# Susceptibility of cattle given organic iodine and urea to respiratory disease and foot rot

by

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# I. INTRODUCTION

## A. Statement of Problem

Increased nasal discharge and coughing have been associated with the use of expectorants. Several drugs may produce such effects, either by opening the air passages or augmenting the secretion of normal respiratory fluid. A list of such expectorants includes ethylenediamine dihydriodide (EDDI), potassium iodide, potassium and ammonium chloride, guaiacol, oil of eucalyptus, creosote, carbon dioxide, and sulfathiazole (Jones, 1965). It is generally considered that these expectorants have a beneficial effect by aiding the clearing of tenacious exudate from the upper respiratory tract.

Iodine compounds have been used as expectorants, increasing the output of respiratory exudates in animals suffering from mild chronic or subacute respiratory diseases. Oral administration of organic iodine compounds such as EDDI has been preferred to inorganic iodides because of the less irritant effect of the organic compounds on the gastric mucosa.

Recently certain beef producers and veterinarians have suspected that EDDI has adverse effects on calves suffering from respiratory disease. They have postulated that EDDI as an expectorant causes inflammation of the respiratory tract and consequently makes exposed animals more susceptible to microbial invasion (McCauley and Johnson, 1972; McCauley et al., 1971, 1972).

EDDI is recommended for treatment of foot rot, lumpy jaw, and mild respiratory diseases in cattle at a dosage of 400-500 mg/head/day for 2-3 weeks. Feeding EDDI at a continuous level of 50 mg/head/day is recommended

as a preventative for foot rot and lumpy jaw (Herrick, 1972; Miller Publishing Company, 1975).

Livestockmen have suspected similar detrimental effects from feeding urea due to the release of ammonia upon hydrolysis. Urea is commonly used as a substitute for natural proteins. A level of 0.1 lb urea/head/day is recommended for a 500-lb calf (Lloyd, 1970). In addition, it has been postulated that increased release of ammonia due to urea hydrolysis may increase EDDI breakdown and consequently result in a release of ethylenediamine, a proven bronchodilatator (Lulling et al., 1958; Noel, 1969).

Recent studies by Brown (1973) make it possible to experimentally reproduce a respiratory disease complex in susceptible cattle by interaction of Haemophilus somnus, infectious bovine rhinotracheitis (IBR) virus, and bovine virus diarrhea (BVD) virus. In addition, foot rot has been experimentally reproduced in cattle by interaction of Spherophorus necrophorus and Bacteriodes melaninogenicus (Berg, 1972).[1]

## B. Objectives

The objectives of this experiment were to: (1) determine the effects of high EDDI exposure (500 mg/head/day) upon experimentally induced bovine respiratory disease complex as manifested by weight gains, body temperature, and clinical signs, (2) determine the effects of low EDDI exposure to calves (50 mg/head/day), alone or combined with 0.1 lb urea/head/day, on susceptibility to, and severity of, the respiratory disease complex and foot rot agents, (3) monitor those parameters (packed cell volume, white

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[1] Berg, John, 1972, Personal communication, University of Missouri, Department of Veterinary Microbiology, Columbia, Missouri.

blood cell count, plasma proteins, fibrinogen, blood urea nitrogen, serum glutamic oxaloacetic transaminase, and white blood cell differentials) that reflect hematic cellular changes and certain serum enzyme activities, (4) study blood ammonia and total blood iodine levels, indicative of urea and EDDI absorption and metabolism, and (5) perform viral and bacterial isolations plus antibody determinations to assess infectivity and immunity to induced infectious diseases.

# II. LITERATURE REVIEW

## A. Iodides and Respiratory Tract Fluid

### 1. Mechanism

The expectorant action of iodides has been studied by Boyd et al. (1945) using potassium iodide at a dosage of 0.1-5.0 g/kg in cats. These animals with severed anterior and posterior branches of the vagus nerve had no increased output of the respiratory tract fluid (RTF) as compared to intact animals, which experienced increased nasal discharge at a maximum degree 2 hours later. This study indicated that the expectorant action of iodides in the cat was by way of vagal reflex from the stomach. Two organic iodide compounds, Siomine (hexamethylenetetramine tetraiodide, 79 percent iodine) and Iod-ethamine (ethylenediamine dihydriodide, 80 percent iodine) at 20 mg/kg increased output of the RTF; but no other organic compounds, such as iodized proteins, fatty acids, or oils, had this effect.

Boyd and Blanchaer (1945) reported that the reputed mucus-liquifying effect of iodides in rabbits and cats was due to a simple increase in output of normal RTF, which had a low viscosity and a pH near the neutral point. This could account for the therapeutic effect of iodides on mild respiratory diseases associated with thick mucus, coughing and reduced flow in the air passages. These workers also suggested that the appearance of iodine-containing compounds in the RTF are of a nature suggesting simple diffusion from the blood.

Organic iodides such as EDDI have been used in cattle as expectorants in the treatment of mild respiratory infections and as nutritional iodide sources (Miller Publishing Company, 1975). In recent field observations,

McCauley and Johnson (1972) suggested that caution should be taken in the use of iodides for the treatment of respiratory diseases. A similar caution is also given on labels of feeds containing EDDI for aid in the treatment of mild respiratory diseases, foot rot, and lumpy jaw: "do not administer to animals showing symptoms of acute respiratory conditions; treat animals with caution until tolerance is determined because of variation in susceptibility to iodides" (Miller Publishing Company, 1975).

B. Effects of Iodides on the Inflammatory Process

Kolmer et al. (1916) found a marked positive Luetin reaction (Noguchi's syphilis reaction) among a group of healthy, nonsyphilitic persons who were simultaneously receiving potassium iodide (KI). This reaction caused inflammatory phenomena to develop and progress to pustulation at the site of a former Luetin reaction. Sherrick (1915) has observed similar effects among guinea pigs following administration of KI. A positive pustular or nodular Luetin reaction was obtained in 99 percent of all cases, irrespective of the presence of syphilis.

Woody (1951), in attempts to treat chronic inflammatory processes in animals, found that the combined effects of KI and streptomycin caused enhancement of the inflammatory conditions. Marchese et al. (1952) found similar effects from iodized oil used in treating pulmonary tuberculosis.

Sutter et al. (1958) demonstrated that cuprous iodide (CuI) fed at 250 mg/kg/day succeeded in causing a reduction of granuloma pouch inflammation in guinea pigs. However, Stone and Carolyn (1967) reported that 33 mg KI/head/day enhanced rather than reduced a dermal inflammatory process in guinea pigs. Oral administration of KI significantly enhanced the

diameter of dermal inflammations. In Stone and Carolyn's experiment, results were evaluated after 24, 48, and 72 hours. After local injection of collagenase, results were positive at 24 and 48 hours but not at 72 hours. Stone and Carolyn (1967) also made topical applications of KI on skin of human volunteers and found that lesions of those treated were greater than those of the controls. Two volunteers in this study noted flare-ups of pain in the joints in which they had previously had discomfort. It was concluded that iodides enhance rather than inhibit certain types of dermal inflammations.

Mielenz and Rozitis (1968) initiated an investigation to determine whether or not orally administered iodides would have anti-inflammatory properties. Five types of experimental chronic inflammations were induced: granuloma pouch, cotton granuloma, corrogenan croton oil edema, turpentine-induced edema, and abscess. Administration of KI resulted in inhibition of granuloma pouch but no inhibition of the other types of inflammation. These data are suggestive of a specific anti-fibrotic effect of KI and corroborate the findings of Sutter et al. (1958).

### C. Iodine Toxicity

Iodine administered as KI or EDDI has been reported to produce toxicosis in sheep at dosages ranging from 0.15 to 0.62 g iodine/head/day for 3 weeks (McCauley et al., 1971). Treated animals had higher body temperature, appeared sluggish, and consumed less feed than controls, particularly at high iodine intake. Weight gains for sheep on zero and 0.15 g iodine/head/day levels were similar. Iodine from a KI source at 0.62 g/head/day was associated with reduced weight gains to a greater extent than iodine

from EDDI sources. At 7 days, serum protein bound iodine levels were 6.3 to 7.9 μg/100 ml for controls and 5.4 to 45 μg/100 ml for lambs receiving iodine. No gross lesions were observed at necropsy of treated animals.

Buck (1970) reported the following signs in 500-600 lb calves fed 2-24 g EDDI/head/day. Seromucoid nasal discharges occurred intermittently throughout the experiment once the exposure to EDDI had started. In addition, an occasional cough; scaliness of the skin of the dorsum, neck, ears, brisket, shoulders, and head of the tail; and slight sloughing of the epidermis were noted. These changes appeared more pronounced at 8 g EDDI/head/day and were very evident at 20 g/head/day and over. The signs disappeared 2 weeks after EDDI exposure was suspended. No temperature variation, hematologic alterations, nor changes in cholinesterase activity were observed. In this experiment, the calves refused to eat the high iodine-containing feed, as opposed to McCauley et al.'s field findings (1972) where animals were eating vigorously. It is important to note, however, that in McCauley's findings 50 mg EDDI/head/day was given, whereas EDDI levels varied from 2 g EDDI/head/day up to 20 g/head/day in Buck's experiment. At this point, it is important to clarify that coughing and increased nasal discharge are iodine expectorant effects. They are considered by some writers, however, to be signs of iodine toxicosis. In cases of true iodine toxicosis, coughing and increased nasal discharge are continuous and more severe, and erythema of the skin is also observed (Garner et al., 1967; Buck, 1970). Vomiting, loss of appetite, central nervous and cardiac depression, muscular spasms, and drowsiness are also reported in acute iodine toxicity.

Decreased weight gains in calves receiving high dietary iodine has been postulated to be due to increased thyroid activity or failure of iron absorption from the intestinal tract. This is reportedly due to decreased gastric pH and degeneration of the gastric parietal cells (Newton et al., 1974).

## D. Urea Toxicity

Urea has been blamed as a detrimental factor in some bovine respiratory diseases. The toxicity of urea formulations is dependent upon their hydrolysis to ammonia. Cattle and other ruminants are more susceptible than monogastric animals due to their high ruman urease content. Toxicosis from nonprotein nitrogen compounds results from the absorption of ammonia from the gastrointestinal tract into the blood stream. An alkaline rumen pH enhances urea hydrolysis (Lloyd, 1970).

Although alkalosis of the rumen occurs during urea toxicosis, a metabolic acidosis develops. This may indicate an inhibition of the citrate cycle. A concomitant decrease in blood pH and urine excretion appears. Death is probably due to a hyperkalemic cardiac blockage and cessation of respiration (Lloyd, 1970).

The possibility of ammonia being aspirated at the moment of eructation has been theorized. Thus, aspiration of eructated ammonia could cause irritation and increased susceptibility to respiratory infectious agents. Such a theory is not plausible; however, because ammonia is bound in liquid form, ammonium hydroxide, and unless the rumen pH is elevated to 8-9, gaseous ammonia would not be available for eructation (Lloyd, 1970).

Doses of 1.0-1.5 g urea/kg are considered to be lethal in ruminants, but 0.3-0.5 g urea/kg may also be toxic. Factors such as fasting, age of

the animal, high roughage diets, lack of conditioning to high urea diets, and high ruminal pH may augment toxic effects of urea (Buck et al., 1973).

In urea toxicosis, areas of congestion in the lungs and brain have been reported. Extravascular erythrocytes, suggestive of antemortem hemorrhages, were also mentioned. Renal congestion, swelling, and an amorphous hyaline substance localized in the glomerulli have been described (Clark et al., 1951).

## E. Infectious Bovine Rhinotracheitis

McIntyre (1954) first experimentally reproduced an upper respiratory infection in cattle by injecting defibrinated blood from typical field cases by either subcutaneous or conjunctival sac route. Postmortem changes were described as congestion and mucopurulent exudate in the upper respiratory tract.

Isolation and identification of infectious bovine rhinotracheitis (IBR) virus in tissue cultures were carried out by Gillespie et al. (1957). Experimental transmission by intratracheal inoculation of tissue culture fluid induced temperature elevation, lacrimation, inappetence, and depression. In calves inoculated intranasally, the virus concentration was greater in nasal exudate, but calves inoculated intratracheally showed a high concentration initially in the lungs and later in nasal mucosa. They also found a high concentration of virus in nasal discharge 5 days post-inoculation.

Clinical signs and virus identification were also described by McKercher and Straub (1960). These consisted of ocular discharges, redness and congestion of the muzzle (red nose), stiff joints, weight loss, and

diarrhea. In addition, Kendrick and Straub (1967) reported respiratory lesions, fetal infection, and death in utero several days before abortion occurred. Characteristic focal necrosis of the liver and renal cortex were also reported.

Antibody formation has been described by McKercher and Straub (1960). A group of calves inoculated with IBR virus showed a rapid rise in antibody titers after 12 days, although there were some variations. Some titers fluctuated widely, while others remained fairly constant. In some animals the titers still were rising 10 months after initial exposure to the virus. It has been shown that IBR virus produces different syndromes, such as conjunctivitis, abortion, balanopostitis, fatal calfhood disease, encephalitis, infectious postular vulvovaginitis, infertility, mastitis, and endometritis (House, 1972).

### F. Haemophilus somnus Infection in Feedlot Cattle

Thromboembolic meningoencephalitis (TEME) was first reported in the United States in 1956 by Griner et al. This disease was described as an acute or chronic infectious embolic meningoencephalitis, a secondary disease of cattle. It was described as a random dissemination of infected emboli in the blood vessels of the brain and meninges. The first report was based on postmortem examination of cattle that had died of clinically diagnosed infectious TEME. Macroscopic and microscopic changes indicated multiple necrotic foci in the brain and meninges, infiltrated with inflammatory cells. Thrombosed blood vessels of the brain frequently contained fibrin and bacteria.

Kennedy et al. (1960) further characterized the pathologic changes in this disease. They succeeded in producing these changes by infecting calves with a Haemophilis-like organism. A gram negative Haemophilis-like organism was isolated from cattle suffering from an epizootic bacterial encephalitis. The characteristic pathologic changes were described microscopically as a bacterial vasculitis of the brain leading to thrombosis and infarction.

Panciera et al. (1968) described an experimental reproduction of a septicemic state caused by a Haemophilis-like organism. Clinical signs were described in 3 syndromes: those of the central nervous system, respiratory tract, and joints. The first syndrome was characterized by fibrinopurulent meningitis with hemorrhagic necrotic foci, localized in the brain near the cortical gray matter. The second syndrome involved the respiratory tract, primarily lamina propria and submucosa of the larynx. Changes in the synovial membrane were involved in the third syndrome, consisting of congestion, edema, and fibrinopurulent exudate which progressed to a chronic state and manifested villous proliferation and stratification of synovial cells. The Haemophilus-like organism was best isolated by yolk sac inoculation of 6- to 8-day-old chicken embryos. The septicemic state was also reproduced in a cow by intravenous inoculation of the Haemophilus-like organism suspension; lesions produced were similar to those of the field cases.

Bailie (1969) described morphologic and biochemical characteristics of the TEME agents. Bailie also gave the new term of Haemophilus somnus to this TEME agent. The lesions that commonly had been ascribed to this condition refer to the central nervous system, respiratory tract, and joints;

however, Brown et al. (1970a) have referred to skeletal muscle lesions that may superficially resemble those of black leg. These lesions appear to be a consequence of endothelial damage to blood vessels. Lesions of kidney and gastrointestinal tract suggestive of Clostridium perfringes enterotoxemia were also observed.

Dillman (1969) gave the name of polypoid tracheitis to the tracheal lesion consistently observed in chronically coughing feedlot cattle. It is suspected that this lesion is due to a chronic bacterial infection, often following the more acute H. somnus infections.

Brown et al. (1970b) described the epidemiology, gross and microscopic tissue changes, and serologic and differential diagnostic procedures of H. somnus infections. They considered H. somnus to be a primary pathogen in the shipping fever syndrome. Intranasal inoculation of susceptible cattle with H. somnus resulted in pneumonia and septicemia not unlike shipping fever.

