours followed by a rise to 143.3 mEq/L at 18 hours of age. Sodium stability occurred at 24 hours of age and from then until 216 hours of age was maintained between the mean values of 137.2 mEq/L and 133.1 mEq/L. A mean value of 123.6 mEq/L at 240 hours appears to be somewhat out of line; however there was only a sample size of 3 at that hour and calf number 104 (appendix) has a serum sodium value of 117 mEq/L at 240 hours of age with no visible physiological problems evident indicating an equipment error. These values as observed after 24 hours were usually lower than those observed by other workers (8, 9, 10, 55).

The most logical cause of the very early high sodium values (coupled with high bicarbonate values) is undoubtedly a result of early high level kidney function. There is at this time a post parturient metabolic acidosis that is being corrected by kidney extrusion of acid (H^+) and at the same time a conservation (perhaps resulting in overcompensation) of bicarbonate and sodium. The net effect being very high levels of serum bicarbonate and sodium during this 16 to 18 hour time period.

A period of relative fractional instability for proteins persisted for

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*Appendix, page 222.

approximately 120 to 140 hours. During this period there was a pronounced rise in total proteins from 6.1 Gms/100 ml to 8.85 Gms/100 ml at 96 hours; this being higher than values found by other workers (15, 17, 18), for this approximate age; although equal to those values found by Tennant (17) in Jersey calves in spite of the fact the calves in this experiment received colostrum from Holstein cows. Gamma globulin showed the most marked increases from 1.07 Gms/100 ml at 1 hour to 2.57 Gms/100 ml at 96 hours of age.

Albumin rose gradually; with some fluctuations after 6 hours of age; and remained at approximately 35% of total proteins from 96 hours on. This rise being related to early metabolic formation and colostrum absorption. Alpha 1 showed a very early loss from the 1 hour 0.38 Gms/100 ml value, to 0.05 Gms/100 ml at 48 hours. Then showed a gradual recovery to 0.21 Gms/100 ml at 120 hours and remained stable through 240 hours. Alpha 2 showed a continual gradual increase; following an early small decline; from 0.69 Gms/100 ml at 1 hour to 1.27 Gms/100 ml at 240 hours and composing 15% of total protein at this time.

Beta 1 proteins followed alpha 2 in rate of increase and stability from 1 hour on. Beta 2 showed a very rapid and marked decrease from 1 hour 2.9 Gms/100 ml value to 6 and 12 hours values of 0.6 and 1.0 Gms/100 ml, respectively. Then it increased and stabilized at 1.4 and 1.6 Gms/100 ml at 168 to 240 hours of age. Gamma globulin showed the expected gradual climb to approximately 20% of total protein (2.2 Gms/100 ml) at 240 hours with a peak of 2.73 Gms/100 ml at 36 hours of age and a stable range from 2.21 Gms/100 ml to 1.83 Gms/100 ml between 120 and 240 hours of age. The 6 hour slight decrease in all proteins except gamma globulins may be explained as a factor of relative body hydration and fluid control. Rapid gamma globulin elevation; being effected by colostral absorption; in spite of the stable PCV for this six hour age period. This was

then followed by a PCV decrease (RBC may also have been hydrated at 6 hours, this probably contributing to the 6, 12 and 18 hour highs of HCO_3^-; along with metabolic, kidney and respiratory regulation as discussed previously.

Therefore it would appear that the neonatal calf has a very dynamic activity of gains and losses of different protein with an overall total increase until 168 hours of age; that then stabilized through 240 hours of age.

Group II

Intravenous Endotoxin Challenge Calves

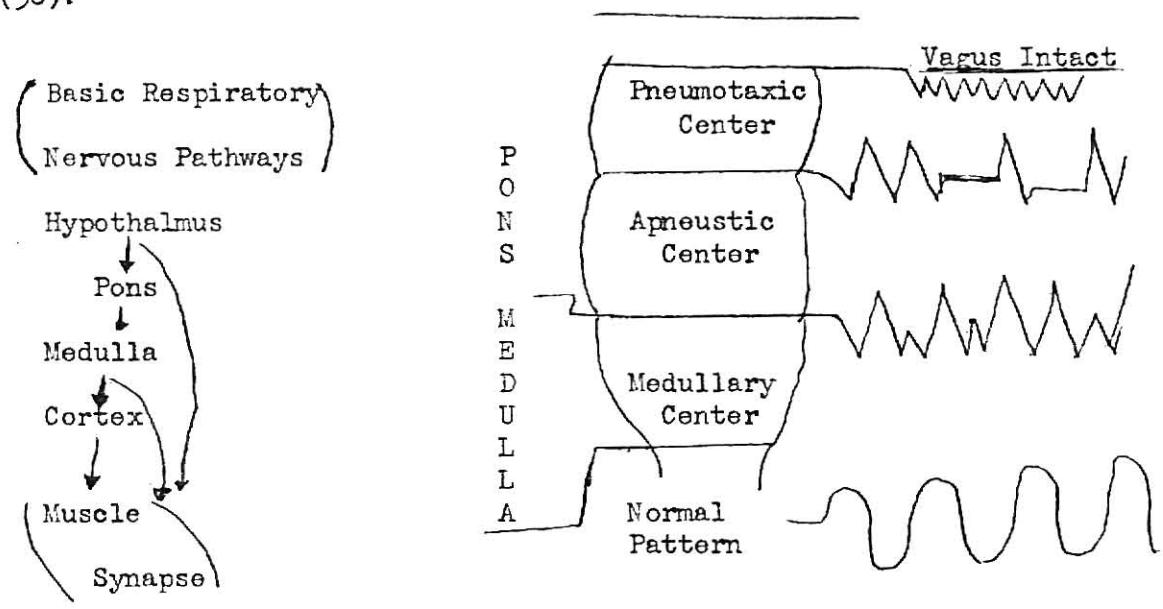
Calves Nos. 207, 209, 210, 216

Respiratory patterns in intravenous endotoxin challenge, Group II calves; were dramatically and severely effected post endotoxin challenge. Calf no. 207 showed very early (T^1 + 1 to 5 minutes) respiratory pattern changes that closely resemble those patterns seen in decerebration; medullary and pons sectioning and thermal cooling (38). There was in all calves an eventual marked decrease in the respiratory rate coupled with pattern alterations to effect depression of blood gas P_aO_2 and variably elevated P_aCO_2. This degree of respiratory pattern change appeared to have some relation to the dosage given. Following T^1 calf 207 (T^1 0.75 mg/Kg) showed profound respiratory collapse; the respiratory rate decreased from 60/min to 10/min immediately. Calf no. 209's (T^1 .38 mg/Kg) respiratory rate initially increased to 100/min but were very shallow in nature as seen in anterior pons sectioning; (ahead of pneumotaxic center) or pons cooling (38); this was followed by a reduction to 30/min and interspersed with a period of hyperventilation prior to T^2, T^3 and T^4 and also following T^4; all occurring during a period of 5 hours and twelve

minutes.

Following endotoxin challenge calf 207 showed four periods of hyperventilation; slight changes in the respiratory pattern between the hyperventilatory episodes and no rate increase (4-10/min); except during the last 30 minutes when the respiratory rate was rapid and shallow. Total time before death 2 hours and 42 minutes. During this time P_aO_2 decreased sharply to a level of low 20's at T^1 + 1.5 hours; was elevated to the high 50's just prior to T^2 and declined sharply to 15 mmHg at T^2 + 30 minutes. P_aCO_2 showed an opposite effect.

Respiratory patterns established with medulla and pons sectioning and cooling (38):



Thus it may appear in calf no. 207 there was a direct and early obliteration of the entire pontine section of the CNS; causing respiratory collapse; marked P_aO_2 decline, P_aCO_2 elevation and respiratory acidosis. This was followed by a slight recovery and an overriding effect of pH which caused hyperventilation and what appears to be a slightly higher center of stimulation (upper pons) at 50.0 + hours of age. All this being overcome following T^2, effecting an

irreversible respiratory acidosis and secondary metabolic acidosis; as a result of further depression of the respiratory centers.

Calf 209 continually showed what may be interpreted as upper pontine or pneumotaxic center involvement and periods of overriding effects (hyperventilation) suspected to be brought on by increased pH and/or hypoxia. The degree of severity also reflected in pH, P_aO_2, P_aCO_2 and attempts to recovery of the resulting acidosis. Calves 207, 209, 210 all showed apnea (cessation of breathing on the expiratory phase); however calf 216 showed apnea on the inspiratory phase and usually the periods of apnea were quite long and frequent as indicated by the respiratory rate. Therefore I will attempt to describe a specific area involved as per the patterns; yet it will be noted that most prior patterns apply to the pneumotaxic and apneustic center (pons) and apnea (as properly defined is in the expiratory phase. This indicating no clear involvement of one area in preference to another; Calf 216 showed cessation of breathing in the inspiratory phase. This response apparently being mediated by the lower apneustic or medullary center; with no regulation (expiratory mediation) from the upper apneustic center; although this is not clear cut (38).

Calf 210 (T^1 3 mg/Kg--Total dose 109.4 mg) showed less marked and apparently reversible effects on the respiratory centers. The rate was not affected initially but the pattern indicated upper pons involvement followed by hyperventilation and blood gas recovery and some pH recovery and stabilization; but a return again to upper pontine involvement indicated by the type of breathing. At this time there was a rate/minute reduction indicating a greater involvement or lower brainstem effect. This was followed by a recovery in the respiratory pattern to an almost normal pattern but not a recovery in the rate/minute and this pattern recovery was quite evident as P_aO_2 increased and P_aCO_2 decreased.

pH was dropping undoubtedly due to the initial respiratory acidosis and now secondary metabolic acidosis. This occurring concurrent with the administration of T^2 (T^2 .3 mg/Kg--T^1 + T^2 .6 mg/Kg) at 49.8 hours. Everything appears quite stable and the animal appeared to be showing some "tolerance" to T^2 (or over-riding physiological action); but following T^3 (0.3 mg/Kg; T^1 + T^2 + T^3 .9 mg/Kg) respiration took on the characteristic's of medullary involvement and this was maintained for about $\frac{1}{2}$ hour. This was followed by a period of hyper-ventilation but no decline in P_aCO_2; but an increase in P_aO_2 occurred; and pH stabilized with a slight lagging rise. Thus there again appeared to be a second recovery by the respiratory pattern. At this time T^4 was given (.6 mg/Kg--total dose 1.5 mg/Kg) and there was a return to a pattern similar to medullary center involvement and P_aCO_2 rose and stabilized; P_aO_2 dropped to a new low and stabilized; but pH was gradually dropping and at T^4 + 1 hour the calf was destroyed. The respiratory rate remained very stable at about 50% of normal throughout the endotoxin period indicating an ability to overcome, or a "tolerance" to the endotoxin by the respiratory center.

Calf 216 succumbed very rapidly to endotoxin challenge as did calf 207, even though the initial dose was considerably less (0.40 mg/Kg versus 0.75 mg/Kg). Immediately following endotoxin injection (T^1) calf 216 had a rapid, shallow, panting type of respiration and the rate was increased to 120-150/minute (2.5 to 3 times the pretoxin rate); this persisted for approximately 30 minutes during which time P_aO_2 decreased to 32.0 mmHg immediately; and P_aCO_2 steadily rose to 75.0 mmHg in 1 hour with respiratory acidosis occurring at T^1 + 12 min and mixed acidosis occurring at T^1 + 54 minutes. This indicated the probability of an immediate and profound general shock syndrome, encompassing

cellular oxygen consumption and decreased cardiac output; the degree of which was probably not witnessed in calves 209 and 210; but is more evident in calf 207. In spite of this severe shock syndrome the pneumotaxic center or upper pons area would appear to be the lowest center of involvement initially; considering the pattern of respiration (38). This however was short lived for at approximately 48.5 hours of age (T^1 + 30 min) the pattern regressed to that of mid pontine character and the rate was reduced to 48/minute.

However P_aO_2 was fairly stable during this half hour; while pH dropped rapidly. Respiratory rate changed to a new low of 16 to 10 per minute with inspiratory cessation (apneusis) of breathing; indicating a lower pontine involvement or cutting off of upper pontine regulation of expiratory initiation. This continued for approximately 45 minutes until the frequency was maintained at 10 per minute but were quickened on inspiration with total expiration and apnea was prolonged. This continued till death.

In summary Calves 207 and 216 showed a more profound response to endotoxin than did calves 209 and 210. Despite a two-fold difference in their initial doses there was in both 207 and 216 an immediate and sustained fall in P_aO_2 and concurrent but often delayed rise in P_aCO_2 with very early pH decrease and base excess deficits occurring. This was brought about by what was believed to be several concurrent mechanisms in these calves:

1. Immediate oxygen deficit.
    a. Respiratory collapse as previously discussed; effecting immediate oxygen deficit. This is not seen in the usual research animal (the dog) as it experiences hyperventilation (60) with dosage of 2 mg/Kg of E. coli endotoxin; effecting comparatively good alveolar ventilation.

b. Initial increased oxygen consumption effected by the increased cellular demand (60) following endotoxin challenge.

c. Secondary oxygen deficit for cellular metabolism due to endotoxin effect on the "ability" to transport O_2 across the cellular membrane and resultant cellular acidosis that then exerts it's effect on the circulating fluid pH.

d. Possible increased right to left shunting following endotoxin challenge, which may be present in these calves and may be common or normal in calves of this age (23, 26, 30, 31, 32). P_aO_2 values observed were considerably lower than those found by other workers (33). Calf 216 may have had a continuing clinically undetectable shunting problem as possibly evidenced by the post partum dyspnea that was transient.

e. What has been described as marked; to negligible; to transient elevation of pulmonary vasoconstriction and peripheral vascular constriction due to endotoxins and hypoxia (23, 26, 30, 21, 32).

f. The effects of endotoxic shock in relation to the "Swartzman reaction" (32, 24, 25, 28) and peripheral vasculature.

g. An apparent decrease in the ability of O_2 to traverse the alveolar-vascular tissues and effect plasma oxygenation. This appears to be quite evident in calf 209 and 315, when P_aCO_2 was maintained at a rather low level and P_aO_2 showed no indications of elevation.

2. Immediate and marked increase in P_aCO_2.

a. Respiratory collapse as described previously effecting initial rapid respiratory acidosis compounded by secondary metabolic acidosis.

b. Early initial increased cellular metabolism and secondary hypoxia.

c. Decreased pulmonary perfusion (23, 26, 30, 31, 32).

d. Possible increased right to left shunting as effected by 1d, e, f, g above.

3. Rapidly declining pH.

a. Uncompensated respiratory acidosis (35).

b. Metabolic acidosis: Increased lactic acid from early cellular metabolism increases and secondary hypoxia of cell effecting incomplete metabolism (60, 46).

c. Decreased kidney function (24, 25, 28).

In summary it is concluded that the very initial acid contribution in calf 207 and 216 was respiratory in nature but the secondary contribution of metabolic acidosis and hypoxia was quantitatively much greater and pH dropped; while P_aCO_2 became elevated and rapidly contributed to the total acidity and terminally low pH and death. There is undoubtedly a damaging contribution from terminal kidney shutdown also.