### G. Bovine Virus Diarrhea

As early as 1946, Olafson et al. described an acute contagious and transmissible disease of cattle characterized by leukopenia, high temperature, salivation, nasal discharges, depression, anorexia, dehydration, and subsequent abortion. Lesions consisted of ulcers and necrosis of the mucous membrane of the lips, cheeks, tongue, pharnyx, and esophagus (Olafson and Richard, 1947). Pritchard et al. (1956) reported a transmissible disease of cattle in Indiana which had many features similar to those described by Olafson in New York. Ramsey and Chivers (1953) described a more severe condition in Iowa, differing in some clinical features. The

3 bovine diseases from New York, Indiana, and Iowa possessed fundamentally similar lesions, and the virus isolated from each area was identical. In addition to the previous characterizations, Ramsey and Chivers (1953) described coughing, salivation, conjunctivitis, oral erosions, and necrotic lesions in the upper alimentary tract, such as hemorrhagic abomasitis. Inflammation of the lower digestive tract as well as deep necrosis of the Peyer's patches were also reported. Dermatitis and scab formation at the junction of the skin and hoof, at the base of the horn, and occasionally on the perineum were seen.

Gillespie et al. (1960) made a major finding in identification of BVD virus when they isolated a cytopathogenic virus from the spleen of a calf that had died of BVD in Oregon. The clinical signs fit very well with those described above. Findings of a cytopathogenic strain offered possibilities for measurements of virus and antibodies. This strain also has become the prototype virus used in many diagnostic laboratories.

After the cytopathogenic virus isolation of BVD disease and the demonstration that serum from recovered cattle neutralized the virus, a diagnostic test was developed. Malmquist (1968) studied the relationship between immunity and neutralizing antibodies. It was determined that the serum neutralization test is at least 95 percent accurate and hence usable as a substitute for a direct challenge.

Attempts to demonstrate BVD pathogenesis failed when Malmquist (1968) used a BVD virus isolated and adapted to tissue culture. Several calves artificially inoculated with the BVD virus had a persistent viremia and failed to develop neutralizing antibodies for up to 4 months, the longest period attempted. These animals also failed to produce complement-fixing

antibodies. This failure to respond immunologically is often attributed to immunologic tolerance. In this case, previous intrauterine exposure was the suspected cause of the failure. Lymphoid depletion is a consistent clinical finding in this disease. Animals suffering lymphocyte depletion are immunologically incompetent, and consequently the defense mechanism of the host is adversely affected. The suppression of interferon formation by BVD virus is considered to be responsible for exalting the action of a more benign virus. By far the most common form of BVD virus infection in older animals is the subclinical form; it probably accounts for the high incidence of animals with high serum titers.

Passive immunity duration on the average is approximately 30 weeks after birth. Whenever this parental immunity ends, a higher incidence of BVD disease is reported. This usually occurs in calves from 6 to 14 months old. Active immunity develops following artificial exposure, since complement fixation antibodies and virus neutralizing antibodies are produced first and reach a peak about 5 to 6 weeks postinfection.

## H. Shipping Fever

Several attempts to reproduce the shipping fever syndrome have failed; however, one of the most common microorganisms isolated from affected animals has been Pasteurella spp. (Gale and King, 1961; Hamdy et al., 1963). A pure culture of Pasteurella spp. failed to reproduce this syndrome. It was suggested that this genus was not the primary cause. Hamdy et al. isolated a virus using nasal washings of animals suffering from shipping fever; a mild disease was induced in calves exposed to this virus. The most severe symptoms and lesions were found in calves that were simultaneously exposed

to P. multocida, P. hemolytica, Myxovirus parainfluenza, and physical stress.

Observations at the Veterinary Diagnostic Laboratory, Iowa State University, have found that susceptible calves naturally exposed to BVD carriers and/or vacinnated against BVD died 2 weeks later due to H. somnus infection. This substantiated a close relationship between BVD and H. somnus (Brown, 1973). Calves are usually stressed due to shipment or severe climatic changes. Unfortunately, this stress may coincide with exposure to a respiratory infection due to IBR virus or H. somnus. Lymphocytic depletion and interferon suppression due to BVD infection plus stress may enhance the susceptibility to H. somnus and IBR virus to an extent that carriers are converted to clinically sick animals.

## I. Foot Rot

Gupta et al. (1964) defined foot rot as an infectious disease of the feet of cattle, characterized by erosions, foul-smelling sores, and deep dermatitis. Foot rot is localized either between the claw or in soft tissue of the feet; it usually starts at the heels and spreads under the hooves or through the upper foot, where it may involve the joints and deep structures of the foot.

Clinically, foot rot is first evidenced by swelling and slight lameness which becomes marked as the infection progresses. Several predisposing factors have been established: (1) wet feces and mud that may soften and macerate the interdigital epidermis, (2) dried and frozen mud and stones that may bruise the tissue and lower its resistance, (3) anaerobiosis

created by mud, feces, and straw layers, and (4) other conditions involving any sore in the foot.

Several experimental designs have been employed in at attempt to isolate the true foot rot agent. Moore (1898) has shown that the injection of pure Spherophorus necrophorus was not successful in reproducing the disease. Gupta et al. (1964) utilized pure bacterial cultures isolated from lesions of the infections, but he also was unsuccessful in reproducing foot rot. A mixture of a gram-negative Fusiform-like bacteria and Staphylococci was associated with a lesion that resembled foot rot. Staphylococci alone did not produce this condition.

Egerton and Parsonson (1969) ascertained that Fusiformis nodosus and S. necrophorus were the organisms that penetrated into normal epidermal tissue and referred to other bacteria as secondary invaders. It was also reported that mild lesions produced by F. nodosus were aggravated by S. necrophorus. Thus, it was concluded that foot rot is caused by F. nodosus (a transmitting agent) in conjunction with S. necrophorus and possibly actively influenced by other microorganisms.

Egerton et al. (1969) examined several hundred smears from foot rot in cattle and sealed foot rot in sheep, showing the similarity of the 2 conditions. On smears stained using the method of May-Greenwald Giemsa, it was found that F. nodosus, Spirochaetes, and 5 species of Fusiformis bacteria were prevalent; S. necrophorus was not discerned at all.

Wright et al. (1972) emphasized the need of a lacerating factor for experimental foot rot induction in pigs. In their experiment, a rough concrete floor surface was shown as a decisive factor in the foot rot induction.

There is an established connection between respiratory disease in cattle caused by H. somnus and subsequent occurrence of epidemic foot rot. Epidemic foot rot is a misnomer for suppurative polyarthritis.

In our experiment, we are dealing with true foot rot as opposed to polyarthritis, which is produced by injecting a combined suspension of S. necrophorus and Bacteriodies melaninogenicus.[2] True foot rot has been clinically identified by lameness, swelling of the lower end of the leg, and interdigital necrotic pododermatitis. The right combination of the 2 bacteria mentioned above plus the initial injury or penetration of the skin are apparently necessary to develop true foot rot.

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[2]Berg, John, 1972, Personal communication, University of Missouri, Department of Veterinary Microbiology, Columbia, Missouri.

# III. MATERIALS AND METHODS

## A. Animals

Forty heifers of crossed Shorthorn, Hereford, and Angus breeds[3] were used. These heifers were approximately 9 months old with a mean weight of 423.1 pounds. They were randomly arranged in 5 groups of 8 each. An ear tag with a number was used for identification. The experiment was continued from February 20 to April 28. These 10 weeks were divided into 3 periods: Period 1 consisted of a 2-week acclimatization period; Period 2 consisted of the following 3 weeks; and Period 3 included the remaining 5 weeks.

## B. Facilities

The cattle were housed in a shed open to the south. A wooden fence-line bunk for feeding the concentrate was installed in each pen. Water was provided by automatic electrically heated waterers. In order to periodically record weights, a scale was placed in the runway leading to the handling chute.

## C. Feed and Care

### 1. Basal ration

The basal ration consisted of the concentrate, hay, and salt ad libitum. The concentrate consisted of 73 percent ground corn, 18 percent protein supplement (90 percent soybean oil meal and 10 percent wheat middlings), and 9 percent of a vitamin and mineral mixture (vitamins A and E,

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[3] On loan from Walnut Grove Products, Atlantic, Iowa.

calcium, phosphorus, and 90 percent soybean oil meal as vehicle).[4] The concentrate was fed twice a day at a rate of 6 lb/head/day.

2. Chemical additives

The feeding program was as follows (Table 1): The 5 groups of animals were fed the basal ration during the 2-week acclimatization period (Period 1). During infectious challenge (Periods 2 and 3), the feeding program was as outlined below:

Group 1 Thirty percent of the total protein supplement of the basal ration was replaced by 0.1 lb urea/head/day.

Group 2 The basal ration plus ethylenediamine dihydriodide (EDDI) as a feed additive were given. Five hundred mg EDDI/head/day was fed during Period 2 (21 days), followed by 50 mg EDDI/head/day during Period 3, until the experiment was completed 35 days later.

Group 3 Thirty percent of the protein supplement of the basal ration was replaced by 0.1 lb urea/head/day plus 50 mg EDDI/head/day.

Groups 4 and 5 The basal ration with no additives was fed.

D. Challenge Studies

Two serum samples were taken during Period 1 before challenge of infectious agents in order to determine the immune status of each animal. After acclimatization and at the beginning of Period 2, BVD vaccine[5] was given to 4 animals in each of Groups 1, 2, 3, and 4 that had no BVD anti-

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[4] Topper 10 Plain,® Walnut Grove Products, Atlantic, Iowa.

[5] Jensine® BVD vaccine, modified live virus, Jensen-Salsbery Laboratories, Kansas City, Kansas.

Table 1. Schedule for administration of EDDI, urea, and infectious agents to cattle

| Week | Chemicals in feed | | | | |
|---|---|---|---|---|---|
| | Group 1<br>Urea<br>0.1 lb/hd/dy<br>8 weeks | Group 2<br>EDDI<br>500 mg/hd/dy<br>3 weeks;<br>50 mg/hd/dy<br>5 weeks | Group 3<br>EDDI-Urea<br>50 mg EDDI/hd/dy-<br>0.1 lb urea/hd/dy<br>8 weeks | Group 4<br>None<br>(chemical<br>control) | Group 5<br>None<br>(infectious<br>control) |
| | Period 1 (2 weeks) | | | | |
| 1<br>2 | Acclimatization period | | | | |
| | Period 2 (3 weeks) | | | | |
| 3 | Feed chemicals started (Groups 1, 2, 3); bovine virus diarrhea vaccination -- 16 calves, 4 in each of Groups 1, 2, 3, 4 | | | | |
| 4 | *Haemophilus somnus*-infectious bovine rhinotracheitis challenge -- 32 calves, 8 in each of Groups 1, 2, 3, 4 | | | | |
| 5 | | | | | |
| | Period 3 (5 weeks) | | | | |
| 6<br>7<br>8 | Foot rot challenge (*Spherophorus necrophorus* and *Bacteriodes melaninogenicus*) -- 16 calves, 2 bovine-virus-diarrhea vaccinated and 2 nonvaccinated, in each of Groups 1, 2, 3, 4 | | | | |
| 9<br>10 | | | | | |

bodies or at least had the lowest titers. The other 4 calves in each group were designated vaccination controls. The 2-ml dose of BVD vaccine produced 2 X $10^4$ plaque forming units (PFU)/ml.

One week after BVD vaccination, the first 4 groups were challenged with H. somnus and IBR virus using nasal spray administration (Table 1). The H. somnus-IBR virus mixture had 1 X $10^6$ PFU/ml of IBR virus and 5 X $10^5$ H. somnus cells/ml. A total suspension of 5 ml was divided in 2 aliquots of 2.5 ml each for spraying in each nostril.

After 2 weeks, 2 heifers in each of the 5 groups were inoculated with an H. somnus suspension by the intravenous route. This suspension contained 2.23 X $10^4$ H. somnus cells/ml.

At the end of the third week during Period 3, 4 animals (2 BVD vaccinated and 2 nonvaccinated) from Groups 1, 2, 3, and 4 were inoculated with foot rot bacteria, a mixture of S. necrophorus and B. melaninogenicus. This mixture had equal concentrations of both species in a 3-ml volume that was injected by the intradermal, interdigital route.

The challenge schedule for foot rot was as follows:

| | |
|---|---|
| Left front foot | S. necrophorus plus B. melaninogenicus strain "A". |
| Left rear foot | S. necrophorus plus B. melaninogenicus strain "B". |
| Right rear foot | B. melaninogenicus only (3 ml). |
| Right front foot | Uninoculated control. |

## E. Bacterial and Viral Isolations

### 1. Bacterial isolations

Two nasal swabs were taken from each heifer at the end of the first and second weeks before any infectious agent was inoculated. Nasal swabs

were again collected 1, 2, and 3 weeks after the challenge period had started. Nasal swabs were tested for aerobic and anaerobic bacteria. Those bacteria that were considered pathogenic due to colony shape were either stained or streaked in selective growth media and biochemically differentiated.

2. Haemophilus somnus isolations

H. somnus isolations were attempted on blood agar from nasal swabs (Brown et al., 1970b). Blood agar plates were streaked and incubated at 37°C anaerobically for about 24 hours; after the inoculation period, small, transparent colonies were sought. Confirmation of H. somnus colony suspects required Gram staining and differential growth media or biochemical assays.

3. Infectious bovine rhinotracheitis virus isolations

One and 3 weeks after IBR virus challenge, attempts were made to recover IBR virus from nasal swabs. Primary bovine testicle cell cultures were inoculated. Cells in a confluent monolayer of 60 X 15 ml Falcon tissue culture bottles were exposed to 10 and $10^{-1}$ dilution of inoculum. This inoculum was previously treated with antibiotics. After a 30-minute incubation period, plates were overlayed with agar. The IBR plaques appeared in approximately 2 days.

## F. Serology

Attempts were made to monitor the immune response of the BVD vaccinated and nonvaccinated animals that were subsequently challenged by IBR virus and H. somnus bacteria.

Serum specimens were collected according to the following schedule: 1 and 2 weeks before any artificial infectious agent exposure; at 1, 2, 3, 4, 6, 7, and 10 weeks following BVD vaccination (1, 3, 5, 6, and 9 weeks following the IBR exposure). BVD and IBR antibodies were titered according to the technique used at the Iowa State University Veterinary Diagnostic Laboratory (Brown et al., 1970b). The serum samples were screened at a final dilution of 1:16 to detect specific BVD virus neutralizing activity and 1:128 to detect IBR virus neutralizing activity. A positive result was recorded for specimens which neutralized 50 percent or more of the respective test virus as compared to controls. End titers were not determined.

H. somnus antibodies were titered by the microtiter adaptation of the complement fixation test (Brown et al., 1970b) using serial 2-fold dilutions of sera taken according to the schedule established following IBR virus challenge. These serum samples were tested against a standard 1:30 dilution of sonicated H. somnus antigen. The results reported are the reciprocal of the highest dilution which exhibited 50 percent or greater inhibition of hemolysis.

## G. Clinical Signs

Each lot of cattle was observed for signs of clinical illness. Clinical signs for each animal were recorded about 30 minutes before and after the feeding time. Two recordings of clinical signs were made each day, the first between 8:00-9:00 a.m. and the second between 4:00-5:00 p.m.

Body temperatures and weights were measured before each of the 8 times that blood samples were taken. Special care was taken following exposure to IBR virus to note mucus nasal discharge, lacrimation, and coughing.

Following challenge with foot rot agents, the incidences of lameness, swelling of the lower extremities of the limbs, and interdigital lesions were recorded.

## H. Clinical Pathology

Clinical chemistry and hematologic studies were done in all groups. Serum glutamic oxaloacetic transaminase (SGOT) and blood urea nitrogen (BUN) values, indicative of liver degeneration and renal function, respectively, were determined twice during Period 1 and 6 times during Periods 2 and 3.

### 1. Packed cell volume

Packed red blood cell volumes were assayed utilizing the microhematocrit technique (McGovern et al., 1955).