Hemoglobin oxygen percent saturation in calves 207 and 216 showed very early and sustained low values (42, 44, 41) following endotoxin challenge.

Calf 209 and 210 in this group showed less pronounced and a partially compensating response to endotoxin challenge. Their ability to maintain their physiological responsiveness appeared to be positively related to their ability to maintain adequate ventilatory processes, was effected by adequate CNS respiratory center function predominatly; a controlled or reduced degree of cellular endotoxic shock and subsequently a less severe metabolic acidosis. Respiratory patterns showed periods of near-normal recovery and also showed near-normal P_aO_2 and P_aCO_2 values during these comparable recovery intervals.

The periods of depression and recovery extended through four challenges and four plus hours beyond the initial challenge.

Calf no. 209 was challenged at T^1 with .38 mg/Kg and showed a transient but marked decline in P_aO_2 but it did not reach the depth of depression or persist for the duration of time as seen in calf 207 and 216. There was no increase in P_aCO_2 and a slight rise in pH at T^1 + 18 minutes. This was followed by a 40%(+) recovery in depressed P_aO_2 in 48 minutes during which time pH, base excess and total bicarbonate was equal to or above prechallenge levels.

Thus I believe it may be fair to assume; following endotoxin challenge T^1; we did not experience a crippling effect on the pontine and medullary respiratory centers, permitting an almost complete recovery or overriding response and return of the respiratory pattern to near normal. This also indicates a good ability of the kidney to concentrate and eliminate probable developing acids. Cellular shock and hypoxia must also be much less following the initial dose of endotoxin, there was a very stable pH early in the case of calf 209 extending for a period of almost 4 hours. In calf 210 cellular oxygen supply was not maintained as well but certainly was much better than in calves 207 and 216 (in view of the higher hemoglobin oxygen saturation values in 210). We must, however, keep in mind the fact that peripheral circulation and O_2 perfusion has undoubtedly been effected. I believe this to be indicative of the fact that the primary and most sustained effects were in the following order detrimental contributions in calves 209 and 210--(1) CNS respiratory center involvement, (2) cellular "shock"--thus basically no different than calf 207 and 216.

There is in calf 209 some early contributing mild respiratory acidosis as effected by elevated P_aCO_2 and related pH change. However P_aCO_2 was then equal

to or lower than prechallenge values while P_aO_2 declined. Therefore there may be an early undetectable metabolic acidosis related to a degree of hypoxia when P_aO_2 declined immediately post T^1. Thus an appearing paradox between decreased P_aO_2 and non elevation of P_aCO_2. The most likely conclusion being that O_2 transfer from the alveoli to vascular plasma has been interferred with, while CO_2 diffusion and exchange is adequately maintained in spite of the seemingly lowered minute volume.

One of the initial cellular responses to endotoxin challenge is an immediate increase in uptake of oxygen, followed by a decrease (minutes), followed by another increase that is variable in degree and duration (60). Coupled with oxygen consumption interferences are interferences with intracellular metabolims of the mitochondria effecting decreased formation of the high energy bonded AMP, ADP and ATP molecules for cellular energy; ribosomal amino acid metabolism and finally deterioration of the lysosomal membrane and release of it's destructive contents. The net effect being high intracellular acidity (predominatly lactic acid) and cell death.

Therefore the question arises as to which component (cellular endotoxic shock or hypoxia) has effected the greatest insult at this time in calf 209.

Following the second challenge (T^2) of calf 209 (T^1 + 42 minutes--Dose T^1 + T^2 .75 mg/Kg); P_aCO_2 rose approximately 26% in 1 hour and pH declined to 7.29 and P_aO_2 dropped to 42.6 mmHg. This was followed by a period of P_aO_2 and pH rise and P_aCO_2 decline as a result of increased ventilation and apparent partial recovery of the respiratory brain stem center and kidney acid elimination. This being 2 hours 12 minutes post T^1 and 1 hour and 30 minutes post T^2.

Immediately following T^2 there was an extended period of marginal

respiratory acidosis (49.0 to 49.9 hours) and probably metabolic acidosis that was being partially controlled by the kidney and other buffers system (Hb and protein); as pH was dropping gradually at this time and P_aCO_2 rising as a result, aiding in the acid base control by pushing more HCO_3^- into the building acid pool (pH at 49.0 hours 7.41; pH at 49.9 hours 7.29). It was at 50.4 hours that metabolic acidosis became markedly evident. This following the initial low period of P_aO_2 (48.6 mmHg and 42.6 mmHg at 49.5 and 49.9 hours). At this time base excess was 1.1 mEq/L and pH had risen from 7.29 to 7.39 and Hb saturation was 87% (44); P_aO_2 55.1 mmHg and P_aCO_2 35.5 mmHg, and oxygen supply was probably marginal at best at this time. Following the third endotoxin (T^3) challenge, however, the respiratory pattern again deteriorated, but a period of hyperventilation effected a P_aO_2 increase; followed by a decline; and a new low that probably markedly effected cellular hypoxia. Following the hyperventilation P_aCO_2 was on a continual and unabated increase just prior to T^4; and metabolic acidosis became strongly influential as pH declined rapidly. This is apparently related to a marked oxygen deficit that occurred for several reasons: cardiac output following T^4 was probably reduced as may be indicated by the rising heart rate; kidney function probably was declining; metabolic acids increased rapidly and respiratory function worsened effecting a decline (and a new low) for P_aO_2. The blood buffers (hemoglobin, bicarbonate and protein) were already functioning at a maximum; as a result pH dropped extremely abruptly and death was short in coming.

Calf number 210 following T^1, showed a very similar blood gas and bicarbonate pattern in relation to calf 209; but a slightly lower pH and higher P_aCO_2; but had consistently maintained a better respiratory pattern and higher P_aO_2 and percent Hb saturation prior to T^3; therefore prior to and following T^3

the metabolic acid contribution was minimal but evident; and had been gradually and decidedly reducing the pH. At this time one might surmise kidney functions in this calf were less able to combat the early metabolic acidosis. Following T^3 P_aO_2 dropped to levels seen in calves 207 and 216 following T^1 and marked tissue hypoxia undoubtedly occurred and P_aCO_2 rose markedly only to be halted by the respiratory center effecting a period of hyperventilation. Following T^4 P_aO_2 was dropping terminally as was pH due to an apparently rapidly developing tissue hypoxia with metabolic acidosis and a contributory respiratory acidosis. Therefore at this time (50.0 hours of age; T^1 + 4.8 hours) the perimeters were: P_aO_2 30.6 mmHg, P_aCO_2 50.8 mmHg, pH 7.11, base excess -13.0 mEq/L, total HCO_3^- 14.5 mEq/L and total CO_2 16 mm/L and death occurred.

With these findings in mind it is conceivable in the marginal case of cellular "endotoxin shock" (as may be the case in calf 209 and 210); that even with improved conditions (respiratory and circulatory) effecting improved gaseous exchange resulting in better than pre T^1, T^2 or T^3 conditions; these improved circumstances may be unable to provide the necessary oxygen demand and acid removal in sufficient time or quantity to repair or improve cellular activity.

Hemoglobin and Packed Cell Volume

Hemoglobin and packed cell volume in the intravenous toxin group of calves show absolutely no detectable effect following endotoxin challenge in numbers 207, 210 and 216. Calf 209 showed a sustained increase in hematocrit (PCV) following T^2 at 48.9 hours of age, that regressed at T^2 + 1.5 hours (50.4 hours) and rose again at T^3 + 6 minutes (51.0 hours). These elevations were however small in magnitude; T^2 - 2.5%; T^3 - 6%.

Hemoglobin Oxygen Saturation and Temperature

Temperature in calf 207 and 216 were extremely stable throughout the experiment with a total temperature decrease of 0.1°C in calf 207 and 0.3°C in calf 216. Following endotoxin injection in calf 207 it's temperature rose 0.6° at T^1 + 12 minutes and regressed gradually to 39.0°C at T^1 + 1 hour 24 minutes and remained as such. Calf 209 and 210 both showed a mild post T^1 temperature elevation of 0.8°C and subsequent gradual regression to normal and then sub-normal until at death calf number 209 was 36.0°C at T^1 + 5.2 hours and calf 210 was 35.0°C at T^1 + 4.8 hours. These depressions being related unquestionably to decreased peripheral circulation and reduced rate of metabolism. Initial temperature rises following endotoxin administration are believed caused by decreased peripheral vascular circulation and reduced heat loss.

Hemoglobin oxygen saturation in all four calves was maintained at very high levels (44) with very low P_aO_2--at P_aO_2 29.7 mmHg and pH 7.38 there was 67% saturation in calf 209 and P_aO_2 of 29.7 mmHg with pH 7.26 it was 60% in calf 210.

Sodium and Potassium

Serum potassium values in general were higher than controls and those previously reported (8, 9, 10, 12). Following endotoxin challenge both sodium and potassium showed elevations and depressions (calf 216, 207) with a potassium high of 8.9 mEq/L in calf 207 at a pH of 6.78. While potassium in calf 216 was 4.8 mEq/L at a pH of 6.12; calf 209 and 210 showed comparatively low values for all the calves of 5.8 and 4.7 mEq/L prechallenge. Calf 209 had 8.6 mEq/L of potassium terminally at a pH of 6.51 and calf 210 had 5.4 mEq/L at a pH of 7.12 thus there may be some relevance to potassium elevation in endotoxemia but only

at very low pH values. Hemolysis seemed to be a problem with some calves although it did not appear to be related to endotoxin challenge except in calf 314. High potassium values associated with hemolysis were not retained for research evaluation.

Serum sodium values in the intravenous group II calves were effected as follows. Post endotoxin challenge all calves but 210 in this group showed an early serum sodium decrease as follows: 207--T^1 + 12 minutes (103.2 mEq/L) with a recovery to 151.3 mEq/L, then a decrease at T^1 + 72 minutes (119.8 mEq/L); 209--T^1 + 26 minutes at (134.4 mEq/L); 210--was generally lower; 216--T^1 + 24 minutes (125.0 mEq/L). Serum sodium values continued to increase in spite of subsequent challenges. These changes are probably related to kidney action and minimal cellular shock.

Endotoxic shock has been held responsible for sodium pump interference; this being considered an active mechanism of electrolyte regulation at the cellular membrane level. Intracellular concentrations of electrolytes are determined by active and passive means. Passive permeability is regulated by the gradient across the membrane in relation to the ion considered; there is no metabolic energy or oxygen consumed in it's crossing or transfer. Active transfer is that seen in the sodium pump--energy is needed and oxygen is consumed and a carrying mechanism may be involved. The gradients across cellular membranes is very high: intracellular sodium--aproximately 10 mEq/L, extracellular approximately 135-140 mEq/L; potassium--intracellular approximately 145 mEq/L, extracellular approximately 5 mEq/L; obviously this is not being controlled by the simple mechanism of passive equilibration (RBC's show

considerable species difference). Therefore we may be seeing an interference with the sodium pump in several instances in these experimental models and a secondary passive activity occurring. The initial consistent decrease of serum sodium post challenge; may be considered as such an action; followed by what may be a secondary pump recovery and return of serum sodium to normal values. Why potassium (which is considered more permeable than sodium) is not seen to increase markedly in the extracellular fluid at this time may indicate another means of maintaining its gradient or at least different circumstances than are observed here are needed to destroy it's activity. However in calf no 315 there appears to be a breaking down of the means of regulation for both potassium and sodium terminally. However this terminal action may also be coupled with terminal kidney failure.

Serum Proteins

Group II serum protein changes following endotoxin challenge were of little or no consequence. Alpha 1 shows a decrease in calves 207, 209 and 210 and albumin appears to decrease in calf 217 immediately post toxin. They show a quick recovery with resulting higher levels.

Group III

Oral Endotoxin Challenge Calves

Calves Nos. 313, 314, 315, 317

Following oral endotoxin challenge there were two distinct types of response; with calf 315 deviating from the others in Group III. This calf (315) prior to challenge had developed a severe case of diarrhea and this unquestionably

had a bearing on the outcome. Therefore this calf will be discussed separately. Calf 313 had viscid diarrhea at T^2 + 60 minutes and this time only. Calf 314 showed uneasiness and slight transient depression; with the ears lowered; that lasted a matter of 15 to 20 minutes. Calf 217 showed no clinically evident response.

Laboratory wise these three calves showed some mild and persistent effects. Following T^1 calves 314 and 317 showed a small increase in P_aCO_2 that were transitory in nature and peaked at 1.6 and 1.8 hours post T^1 respectively and in calf 317 was normal as compared to controls at T^1 + 3.6 hours. Simultaneous with this P_aCO_2 elevation both calves pH rose to new highs (314: Prechallenge 7.47, T^1 + 1.6 hours 7.49) (317: Prechallenge 7.46, T^1 + 1.8 hours 7.54) calf 313, even though it showed no clinical changes, went from prechallenge pH of 7.42 to 7.45 at T^1 + 2.0 hours; base excesses in all calves were elevated. Following T^2 in calf 313 there was no identifiable response. But in all three calves pH and base excess remained high. Concurrent with this, sodium values although generally unstable, appeared to have a general decline followed by a recovery (especially in calves 313 and 314). Potassium had a reverse effect. Respiratory patterns and rate did not appear to be affected nor did heart rate.

Temperature; PCV; hemoglobin, percent hemoglobin oxygen saturation and proteins did not appear to be affected in these three calves.

The effects above were certainly minimal; except in the case of pH and base excess. These effects appeared to be longer lasting (pH and base excess) than one might expect but endotoxins have been known to have residual effects. Speculation as to the mechanism involved may be (1) Kidney function probably has been interferred with to effect preservation and elevation of serum bicarbonate; (2) Initially there was probably some cellular metabolic effects causing

a rise in cellular metabolism with no concurrent hypoxia as evidenced in Group II calves; as a result metabolism was complete to effect a P_aCO_2 increase and not intermediate metabolic acid (lactic acid, etc.) formation; (3) The "sodium pump" may have been slightly disturbed giving short lived altered sodium and potassium changes; this however may also be kidney related; (4) These responses may have been coupled with a clinically undetectable respiratory minute volume decline; (5) The other mechanism of change may have been medicated through the vaso pressor effect on pulmonary circulation and/or cardiac output; although these are usually transitory in dogs and P_aO_2 was not effected in the calves. Thus the modes of response may have been operating separately or in concert and are merely suspicions at this time. The consistently high value of all protein fractions pre and post endotoxin in calf 317; coupled with high sodium values; may have been contributing to osmolarity control, but this seems highly unlikely as all fractions except albumin contribute extremely little to osmotic effect in the vascular system.

Calf No. 315

Calf number 315 showed clinical evidence of a progressive severe case of diarrhea; with profuse bowel evacuations; no apparent visible dehydration or temperature elevation were evident prior to the 48 hour oral endotoxin challenge. Thus as evidenced by others (39, 60) it appears inevitable that some calves will become actively affected by colibacillosis in the course of prolonged studies in confinement.