### 2. White blood cell count

White blood cell counts were determined using whole blood diluted with a 2 percent solution of acetic acid to remove the erythrocytes.[6]

### 3. Plasma proteins

Plasma proteins were analyzed using a refractometer.[7]

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[6] Coulter electronic cell counter, Model F, Coulter Electronics, Inc., Hialeah, Florida.

[7] TC/refractometer concentrimeter, American Optical Co., Buffalo, New York.

4. Fibrinogen

Fibrinogen was quantitated in plasma fluid once plasma proteins had been quantitated. The same refractometer was used for fibrinogen and plasma proteins measurements.

5. Blood urea nitrogen

Whole blood was mixed in commercially prepared test tubes containing potassium ethylenediaminetetracetate (EDTA) as anticoagulant and assayed for blood urea nitrogen using the colorimetric Berthelo's reaction.[8]

6. Serum glutamic oxaloacetic transaminase

Serum glutamic oxaloacetic transaminase was determined in serum samples colorimetrically.[9]

7. White blood cell differentials

White blood cells differentials were done on blood smears stained by Wright's method (Coles, 1967). They were examined under oil immersion of a light microscope.

## I. Chemical Analyses

Chemical analyses for ammonia nitrogen ($NH_3$-N) and total blood iodine were conducted in those groups given urea, EDDI, and in the chemical control group.

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[8] BUN test, Bio-Dynamics, Inc., Indianapolis, Indiana.

[9] Dade Division, American Hospital Supply Co., Miami, Florida.

1. Blood ammonia nitrogen

Blood ammonia nitrogen values were determined twice during Period 1 and 5 times during Periods 2 and 3 using a modification of Conway's micro-diffusion method (Conway, 1957; Lloyd, 1970).

2. Total blood iodine

Total blood iodine values were determined twice before EDDI administration was commenced and 6 times during the feeding trials. Analyses were conducted in both groups receiving EDDI and the infectious control group. The analyses were done by Whitmoyer Laboratories[10] using a procedure based on the method described by Benotti and Benotti (1963).

## J. Analyses of Data

Mean values for all parameters were plotted on a curve design, as shown in Figures 1-14. The 10 weeks of the experiment were divided into the 3 periods previously described. Mean values of each period for each parameter in each group were computed. A student t test for analysis between 2 groups at 1 specific period was performed. For this approach, values that showed a gross difference were selected. Period 2 of Group 2 was selected as a main point of reference, due to the fact that it corresponded to high EDDI levels. However, any differences between other groups and periods were examined.

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[10]Method 690-0, Whitmoyer Laboratories, 1963.

# IV. RESULTS AND DISCUSSION

Data from this project are grouped around 5 primary categories: (1) clinical signs, (2) performance, (3) serologic and microbiologic isolations (bacterial and viral), (4) clinical pathology studies, and (5) chemical analyses. A complete tabulation of data from each of the parameters investigated is presented in the Appendix.

## A. Clinical Signs

The incidence of coughing, nasal discharge, and lacrimation was recorded during Period 2 (21 days). All animals in all groups given 0, 50 mg EDDI plus 0.1 lb urea/head/day, 500 mg EDDI/head/day, and 0.1 lb urea/head/day coughed during the week following IBR virus-H. somnus challenge (Appendix Figure 1). Those receiving 500 mg EDDI, however, had a greater incidence of coughing before challenge which lasted longer following challenge than the other groups, and those receiving 50 mg EDDI plus 0.1 lb urea had a somewhat greater incidence of coughing than the group receiving urea alone and the control group.

All animals given 500 mg EDDI/head/day had nasal discharge within 1 week following IBR virus-H. somnus challenge, whereas only 50 percent of those given 0.1 lb urea and those given 50 mg EDDI plus 0.1 lb urea exhibited nasal discharge during this period (Appendix Figure 2). Also, those given 500 mg EDDI exhibited an increased incidence of nasal discharge a few days prior to and the week following challenge with IBR virus and H. somnus.

Approximately 50 percent of those animals given 500 mg EDDI/head/day exhibited lacrimation for about 7 days, beginning 1 week after IBR virus

and H. somnus challenge (Appendix Figure 3). Those given 0, 50 mg EDDI, and 0.1 lb urea also manifested lacrimation but to a lesser extent.

The above mentioned clinical signs, i.e., coughing, nasal discharge, and lacrimation, reflect not only the expectorant effects of EDDI but also those of a respiratory viral infection such as IBR. In all animals, signs were more pronounced during the period of peak IBR infection approximately 7-14 days following challenge. Most of the clinical signs ceased within 3 days after removal of EDDI from the diet, including in the control group that received no EDDI and the group that received 0.1 lb urea. Signs of H. somnus infection were not observed.

Clinical signs of experimental foot rot commenced 2 to 4 days after inoculation in those groups receiving 50 mg EDDI daily (Groups 2 and 3) as well as those not receiving EDDI (Groups 1 and 4) (Table 2). Clinical signs commenced 2-4 days after inoculation. Six of 8 animals experienced lameness, swelling of the lower left front and rear legs, and interstitial necrotic pododermatitis at the site of inoculation. These signs were observed for 4 days but subsided after antibiotic treatment. The right front feet (uninoculated) were unaffected as were all feet of those animals that were not inoculated with the foot rot agents.

Both groups of calves being given 50 mg EDDI/head/day contracted "foot rot" (pododermatitis) within 2-3 days following inoculation by S. necrophorus and B. melaninogenicus suspensions, as did those animals not receiving EDDI. This phase of the study is inconclusive, however, because a very large inoculum of S. necrophorus and B. melaninogenicus was used, and test animals were receiving only 50 mg EDDI/head/day. Other experimentation should include studies with animals given 500 mg EDDI/head/day at

Table 2. Incidence of clinical signs in calves fed EDDI, urea, and no feed additives following interdigital-intradermal inoculation of Spherophorus necrophorus and Bacteriodes melaninogenicus[a]

| Clinical signs | Chemicals in feed | | | | |
|---|---|---|---|---|---|
| | Group 1 Urea 0.1 lb/hd/dy 8 weeks | Group 2 EDDI 500 mg/hd/dy 3 weeks; 50 mg/hd/dy 5 weeks | Group 3 EDDI-Urea 50 mg EDDI/hd/dy-0.1 lb urea/hd/dy 8 weeks | Group 4 None (chemical control) | Group 5 None (infectious control) |
| | Days after challenge clinical signs observed | | | | |
| Lameness | 2-4 (2/4)[b] | 2-6 (3/4) | 2-5 (3/4) | 4-6 (3/4) | Not challenged |
| Swelling of inoculated feet | 2-4 (2/4) | 2-6 (3/4) | 2-5 (3/4) | 4-6 (3/4) | |
| Necrotic pododermatitis | 2-4 (2/4) | 2-6 (3/4) | 2-5 (3/4) | 4-6 (3/4) | |

[a]Animals were inoculated at the beginning of the third week of Period 3 (2 weeks after Group 2 EDDI exposure had been reduced to 50 mg/hy/dy).

[b]Numbers in parentheses indicate number of affected animals of the total challenged in the group.

the time of bacterial inoculation, and various dosage levels of inoculum should be used to adequately determine the effectiveness of EDDI as a preventative and treatment for foot rot.

In Group 4, not given EDDI, clinical signs commenced 3 to 4 days after inoculation and lasted 2 to 4 days. Three of 4 animals had affected left rear feet, 2 had affected left front feet, and 1 had affected right rear foot but to a lesser degree. Antibiotic treatment was given to those animals most severely affected, and recovery was usually within 2 days.

Only 2 borderline foot rot cases were detected in Group 1, given urea (0.1 lb/head/day) with no EDDI. The rear feet on both animals were affected for 2 days. Interdigital lesions consisted of superficial skin necrosis which healed 2 days later. No antibiotic treatment was given.

1. Body temperature

No statistically significant differences were found in mean body temperatures in calves exposed to both levels of EDDI, urea, and the controls (Appendix Figure 4). A significant difference in mean body temperature occurred during Period 1 when no EDDI or urea was being fed. Calculated T (Tc) and tabulated T (Tt) of the chemical control group (Group 4) and the 500 mg EDDI/head/day group (Group 2) during Period 1 were 3.26 and 1.69, respectively. A similar difference was also seen between the infectious control group (Group 5) and Group 2 during Period 2 (Tc = 3.3 and Tt = 1.69), but it was considered null because of the prior difference seen during Period 1 when no EDDI and urea were fed. The changes in body temperature in any of the groups during any week were not significant when compared to those changes experienced by other groups.

## B. Body Weight Gain

Body weights of the calves measured during the 10-week period are summarized in Appendix Figure 5 and detailed in Appendix Table 1. Their overall mean weight was 423 lb at the beginning and 540 lb after 10 weeks on the experiment. Their average daily gains (pounds) during the 10-week experiment were as follows: Group 1, 1.79; Group 2, 1.56; Group 3, 1.53; Group 4, 1.97, and Group 5, 1.70.

An F test was performed to determine if the weight gains in all 5 groups were significantly different (Appendix Figure 5). $F = 4,33\ \frac{631}{520} = 1.21$ which is not significant. There is no evidence that the gain in weight differed significantly among the 5 groups.

## C. Microbiologic Isolations and Serology

Antibodies for IBR virus were not present in any of the calves before the experiment was begun and remained undetectable through the second week after challenge. IBR was confirmed by isolation of the virus from random blood samples taken from affected animals. Subsequent antibody titrations indicated that a general IBR infection had occurred in all 4 groups. Within 3 weeks after IBR virus exposure, antibodies were detected in 17 of 32 of the experimentally exposed calves (Table 3, Appendix Table 3). It is noteworthy that 3 calves in Group 2 and 1 animal in each of Groups 1 and 4 failed to develop detectable circulating IBR antibodies, even though these animals were clinically indistinguishable from the other affected calves which developed antibodies. This is not too surprising, however, in light of previous reports of variations in circulating antibodies in convalescent animals (McKercher and Straub, 1960).

Table 3. Infectious bovine rhinotracheitis antibody titers (before and after challenge) in calves fed EDDI, urea, and no feed additives (8 animals in each of Groups 1, 2, 3, 4 were challenged)

| Week | Chemicals in feed | | | | |
|---|---|---|---|---|---|
| | Group 1 Urea 0.1 lb/hd/dy 8 weeks | Group 2 EDDI 500 mg/hd/dy 3 weeks; 50 mg/hd/dy 5 weeks | Group 3 EDDI-Urea 50 mg EDDI/hd/dy-0.1 lb urea/hd/dy 8 weeks | Group 4 None (chemical control) | Group 5 None (infectious control) |
| 1 | 8/0[a] | 8/0 | 8/0 | 8/0 | 8/0 |
| 2 | 8/0 | 8/0 | 8/0 | 8/0 | 8/0 |
| 3 | 8/0 | 8/0 | 8/0 | 8/0 | 8/0 |
| | Infectious bovine rhinotracheitis challenge | | | | |
| 4 | 8/0 | 8/0 | 8/0 | 8/0 | 8/0 |
| 5 | 4/4 | 5/3 | 3/5 | 6/2 | 8/0 |
| 6 | 4/4 | 5/3 | 2/6 | 4/4 | 8/0 |
| 8 | 4/4 | 5/3 | 2/6 | 2/6 | 7/1 |
| 10 | 3/5 | 7/1 | 4/4 | 6/2 | 8/0 |

[a]Numerator indicates number of animals negative to infectious bovine rhinotracheitis antibodies at a 1:16 serum dilution; denominator indicates number of animals with positive titers above 1:16 serum dilution.

Since a majority of the calves were found to have circulating antibodies for BVD virus (Table 4, Appendix Table 4) and H. somnus bacteria prior to BVD vaccination and subsequent challenge to IBR-H. somnus agents, enhancement of H. somnus infectivity by BVD vaccination was not expected. This indeed was the case based upon the following observations: (1) white blood cell counts did not decrease in the vaccinated calves, (2) the clinical signs observed subsequent to IBR-H. somnus challenge were not indicative of H. somnus infection, and (3) H. somnus bacteria were not isolated from the blood of affected animals although attempts were made to do so. It is apparent, however, that both BVD vaccination and H. somnus challenge stimulated the production of their respective circulating antibodies (Tables 4 and 5, Appendix Tables 4 and 5). Although serum dilutions were not extended beyond 1:16, it is evident that the BVD-vaccinated calves had circulating antibodies for a longer time than the nonvaccinated calves.

The bacteria isolated from nasal swabs are listed below (only the pathogenic bacteria are included:

The first nasal swab sampling taken 1 week after BVD vaccination resulted in P. multocida isolation from only 1 animal from each of Groups 1, 3, 4, and 5. After 2 weeks, P. multocida was isolated from 2 nasal swabs from Group 4, from 3 nasal swabs of Group 3, and from only 1 from Groups 1, 3, and 5. Hemolytic streptococci and moraxella were isolated from nasal swabs of Group 4 after 3 weeks. From a sampling after 4 weeks, P. multocida was isolated from 6 nasal swabs from 2 animals in each of Groups 2, 3, and 4. A week after exposure, H. somnus was recovered from nasal swabs from Groups 2 and 3.

Table 4. Bovine virus diarrhea antibody titers in calves receiving EDDI, urea, and no feed additives (4 animals in each of Groups 1, 2, 3, 4 were vaccinated with BVD virus)

| | Chemicals in feed | | | | |
|---|---|---|---|---|---|
| Week | Group 1<br>Urea<br>0.1 lb/hd/dy<br>8 weeks | Group 2<br>EDDI<br>500 mg/hd/dy<br>3 weeks;<br>50 mg/hd/dy<br>5 weeks | Group 3<br>EDDI-Urea<br>50 mg EDDI/hd/dy-<br>0.1 lb urea/hd/dy<br>8 weeks | Group 4<br>None<br>(chemical<br>control) | Group 5<br>None<br>(infectious<br>control) |
| 1 | 1/7[a] | 5/3 | 4/4 | 3/5 | 3/5 |
| 2 | 0/8 | 0/8 | 0/8 | 1/7 | 1/7 |
| | Bovine virus diarrhea vaccination | | | | |
| 3 | 1/7 | 1/7 | 1/7 | 0/8 | 2/6 |
| 4 | 2/6 | 3/5 | 3/5 | 1/7 | 4/4 |
| 5 | 4/4 | 4/4 | 4/4 | 4/4 | 6/2 |
| 6 | 2/6 | 3/5 | 4/4 | 4/4 | 7/1 |
| 8 | 4/4 | 4/4 | 4/4 | 4/4 | 8/0 |
| 10 | 4/4 | 5/3 | 4/4 | 4/4 | 7/1 |

[a]Denominator denotes number of animals positive to bovine virus diarrhea antibodies at a 1:16 dilution; numerator denotes the number of animals with a bovine virus diarrhea antibodies titer below 1:16 serum dilution.

Table 5. Haemophilus somnus antibody titers (before and after challenge) in calves fed EDDI, urea, and no feed additives (8 animals in each of Groups 1, 2, 3, 4 were challenged

| Week | Chemicals in feed | | | | |
|---|---|---|---|---|---|
| | Group 1<br>Urea<br>0.1 lb/hd/dy<br>8 weeks | Group 2<br>EDDI<br>500 mg/hd/dy<br>3 weeks;<br>50 mg/hd/dy<br>5 weeks | Group 3<br>EDDI-Urea<br>50 mg EDDI/hd/dy-<br>0.1 lb urea/hd/dy<br>8 weeks | Group 4<br>None<br>(chemical<br>control) | Group 5<br>None<br>(infectious<br>control) |
| 1 | 1/7[a] | 1/7 | 2/6 | 2/6 | 0/8 |
| 2 | 1/7 | 0/8 | 1/7 | 0/8 | 1/7 |
| 3 | 0/8 | 1/7 | 0/8 | 0/8 | 0/8 |
| | Haemophilus somnus challenge | | | | |
| 4 | 0/8 | 1/7 | 0/8 | 0/8 | 0/8 |
| 5 | 0/8 | 2/6 | 0/8 | 0/8 | 0/8 |
| 6 | 0/8 | 1/7 | 1/6 | 0/8 | 0/8 |
| 8 | 0/8 | 2/6 | 0/8 | 0/8 | 0/8 |
| 10 | 0/8 | 3/5 | 0/8 | 0/8 | 0/8 |

[a]Denominator denotes number of animals positive to Haemophilus somnus antibodies at a 1:8 serum dilution; numerator denotes number of animals with a Haemophilus somnus antibodies titer below 1:8 serum dilution.