Prechallenge values (48.0 hours) were showing signs of alteration from normal values: Blood gases and pH were: P_aO_2 75.3 mmHg, P_aCO_2 37.7 mmHg, pH 7.40 but base excess was -1.0 mEq/L; sodium 122.0 mEq/L, K 6.0 mEq/L, and PCV

showed indication of elevation (31.0--37.5 Vol %) although proteins appeared stable. Sodium increased even in the face of profuse diarrhea following endotoxin at T^1 + 5.6 hours and 10.1 hours (139.6 and 154 mEq/L) as did potassium while pH was dropping gradually (7.35 at T^1 + 5.6 hours and 7.24 at T^1 + 10.1 hours). At this time, T^1 + 10.1 hours, P_aO_2 was 47.2 and P_aCO_2 was 35.6. Heart rate at this time had returned to slightly above pretoxin levels (140 to 130) and the respiratory rate was maintained at prechallenge levels.

The respiratory pattern became frequently altered from normal to pneumotaxic in nature, and from the indications of blood gases was adequately ventilating periodically (at least) to blow off the accumulating CO_2; however P_aO_2 remained at a very low level. It must also be remembered that CO_2 can diffuse more readily through the tissue than O_2 and if pulmonary perfusion was poor due to increased right to left shunting there could be poor oxygen saturation. This however would not appear to be sufficient explanation considering the magnitude of difference in decreased P_aO_2 and maintained low levels of P_aCO_2 over such a long period of time. But coupled with cellular metabolic disturbance and marginal levels of oxygenation effected by poor transfer of O_2 from alveoli to blood plasma as discussed previously this seeming P_aO_2; P_aCO_2 paradox is probable. Then suddenly cellular hypoxia became pronounced and pH dropped rapidly and death occurs.

Thus once again the animal was confronted with marginal to inadequate respiratory function; marginal to inadequate oxygen supplies; probable secondary circulatory deficiencies; tissue hypoxia as a direct result of the endotoxin and low circulating O_2 tensions; resulting in respiratory and metabolic acidosis.

While hematocrit (PCV) was elevated to 40 and 45 percent this is not

considered to be in a critical range; but considered by some to be an optimal functioning level. Temperature remained stable until the terminal hours. Serum proteins appeared generally uneffected in calf 315.

In conclusion it is apparent that oral endotoxin while it may have mild and transient effects in a normal calf with no gastro intestinal involvement is had marked effects in a calf with presumed epitehlical degradation as related to E.coli enteritis. These findings were evidenced by other works (39, 57).

SUMMARY

1. Controls

   A. Normal newborn Holstein calves showed a marked early physiological instability in all parameters examined; with stabilization as indicated below:

      1. P_aO_2--96 to 121 hours of age 77.8 ± 3 mmHg
      2. P_aCO_2--48 hours of age 40.1 ± 3 mmHg
      3. pH--18 hours of age 7.46 ± 0.02
      4. Base excess 2.7 ± 0.4 mEq/L

         Total HCO_3^---192 hours of age 26.3 ± 0.3 mEq/L

         Total CO_2 27.3 ± 0.3 mm/L
      5. Sodium--24 hours of age 135.5 ± 1.6 mEq/L
      6. Heart rate and respiratory rate--72 to 96 hours of age
      7. Potassium--normal throughout, 6.5 ± 0.8 mEq/L
      8. Proteins--agreed with previously reported changes associated with usual postpartum colostral feeding but slightly higher values were observed.

2. Endotoxin Challenge Calves

   A. Intravenous Endotoxin

      1. The respiratory system appears to be the first and most drastically effected system following E. coli endotoxin challenge in newborn Holstein calves.

         a. This response appears to be mediated as a result of the endotoxins effect on the CNS respiratory centers: reticular activity system; hypothalmus; pontine and medullary centers of the brain stem.

b. This effect appears to be reversible; depending on the initial severity and it's effect on related systems (2, 3 and 4 below).

2. Secondary effects are an early initial respiratory acidosis, hypoxia of varying degrees and cellular endotoxic shock with resulting metabolic acidosis.

   a. Cellular shock may be reversible depending on the initial severity.

3. Pulmonary circulation and perfusion appear to be adequate following endotoxin challenge.

4. Transfer of CO_2 is responsive and adequate; O_2 shows some periods of poor transfer even when alveolar ventilation appeared adequate. These are evident even after long periods of endotoxin effects.

5. Hemoconcentration does not appear to be an early complication of endotoxin challenge and shock in newborn Holstein calves in contrast to the dog.

6. There appears to be a definite lowering of serum sodium values immediately following endotoxin challenge. This is considered to be related to interference with cellular membrane active transport of sodium by the sodium pump. This sodium depression is reversible.

7. Endotoxin had little effect on proteins; except that alpha 1 globulin was markedly reduced but quickly returned to pre-challenge values.

8. Potassium values were consistently higher than those normally reported but the outcome did not appear to have any relevance to these values.

9. Clinical observation would indicate marked disturbance of cerebral and cerebellar centers.
    a. Early loss of muscle tone prior to recumbency.
    b. Depression prior to recumbency.
    c. Persistence of a cutaneous trunchi sensory reflex but absence of any ascending and descending motor response.

3. Oral Endotoxin
    A. Persistently elevated base excess; HCO_3^- and total CO_2.
    B. Transient elevation of P_aCO_2
    C. Mild transiently lowered sodium values
    D. Oxygen alveolar-plasma transfer is apparently affected as seen in calf 315.

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VITA

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APPENDIX

Table 5. Mean arterial blood values for P_aO_2, P_aCO_2 expressed in millimeters of Hg and pH in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III, 0-48 hours (pre-challenge period). See Figure 3, page 64.

Time (Hours)	Sample Size	P_aO_2 mmHg	P_aCO_2 mmHg	pH
1	5	75.90	43.04	7.37
6	4	79.50	45.88	7.39
12	5	78.20	39.56	7.45
18	5	70.34	48.52	7.46
24	9	71.39	46.00	7.44
36	5	80.90	40.86	7.46
48	14	81.07	40.09	7.46
72	5	82.68	36.34	7.47
96	5	75.14	41.20	7.45
120	5	77.21	39.50	7.47
144	5	80.56	43.94	7.45
168	4	77.75	40.33	7.48
192	5	76.98	39.56	7.44
216	5	76.72	39.96	7.45
240	4	70.95	39.83	7.43

Table 6. Mean arterial blood values for total bicarbonate and base excess expressed in milliequivalents per liter; and total carbon dioxide expressed in millimoles per liter in newborn Holstein calves--Group I experimental control calves. Control period: Group I, 0-240 hours; Group II, III 0-48 hours. See Figure 4, page 65.

Time (Hours)	Sample Size	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mm/L)
1	5	23.70	0.94	24.70
6	4	26.50	1.25	27.88
12	5	28.50	2.66	27.46
18	5	32.90	7.96	33.90
24	9	30.11	5.37	31.28
36	5	28.10	4.36	29.10
48	14	27.41	3.94	28.40
72	5	25.84	2.94	26.94
96	5	26.40	3.32	27.60
120	5	28.50	4.62	29.50
144	5	30.30	6.34	31.30
168	4	29.20	5.95	30.15
192	5	26.60	3.08	27.60
216	5	26.60	3.10	27.60
240	4	25.75	2.38	26.75

Table 7. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III, 0-48 hours. See Figure 3, page 64.

Time (Hours)	Sample Size	Temperature (centigrade)	Sample Size	Hb Sat. (%)
1	7	38.81	5	92.00
6	4	38.75	4	92.25
12	6	38.53	5	92.60
18	5	39.16	5	91.00
24	10	39.13	9	90.56
36	6	38.93	5	93.40
48	15	39.30	14	93.14
72	7	39.41	5	94.10
96	7	39.41	5	89.80
120	7	39.44	5	92.00
144	7	39.53	5	93.00
168	6	39.21	4	90.00
192	7	39.26	5	91.40
216	7	39.48	5	91.80
240	4	39.23	4	91.00

Table 8. Mean arterial blood hemoglobin values expressed in grams per 100 milliliters and mean arterial blood packed cell volume expressed in volumes percent in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III, 0-48 hours (pre-challenge period). See Figure 5, page 66.

Time (Hours)	Sample Size	Hemoglobin Gms/100 ml	Volume %
1	14	10.37	33.32
6	4	10.43	33.25
12	7	9.57	29.64
18	7	9.54	29.79
24	11	10.16	31.64
36	7	9.13	26.64
48	16	9.46	30.16
72	7	8.77	26.29
96	7	8.81	27.36
120	7	8.46	27.21
144	7	8.17	27.00
168	6	7.97	25.75
192	7	8.28	26.71
216	7	8.31	27.36
240	4	7.85	25.75

Table 9. Mean serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III 0-48 hours (pre-challenge period). See Figure 2, page 63.

Time (Hours)	Potassium		Sodium	
	Sample Size	Mean mEq/L	Sample Size	Mean mEq/L
1	12	6.87	13	136.95
6	3	6.23	3	146.13
12	8	6.21	9	140.59
18	6	6.42	6	143.27
24	11	6.37	11	137.15
36	7	6.34	7	133.44
48	12	6.43	14	134.46
72	7	5.61	7	132.73
96	6	7.28	6	135.90
120	6	6.35	7	133.20
144	7	5.81	7	133.14
168	6	8.43	4	134.33
192	7	7.13	7	136.57
216	7	6.59	7	134.77
240	3	6.80	3	123.60

Table 10. Mean serum protein electrophoresis values expressed in grams per one hundred milliliters in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III 0-48 hours (pre-challenge period). See Figure 6, page 67.

Time (Hours)	Sample Size	Total Protein	Albumin	Gamma Globulin
1	14	6.05	2.33	1.07
6	3	5.43	2.20	1.47
12	9	6.67	2.26	1.98
18	7	8.84	3.26	2.16
24	11	6.79	2.36	2.02
36	7	8.37	2.71	2.73
48	16	8.26	2.76	2.51
72	7	7.07	2.21	2.07
96	6	8.85	2.70	2.57
120	7	7.53	2.29	2.21
144	7	6.69	1.99	1.83
168	6	9.02	2.65	2.03
192	7	8.21	2.76	1.96
216	7	8.43	2.54	2.03
240	3	8.07	2.13	2.20

Table 11. Mean serum protein electrophoresis values expressed in grams per one hundred milliliters in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III 0-48 hours (pre-challenge period). See Figure 6, page 67.

Time (Hours)	Sample Size	Alpha 1	Alpha 2	Beta 1	Beta 2
1	14	0.38	0.69	0.6	0.9
6	3	0.20	0.50	0.4	0.6
12	9	0.16	0.59	0.7	1.0
18	7	0.20	0.99	0.9	1.4
24	11	0.10	0.76	0.6	0.9
36	7	0.20	0.70	0.8	1.2
48	16	0.05	0.86	0.8	1.3
72	7	0.11	0.79	0.7	1.2
96	6	0.12	1.08	0.9	1.5
120	7	0.21	0.91	0.7	1.2
144	7	0.16	0.86	0.7	1.2
168	6	0.18	1.41	1.1	1.6
192	7	0.11	1.07	0.9	1.4
216	7	0.19	1.19	0.9	1.5
240	3	0.17	1.27	0.9	1.4

Table 12. Mean heart rate (taken by cardiac auscultation) and mean respiratory rate (clinical observation) in newborn Holstein calves--Group I, experimental control calves. Control period: Group I, 0-240 hours; Group II, III, 0-48 hours (pre-challenge period). See Figure 2, page 63.

Time (Hours)	Sample Size	Respiratory Rate	Heart Rate
6	5	57	138
24	8	60	125
48	8	66	135
72	5	75	132
96	5	66	121
120	5	50	100
144	5	58	115
168	4	52	118
192	4	52	120
216	4	48	109
240	4	46	115

Table 13. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 207--Group II intravenous endotoxin. See Figure 8, page 71.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	--	--	--
12.0	97.1	36.2	7.47
18.0	--	--	--
36.0	84.6	36.1	7.47
48.0	97.0	37.1	7.50
T^1-48.0	Endotoxin Challenge		
48.2	41.8	53.8	7.30
48.5	28.2	69.5	7.13
48.8	23.1	66.4	7.01
49.2	16.2	71.1	7.01
49.7	28.1	55.9	6.96
49.8	58.6	43.4	7.04
T^2-50.0	Endotoxin Challenge		
50.2	20.5	62.7	6.98
50.5	17.5	74.8	6.78

Table 14. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 207--Group II intravenous endotoxin. See Figure 9, page 72.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mm/L)
1.0	--	--	--
12.0	25.0	2.3	26.0
18.0	--	--	--
36.0	26.0	2.7	27.0
48.0	28.0	5.6	29.0
T^1-48.0	Endotoxin Challenge		
48.2	25.0	- 0.6	26.0
48.5	22.0	- 6.3	23.5
48.8	17.0	-14.2	17.5
49.2	15.0	-15.7	16.5
49.7	12.0	-19.0	13.5
49.8	11.0	-18.5	12.0
T^2-50.0	Endotoxin Challenge		
50.2	13.5	-17.0	15.0
50.5	10.0	-25.0	11.5

Table 15. Temperature expressed in centigrade and arterial blood hemoglobin oxygen saturation values expressed in volumes percent in newborn Holstein calf number 207--Group II intravenous endotoxin. See Figure 8, page 71.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	--	--
12.0	38.4	95.0
18.0	--	--
36.0	38.9	95.0
48.0	40.0	95.0
T^1-48.0	Endotoxin Challenge	
48.2	40.0	75.0
48.5	40.0	52.0
48.8	39.9	32.0
49.2	39.9	15.0
49.7	40.0	30.0
49.8	40.0	80.0
T^2-50.0	Endotoxin Challenge	
50.2	40.0	20.0
50.5	40.0	12.0

Table 16. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 207--Group II intravenous indotoxin. See Figure 10, page 73.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	10.0	30.0
12.0	10.0	30.0
18.0	9.0	28.0
36.0	8.7	26.0
48.0	9.0	26.0
T^1-48.0	Endotoxin Challenge	
48.2	9.0	26.0
48.5	9.0	26.0
48.8	9.0	26.0
49.2	9.0	26.0
49.7	9.0	26.0
49.8	9.0	26.0
T^2-50.0	Endotoxin Challenge	
50.2	9.0	26.0
50.5	9.0	26.0

Table 17. Serum sodium and potassium values expressed in milliequivalents per litor in newborn Holstein calf number 207--Group II intravenous endotoxin. See Figure 7, page 70.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	5.8	72.8
12.0	--	138.2
18.0	--	152.0
36.0	7.5	143.6
48.0	5.1	--
T^1-48.0	Endotoxin Challenge	
48.2	4.1	103.2
48.5	7.4	151.3
48.8	--	--
49.2	6.5	119.8
49.7	6.8	129.2
49.8	--	--
T^2-50.0	Endotoxin Challenge	
50.2	--	--
50.5	*Hemolysis 8.9	137.5