Although an objective of this experiment was to produce a complex IBR-*H. somnus* infection, this was not accomplished because the calves were immune to both BVD and *H. somnus* agents, Therefore, an uncomplicated IBR infection was produced in these calves.

## D. Clinical Pathology Studies

### 1. Serum glutamic oxaloacetic transaminase

During the entire experiment, serum glutamic oxaloacetic transaminase groups were consistently within the normal range, and no statistically significant differences were found among the groups (Appendix Figure 6, Appendix Table 6).

### 2. Blood urea nitrogen

Variations in blood urea nitrogen values in animals among the 5 groups and at any specific time were not statistically significant during the 10-week experiment (Appendix Figure 7, Appendix Table 7).

### 3. Hematologic studies

There were not statistically significant differences among the 5 groups in white blood cell count, lymphocytes, segmented and band neutrophils, eosinophils, and packed cell volume values (Appendix Figures 8, 9, 10, 11, 12, 14). At the eighth week of the experiment (6 weeks of exposure to EDDI and urea), there were significant increases (TC = 2.75; Tt = 1.96) in mean fibrinogen and corresponding total protein values in all except the 2 control groups. Not all individuals within a group had increased values (Appendix Figures 14 and 15, Appendix Tables 15 and 16), and this phenomenon has not been explained. At this point in the experiment, the respira-

tory infection has completely subsided, and those on EDDI were being given only 50 mg/head/day. One possible attributing factor was a severe snowstorm (36-hour blizzard) which occurred 1 week before the increased fibrinogen-total protein levels were detected.

## E. Chemical Analyses

### 1. Blood ammonia nitrogen

The blood ammonia nitrogen levels are not reported because laboratory errors resulted in erratic and unacceptable data. It was determined that glassware used in the test had been cleaned with an alkaline detergent and was not properly rinsed, resulting in inordinately high and erratic levels of sulfuric acid necessary for titration to the neutral end point required in the test procedure.

### 2. Total blood iodine

Total blood iodine levels were significantly increased in those groups given EDDI. The mean levels peaked at 1400 ng/ml after 2 weeks in the 500 mg/head/day group, whereas those on 50 mg/head/day peaked at about 300 ng/ml. When EDDI exposure was maintained at 50 mg/head/day (Groups 2 and 3), the total blood iodine levels remained slightly under 275 ng/ml, and the control animals (Group 5) averaged 140 ng/ml.

Differences in mean total blood iodine levels were highly significant between EDDI groups and the controls. Total blood iodine levels compared between Group 2 Period 2 to Group 5 Period 2 had the following T values: Tc = 66 and Tt = 1.96; Group 3 (50 mg EDDI plus 0.1 lb urea/head/day). Period 3 compared to Group 5 Period 3 had Tc = 8.07 and Tt = 1.96.

# V. CONCLUSIONS

Attempts to confirm field observations that cattle suffering adverse effects from bovine virus diarrhea (BVD) vaccination and concomitant exposure to infectious bovine rhinotracheitis (IBR) virus and Haemophilis somnus bacteria were unsuccessful since this group of calves were already resistant to BVD and H. somnus infection. Antibody titers before BVD vaccination and H. somnus challenge were inconsistent but present in all the calves, although only a maximum serum dilution of 1:16 was titrated.

No adverse effects from BVD vaccination were demonstrated. Immunosuppression and delayed hypersensitivity reactions were not associated with BVD vaccination and H. somnus-IBR virus challenge.

This group of calves was susceptible to IBR virus infection. No antibodies were present before IBR challenge, but 2 weeks later antibody titers were consistently present in all exposed calves. A natural spread of the disease was evident and confirmed by IBR virus isolation from blood and nasal swabs of challenged and control groups.

Clinical signs manifested by the calves were indicative of both the expectorant action of EDDI and IBR infection. Those animals given 500 mg EDDI/head/day had more coughing, nasal discharge, and lacrimation than those given 50 mg EDDI/head/day or 0.1 lb urea/head/day or the controls. The period of time required for recovery from IBR infection, however, appeared to be about the same in the EDDI exposed, those fed 0.1 lb urea/head/day, and the control animals.

Mean temperature changes experienced by this herd of calves were not significantly different at any week neither among groups. Mean weight

gains rate was not significantly different among any groups neither at any week.

The replacement of natural dietary protein with 0.1 lb urea/head/day in these calves did not appear to affect their susceptibility to or the course of IBR infection.

This report has attempted to distinguish between epidemic foot rot or suppurative polyarthritis, a sequellae to H. somnus infection, and "true" foot rot or infectious pododermatitis produced by the interaction of Spherophorus necrophorus and Bacteriodes melaninogenicus when introduced intradermally into the interdigital space. Classical foot rot lesions were produced in 14 of 16 animals inoculated with a suspension of these 2 bacterial species. Calves given 500 mg EDDI/head/day for 3 weeks followed by 50 mg/head/day and calves given 50 mg/head/day for 6 weeks were equally susceptible to pododermatitis infection by S. necrophorus and B. melaninogenicus as the non-EDDI controls. This experiment is inconclusive and should be repeated using different levels of EDDI as well as varied numbers of bacteria in suspension. In our experiments, a high concentration of organisms was used for the inoculum, and only 50 mg EDDI/head/day were given. Other experimentation should include studies with animals given 500 mg EDDI/head/day at the time of bacterial inoculation.

Other experimentation should include studies with animals given 500 mg EDDI/head/day at the time of bacterial inoculation, and various dosage levels of inoculum should be used to adequately determine the effectiveness of EDDI as a preventative or treatment for foot rot.

# VI. SUMMARY

Forty crossbred beef calves weighing an average of 423 lb each were placed in 5 lots consisting of 8 animals/group. Each group was fed a basal ration consisting of concentrate and alfalfa hay. The concentrate was made up of corn and soybean oil meal plus minerals and vitamins. Three groups were given urea and ethylenediamine dihydriodide (EDDI) in their diet as follows: Group 1 was given 0.1 lb urea/head/day for 56 days in place of an equivalent amount of natural protein; Group 2 was given 500 mg EDDI/head/day for 21 days, followed by 50 mg EDDI/head/day for an additional 35 days; Group 3 was given 0.1 lb urea/head/day as a replacement for an equivalent amount of natural protein and 50 mg EDDI/head/day for 56 days; and Groups 4 and 5 were given basal rations with no chemical additives and served as chemical control and infectious control, respectively.

The 10-week experiment was divided into 3 periods as follows: Period 1--2 weeks of acclimatization prior to the adding of EDDI and urea to the basal ration; Period 2--the following 3 weeks during which Group 2 was given 500 mg EDDI/head/day; and Period 3--the remaining 5 weeks during which Groups 2 and 3 were given 50 mg EDDI/head/day.

At the beginning of Period 2, 16 calves, 4 from each of Groups 1, 2, 3, and 4, were given bovine virus diarrhea (BVD) vaccine. One week later, all 32 calves in Groups 1, 2, 3, and 4 were challenged with infectious bovine rhinotracheitis (IBR) virus and Haemophilus somnus bacteria in an attempt to produce a shipping fever-like respiratory infection. Group 5 remained as an unexposed control.

At the beginning of the third week of Period 3, 4 animals (2 BVD vaccinated and 2 nonvaccinated) from Groups 1, 2, 3, and 4 were inoculated with a mixture of Spherophorus necrophorus and Bacteriodes melaninogenicus in an attempt to produce classical foot rot, infectious pododermatitis. The inoculum was injected intradermally in the interdigital spaces of the left front and rear feet. The right rear foot was injected with a culture of B. melaninogenicus only, and the right front foot of each animal remained as an uninoculated control.

All animals given IBR virus developed clinical signs of the disease within 7 days. No signs of H. somnus infection were observed. Clinical signs were primarily manifested by coughing, nasal discharge, lacrimation, and temperature rise. Those animals receiving 500 mg EDDI/head/day were coughing and had nasal discharge sooner than and for a more prolonged period of time than animals in the other groups. Also, those animals receiving 50 mg EDDI/head/day had a slightly increased incidence of coughing and nasal discharge over those animals receiving no EDDI. There were no significant differences in temperature elevations, weight gain, clinical pathologic, and hematologic parameters measured between those animals given EDDI and/or urea and the controls.

It was concluded that coughing, nasal discharge, and lacrimation reflected not only the expectorant effects of EDDI but also those of a respiratory viral infection such as IBR. Even though these clinical signs were more pronounced in the high EDDI exposed group, the overall outcome of IBR infection was essentially the same in all groups of animals, whether exposed to EDDI or not. Although the study was not designed to be a feed-

ing trial, average daily weight gains were not statistically different among the 5 groups of calves.

The total blood iodine levels peaked at the end of the second week of feeding EDDI. Those calves given 500 mg EDDI/head/day reached a mean total blood iodine level of 1,400 ng/ml while those receiving 50 mg EDDI/head/day reached a peak of 330 ng/ml. The control animals also had slight increases in total blood iodine, reaching a peak of 142 ng/ml. This finding reflects the ease with which iodine may contaminate the environment by urine, feces, and perhaps feed dust.

Both groups of calves being given 50 mg EDDI/head/day contracted "foot rot" (pododermatitis) within 2-3 days following inoculation by S. necrophorus and B. melaninogenicus suspensions, as did those animals not receiving EDDI. This phase of the study is inconclusive because a very large inoculum of S. necrophorus and B. melaninogenicus was used, and test animals were receiving only 50 mg EDDI/head/day.

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# IX. APPENDIX

Figure 1. Percent incidence of coughing in experimental and control calves (8 animals per group) during Period 2 (21 days) (see Table 1 for experimental paradigm)

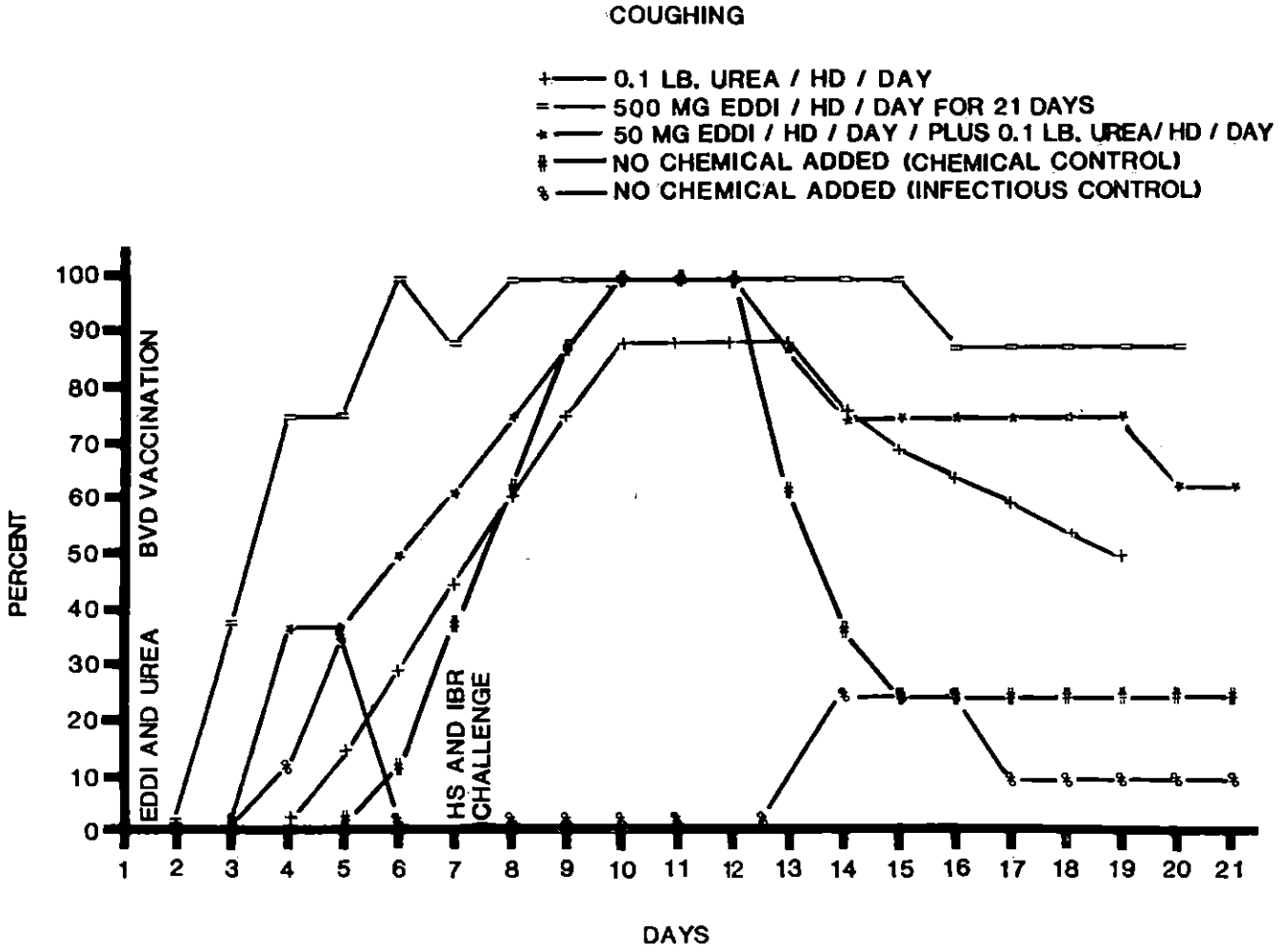
COUGHING
+ 0.1 LB. UREA / HD / DAY
= 500 MG EDDI / HD / DAY FOR 21 DAYS
* 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
# NO CHEMICAL ADDED (CHEMICAL CONTROL)
% NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
EDDI AND UREA
BVD VACCINATION
HS AND IBR
CHALLENGE
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
DAYS

Figure 2. Percent incidence of nasal discharge in experimental and control calves (8 animals per group) during Period 2 (21 days) (see Table 1 for experimental paradigm)

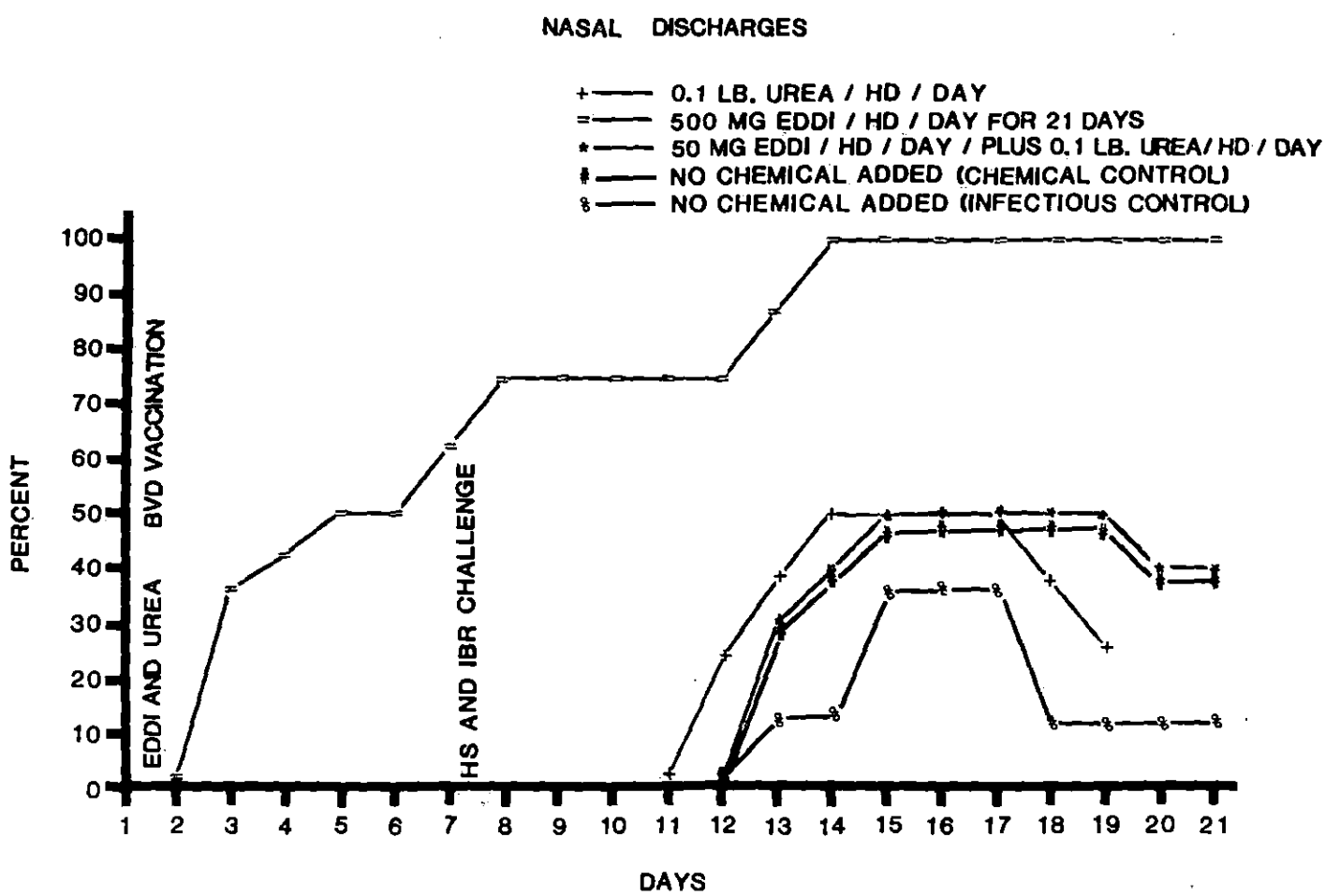
NASAL DISCHARGES
+—— 0.1 LB. UREA / HD / DAY
=—— 500 MG EDDI / HD / DAY FOR 21 DAYS
*—— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
#—— NO CHEMICAL ADDED (CHEMICAL CONTROL)
%—— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
DAYS

Figure 3. Percent incidence of lacrimation in experimental and control calves (8 animals per group) during Period 2 (21 days) (see Table 1 for experimental paradigm)

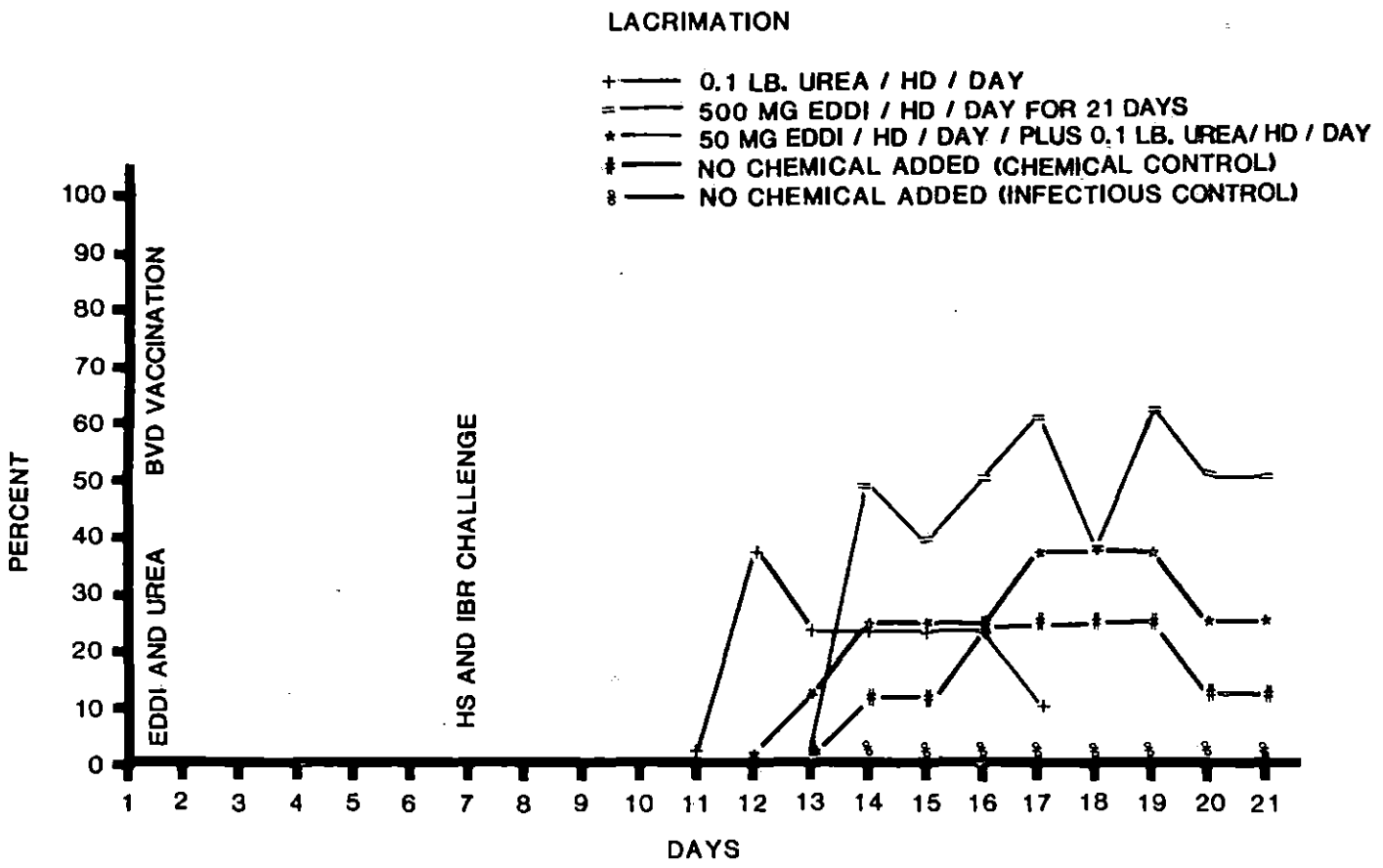
LACRIMATION
0.1 LB. UREA / HD / DAY
500 MG EDDI / HD / DAY FOR 21 DAYS
50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
NO CHEMICAL ADDED (CHEMICAL CONTROL)
NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
DAYS

Figure 4. Weekly mean body temperatures in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

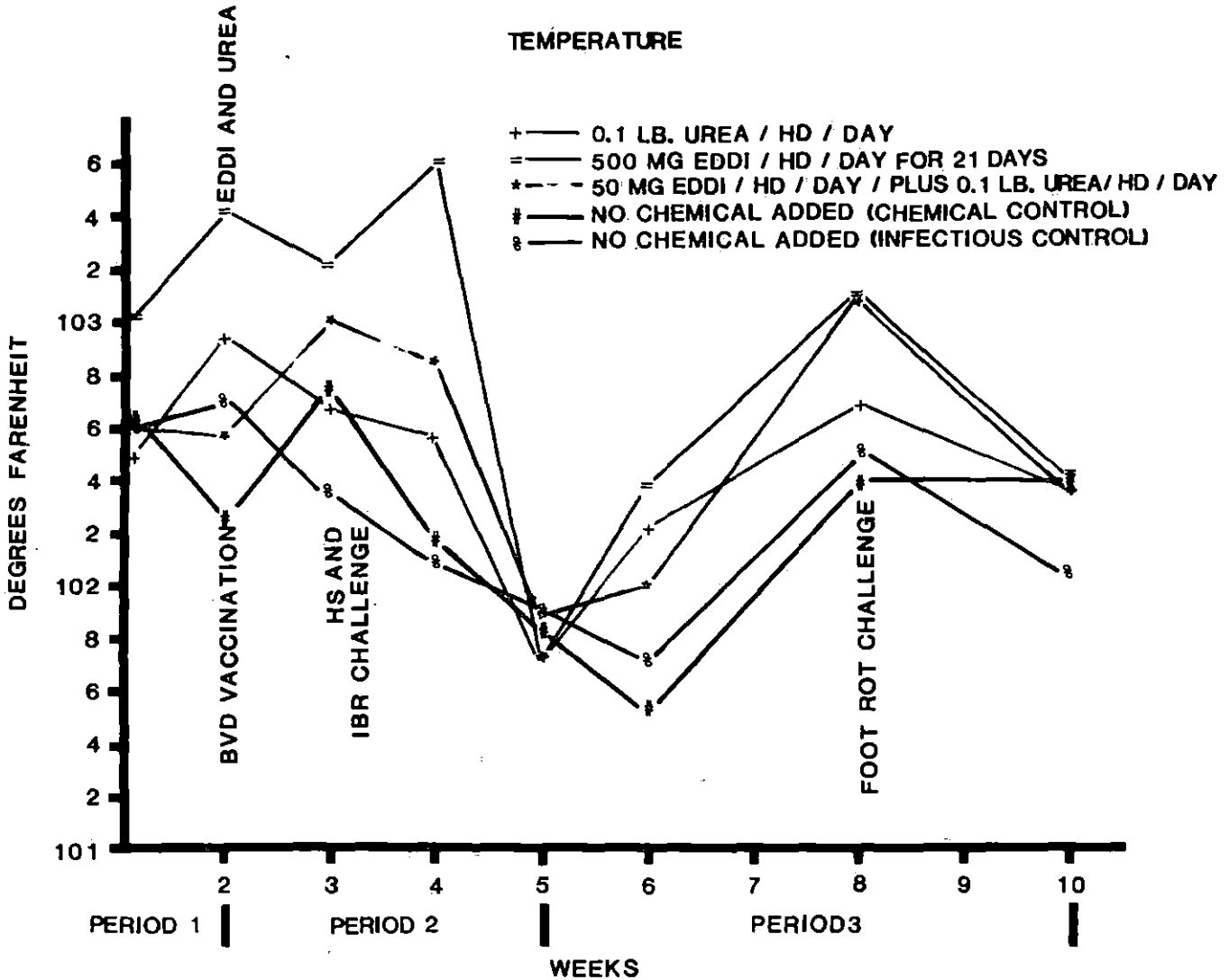
TEMPERATURE
+—— 0.1 LB. UREA / HD / DAY
=—— 500 MG EDDI / HD / DAY FOR 21 DAYS
*– – – 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
#—— NO CHEMICAL ADDED (CHEMICAL CONTROL)
8—— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
DEGREES FARENHEIT
6
4
2
103
8
6
4
2
102
8
6
4
2
101
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD3
WEEKS

Figure 5. Weekly mean body weights in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

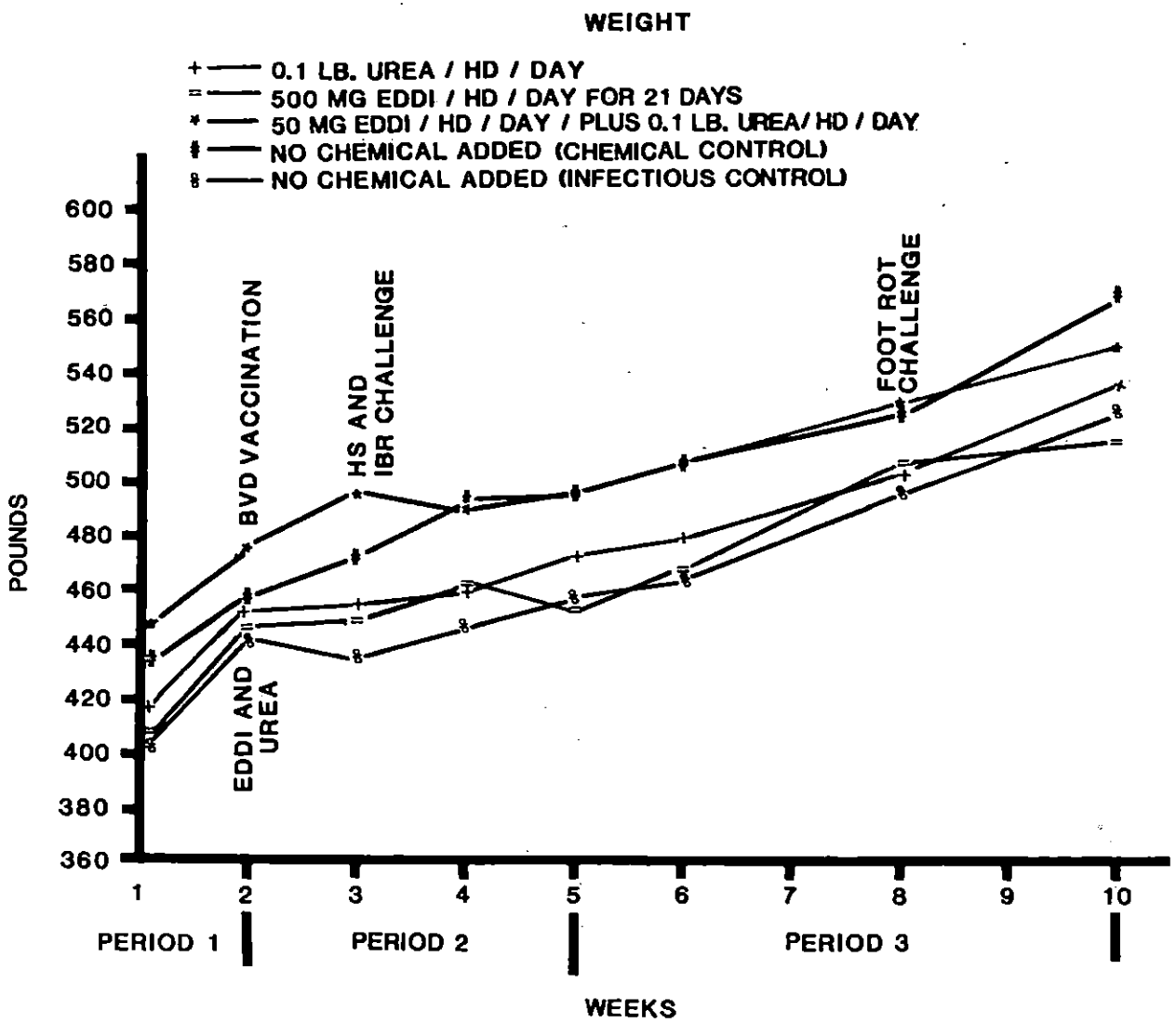
WEIGHT
+ —— 0.1 LB. UREA / HD / DAY
= —— 500 MG EDDI / HD / DAY FOR 21 DAYS
* —— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
# —— NO CHEMICAL ADDED (CHEMICAL CONTROL)
8 —— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
POUNDS
600
580
560
540
520
500
480
460
440
420
400
380
360
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 6. Weekly mean serum glutamic oxaloacetic transaminase activities in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