Table 18. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 207 --Group II intravenous endotoxin. See Figure 11, page 74.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	5.2	2.5	0.0	0.2	0.8	0.8	0.9
12.0	11.8	4.4	0.0	0.8	1.4	1.8	3.4
18.0	14.6	5.3	0.0	1.0	2.2	2.0	4.1
36.0	7.6	2.2	0.3	0.8	0.8	1.0	2.5
48.0	9.6	2.7	0.0	1.1	1.1	1.6	3.1
T^1-48.0			Endotoxin Challenge				
48.2	6.2	1.6	0.4	0.5	0.6	1.0	2.1
48.5	6.0	1.9	0.2	0.8	0.8	0.9	1.4
49.2	6.0	3.0	0.0	0.4	0.9	0.8	0.9
49.7	6.2	2.8	0.0	0.4	0.9	0.7	1.4
T^2-50.0			Endotoxin Challenge				
50.5	7.5	2.1	0.5	0.7	1.2	1.2	1.8

Table 19. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 13, page 79.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	67.1	41.0	7.40
12.0	69.1	35.8	7.43
24.0	80.7	41.6	7.43
48.0	80.9	38.7	7.44
48.0	82.4	37.5	7.48
T^1-48.2	Endotoxin Challenge		
48.5	52.0	38.5	7.52
48.8	62.9	38.9	7.50
T^2-48.9	Endotoxin Challenge		
49.0	63.4	37.3	7.41
49.5	48.6	41.6	7.40
49.9	42.6	48.9	7.29
50.9	55.1	35.5	7.39
T^3-50.9	Endotoxin Challenge		
51.0	29.7	34.7	7.38
51.1	21.9	25.8	7.40
51.4	21.7	25.1	7.41
51.6	28.0	26.5	7.36
51.8	43.6	31.5	7.25
52.0	43.2	31.4	7.22
T^4-52.1	Endotoxin Challenge		
52.6	22.3	43.1	7.08

Table 19. (Contd) Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 13, page 79.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
52.8	23.2	55.6	6.94
53.3	24.8	74.8	6.64
53.4	23.3	81.5	6.51

Table 20. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 14, page 80.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mm/L)
1.0	24.0	0.3	25.0
12.0	24.0	0.2	25.0
24.0	24.5	1.6	25.5
48.0	26.0	2.5	27.0
48.0	27.5	4.2	28.5
T^1-48.2	Endotoxin Challenge		
48.5	31.5	8.4	32.5
48.8	30.0	7.3	31.0
T^2-48.9	Endotoxin Challenge		
49.0	25.5	+3.0	26.5
49.5	23.0	-0.5	24.0
49.9	22.0	-1.1	23.0
50.9	22.0	-1.1	23.0
T^3-50.9	Endotoxin Challenge		
51.0	20.5	-2.3	21.5
51.1	20.5	-1.7	21.5
51.4	21.0	-1.2	21.5
51.6	19.5	-4.3	19.5
51.8	14.0	-11.7	14.7
52.0	12.0	-13.9	12.5
T^4-52.1	Endotoxin Challenge		
52.6	11.0	-16.6	12.0

Table 20. (Contd) Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 14, page 80.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mm/L)
52.8	10.5	-19.8	11.0
53.3	7.0	-22.3	8.5
53.4	6.5	-32.2	7.5

Table 21. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 209--Croup II intravenous endotoxin. See Figure 13, page 79.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	39.2	90.0
12.0	38.3	92.0
24.0	38.8	93.0
48.0	38.6	93.0
48.0	38.9	93.0
T^1-48.2	Endotoxin Challenge	
48.5	39.0	90.0
48.8	39.2	92.0
T^2-48.9	Endotoxin Challenge	
49.0	39.4	92.0
49.5	38.7	86.0
49.9	38.5	75.0
50.9	38.0	87.0
T^3-50.9	Endotoxin Challenge	
51.0	37.5	67.0
51.1	37.0	50.0
51.4	36.8	50.0
51.6	36.8	50.0
51.8	36.6	72.0
52.0	36.4	72.0
T^4-52.1	Endotoxin Challenge	
52.6	36.0	35.0

Table 21. (Contd) Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 13, page 79.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
52.8	36.0	23.0
53.3	36.0	22.0
53.4	36.0	17.0

Table 22. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 15, page 81.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	13.0	45.0
24.0	12.0	40.0
48.0	12.0	38.5
48.0	11.5	37.0
T^1-48.2	Endotoxin Challenge	
48.5	11.5	38.0
48.8	12.0	39.0
T^2-48.9	Endotoxin Challenge	
49.0	12.0	39.4
49.5	13.0	41.5
49.9	12.5	41.5
50.9	12.1	39.0
T^3-50.9	Endotoxin Challenge	
51.0	12.1	40.0
51.1	14.1	45.0
51.4	14.0	45.0
51.6	14.0	45.0
51.8	13.8	45.0
T^4-52.1	Endotoxin Challenge	
52.2	13.2	44.0
52.6	13.2	45.0
52.8	13.2	45.0

Table 22. (Contd) Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 15, page 81.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
53.3	13.2	45.0
53.4	13.2	45.0

Table 23. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 12, page 78.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	0.0	137.4
12.0	8.9	119.0
24.0	5.8	116.4
48.0	--	140.4
48.0	--	140.0
T^1-48.2	Endotoxin Challenge	
48.5	--	--
48.8	6.1	124.4
T^2-48.9	Endotoxin Challenge	
49.0	--	--
49.5	5.4	146.2
49.9	--	--
50.9	--	134.2
T^3-50.9	Endotoxin Challenge	
51.0	5.6	146.3
51.1	--	--
51.4	--	--
51.6	--	--
51.8	5.3	142.8
52.0	--	--
T^4-52.1	Endotoxin Challenge	
52.6	--	--

Table 23. (Contd) Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 12, page 78.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
52.8	--	--
53.3	--	--
53.4	8.6	151.6

Table 24. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 209--Group II intravenous endotoxin. See Figure 16, page 82.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	5.7	1.7	0.2	0.6	0.8	0.7	0.9
12.0	6.2	1.4	0.1	0.9	0.7	0.8	2.3
24.0	8.8	1.9	0.3	0.9	0.9	1.0	3.8
48.0	8.3	2.6	0.0	0.5	0.5	1.1	3.6
T^1-48.2			Endotoxin Challenge				
48.8	12.4	3.4	0.0	1.1	1.2	2.1	4.6
T^2-48.9			Endotoxin Challenge				
49.5	8.3	2.5	0.3	0.4	0.7	1.4	3.0
50.9	8.9	2.6	0.0	0.8	0.8	1.2	3.5
T^3-50.9			Endotoxin Challenge				
51.0	8.6	2.5	0.3	0.4	0.8	1.2	3.4
T^4-52.1			Endotoxin Challenge				
53.4	9.0	2.5	0.2	0.6	0.9	1.4	3.4

Table 25. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein Calf number 210--Group II intravenous endotoxin. See Figure 18, page 86.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	72.4	42.0	7.39
6.0	71.9	43.5	7.39
18.0	70.2	44.5	7.41
48.0	77.2	35.5	7.46
48.0	85.3	34.2	7.52
T^1-48.1	Endotoxin Challenge		
48.7	46.6	46.5	7.38
49.0	59.4	39.7	7.41
49.3	66.6	36.5	7.41
49.4	64.4	41.0	7.40
49.5	48.7	50.5	7.33
49.7	55.4	45.0	7.36
T^2-49.8	Endotoxin Challenge		
49.9	59.1	40.2	7.33
50.1	63.7	43.6	7.31
50.2	63.7	43.6	7.31
50.6	60.0	43.1	7.31
T^3-50.7	Endotoxin Challenge		
50.8	60.0	41.8	7.31
51.0	29.7	48.3	7.26
51.1	32.6	49.7	7.23
51.2	36.4	61.9	7.13
51.5	38.3	63.1	7.13

Table 25. (Contd) Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 18, page 86.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
51.8	51.2	49.5	7.18
52.0	42.5	45.9	7.21
T4-52.0	Endotoxin Challenge		
52.1	35.4	47.7	7.23
52.4	27.8	50.7	7.18
52.6	30.5	50.7	7.12
52.8	29.0	54.8	7.13
52.9	30.6	50.8	7.11

Table 26. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 19, page 87.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
1.0	24.5	0.2	25.5
0.6	25.5	1.3	26.5
18.0	26.5	2.3	27.5
48.0	23.5	0.2	24.5
48.0	26.5	4.6	27.5
T^1-48.0		Endotoxin Challenge	
48.7	25.5	1.5	26.5
49.0	27.0	2.6	28.0
49.3	22.5	0.8	23.5
49.4	25.5	1.2	26.5
49.5	26.0	0.4	27.0
49.7	24.0	0.7	25.5
T^2-49.8		Endotoxin Challenge	
49.9	20.0	-4.7	21.0
50.1	21.5	-3.7	22.5
50.2	21.5	-3.7	22.5
50.6	21.5	-3.7	22.5
T^3-50.7		Endotoxin Challenge	
50.8	20.5	-4.7	21.5
51.0	20.5	-6.4	21.5
51.1	20.5	-6.4	21.5
51.2	20.0	-8.0	22.0

Table 26. (Contd) Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 19, page 87.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
51.5	20.5	-8.0	22.0
51.8	19.0	-9.4	19.5
52.0	18.0	-7.5	19.0
T^4-52.0		Endotoxin Challenge	
52.1	19.5	-7.3	20.5
52.4	18.5	-10.2	20.0
52.6	16.0	-13.2	17.5
52.8	17.5	-11.8	19.5
52.9	14.5	-13.0	16.0

Table 27. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 18, page 86.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	38.9	92.0
6.0	38.9	92.0
18.0	38.9	91.0
48.0	38.8	94.0
48.0	38.9	95.0
T^1-48.1	Endotoxin Challenge	
48.7	39.7	82.0
49.0	39.3	90.0
49.3	39.0	91.0
49.4	38.8	91.0
49.5	38.8	80.0
49.7	38.8	85.0
T^2-49.8	Endotoxin Challenge	
49.9	38.3	85.0
50.1	38.3	85.0
50.2	38.3	85.0
50.6	38.0	84.0
T^3-50.7	Endotoxin Challenge	
50.8	37.5	84.0
51.0	37.2	60.0
51.1	36.9	65.0
51.2	36.6	60.0

Table 27. (Contd) Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 18, page 86.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
51.8	36.4	62.0
52.0	36.1	75.0
T^{4}-52.0	Endotoxin Challenge	
52.1	35.9	72.0

Table 28. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 20, page 88.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	10.7	38.0
6.0	9.0	33.0
18.0	9.2	33.1
48.0	8.2	31.0
48.0	8.1	29.0
T^1-48.1	Endotoxin Challenge	
48.7	8.7	31.0
49.0	8.2	30.0
49.3	8.2	30.0
49.4	8.2	30.0
49.5	8.1	29.0
49.7	8.4	30.0
T^2-49.8	Endotoxin Challenge	
49.9	8.4	30.0
50.1	8.4	30.5
50.2	8.4	30.6
50.6	8.5	30.5
T^3-50.7	Endotoxin Challenge	
50.8	8.6	31.0
51.0	8.6	31.0
51.1	8.7	31.0
51.2	8.5	31.0

Table 28. (Contd) Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 20, page 88.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
51.5	8.7	31.0
51.8	8.7	31.0
52.0	8.7	31.0
T_4-52.0	Endotoxin Challenge	
52.1	8.7	31.0
52.4	8.7	31.0
52.6	8.7	31.0
52.8	8.7	31.0
52.9	8.7	32.0

Table 29. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 17, page 85.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	5.7	143.3
6.0	--	--
18.0	5.1	136.6
48.0	4.4	121.0
48.0	4.7	128.4
T^1-48.1	Endotoxin Challenge	
48.7	5.0	133.2
49.0	4.3	129.5
49.3	--	--
49.4	--	--
49.5	--	--
49.7	4.4	138.1
T^2-49.8	Endotoxin Challenge	
49.9	--	--
50.1	4.1	140.2
50.2	--	--
50.6	--	--
T^3-50.7	Endotoxin Challenge	
50.8	--	--
51.0	--	--
51.1	--	--
51.2	4.4	136.8
51.5	--	--

Table 29. (Contd) Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 17, page 85.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
51.8	--	--
52.0	--	--
T^4-52.0	Endotoxin Challenge	
52.1	--	--
52.4	--	--
52.6	--	--
52.8	--	--
52.6	5.4	137.4
52.8	--	--
52.9	--	--

Table 30. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 210--Group II intravenous endotoxin. See Figure 21, page 89.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	5.2	2.7	0.1	0.8	0.4	0.7	0.5
0.6	--	--	--	--	--	--	--
18.0	5.6	1.5	0.4	0.5	0.5	0.8	1.9
24.0	--	--	--	--	--	--	--
48.0	10.2	3.9	--	0.9	0.7	1.4	3.3
48.0	4.8	1.4	0.2	0.6	0.5	0.7	1.4
T^1-48.1			Endotoxin Challenge				
48.7	10.0	3.4	0.4	1.1	0.8	1.5	2.8
49.0	5.5	1.6	0.2	0.5	0.7	0.8	1.7
49.7	5.4	1.7	0.2	0.4	0.6	0.8	1.7
T^2-49.8			Endotoxin Challenge				
50.1	4.7	1.7	0.1	0.6	0.4	0.7	1.2
T^3-50.7			Endotoxin Challenge				
51.2	5.2	1.6	0.3	0.5	0.6	0.8	1.4
T^4-52.0			Endotoxin Challenge				
52.6	5.4	1.5	0.1	0.7	0.6	0.8	1.7

Table 31. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 23, page 92.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	--	--	--
18.0	69.3	48.0	7.50
24.0	79.8	46.0	7.52
48.0	79.7	45.9	7.49
T^1-48.0	Endotoxin Challenge		
48.1	--	--	--
48.2	31.1	47.5	7.47
48.4	31.8	53.8	7.37
48.6	31.7	59.8	7.28
48.9	33.6	62.4	7.16
49.1	29.7	77.2	7.12
49.4	22.2	81.4	6.94
49.7	27.3	84.0	6.92
T^2-49.8	Endotoxin Challenge		
49.9	19.6	92.5	6.78
50.2	8.6	99.9	6.12

Table 32. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 24, page 93.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mm/L)
1.0	--	--	--
18.0	36.0	11.0	37.0
24.0	37.0	12.0	38.0
48.0	34.0	9.0	35.0
T^1-48.1	Endotoxin Challenge		
48.2	29.0	8.5	30.0
48.4	30.7	6.4	32.0
48.6	26.5	0.0	28.0
48.9	20.0	- 7.5	22.0
49.1	22.0	- 7.5	24.0
49.4	16.5	-10.6	18.5
49.7	16.3	-18.0	18.0
T^2-49.8	Endotoxin Challenge		
49.9	12.8	-20.6	14.5
50.2	6.5	-32.3	7.8

Table 33. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 23, page 92.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	--	--
18.0	39.4	92.0
24.0	39.2	93.0
48.0	39.3	99.0
T^1-48.0	Endotoxin Challenge	
48.1	--	--
48.2	39.6	77.0
48.4	39.9	69.0
48.6	39.4	60.0
48.9	39.5	55.0
49.1	39.6	55.0
49.4	39.3	40.0
49.7	39.0	25.0
T^2-49.8	Endotoxin Challenge	
49.9	39.0	25.0
50.2	39.0	15.0

Table 34. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 25, page 94.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	10.7	36.0
18.0	10.7	36.0
24.0	10.7	34.0
48.0	9.2	31.0
T^1-48.0	Endotoxin Challenge	
48.1	10.7	34.0
48.2	10.7	34.0
48.4	11.0	38.0
48.6	10.1	34.0
48.9	10.1	34.0
49.1	10.1	34.0
49.4	10.4	33.0
49.7	9.5	31.0
T^2-49.2	Endotoxin Challenge	
49.9	9.5	31.0
50.2	10.1	31.0

Table 35. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 22, page 91.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	8.0	146.0
18.0	5.3	138.0
24.0	6.4	142.9
48.0	4.8	139.0
T^1-48.0	Endotoxin Challenge	
48.1	5.1	131.5
48.2	5.4	137.0
48.4	4.6	125.0
48.6	4.9	125.0
48.9	6.6	133.0
49.1	--	--
49.4	5.6	132.0
49.7	6.6	141.0
T^2-49.8	Endotoxin Challenge	
49.9	--	--
50.2	4.8	138.0

Table 36. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 216--Group II intravenous endotoxin. See Figure 26, page 95.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	4.6	2.4	0.2	1.0	0.1	0.6	0.3
6.0	--	--	--	--	--	--	--
12.0	--	--	--	--	--	--	--
18.0	11.4	3.8	0.2	1.2	1.0	1.6	3.6
24.0	9.8	3.3	0.2	2.0	0.3	1.1	2.9
48.0	6.7	2.5	0.1	1.3	0.2	0.9	1.7
T^1-48.0			Endotoxin Challenge				
48.1	7.1	2.4	0.1	1.5	0.2	1.0	1.9
48.2	8.4	3.2	0.2	1.6	0.4	1.1	1.9
48.4	8.7	2.6	0.1	1.9	0.1	1.4	2.6
48.6	5.6	2.3	0.1	1.4	0.1	0.2	1.5
48.9	7.4	2.4	0.7	0.9	1.0	1.3	1.1
49.4	6.1	1.8	0.1	1.2	0.3	1.0	1.7
49.7	6.0	2.2	0.1	1.2	0.2	0.8	1.5
T^2-49.8			Endotoxin Challenge				
50.2	5.6	2.0	0.1	1.0	0.2	0.7	1.6

Table 37. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 28, page 99.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
6.0	90.7	47.5	7.40
24.0	76.1	41.4	7.57
48.0	89.3	42.9	7.42
T^1-48.0	Endotoxin Challenge		
49.0	86.7	49.1	7.42
60.0	82.9	42.4	7.43
72.0	75.4	42.0	7.45
96.0	84.4	42.5	7.47
T^2-96.2	Endotoxin Challenge		
96.5	86.3	42.5	7.48
97.5	85.3	42.0	7.48
99.9	83.7	46.0	7.48
120.0	51.9	40.8	7.48

Table 38. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 29, page 100.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
6.0	27.5	3.0	29.0
24.0	36.0	13.0	37.0
48.0	27.5	3.0	28.5
T^1-48.0	Endotoxin Challenge		
49.0	31.0	6.0	32.0
60.0	27.0	3.0	28.0
72.0	28.0	4.5	29.0
96.0	31.0	7.2	32.0
T^2-96.2	Endotoxin Challenge		
96.5	31.3	7.0	32.3
97.5	31.3	7.0	32.3
99.9	33.0	9.0	34.0
120.0	29.0	6.0	30.0

Table 39. Temperature expressed in centigrade and arterial blood hemoglobin oxygen saturation values expressed in volumes percent in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 28, page 99.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	--	--
6.0	39.3	95.0
24.0	39.7	93.0
48.0	39.4	94.0
T^1-48.1	Endotoxin Challenge	
49.0	40.0	93.0
60.0	39.7	93.0
72.0	39.0	92.0
96.0	38.9	93.0
T^2-96.2	Endotoxin Challenge	
96.5	39.2	93.0
97.5	38.9	93.0
99.9	40.0	93.0
120.0	40.0	90.0

Table 40. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 30, page 101.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	15.3	46.0
6.0	15.3	46.0
24.0	13.0	43.5
48.0	13.6	47.0
T^1-48.1	Endotoxin Challenge	
49.0	14.1	46.0
60.0	13.6	43.0
72.0	14.2	44.0
96.0	12.7	42.0
T^2-96.2	Endotoxin Challenge	
96.5	13.0	41.0
97.5	13.4	43.0
99.9	12.5	41.0
120.0	14.0	45.0

Table 41. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 27, page 98.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	5.1	150.5
6.0	5.8	144.6
24.0	8.4	137.0
48.0	9.7	169.8
T^1-48.1	Endotoxin Challenge	
49.0	7.8	134.6
60.0	7.4	144.4
72.0	8.2	141.7
96.0	6.6	141.7
T^2-96.2	Endotoxin Challenge	
96.5	6.4	142.0
97.5	--	--
99.9	7.0	125.0
120.0	4.8	146.0

Table 42. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 313--Group III oral endotoxin. See Figure 31, page 102.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	5.5	2.1	0.8	0.8	0.9	0.6	0.3
6.0	5.2	2.0	0.4	0.5	0.6	0.6	1.1
24.0	8.4	2.8	0.0	1.0	0.9	1.3	2.4
48.0	7.4	2.8	0.0	0.7	0.9	1.1	1.9
T^1-48.1			Endotoxin Challenge				
49.0	9.5	3.4	0.0	1.0	1.0	1.5	2.6
60.0	7.9	2.8	0.2	1.1	0.9	1.0	1.9
72.0	6.3	3.0	0.0	0.6	0.5	1.0	1.2
96.0	5.8	1.8	0.1	1.0	0.5	0.9	1.5
T^2-96.2			Endotoxin Challenge				
96.5	6.8	2.6	0.2	1.2	0.3	0.9	1.6
97.5	6.3	2.1	0.1	1.3	0.3	0.9	1.6
99.9	5.5	2.1	0.1	1.0	0.3	0.7	1.3
120.0	5.5	2.3	0.1	1.2	0.3	0.9	0.7

Table 43. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 33, page 105.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	--	--	--
18.0	50.7	64.0	7.41
24.0	48.3	66.3	7.36
36.0	83.0	39.5	7.45
48.0	86.2	43.0	7.47
T^1-48.1	Endotoxin Challenge		
48.2	78.6	44.6	7.48
48.7	76.4	46.5	7.49
51.7	76.0	52.3	7.47
57.7	--	--	--
72.0	78.6	48.0	7.51
96.0	77.6	38.5	7.51

Table 44. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 34, page 106.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
18.0	40.0	2.0	41.5
24.0	37.0	4.8	39.0
36.0	27.0	3.0	28.0
48.0	30.7	7.2	32.0
T^1-48.1	Endotoxin Challenge		
48.2	32.5	8.7	33.5
48.7	35.0	10.8	36.0
51.7	38.0	11.0	39.0
57.7	--	--	--
72.0	38.3	13.0	39.5
96.0	30.5	7.0	31.4

Table 45. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 33, page 105.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
18.0	38.9	86.0
24.0	38.9	82.0
36.0	38.8	93.0
48.0	38.4	95.0
T^1-48.1	Endotoxin Challenge	
48.2	38.3	93.0
48.7	38.3	91.0
51.7	38.3	93.0
57.7	--	--
72.0	39.0	94.0
96.0	39.0	93.0

Table 46. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 35, page 107.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
18.0	14.1	33.0
24.0	9.7	32.0
36.0	8.4	28.5
48.0	8.4	28.5
T^1-48.1	Endotoxin Challenge	
48.2	9.2	30.0
48.7	9.2	30.0
51.7	9.1	30.0
57.7	9.0	30.0
72.0	9.0	30.0
96.0	9.8	31.0

Table 47. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 32, page 104.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
18.0	7.5	145.5
24.0	7.0	149.7
36.0	5.5	141.1
48.0	Hem.	125.0
T^1-48.1	Endotoxin Challenge	
48.2	--	--
48.7	Hem.	125.6
51.7	8.4	119.0
57.7	9.5	167.6
72.0	7.4	156.0
96.0	5.1	143.0

Table 48. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 314--Group III oral endotoxin. See Figure 36, page 108.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	--	--	--	--	--	--	--
18.0	6.7	3.3	0.0	0.7	0.7	1.3	0.7
24.0	5.4	2.2	0.0	0.6	0.5	1.0	1.1
36.0	6.7	3.2	0.0	0.7	0.5	1.1	1.2
48.0	5.4	1.7	0.0	1.0	0.9	0.8	1.0
48.0	8.0	3.2	0.0	0.6	1.6	1.1	1.5
T^1-48.1			Endotoxin Challenge				
48.2	--	--	--	--	--	--	--
48.7	5.4	2.2	0.0	0.5	1.0	0.8	0.9
51.7	6.9	2.7	0.0	0.6	1.4	1.1	1.1
57.7	5.0	1.8	0.0	0.7	1.0	0.7	0.8
72.0	3.8	1.6	0.1	0.8	0.1	0.6	0.6
96.0	4.8	2.1	0.1	1.1	0.2	0.8	0.5

Table 49. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 38, page 112.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	--	--	--
12.0	--	--	--
18.0	74.5	45.5	7.45
24.0	80.4	40.3	7.45
48.0	75.3	37.7	7.40
T^1-48.1	Endotoxin Challenge		
48.6	76.6	35.8	7.42
49.5	52.6	40.9	7.39
53.7	45.9	36.8	7.35
58.2	47.2	35.6	7.24
59.2	21.7	68.0	6.34

Table 50. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 39, page 113.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
1.0	--	--	--
18.0	30.0	6.0	31.0
24.0	32.0	8.7	33.0
48.0	22.5	- 1.0	23.5
T^1-48.1	Endotoxin Challenge		
48.6	22.5	- 1.0	23.5
49.5	24.3	- 1.0	25.5
53.7	20.0	- 5.0	21.0
58.2	14.0	-11.2	16.0
59.1	5.0	-33.5	6.0

Table 51. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 38, page 112.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	--	--
12.0	--	--
18.0	39.7	92.0
24.0	39.7	92.0
48.0	39.7	92.0
T^1-48.1	Endotoxin Challenge	
48.6	39.4	92.0
49.5	39.4	87.0
53.7	39.4	80.0
58.2	37.8	73.0
59.2	37.0	20.0

Table 52. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 40, page 114.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	9.2	31.0
12.0	9.2	31.0
18.0	9.2	32.5
24.0	10.0	30.5
48.0	12.0	37.5
T^1-48.1	Endotoxin Challenge	
48.6	12.5	40.0
49.5	12.0	40.5
53.7	12.5	50.5
58.2	14.7	47.0
59.1	12.7	40.0

Table 53. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 37, page 111.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	5.5	141.7
12.0	5.4	140.8
18.0	5.5	141.7
24.0	6.3	122.8
48.0	6.0	124.0
T^1-48.1	Endotoxin Challenge	
48.6	--	--
49.5	12.7	205.0
53.7	8.0	139.6
58.2	8.6	154.0
59.1	14.8	56.0

Table 54. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 315--Group III oral endotoxin. See Figure 41, page 115.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	11.3	4.1	0.6	1.6	1.0	1.5	2.5
12.0	5.8	2.3	0.2	0.7	0.7	0.7	1.2
18.0	11.3	4.7	0.4	2.8	0.9	1.4	1.1
24.0	4.6	2.8	0.2	0.5	0.2	0.7	0.2
48.0	4.4	2.0	0.1	1.1	0.2	0.5	0.5
T1-48.1			Endotoxin Challenge				
49.5	4.6	2.2	0.1	0.9	0.5	0.6	0.3
53.7	6.3	2.4	0.1	1.3	0.2	1.0	1.3
58.2	4.5	2.0	0.0	0.6	0.6	0.7	0.6
59.1	5.5	2.3	0.1	1.4	0.2	0.6	0.9

Table 55. Arterial blood P_aO_2 and P_aCO_2 expressed in mmHg and pH values in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 43, page 117.

Time (Hours)	P_aO_2 (mmHg)	P_aCO_2 (mmHg)	pH
1.0	--	--	--
6.0	78.1	46.5	7.44
18.0	88.4	40.6	7.53
48.0	80.1	44.0	7.46
T^1-48.1	Endotoxin Challenge		
48.2	84.0	44.5	7.53
48.5	85.1	46.5	7.53
48.9	84.1	51.0	7.54
49.9	90.6	51.0	7.54
51.7	92.9	45.0	7.53
67.4	84.9	40.6	7.54

Table 56. Arterial blood values for total bicarbonate and base excess expressed in mEq/L and total carbon dioxide expressed in millimoles per liter in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 44, page 118.

Time (Hours)	HCO_3^- (mEq/L)	Base Excess (mEq/L)	Total CO_2 (mmol/L)
1.0	--	--	--
6.0	29.0	2.5	31.0
18.0	32.0	8.5	32.5
48.0	29.0	2.5	30.0
T^1-48.1	Endotoxin Challenge		
48.2	35.0	8.5	38.0
48.5	36.0	8.5	37.5
48.9	40.0	9.5	41.5
49.9	45.0	9.5	47.5
51.7	34.5	8.5	35.5
67.4	32.0	8.5	32.5

Table 57. Mean temperature values expressed in degrees centigrade and mean arterial blood percent hemoglobin oxygen saturation in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 43, page 117.

Time (Hours)	Temperature (Centigrade)	Hb Sat. (%)
1.0	--	--
6.0	38.8	9.2
18.0	38.9	9.4
48.0	38.6	9.2
T^1-48.1	Endotoxin Challenge	
48.2	38.8	9.4
48.5	38.8	9.4
48.9	38.9	9.4
49.9	38.9	9.5
51.7	39.0	9.5
57.4	38.6	9.4

Table 58. Arterial blood hemoglobin values expressed in grams per 100 milliliters; and mean packed cell volume values expressed in volumes percent of whole blood in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 45, page 119.

Time (Hours)	Hemoglobin (Gms/100 ml)	P.C.V. (Vol. %)
1.0	6.5	21.0
6.0	5.6	19.0
18.0	5.1	18.0
48.0	5.5	18.0
T^1-48.1	Endotoxin Challenge	
48.2	5.0	16.0
48.5	5.3	18.0
48.9	5.2	17.0
49.9	5.3	16.0
51.7	5.5	18.0
67.4	4.9	15.0

Table 59. Serum sodium and potassium values expressed in milliequivalents per liter in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 42, page 116.

Time (Hours)	Potassium (mEq/L)	Sodium (mEq/L)
1.0	6.3	176.0
0.6	5.0	143.0
18.0	8.0	--
48.0	10.0	--
T^1-48.1	Endotoxin Challenge	
48.2	6.0	136.1
48.5	8.6	144.0
48.9	9.1	--
49.9	--	--
51.7	4.8	132.5
67.4	7.1	144.0

Table 60. Total serum protein and serum electrophoresis values expressed in grams per hundred milliliters in newborn Holstein calf number 317--Group III oral endotoxin. See Figure 46, page 120.