SERUM GLUTAMIC OXALOACETIC TRANSAMINASE

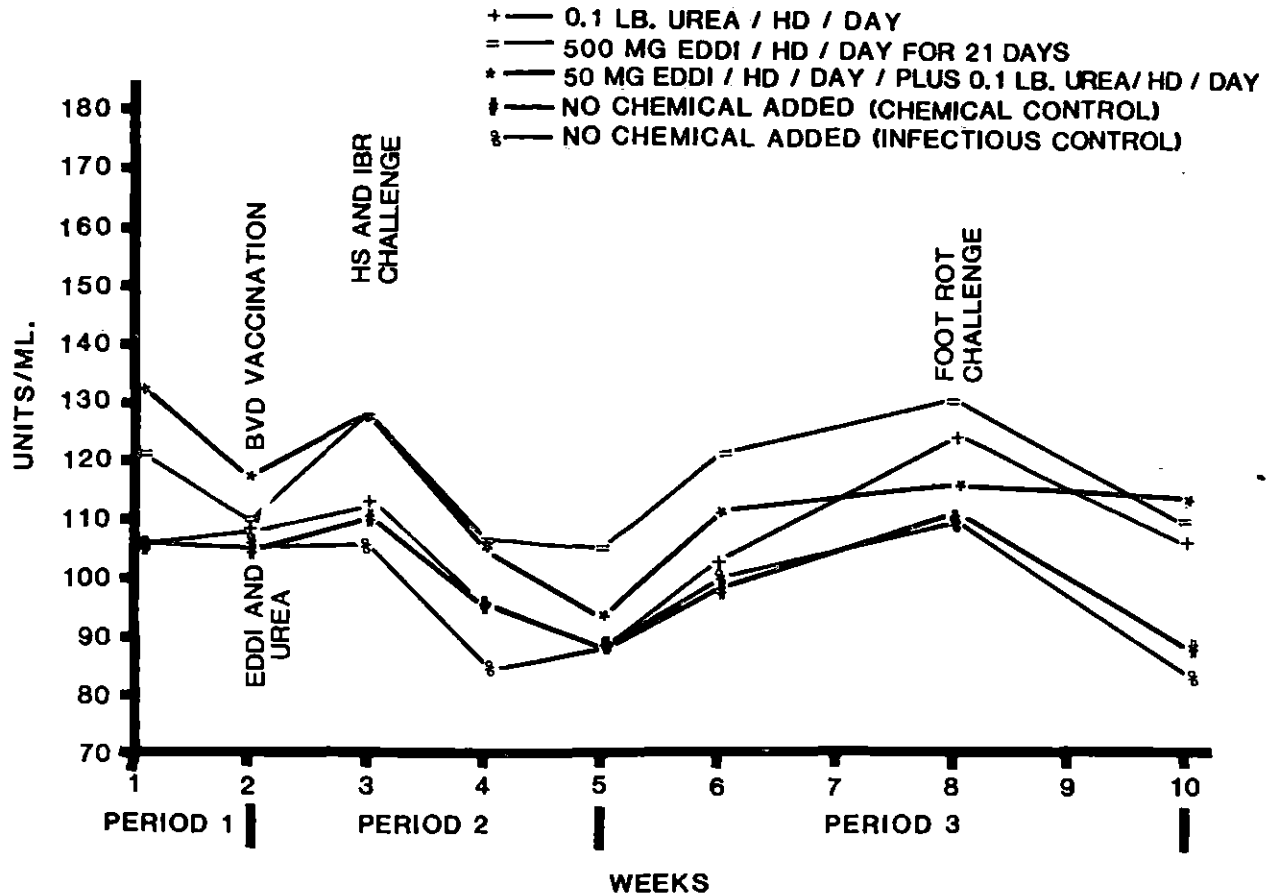

Figure 7. Weekly mean blood urea nitrogen levels in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

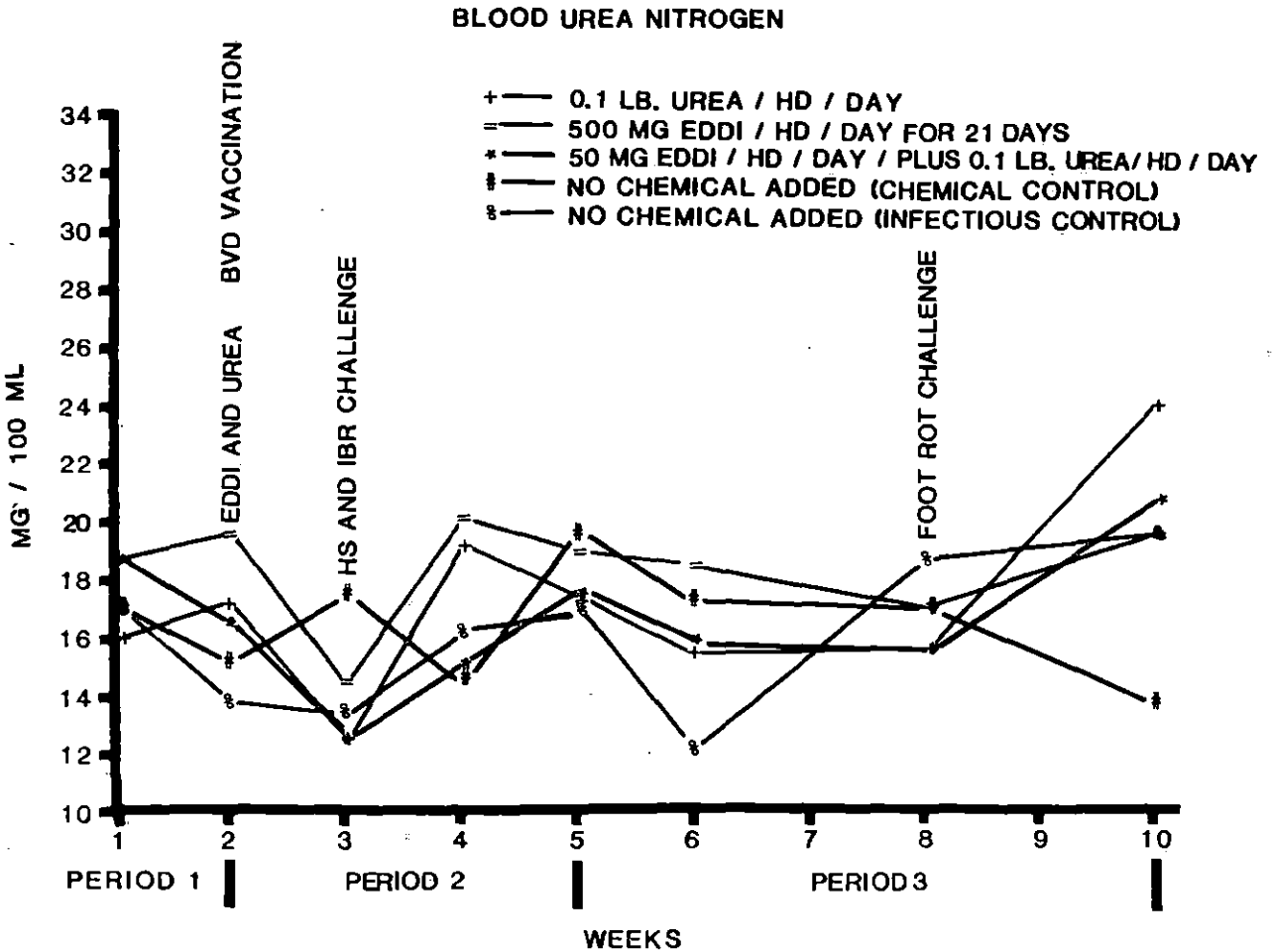
BLOOD UREA NITROGEN
+ 0.1 LB. UREA / HD / DAY
= 500 MG EDDI / HD / DAY FOR 21 DAYS
* 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
# NO CHEMICAL ADDED (CHEMICAL CONTROL)
% NO CHEMICAL ADDED (INFECTIOUS CONTROL)
MG / 100 ML
34
32
30
28
26
24
22
20
18
16
14
12
10
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 8. Weekly mean white blood cell counts in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

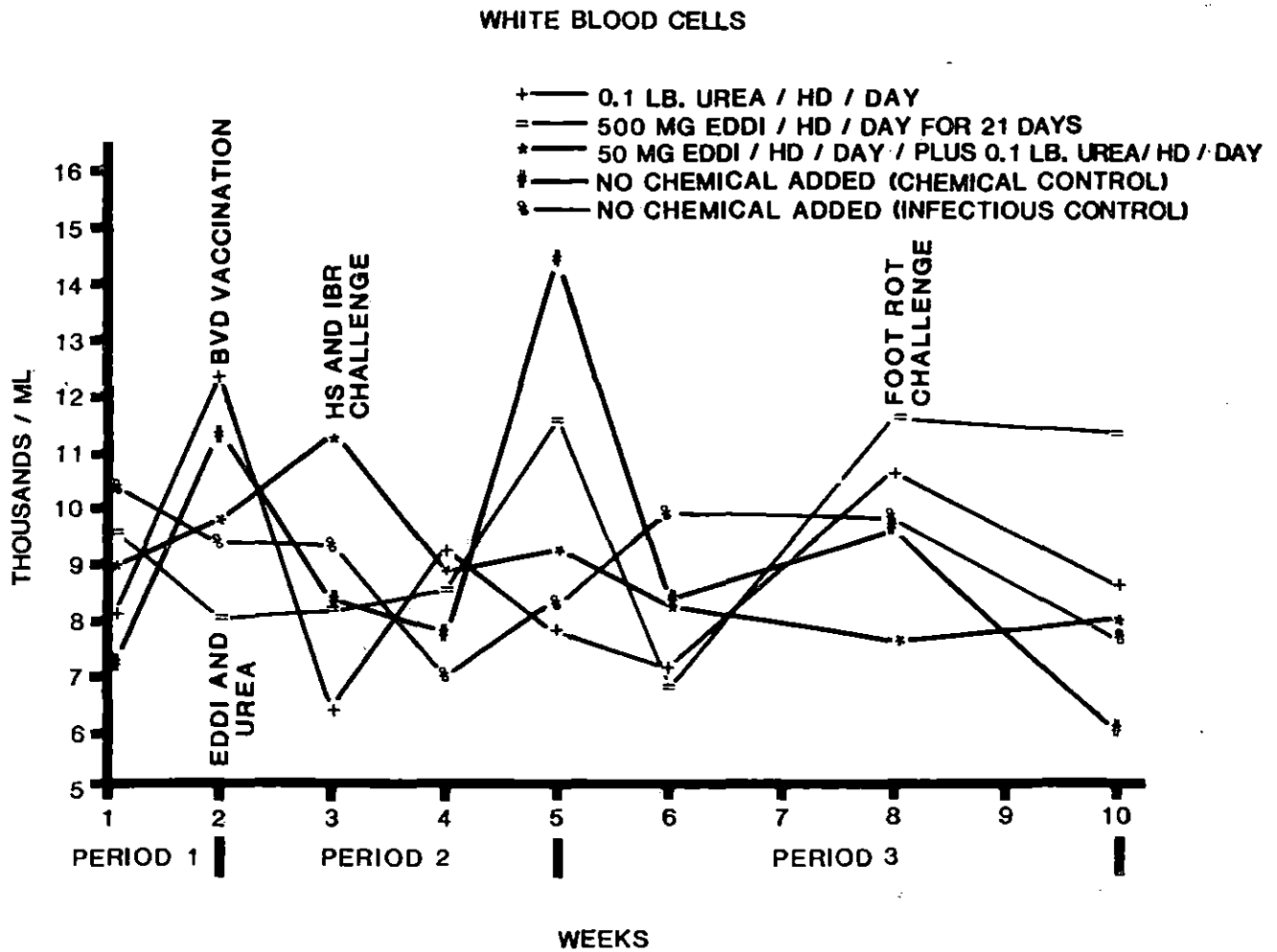
WHITE BLOOD CELLS
+—— 0.1 LB. UREA / HD / DAY
=—— 500 MG EDDI / HD / DAY FOR 21 DAYS
*—— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
#—— NO CHEMICAL ADDED (CHEMICAL CONTROL)
%—— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
THOUSANDS / ML
16
15
14
13
12
11
10
9
8
7
6
5
BVD VACCINATION
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
EDDI AND UREA
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 9. Weekly mean lymphocytes (percent) in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

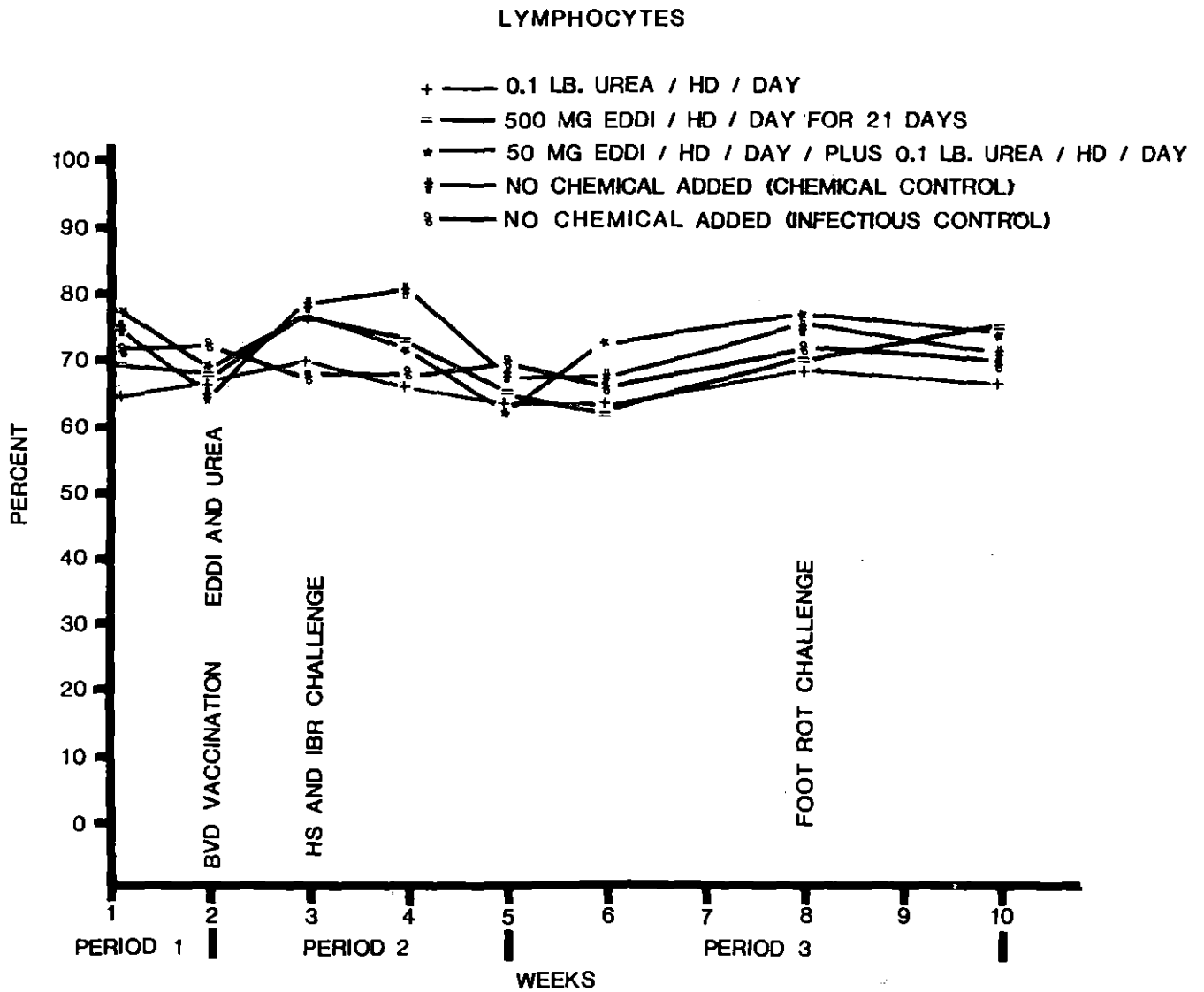
LYMPHOCYTES
+ —— 0.1 LB. UREA / HD / DAY
= —— 500 MG EDDI / HD / DAY FOR 21 DAYS
* —— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA / HD / DAY
# —— NO CHEMICAL ADDED (CHEMICAL CONTROL)
% —— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
BVD VACCINATION
EDDI AND UREA
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 10. Weekly mean segmented neutrophils (percent) in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