Time (Hours)	Total Protein	Albumin	Alpha 1	Alpha 2	Beta 1	Beta 2	Gamma
1.0	5.5	2.1	0.3	0.8	0.5	0.7	1.1
6.0	6.9	2.5	0.2	0.7	0.3	0.8	2.4
18.0	6.9	2.8	0.2	0.4	0.2	1.1	2.2
48.0	14.9	4.3	0.0	1.7	1.4	2.5	5.0
T^1-48.1			Endotoxin Challenge				
48.2	10.2	3.0	0.5	0.6	0.9	1.6	3.6
48.5	13.6	4.1	0.7	0.7	1.3	2.4	4.4
48.9	14.8	3.7	1.4	0.9	2.4	3.6	2.8
51.7	11.4	3.2	1.0	0.8	1.7	3.1	1.6
67.4	12.4	3.8	0.1	2.5	0.5	2.2	3.3

*The following calf and sample hour sodium and potassium were run on Coleman Flame Photometer Model 21:

Calf No.	Hour
12	1.0
	120.0
	144.0
	216.0
13	24.0
	49.0
	49.2
	51.9
	57.6
	60.0
	72.0
14	18.0
	72.0
	96.0
15	1.0
	12.0
	24.0
	48.0
	53.7
16	1.0
	24.0
	48.0
	48.1
	48.4
	48.6
	49.4
	49.7
17	6.0
	18.0
	48.0
	48.2
	48.9

Table 61. Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3^-	Total Co_2
1	01	001	29.0	09.0				39.40	0.41	1.5	0.3	0.4	0.4	0.7	0.8	114.32	08.5									
1	01	024	26.0	08.5				39.55	05.3	1.5	0.0	0.9	0.5	0.7	1.7	114.98	06.2									
1	01	048	25.0	09.0				39.80	07.5	2.3	0.0	0.8	0.6	1.1	2.7	122.1	05.4									
1	01	072	25.0	09.5				38.90	05.3	1.7	0.2	0.5	0.4	0.8	1.7	137.8	04.8									
1	01	096	25.0	09.5				39.10	07.9	2.5	0.2	1.1	0.8	1.3	2.0	130.2	05.4									
1	01	120	27.0	08.2				39.80	08.1	2.6	0.3	0.9	0.9	1.3	2.1	117.6	05.7									
1	01	144	29.0	08.2				39.30	05.2	1.7	0.1	0.7	0.5	0.8	1.4	134.0	05.7									
1	01	168	30.0	09.0				39.30	07.1	2.1	0.2	0.9	0.7	1.3	1.9	128.0	08.0									
1	01	192	30.0	09.0				39.40	09.3	3.0	0.2	1.2	1.0	1.5	2.4	132.6	06.8									
1	01	216	29.0	09.0				39.70	08.1	2.5	0.3	1.0	0.9	1.4	2.0	130.0	06.5									
1	03	001	28.0	08.6				38.40	04.1	1.5	0.4	0.4	0.4	0.6	0.8	137.0	08.5									
1	03	012	27.0	08.3				38.40	05.0	1.5	0.4	0.3	0.4	0.8	1.6	139.5	05.7									
1	03	036	38.0	08.6				38.55	06.5	1.8	0.4	0.6	0.6	0.9	2.2	132.5	06.1									
1	03	072	25.0	09.5				39.20	07.5	2.5	0.1	0.6	0.7	1.3	2.3	130.1	05.0									
1	03	096	26.0	09.5				39.30	08.0	2.7	0.1	0.9	0.7	1.3	2.3	132.0	05.2									
1	03	120	27.0	08.2				38.90	08.1	2.7	0.2	0.9	0.9	1.2	2.2	136.6	05.4									
1	03	144	23.0	07.1				39.45	05.1	1.5	0.1	0.6	0.5	1.0	1.4	141.2	06.2									
1	03	168	22.0	06.9				39.30	05.2	1.4	0.2	0.5	0.6	0.9	1.6	138.0	05.8									
1	03	192	22.0	07.2				39.20	11.5	3.9	0.0	1.3	1.3	2.1	2.9	130.0	07.4									
1	03	216	26.0	08.1				39.20	08.1	2.6	0.1	1.0	0.8	1.4	2.2	134.2	06.1									
1	04	001	35.0	11.5	73.0	44.5	7.333	38.30	13.0	3.8	1.2	1.2	0.8	2.1	3.9	142.0	08.5	66.4	75.0	07.34	90.0	40.9	43.1	-02.8	22.5	23.5
1	04	024	26.0	10.9	61.5	43.0	7.323	38.90	07.0	2.6	0.0	0.4	0.7	0.8	2.5	142.9	04.8	55.9	66.5	07.32	90.0	39.6	43.0	-02.0	21.0	22.0
1	04	048	28.0	10.5	71.5	43.5	7.470	39.40	07.1	2.2	0.0	0.5	0.6	1.2	2.6	130.0	03.8	75.5	81.6	07.46	95.0	40.0	44.5	+07.0	31.6	32.6
1	04	072	29.0	10.1	68.0	35.0	7.475	40.30	09.1	2.6	0.2	0.7	0.9	1.8	2.9	104.5	04.8	71.8	78.3	07.46	94.0	32.2	37.0	+03.0	25.0	26.0
1	04	096	29.0	09.1	61.0	35.0	7.500	40.30	10.3	2.8	0.2	1.3	1.3	1.6	3.1	136.2	08.0	66.5	73.9	07.48	93.0	32.2	37.0	+04.3	25.0	27.0
1	04	120	28.5	09.2	65.5	38.0	7.440	39.40	08.5	2.5	0.4	0.4	0.9	1.4	2.9	124.2	10.6	67.0	74.4	07.43	93.0	34.9	38.8	+01.3	25.0	26.0
1	04	144	31.0	09.2	71.0	44.0	7.485	39.30	08.7	2.6	0.3	0.6	0.6	1.9	2.7	126.4	03.7	75.8	79.6	07.43	94.0	40.5	44.5	+08.0	32.0	33.0

Table 61. (Contd.) Experimental *E. coli* endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. c°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3^-	Total Co_2
1	04	192	29.0	09.2	61.0	39.5	7.440	39.40	06.5	2.0	0.1	0.6	0.5	1.4	1.9	133.6	06.6	62.4	69.3	07.43	92.0	36.3	39.5	+02.5	26.0	27.0
1	04	216	31.0	09.3	52.0	45.5	7.385	39.00	07.4	1.7	0.4	1.2	0.5	1.4	1.9	141.0	05.7	50.6	58.1	07.39	87.0	41.9	45.5	+02.0	26.0	27.5
1	04	240	29.0	09.0	44.5	44.5	7.355	38.90	07.4	1.8	0.3	1.1	0.9	1.1	2.2	117.0	10.9	42.0	48.3	07.36	82.0	40.9	44.5	+00.7	24.0	25.0
1	05	001	26.0	08.5					05.0	2.5	0.1	0.5	0.4	0.9	0.6	138.5	06.9									
1	05	012							06.2	2.3	0.0	0.6	0.5	0.9	1.9	140.7	05.5									
1	05	024	24.0	06.8	68.0	48.0	7.310	39.40	06.5	2.1	0.1	0.6	0.5	1.1	2.1	149.6	06.0	61.3	76.6	07.30	90.0	44.2	49.1	-02.5	23.5	25.0
1	05	036	22.0	06.7	58.0	45.0	7.505	40.00	06.2	2.1	0.1	0.4	0.5	0.8	2.3	126.0	04.0	63.3	68.4	07.48	92.0	41.4	47.0	10.0	34.5	35.5
1	05	048	18.0	07.2	68.0	35.0	7.455	41.10	12.9	3.7	0.2	1.1	1.7	2.3	3.9	141.7	06.0	71.0	72.5	07.43	92.0	32.2	38.3	03.0	24.0	24.5
1	05	072	17.0	05.0	70.5	33.0	7.535	40.30	05.7	1.9	0.0	0.7	0.6	0.9	1.6	139.3	05.0	79.6	83.6	07.52	95.0	30.4	34.9	05.2	27.0	28.5
1	05	096	19.5	06.2	51.0	43.5	7.385	40.30	10.6	3.1	0.0	1.4	1.1	2.1	2.9	152.8	09.7	49.6	61.0	07.37	85.0	40.0	46.0	00.3	24.5	25.5
1	05	120	19.0	05.9	59.5	40.0	7.440	39.20	06.7	2.0	0.2	0.9	0.7	1.1	1.8	142.0	04.9	60.9	65.7	07.44	90.0	36.8	40.4	02.8	26.0	27.0
1	05	144	19.0	06.0	74.0	39.0	7.470	39.80	07.4	2.4	0.2	0.6	0.9	1.1	2.2	146.0	04.5	78.1	85.2	07.46	95.0	35.9	40.3	04.2	27.5	28.5
1	05	168	19.0	06.1	70.0	38.5	7.465	38.90	11.6	3.6	0.2	1.5	1.1	2.4	2.8		09.4	73.1	75.3	07.47	93.0	35.4	38.5	04.3	26.8	27.6
1	05	192	19.0	05.9	73.0	41.0	7.448	39.00	08.2	2.5	0.3	0.9	0.8	1.6	2.1	140.8	04.8	75.5	79.2	07.45	94.0	37.7	41.0	03.8	27.0	28.0
1	05	216	19.0	05.9	73.5	37.5	7.445	38.60	12.9	4.0	0.5	1.3	1.3	2.6	3.2	146.1	06.0	76.8	78.3	07.46	94.0	34.5	36.7	01.8	25.0	26.0
1	05	240	19.0	05.9	74.0	38.5	7.460	39.40										77.3	83.5	07.45	95.0	35.4	39.4	02.3	26.5	27.5
1	06	001	32.0	10.5	64.5	46.0	7.365	39.20	04.9	2.0	0.4	0.3	0.6	0.7	0.9	140.8	05.5	60.9	70.7	07.37	93.0	42.3	46.5	00.8	25.5	26.5
1	06	012	28.0	09.5	86.0	38.6	7.425	39.20	08.0	3.1	0.3	0.5	0.7	1.2	2.2	135.6	04.5	87.1	94.9	07.43	95.0	35.5	39.0	00.5	34.5	25.5
1	06	018	28.0	09.5					05.4	1.4	0.2	0.3	0.5	1.5	1.5	145.8	07.0									
1	06	024	28.0	09.5					06.4	2.3	0.3	0.4	0.6	0.9	1.9	131.2	07.0									
1	06	036	28.0	09.5	86.0	38.6	7.425	39.00	08.5	2.2	0.6	1.0	0.8	1.6	2.3	136.8	09.6	86.2	93.1	07.43	95.0	35.5	38.6	00.9	23.5	24.5
1	06	048	28.0	09.0	67.5	38.5	7.410	39.70	08.7	3.1	0.2	0.8	0.8	1.3	2.5	131.3	09.6	66.9	77.7	07.40	90.0	35.5	39.9	00.9	23.0	24.0
1	06	072	29.0	08.7	82.0	30.5	7.495	39.20	07.1	1.9	0.3	0.8	0.6	1.1	2.4	132.8	04.3	88.5	89.4	07.50	95.0	28.1	30.8	01.3	25.5	26.5
1	06	096	27.0	08.0	69.5	39.0	7.445	39.20	08.7	3.2	0.2	0.7	0.6	1.3	2.7	138.7	06.3	71.1	75.4	07.45	85.0	35.9	39.4	02.3	25.5	26.5
1	06	120	27.0	08.2	72.0	34.5	7.490	39.40	06.6	1.9	0.2	1.1	0.7	1.0	1.7	142.0		77.7	81.6	07.48	90.0	31.7	35.3	02.8	28.0	29.0
1	06	144	25.0	08.0	65.5	38.5	7.470	40.00	09.9	2.4	0.2	1.8	1.2	1.7	2.6	117.6	08.8	69.2	76.1	07.46	90.0	35.4	40.3	04.8	28.0	29.0
1	06	168	25.0	08.0	63.5	37.5	7.485	39.40	11.7	3.0	0.4	2.1	1.6	1.9	2.7	138.5	09.4	67.8	71.2	07.48	80.0	34.5	38.3	04.3	27.0	28.0

Table 61. (Contd.) Experimental *E. coli* endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3^-	Total Co_2
1	06	192	260	080	625	340	7.415	39.20	097	26	0.0	1.7	13	1.4	2.7	1382	07.7	620	688	07.42	850	313	355	-023	210	220
1	06	216	270	077	625	325	7.450	39.90	07.6	1.6	0.0	13	15	15	1.7	1267	07.7	646	724	07.44	900	299	325	-012	220	225
1	06	240	260	077	665	330	7.480	38.90	099	2.4	0.2	1.8	1.2	1.7	2.6	1314	059	710	717	07.48	950	304	330	013	240	250
1	08	001	350	120	810	440	7.320	38.30	0.49	1.4	0.2	0.5	0.6	0.7	1.5	1334	07.8	827	943	07.33	950	405	426	-032	220	230
1	08	006	350	120	760	475	7.330	38.00	0.42	21	0.0	0.3	0.3	0.6	0.9	1501	079	697	774	07.34	900	437	460	-018	240	250
1	08	012	330	115	650	410	7.400	37.90	0.45	1.2	0.0	0.6	0.6	0.7	1.4	1273	066	638	664	07.41	900	377	393	003	245	253
1	08	024	330	115	655	420	7.410	38.00	070	23	0.0	0.6	09	09	23	1366	078	649	669	07.42	900	386	403	022	260	270
1	08	036	340	120	730	445	7.445	38.30	138	4.3	0.0	0.9	1.6	2.0	5.0	1292	074	747	754	07.46	920	409	431	052	295	305
1	08	072	300	101	735	395	7.385	39.00	066	1.9	0.0	0.8	0.8	1.1	2.0	1510	080	715	800	07.39	925	363	395	000	237	247
1	08	096	350	104	785	415	7.420	38.30	07.6	1.9	0.0	1.1	09	1.3	2.4	1255	091	787	818	07.43	930	382	402	022	260	270
1	08	120	310	094	775	440	7.433	39.30	104	2.7	0.2	1.2	0.6	1.7	4.0	1331	049	785	824	07.44	940	405	445	042	285	295
1	08	144	330	095	755	440	7.445	39.20	056	1.6	02	0.6	0.5	1.2	1.5	1352	062	772	826	07.45	940	405	445	052	295	305
1	08	168	320	095	710	430	7.460	39.20	057	1.6	0.1	0.8	0.5	1.1	1.5	1328	079	742	786	07.46	940	396	435	062	300	310
1	08	192	310	092	765	410	7.445	39.20	057	2.5	0.2	0.6	0.8	0.7	0.9	1376	115	783	837	07.45	940	377	415	032	270	280
1	08	216	300	091	725	425	7.450	39.40	082	2.7	0.0	1.2	0.8	1.5	2.0	1248	085	749	817	07.44	930	391	434	047	280	290
1	08	240	290	088	705	410	7.460	39.70	069	2.2	0.0	0.9	0.6	1.4	1.8	1224	036	736	803	07.44	920	377	424	052	285	295
1	12	001	345	097					057	2.3	0.5	0.6	0.8	1.5	0.0	1537	066									
1	12	012	295	085	590	470	7.490	39.00	055	2.0	0.4	0.4	0.7	0.9	1.1	1551	063	616	635	07.49	910	432	475	100	345	355
1	12	024	315	091	605	455	7.490	39.20	055	2.1	0.0	0.5	0.7	0.8	1.3	1297	044	653	672	07.49	910	419	460	105	340	350
1	12	048	30.	090	620	420	7.475	38.90	079	3.2	0.0	0.5	1.1	1.3	1.8	1415	077	655	668	07.48	910	386	420	065	300	310
1	12	072	290	085	755	395	7.469	39.00	082	3.0	0.0	1.4	0.9	1.3	1.6	1336	074	797	821	07.47	940	363	395	052	280	290
1	12	096	300	090	745	425	7.490	39.40										804	836	07.49	930	391	434	075	310	320
1	12	120	310	101	745	385	7.570	39.20	043	1.6	0.0	1.0	0.3	0.6	0.8	1369	066	881	821	07.57	930	354	385	120	350	360
1	12	144	290	092	695	485	7.470	39.70	049	1.7	0.0	1.1	0.7	0.4	1.0	1316	056	734	793	07.46	920	446	501	095	345	355
1	12	168	265	083	780	405	7.495	39.20	123	4.2	0.0	2.7	2.1	2.1	1.7		101	851	859	07.50	930	373	410	090	330	340
1	12	192	300	095	750	450	7.475	39.40	066	2.8	0.0	1.2	0.5	1.3	0.8	1432	051	792	839	07.47	920	362	403	082	320	330
1	12	216	295	091	780	390	7.525	40.55	067	2.7	0.0	1.3	07	0.8	1.2	1416	056	870	931	07.51	950	359	417	082	320	330