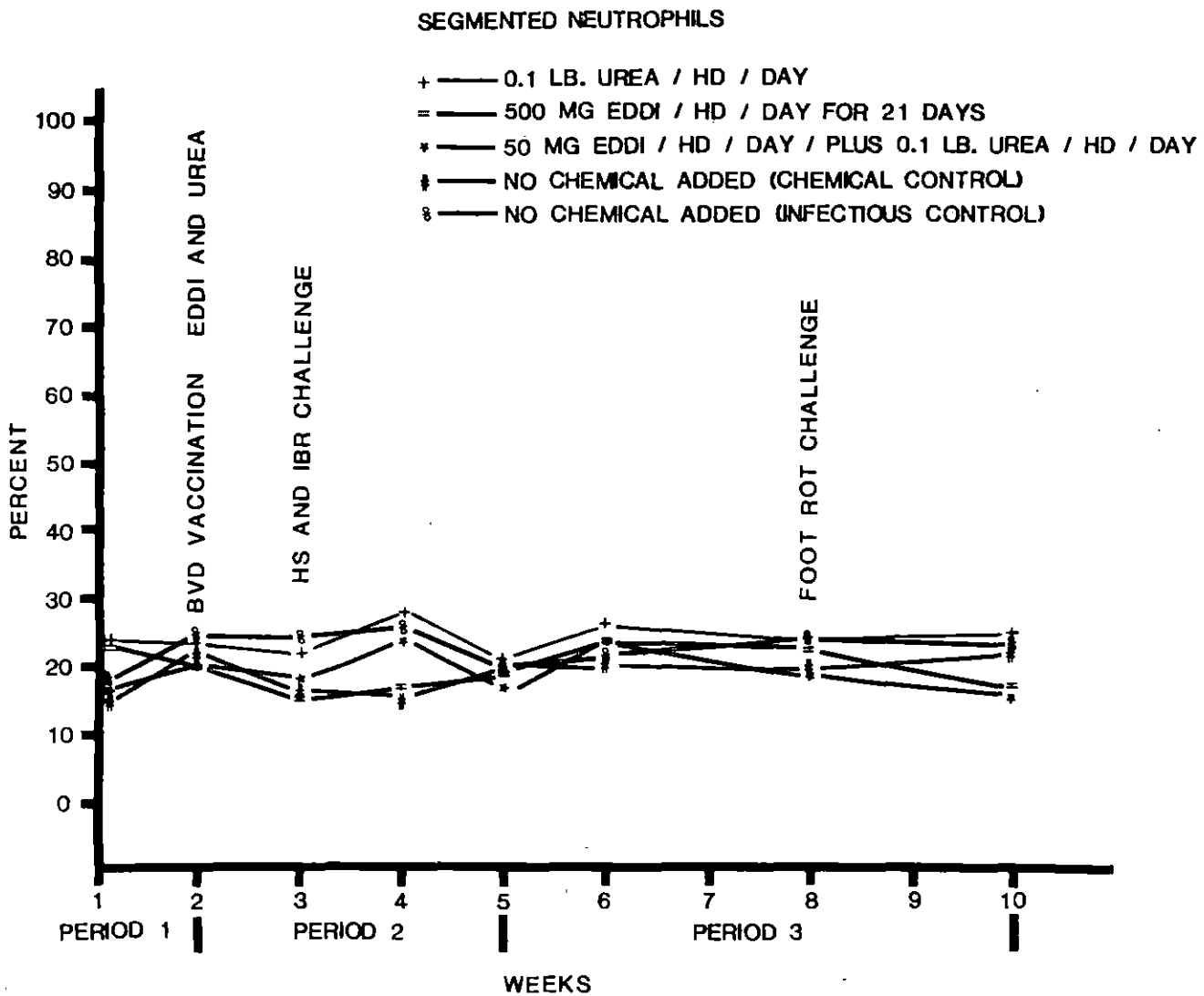
SEGMENTED NEUTROPHILS
+ —— 0.1 LB. UREA / HD / DAY
= —— 500 MG EDDI / HD / DAY FOR 21 DAYS
* —— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA / HD / DAY
# —— NO CHEMICAL ADDED (CHEMICAL CONTROL)
% —— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
BVD VACCINATION EDDI AND UREA
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 11. Weekly mean band neutrophils (percent) in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

BAND NEUTROPHILS

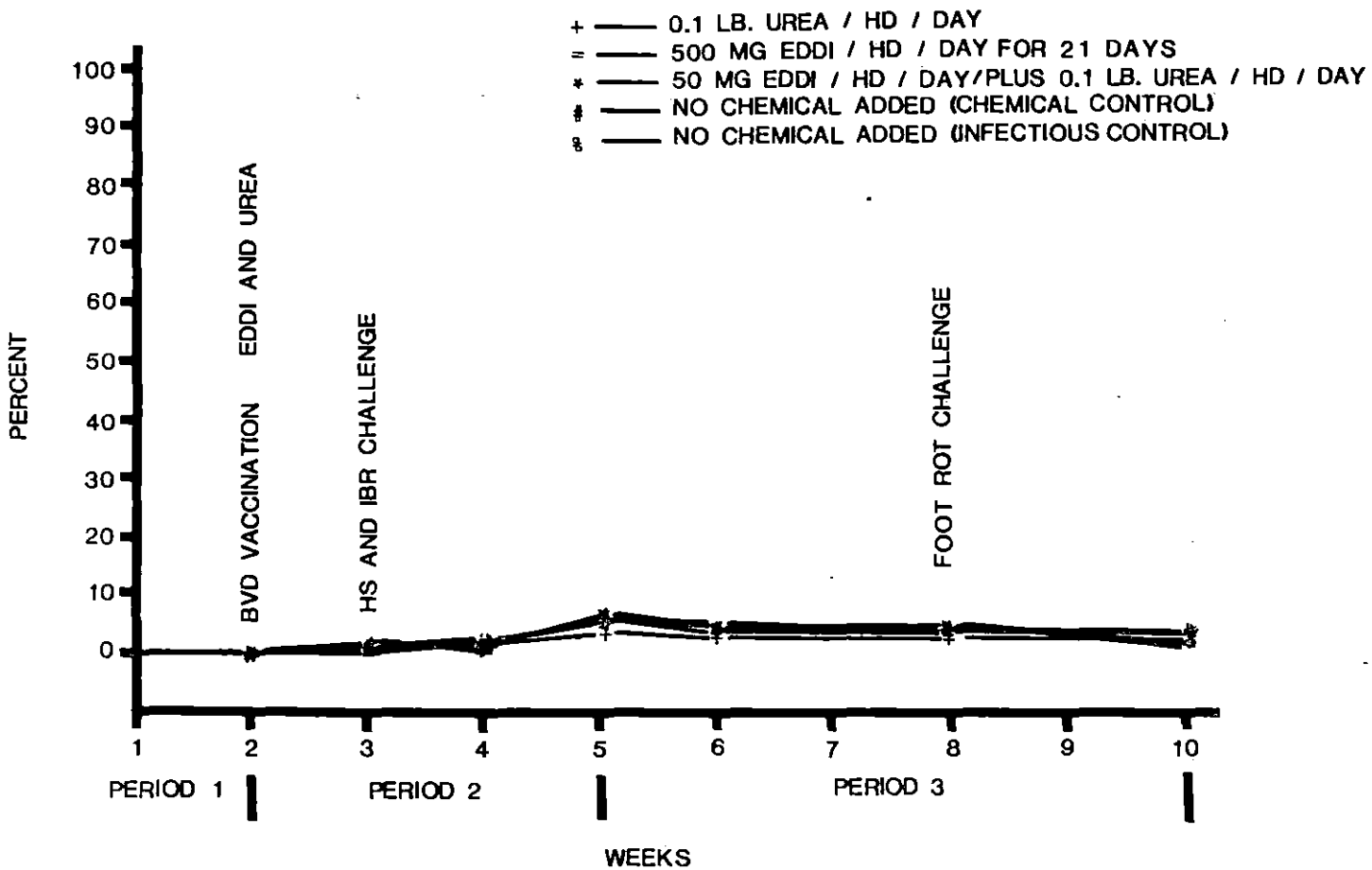

Figure 12. Weekly mean eosinophils (percent) in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

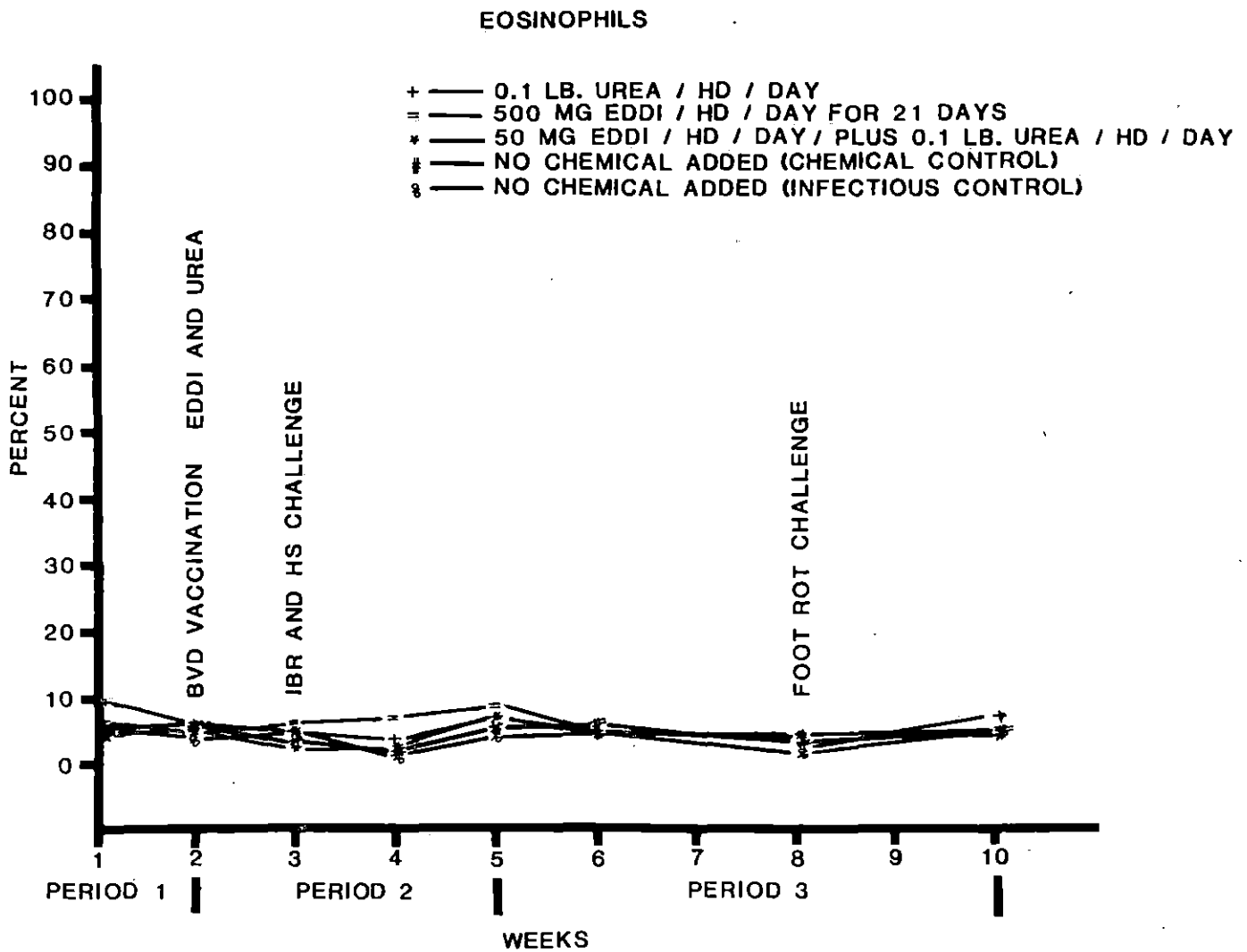
EOSINOPHILS
+ —— 0.1 LB. UREA / HD / DAY
= —— 500 MG EDDI / HD / DAY FOR 21 DAYS
* —— 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA / HD / DAY
# —— NO CHEMICAL ADDED (CHEMICAL CONTROL)
§ —— NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
BVD VACCINATION EDDI AND UREA
IBR AND HS CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 13. Weekly mean packed cell volumes in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

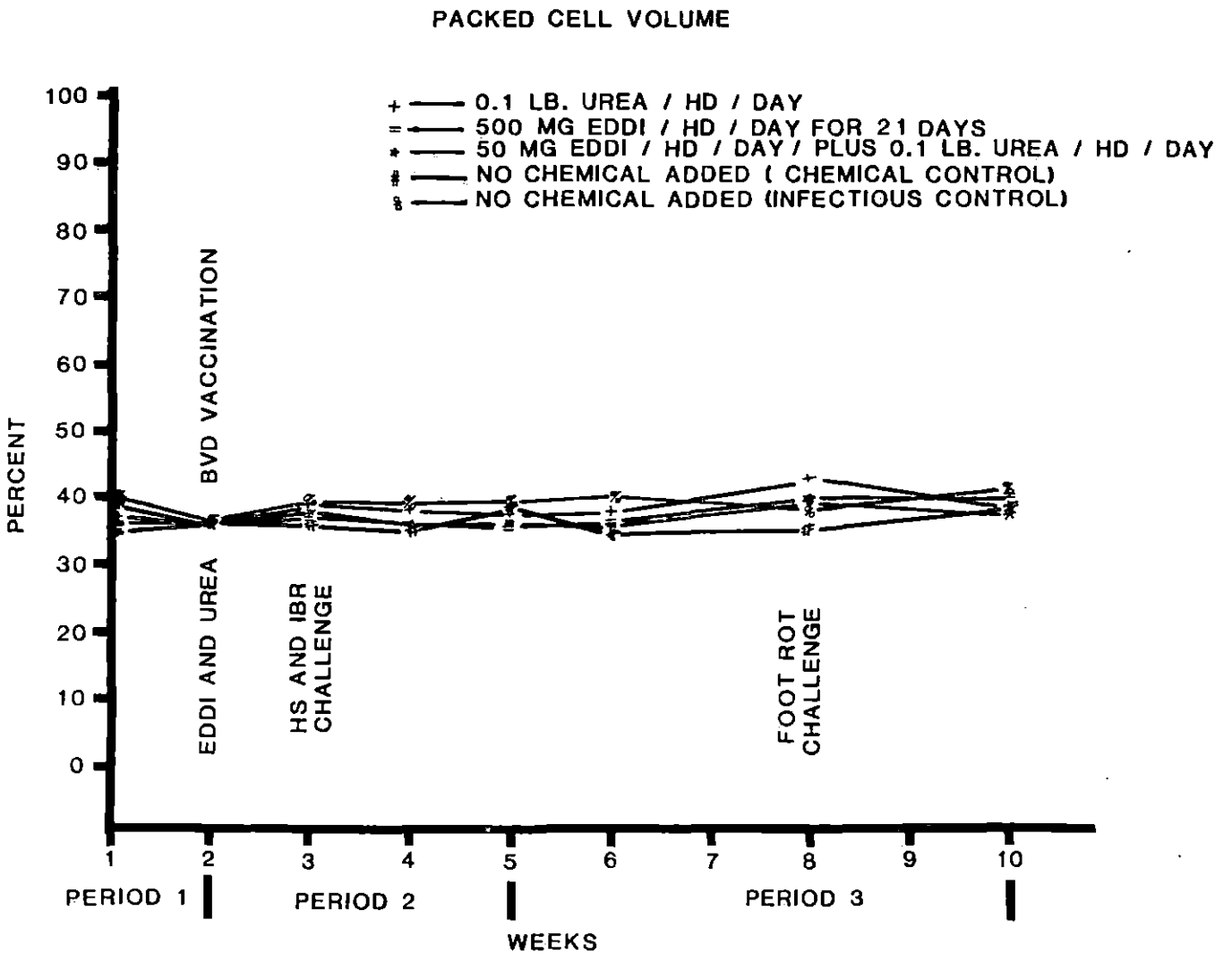
PACKED CELL VOLUME
+ 0.1 LB. UREA / HD / DAY
= 500 MG EDDI / HD / DAY FOR 21 DAYS
* 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA / HD / DAY
# NO CHEMICAL ADDED ( CHEMICAL CONTROL)
% NO CHEMICAL ADDED (INFECTIOUS CONTROL)
PERCENT
100
90
80
70
60
50
40
30
20
10
0
BVD VACCINATION
EDDI AND UREA
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 14. Weekly mean fibrinogen levels in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