Table 61. (Contd.) Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3^-	Total Co_2
2	07	001	30.0	10.0					05.2	2.5	0.0	0.2	0.8	0.8	0.9	072.8	0.58									
2	07	012	30.0	10.0	92.0	37.0	7.456	38.4.0	11.8	4.4	0.0	0.8	1.4	1.8	3.4	138.2		96.1	97.1	07.47	95.0	3.4.0	36.2	02.3	25.0	26.0
2	07	018	28.0	09.0					14.6	5.3	0.0	1.0	2.2	2.0	4.1	152.0										
2	07	036	26.0	08.7	63.0	36.5	7.470	38.85	07.6	2.2	0.3	0.8	0.8	1.0	2.5	143.6	07.5	83.9	84.6	07.47	95.0	33.5	36.1	02.7	26.0	27.0
2	07	048	26.0	09.0	85.5	35.5	7.520	40.00	09.6	2.7		1.1	1.1	1.6	3.1		05.1	95.4	97.0	07.50	95.0	32.7	37.1	05.6	28.0	29.0
T1-48.0 Endotoxin Challenge																										
2	07	0482	26.0	09.0	36.0	51.5	7.310	40.00	06.2	1.6	0.4	0.5	0.6	1.0	2.1	103.2	04.1	32.4	41.8	07.30	75.0	47.4	53.8	-00.6	25.0	26.0
2	07	0485	26.0	09.0	24.0	66.5	7.155	40.00	06.0	1.9	0.2	0.8	0.8	0.9	1.4	151.3	07.4	18.6	28.2	07.13	52.0	61.2	69.5	-06.3	22.0	23.5
2	07	0488	26.0	09.0	20.0	63.5	7.020	39.90										13.5	23.1	07.01	32.0	58.4	66.4	-14.2	17.0	17.5
2	07	0492	26.0	09.0	14.0	68.0	7.020	39.90	06.0	3.0	0.0	0.4	0.9	0.8	0.9	119.8	06.5	09.4	16.2	07.01	15.0	62.6	71.1	-15.7	15.0	16.5
2	07	0497	26.0	09.0	24.0	53.5	6.980	40.00	06.2	2.8	0.0	0.4	0.9	0.7	1.4	129.2	06.8	15.5	28.1	06.96	30.0	49.2	55.9	-19.0	12.0	13.5
2	07	0498	26.0	09.0	50.0	41.5	7.065	40.00										35.1	58.6	07.04	80.0	38.2	43.4	-18.5	11.0	12.0
T2-50.0 Endotoxin Challenge																										
2	07	0502	26.0	09.0	18.0	60.0	6.990	40.00										11.7	20.5	06.98	20.0	55.2	62.7	-17.0	13.5	15.0
2	07	0505	26.0	09.0	11.0	71.5	6.800	40.00	07.5	2.1	0.5	0.7	1.2	1.2	1.8	137.5	08.9	08.1	17.5	06.78	12.0	65.8	74.8	-25.0	10.0	11.5
2	09	001	45.0	13.0	61.0	40.5	7.405	39.20	05.7	1.7	0.2	0.6	0.8	0.7	0.9	137.4		59.9	67.1	07.40	90.0	37.3	41.0	00.3	24.0	25.0
2	09	012			67.0	37.0	7.415	38.30	06.2	1.4	0.1	0.9	0.7	0.8	2.3	149.0	08.9	66.5	69.1	07.43	92.0	34.0	35.8	00.2	24.0	25.0
2	09	024	40.0	12.0	74.5	42.0	7.430	38.80	08.8	1.9	0.3	0.9	0.9	1.0	3.8	116.4	05.8	75.4	80.7	07.43	93.0	38.6	41.6	01.6	24.5	25.5
2	09	048	38.5	12.0	74.5	39.5	7.450	38.60	08.3	2.6	0.0	0.5	0.5	1.1	3.6	114.4		77.0	80.9	07.44	93.0	36.3	38.7	02.5	26.0	27.0
2	09	048	37.0	11.5	76.5	37.5	7.475	38.90	08.3	2.6	0.0	0.5	0.5	1.1	3.6	114.0		80.8	82.4	07.48	93.0	34.5	37.5	04.2	27.5	28.5
T1-48.2 Endotoxin Challenge																										
2	09	0485	38.0	11.5	47.5	38.5	7.520	39.00										53.0	52.0	07.52	90.0	35.4	38.5	08.4	31.5	32.5
2	09	0488	39.0	12.0	56.5	38.5	7.500	39.20	12.4	3.4	0.0	1.1	1.2	2.1	4.6	124.4	06.1	61.7	62.9	07.50	92.0	35.4	38.9	07.3	30.0	31.0
T2-48.9 Endotoxin Challenge																										
2	09	0490	39.0	12.0	56.0	36.5	7.420	39.40										56.1	63.4	07.41	92.0	33.6	37.3	03.0	25.5	26.5
2	09	0495	41.5	13.0	45.0	42.0	7.395	38.70	08.3	2.5	0.3	0.4	0.7	1.4	3.0	146.2	05.4	44.2	48.6	07.40	86.0	38.6	41.6	-00.5	23.0	24.0
2	09	0499	41.5	12.5	40.5	50.0	7.280	38.50										35.2	42.6	07.29	75.0	46.0	48.9	-01.1	22.0	23.0

Table 61. (Contd.) Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Ino. Hb)	HCO_3^-	Total Co_2
2	09	0509	39.0	12.1	54.0	37.0	7.380	38.00	08.9	2.6	0.0	0.8	0.8	1.2	3.5	134.2		52.0	55.1	07.39	87.0	34.0	35.5	-01.1	22.0	23.0
T3-50.9 Endotoxin Challenge																										
2	09	0510	40.0	12.1	30.0	37.0	7.360	37.50	08.6	2.5	0.3	0.4	0.8	1.2	3.4	146.3	05.6	28.3	29.7	07.38	67.0	34.0	34.7	-02.3	20.5	21.5
2	09	0511	45.0	14.1	23.0	28.0	7.370	37.00										21.9	21.9	07.40	50.0	25.8	25.8	-01.7	20.5	21.5
2	09	0534	45.0	14.0	23.0	27.0	7.380	36.80										22.1	21.7	07.41	50.0	24.8	25.1	-01.2	21.0	21.5
2	09	0536	45.0	14.0	30.0	28.5	7.330	36.80										27.5	28.0	07.36	50.0	26.2	26.5	-04.3	19.5	19.5
2	09	0538	45.0	13.8	48.0	33.5	7.210	36.60								142.8	05.3	39.0	43.6	07.25	72.0	30.8	31.5	-11.7	14.0	14.7
2	09	0540	44.0	13.2	47.0	33.5	7.180	36.40										37.2	43.2	07.22	72.0	30.8	31.4	-13.9	12.0	12.5
T4-54.1 Endotoxin Challenge																										
2	09	0546	45.0	13.2	25.0	45.0	7.035	36.00										17.2	22.3	07.08	35.0	41.4	43.1	-16.6	11.0	12.0
2	09	0548	45.0	13.2	26.0	58.0	6.900	36.00										15.5	23.2	06.94	23.0	53.4	55.6	-19.8	10.5	11.0
2	09	0553	45.0	13.2	26.0	78.0	6.600	36.00										11.6	24.8	06.64	22.0	71.8	74.8	-22.3	07.0	08.5
2	09	0554	45.0	13.2	25.0	85.0	6.470	36.00	09.0	2.5	0.2	0.6	0.9	1.4	3.4	151.6	08.6	10.2	23.3	06.51	17.0	78.2	81.5	-32.2	06.5	07.5
2	10	001	38.0	10.7	66.5	42.0	7.390	38.90	05.2	2.7	0.1	0.8	0.4	0.7	0.5	143.3	05.7	64.5	72.4	07.39	92.0	38.6	42.0	00.2	24.5	25.5
2	10	006	33.0	09.0	66.0	43.5	7.390	38.90										64.2	71.9	97.39	92.0	40.0	43.5	01.3	25.5	26.5
2	10	018	33.0	09.2	65.0	44.5	7.405	38.90	05.6	1.5	0.4	0.5	0.5	0.8	1.9	136.6	05.1	63.8	70.2	07.41	91.0	40.9	44.5	02.3	26.5	27.5
2	10	048	31.0	08.2	77.0	35.5	7.440	38.80	10.2	3.9		0.9	0.7	1.4	3.3	121.9	04.4	78.8	77.2	07.46	94.0	32.7	35.5	00.2	23.5	24.5
2	10	048	29.0	08.1	78.0	34.2	7.515	38.90	04.8	1.4	0.2	0.6	0.5	0.7	1.4	128.4	04.7	87.0	85.3	07.52	95.0	31.5	34.2	04.6	26.5	27.5
T1-48.1 Endotoxin Challenge																										
2	10	0487	31.0	08.7	41.0	45.0	7.385	39.70	10.0	3.4	0.4	1.1	0.8	1.5	2.8	133.2	05.0	39.5	46.6	07.38	82.0	41.4	46.5	01.5	25.5	26.5
2	10	0490	30.0	08.2	53.5	43.5	7.415	39.30	05.5	1.6	0.2	0.5	0.7	0.8	1.7	129.5	04.3	53.1	59.4	07.41	90.0	36.1	39.7	02.6	27.0	28.0
2	10	0493	30.0	08.2	61.0	36.5	7.410	39.00										60.5	66.6	07.41	91.0	33.6	36.5	00.8	22.5	23.5
2	10	0494	30.0	08.2	59.0	41.5	7.410	38.80										58.5	64.4	07.40	91.0	38.2	41.0	01.2	25.5	26.5
2	10	0495	29.0	08.1	45.0	51.0	7.330	38.80										41.3	48.7	07.33	80.0	46.9	50.5	00.4	26.0	27.0
2	10	0497	30.0	08.4	51.5	45.5	7.355	38.80	05.4	1.7	0.2	0.4	0.6	0.8	1.7	138.1	04.4	48.6	55.4	07.36	85.0	41.9	45.0	00.7	24.0	25.5
T2-49.8 Endotoxin Challenge																										
2	10	0499	30.0	08.4	57.5	41.5	7.315	38.30										51.8	59.1	07.33	85.0	38.2	40.2	-04.7	20.0	21.0

Table 61. (Contd.) Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	PaO_2 39°C	$PaCO_2$ 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	PaO_2 (7.4 37°C)	PaO_2 Calf	pH Calf	Hb Saturation	$PaCO_2$ (7.4 37°)	$PaCO_2$ Calf	Base Excess (Inc. Hb)	HCO_3	Total Co_2
2	10	0501	305	084	610	450	7300	3830										545	637	7.31	850	414	436	-037	215	225
2	10	0502	305	084	610	450	7300	3830										545	637	7.31	850	414	436	-037	215	225
2	10	0501	305	084					047	17	01	06	04	07	12	1402	041									
2	10	0506	310	085	600	450	7300	3800										536	600	7.31	840	414	431	-037	215	225
T3-50.7 Endotoxin Challenge																										
2	10	0508	210	086	600	445	7290	3755										536	600	7.31	840	409	418	-047	205	215
2	10	0510	310	086	310	520	7225	3720										254	297	7.26	600	478	483	-064	205	215
2	10	0511	310	087	340	540	7200	3690										274	326	7.23	650	497	497	-064	205	215
2	10	0512	310	085	345	680	7100	3675	052	16	03	05	06	08	14	1368	044	286	364	7.13	600	626	619	-080	200	220
2	10	0515	310	087	380	700	7100	3655										314	383	7.13	620	644	631	-080	205	220
2	10	0518	310	087	495	555	7150	3635										424	512	7.18	750	512	495	-094	190	195
2	10	0520	310	087	400	520	7175	3610										363	425	7.21	720	478	459	-075	180	190
T4-52.0 Endotoxin Challenge																										
2	10	0521	310	087	340	540	7190	3590										313	354	7.23	650	497	477	-073	195	205
2	10	0524	310	087	285	580	7130	3570										214	278	7.18	500	534	507	-102	185	200
2	10	0526	310	087	300	580	7070	3560										249	305	7.12	530	534	507	-132	160	175
2	10	0528	310	087	290	640	7070	3520										249	290	7.13	520	589	548	-118	175	195
2	10	0524	032	087				3500																		
2	10	0529	320	087	300	600	7070	3500										258	306	7.11	550	552	508	-130	145	160
2	10	0526	320	087					054	15	01	07	06	08	17	1374	054									
2	16	001	360	107					046	24	02	10	01	06	03	1460	080									
2	16	018	360	107	630	470	7490	3940	114	38	02	12	10	16	36	1380	053	680	693	7.50	920	432	480	110	360	370
2	16	024	340	107	730	455	7520	3920	098	33	02	20	03	11	29	1429	064	815	798	7.52	930	419	460	120	370	380
2	16	048	310	092	725	450	7495	3930	067	25	01	13	02	09	17	1390	048	774	797	7.49	930	414	459	090	340	350
T1-48.0 Endotoxin Challenge																										
2	16	0481	340	107					071	24	01	15	02	10	19	1315	051									
2	16	0482	340	107	275	465	7475	3960	084	32	02	16	04	11	19	1370	054	290	311	7.47	770	428	475	080	330	340

Table 61. (Contd.) Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hbg	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3^-	Total Co_2
2	16	0484	38.0	11.0	28.0	52.0	7.375	39.90	08.7	2.6	0.1	1.9	0.1	1.4	2.6	125.3	04.6	26.7	31.8	07.37	69.0	47.8	53.8	06.4	30.7	32.0
2	16	0486	34.0	10.1	38.5	58.5	7.285	39.40	05.6	2.3	0.1	1.4	0.1	0.2	1.5	125.2	04.9	24.8	31.7	07.28	67.5	53.8	59.8	00.0	26.5	28.0
2	16	0489	34.0	10.1	30.0	61.0	7.165	39.50	07.4	2.4	0.7	0.9	1.0	1.3	1.1	133.9	06.6	23.2	33.6	07.16	60.0	46.1	62.4	07.5	20.5	22.0
2	16	0491	34.0	10.1	26.5	75.5	7.113	39.60										19.6	29.7	07.12	55.0	69.5	77.2	-07.5	22.0	24.0
2	16	0494	33.0	10.4	20.0	80.5	6.940	39.30	06.1	1.8	0.1	1.2	0.3	1.0	1.7	132.8	05.6	12.5	22.2	06.94	40.0	74.1	81.4	-10.6	16.5	18.5
2	16	0497	31.0	09.5	35.0	84.0	6.915	39.00	06.0	2.2	0.1	1.2	0.2	0.9	1.5	141.0	06.6	15.3	27.3	06.92	25.0	77.3	84.0	-18.0	16.3	18.0
T2-49.8 Endotoxin Challenge																										
2	16	0499	31.0	09.5	18.0	92.5	6.780	39.00										09.6	19.6	06.78	25.0	85.1	92.5	-20.6	12.8	14.5
2	16	0502	31.0	10.1	09.5	99.9	6.125	39.00	05.6	2.0	0.1	1.0	0.2	0.7	1.6	138.0	04.8	03.1	08.6	06.12	15.0	91.9	99.9	-32.3	06.5	07.8
3	13	001	46.0	15.3					05.5	2.1	0.8	0.8	0.9	0.6	0.3	150.5	05.1										
3	13	006	46.0	15.3	82.5	47.0	7.395	39.30	05.2	2.0	0.4	0.5	0.6	0.6	1.1	144.6	05.8	81.0	90.7	07.40	95.0	43.2	47.5	03.0	27.5	29.0
3	13	024	43.5	13.0	67.0	40.0	7.575	39.70	08.4	2.8	0.0	1.0	0.9	1.3	2.4	137.0	08.4	79.3	76.1	07.57	93.0	36.8	41.4	13.0	36.0	37.0
3	13	048	47.0	13.6	79.5	42.0	7.435	39.40	07.4	2.8	0.0	0.7	0.9	1.1	1.9	169.8	09.7	80.5	89.3	07.42	94.0	38.6	42.9	03.0	27.5	28.5
3	13	0490	46.0	14.1	74.5	47.0	7.430	40.00	09.5	3.4	0.0	1.0	1.0	1.5	2.6	134.6	07.8	75.4	86.7	07.42	93.0	43.2	49.1	06.0	31.0	32.0
3	13	0500	43.0	13.6	73.0	41.0	7.445	39.70	07.9	2.8	0.2	1.1	0.9	1.0	1.9	144.4	07.4	74.7	82.9	07.43	93.0	37.2	42.4	03.0	27.0	28.0
3	13	072	44.0	14.2	69.5	42.0	7.450	39.00	06.3	3.0	0.0	0.6	0.5	1.0	1.2	141.7	08.2	71.8	75.4	07.45	92.0	38.6	42.0	04.5	28.0	29.0
3	13	096	42.0	12.7	77.5	43.0	7.485	38.90	05.8	1.8	0.1	1.0	0.5	0.9	1.5	141.7	06.6	82.7	84.4	07.47	93.0	39.6	42.5	07.2	31.0	32.0
3	13	0965	41.0	13.0	78.5	42.0	7.480	39.20	06.8	2.6	0.2	1.2	0.3	0.9	1.6	142.0	06.4	83.8	86.3	07.48	93.0	38.8	42.5	07.0	31.3	32.3
3	13	0975	43.0	13.4	77.5	42.0	7.485	38.90	06.3	2.1	0.1	1.3	0.3	0.9	1.6		15.3	83.6	85.3	07.48	93.0	38.6	42.0	07.0	31.3	32.3
3	13	1009	41.0	12.5	71.0	44.0	7.495	40.00	05.5	2.1	0.1	1.0	0.3	0.7	1.3	125.0	07.0	77.5	83.7	07.48	93.0	40.5	46.0	09.0	33.0	34.0
3	13	120	45.0	14.0	71.0	39.0	7.495	40.00	05.5	2.3	0.1	1.2	0.3	0.9	0.7	146.0	04.8	77.5	83.7	07.48	90.0	35.9	40.8	06.0	29.0	30.0
3	14	018	33.0	14.1	41.5	64.0	7.410	38.90	06.7	3.3	0.0	0.7	0.7	1.3	0.7	145.5	07.6	46.1	50.7	07.41	86.0	58.9	64.0	12.0	40.0	41.5
3	14	024	32.0	09.7	44.5	67.0	7.360	38.80	05.4	2.2	0.0	0.6	0.5	1.0	1.1	149.7	07.0	42.0	48.3	07.36	82.0	62.6	66.3	04.8	37.0	39.0
3	14	036	28.5	08.4	76.5	39.5	7.450	38.90	06.7	3.2	0.0	0.7	0.5	1.1	1.2	141.1	05.5	79.1	83.0	07.45	93.0	36.3	39.5	03.0	27.0	28.0
3	14	048	28.5	08.4					05.4	1.7	0.0	1.0	0.9	0.8	1.0	125.0										
3	14	048	30.0	09.2	82.5	44.0	7.465	38.40	08.0	3.2	0.0	0.6	1.6	1.1	1.5	123.2		86.2	86.2	07.47	95.0	40.5	43.1	07.2	30.7	32.0
3	14	0482	30.0	09.2	76.0	46.0	7.473	38.30										80.2	78.6	07.48	93.0	42.3	44.6	08.7	32.5	33.5

Table 61. (Contd.) Experimental E. coli endotoxemia in newborn calves; original and converted data.

Test Group	Test No.	Hour	HCT	Hgb	Pa_{O_2} 39°C	Pa_{CO_2} 39°C	pH 39°C	Calf Temp. C°	Total Serum Protein	Albumin	Alpha I	Alpha II	Beta I	Beta II	Gamma	Sodium	Potassium	Pa_{O_2} (7.4 37°C)	Pa_{O_2} Calf	pH Calf	Hb Saturation	Pa_{CO_2} (7.4 37°C)	Pa_{CO_2} Calf	Base Excess (Inc. Hb)	HCO_3	Total Co_2
3	14	0&8.7	30.0	09.2	68.0	&8.0	7.&80	38.30	05.&	2.2	0.0	0.5	1.0	0.8	0.9	125.6		72.6	70.&	07.&9	91.0	&.2	&.5	10.8	35.0	36.0
3	14	05&.7	30.0	09.1	73.5	54.0	7.&65	38.30	06.9	2.7	0.0	0.6	1.&	1.1	1.1	119.0	08.&	76.8	76.0	07.&7	93.0	&9.7	52.3	11.0	38.0	39.0
3	14	057.7	30.0	09.0					05.0	1.8	0.0	0.7	1.0	0.7	0.8	167.6	09.5									
3	14	072	30.0	09.0	72.0	&8.0	7.510	39.00	03.8	1.6	0.1	0.8	0.1	0.6	0.6	156.0	07.&	79.&	78.6	07.51	9&.0	&.2	&8.0	13.0	38.3	39.5
3	14	096	31.0	09.8	71.0	38.5	7.510	39.00	06.8	2.1	0.1	1.1	0.2	0.8	0.5	11.33	05.1	78.3	77.6	07.51	93.0	35.&	38.5	07.0	30.5	31.&
3	15	001	31.0	09.2					11.3	&.1	0.6	1.6	1.0	1.5	2.5	1&1.7	05.5									
3	15	012	31.0	09.2					05.8	2.3	0.2	0.7	0.7	0.7	1.2	1&0.8	05.&									
3	15	018	32.5	09.2	65.0	&&.0	7.&50	39.70	11.3	&.7	0.&	2.8	0.9	1.&	1.1	1&1.7	05.5	67.2	73.2	07.&5	92.0	&0.5	&5.5	06.0	30.0	31.0
3	15	02&	30.0	10.0	70.5	39.0	7.530	39.70	06.6	2.8	0.2	0.5	0.2	0.7	0.2	122.8	06.3	79.6	80.&	07.52	93.0	35.9	&0.3	08.7	32.0	33.0
3	15	0&.8	37.5	12.0	66.0	36.5	7.&15	39.70	0&.&	2.0	0.1	1.1	0.2	0.5	0.5	12&.0	06.0	65.5	75.3	07.&0	92.0	33.6	37.7	-01.0	22.5	23.5
3	15	0&8.6	&0.0	12.5	67.5	35.0	7.&35	39.&0										69.1	76.6	07.&2	92.0	32.2	35.8	-01.0	22.5	23.5
3	15	0&9.5	&0.5	12.0	&7.0	&.00	7.&00	39.&0	0&.6	2.2	0.1	0.9	0.5	0.6	0.3			&6.2	52.6	07.39	87.0	36.8	&0.9	-01.0	2&.3	25.5
3	15	053.7	50.5	12.5	&2.0	36.0	7.335	39.&0	06.3	2.&	0.1	1.3	0.2	1.0	1.3	139.6	08.0	38.9	&5.9	07.35	80.0	33.1	36.8	-05.0	20.0	21.0
3	15	0582	&7.0	1&.7	&6.5	37.5	7.225	37.80	0&.5	2.0	0.0	0.6	0.6	0.7	0.6	15&.3	08.6	38.&	&7.2	07.2&	73.0	3&.5	35.6	-11.2	1&.0	16.0
3	15	059.1	&0.0	12.7	28.0	7&.0	6.300	37.00	05.5	2.3	0.1	1.&	0.2	0.6	0.9	056.0		09.2	21.7	06.3&	20.0	68.0	68.1	-33.5	05.0	06.0
3	17	001	21.0	06.5					05.5	2.1	0.3	0.8	0.5	0.7	1.1											
3	17	006	19.0	05.6	72.0	&7.0	7.&&0	38.80	06.9	2.5	0.2	0.7	0.3	0.8	2.&	11.3&	05.0	73.6	78.1	07.&&	92.0	&3.2	&6.5	02.5	29.0	31.0
3	17	018	18.0	05.1	82.5	&1.0	7.525	38.90	06.9	2.8	0.2	0.&	0.2	1.1	2.2		08.0	92.1	88.&	07.53	9&.0	37.7	&0.6	08.5	32.0	32.5
3	17	0&8	18.0	05.5	76.0	&5.0	7.&50	38.60	1&.9	&.3	0.0	1.7	1.&	2.5	5.0		10.0	78.6	80.1	07.&6	92.0	&1.&	&&.0	02.5	29.0	30.0
3	17	0&82	16.0	05.0	77.5	&5.0	7.535	38.80	10.2	3.0	0.5	0.6	0.9	1.6	3.6	136.1	06.0	87.5	8&.0	07.53	9&.0	&1.&	&&.5	08.5	35.0	38.0
3	17	0&8.5	18.0	05.3	78.5	&7.0	7.535	38.80	13.6	&.1	0.7	0.7	1.3	2.&	&.&	1&.95	08.6	88.6	85.1	07.53	9&.0	&3.2	&6.5	08.5	36.0	37.5
3	17	0&89	17.0	05.2	77.5	51.5	7.5&0	38.90	1&.8	3.7	1.&	0.9	2.&	3.6	2.8		09.1	88.5	8&.1	07.5&	9&.0	&7.&	51.0	09.5	&.0.0	&.1.5
3	17	0&99	16.0	05.3	83.5	51.5	7.5&5	38.90										95.3	90.6	07.5&	95.0	&7.3	51.0	09.5	&5.0	&7.5
3	17	051.7	18.0	05.5	85.8	&5.0	7.525	39.00	11.&	3.2	1.0	0.8	1.7	3.1	1.6	1325	0&.8	95.7	92.9	07.53	95.0	&1.&	&5.0	08.5	3&.5	35.5
3	17	067.&	15.0	0&.9	80.0	&1.5	7.530	38.60	12.&	3.8	0.1	2.5	0.5	2.2	3.3	1&1.0	07.1	90.3	8&.9	07.5&	9&.0	38.2	&0.6	08.5	32.0	32.5
1	0&	012.	29.0	10.0					07.0	2.1	0.0	0.5	0.7	1.0	2.7	1391	06.8									
1	0&	036.	20.0	10.0					09.3	3.2	0.0	0.5	0.7	1.3	3.6	12&.9	0&.3									
1	0&	060.	20.0	10.0					11.0	3.2	0.&	0.7	1.2	1.8	3.1	132.0	0&.9									

EXPERIMENTAL E. COLI ENDOTOXEMIA IN NEONATAL HOLSTEIN CALVES AND THE CHANGES IN ARTERIAL BLOOD GASES, PH, SELECTED ELECTROLYTES AND PROTEINS AND THEIR EFFECT ON ACID-BASE BALANCE

by

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Fifteen newborn holstein calves were studied to determine normal mean values for arterial blood gases, pH, base excess, total bicarbonate, total carbon dioxide, hemoglobin and packed cell volume. Simultaneous serum values for sodium, potassium and protein were also made. These values were determined at 6 hour intervals from 1 to 24 hours of age, at 12 hour intervals from 24 to 48 hours of age and at 24 hour intervals from 48 to 240 hours of age. Rectal temperatures and heart rates were also recorded for the respective time periods.

Eight of these calves were challenged with E. coli endotoxin, B-055:B5 Difco Laboratories, at 48+ hours of age and these same parameters were serially determined.

The challenge calves were divided into two groups: Group II, intravenous challenge calves and Group III, oral challenge calves. Values obtained on these calves between 1 and 48 hours of age were used in determination of mean values for this time period. Normal mean values were pooled and classed as Group I, control calves.

To obtain arterial blood samples all calves were cannulated via the saphenous and femoral artery with a polyehtelyene cathetor. The tip was projected into the dorsal aorta to a level distal to the renal arteries. This cannula was also used to administer the intravenous endotoxin when given to Group II calves. It was sutured in place with polypropylene suture and remained as such throughout the experimental period, with little or no complications.

Control calves, Group I, showed marked instability during early life in all parameters studied. There was considerable variation in the approximate hour of stabilization for the individual perimeters.

Intravenous challenge calves, Group II, showed mild to severe progressive

endotoxin shock and marked deleterious respiratory pattern changes post-challenge. This change occurred as a result of the endotoxin effect on the central nervous system respiratory centers. There were correspondingly marked deleterious effects on blood gases and acid-base balance. Early mild respiratory acidosis and a delayed but simultaneous metabolic acidosis, coupled with hypoxia effected death of the animal. Circulatory complications were of undeterminable magnitude.

Sodium values were transiently affected, there being a marked reduction immediately post challenge. Hemoconcentration and regular potassium changes were not evident.

Clinical observations in the intravenous challenge calves showed marked central nervous system disturbances evidenced by early loss of muscle tone, depression, weakness, recumbency and persistance of a cutaneous trunchi spinal reflex.

Oral endotoxin challenge in three of the four calves in Group III produced clinical indications of transient apprehension. The changes in the perimeters studied were a mild persistent elevation in base excess and pH, coupled with a mild transient increased P_aCO_2. The fourth calf in this group developed a severe case of enteritis just prior to endotoxin challenge and its response was similar to the intravenous challenge calves.