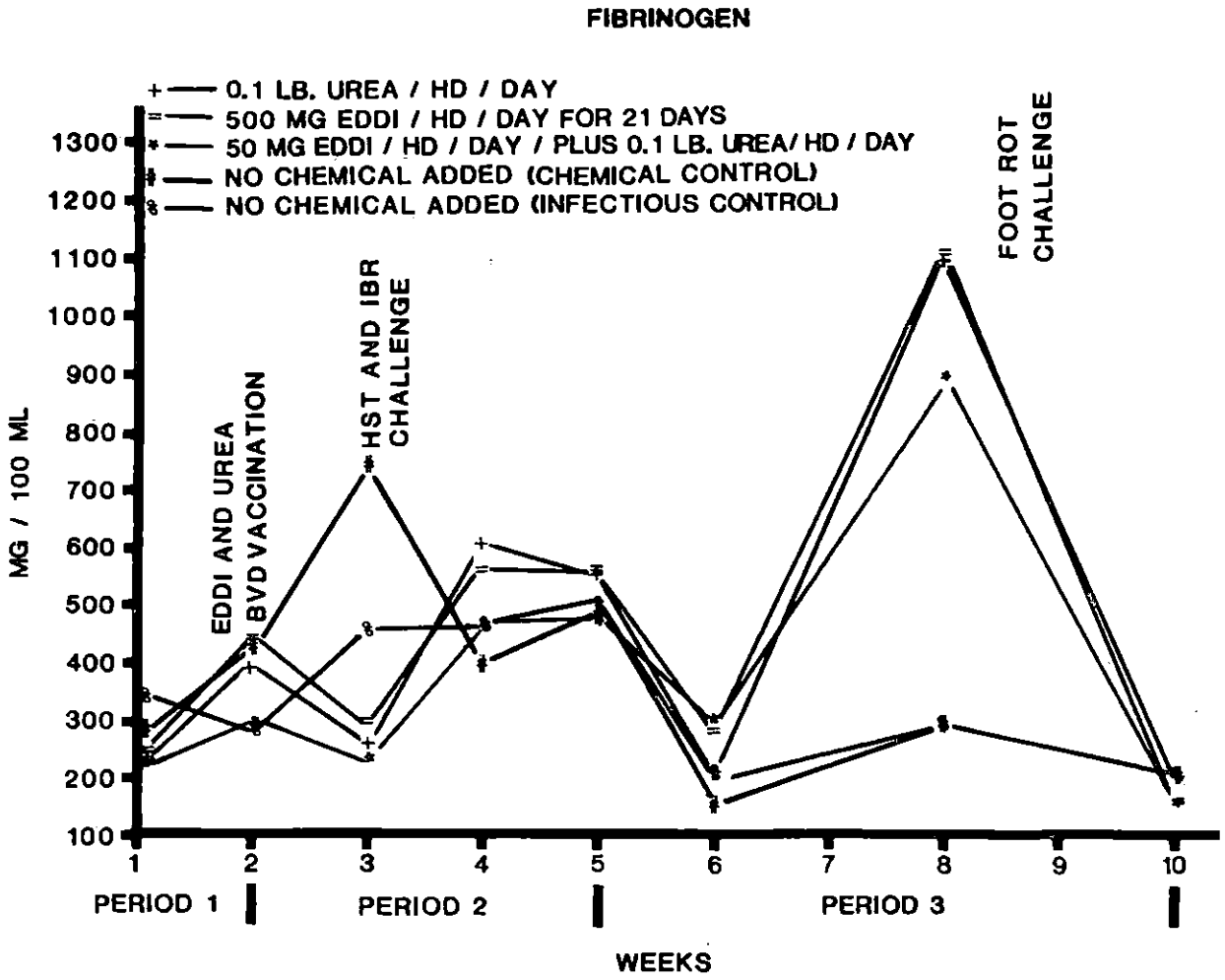
FIBRINOGEN
+ — 0.1 LB. UREA / HD / DAY
= — 500 MG EDDI / HD / DAY FOR 21 DAYS
* — 50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
# — NO CHEMICAL ADDED (CHEMICAL CONTROL)
% — NO CHEMICAL ADDED (INFECTIOUS CONTROL)
MG / 100 ML
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
EDDI AND UREA
BVD VACCINATION
HST AND IBR
CHALLENGE
FOOT ROT
CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 15. Weekly mean total plasma protein levels in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

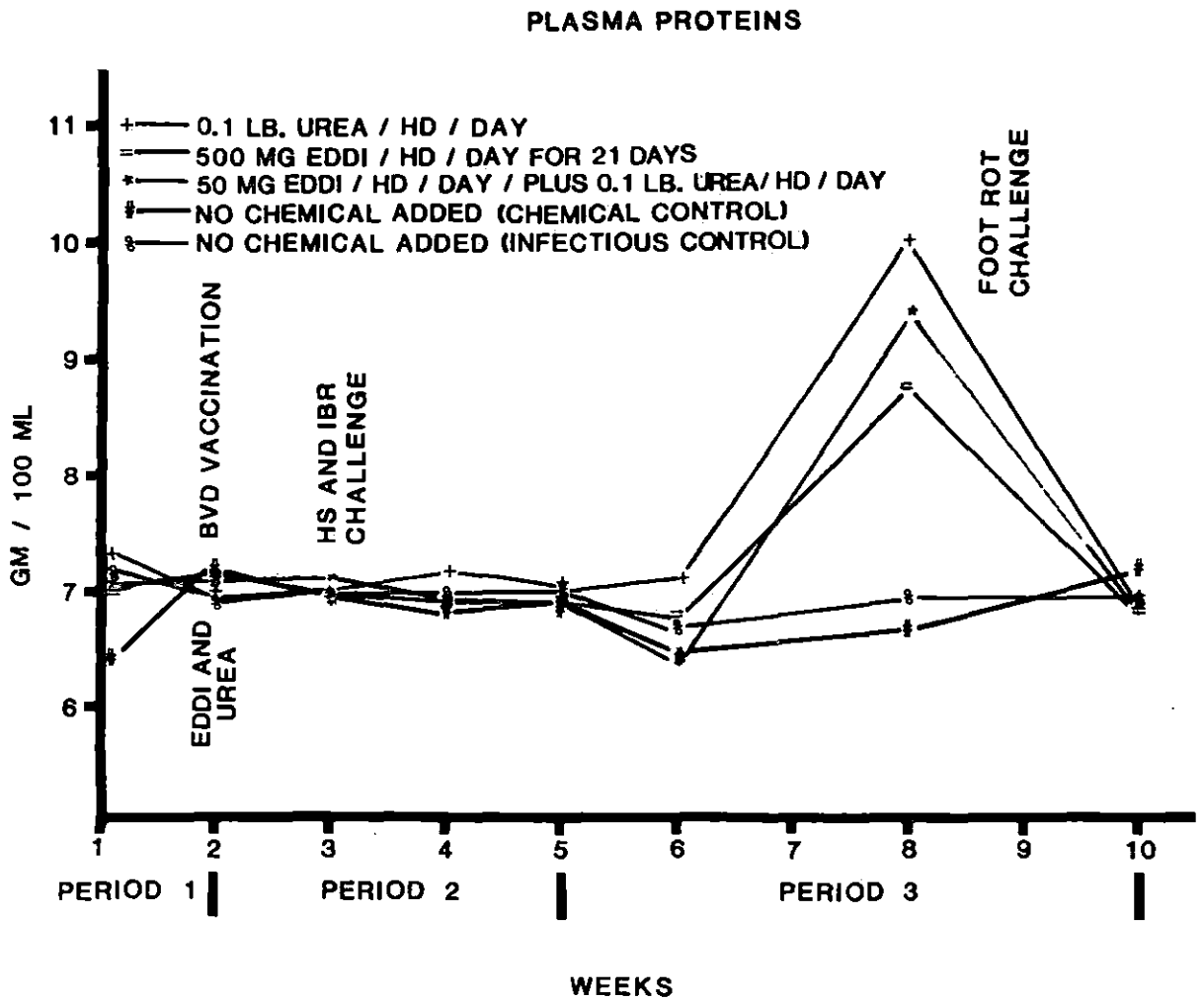
PLASMA PROTEINS
0.1 LB. UREA / HD / DAY
500 MG EDDI / HD / DAY FOR 21 DAYS
50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
NO CHEMICAL ADDED (CHEMICAL CONTROL)
NO CHEMICAL ADDED (INFECTIOUS CONTROL)
GM / 100 ML
11
10
9
8
7
6
EDDI AND UREA
BVD VACCINATION
HS AND IBR CHALLENGE
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Figure 16. Weekly mean total blood iodine levels in experimental and control calves (8 animals per group) during the 10-week experiment (see Table 1 for experimental paradigm)

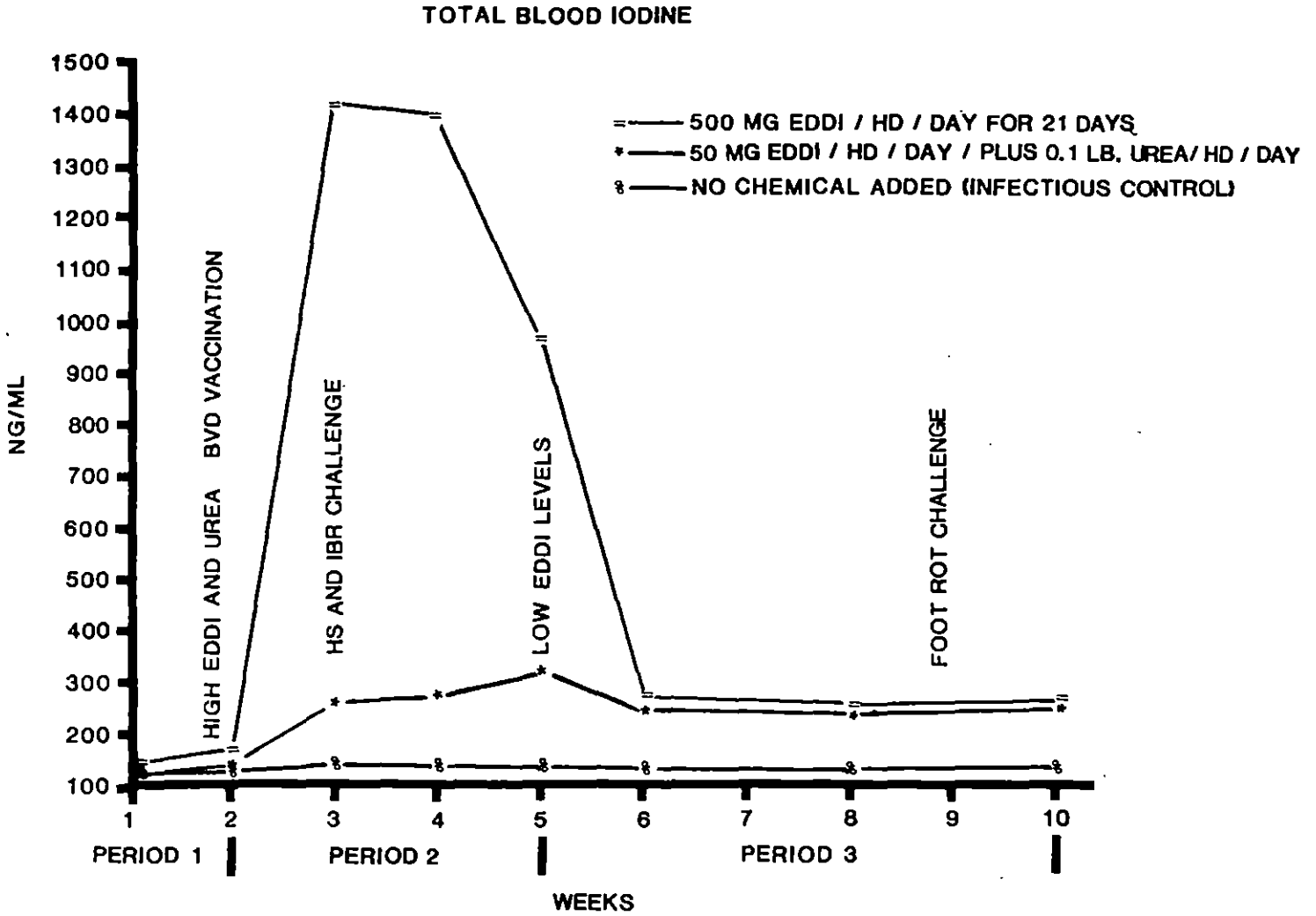
TOTAL BLOOD IODINE
500 MG EDDI / HD / DAY FOR 21 DAYS
50 MG EDDI / HD / DAY / PLUS 0.1 LB. UREA/ HD / DAY
NO CHEMICAL ADDED (INFECTIOUS CONTROL)
NG/ML
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
HIGH EDDI AND UREA BVD VACCINATION
HS AND IBR CHALLENGE
LOW EDDI LEVELS
FOOT ROT CHALLENGE
1
2
3
4
5
6
7
8
9
10
PERIOD 1
PERIOD 2
PERIOD 3
WEEKS

Table A1. Body weight -- pounds

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 420 | 453 | 475 | 483 | 489 | 489 | 500 | 539 |
| Urea | 13 | 383 | 400 | 405 | 386 | 402 | 396 | -- | 435 |
| 0.1 lb/hd/dy | 15 | 391 | 444 | 444 | 455 | 472 | 476 | 481 | 526 |
| 8 weeks | 34 | 434 | 473 | 469 | 479 | 493 | 492 | 510 | 549 |
| | 35 | 466 | 512 | 505 | 508 | 519 | 530 | 545 | 583 |
| | 36 | 408 | 452 | 459 | 457 | 472 | 488 | 502 | 570 |
| | 38 | 422 | 444 | 441 | 451 | 477 | 490 | 505 | 535 |
| | 40 | 390 | 434 | 440 | 456 | 465 | 474 | 484 | 544 |
| Group 2 | 17 | 484 | 500 | 517 | 535 | 530 | 542 | 559 | 597 |
| EDDI | 18 | 355 | 390 | 383 | 395 | 401 | 397 | 414 | 458 |
| 500 mg/hd/dy | 19 | 447 | 426 | 430 | 441 | 453 | 455 | 475 | 514 |
| 3 weeks; | 25 | 530 | 570 | 570 | 590 | 598 | 600 | 622 | -- |
| 50 mg/hd/dy | 26 | 446 | 470 | 472 | 499 | 509 | 501 | 538 | 594 |
| 5 weeks | 28 | 335 | 379 | 385 | 400 | 414 | 415 | 547 | 480 |
| | 31 | 456 | 457 | 455 | 459 | 454 | 457 | 491 | 523 |
| | 32 | 349 | 379 | 375 | 374 | 388 | 388 | 407 | 447 |
| Group 3 | 4 | 449 | 462 | 490 | 485 | 500 | 512 | 520 | 524 |
| EDDI-Urea | 6 | 457 | 463 | 494 | 515 | 525 | -- | 560 | 560 |
| 50 mg EDDI/hd/dy- | 20 | 321 | 365 | 404 | 353 | 365 | 375 | 390 | 421 |
| 0.1 lb urea/hd/dy | 21 | 447 | 463 | 476 | 474 | 498 | 508 | 517 | 550 |
| 8 weeks | 22 | 485 | 557 | 565 | 560 | 571 | 585 | 593 | 630 |
| | 23 | 436 | 475 | 478 | 477 | 490 | 494 | 517 | 557 |
| | 24 | 550 | 590 | 576 | 576 | 548 | 594 | 601 | 613 |
| | 27 | 410 | 455 | 472 | 475 | 485 | 492 | 508 | 555 |

Table A1. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 418 | 425 | 455 | 468 | 473 | 490 | 497 | 534 |
| None | 3 | 410 | 429 | 440 | 477 | 470 | 475 | 502 | 552 |
| (chemical | 5 | 426 | 440 | 479 | 514 | 512 | 530 | 541 | 605 |
| control) | 11 | 429 | 489 | 514 | 521 | 514 | 540 | 560 | 602 |
| | 12 | 493 | 535 | 517 | 540 | 555 | 562 | 572 | 621 |
| | 16 | 424 | 458 | 465 | 483 | 495 | 491 | 521 | 560 |
| | 37 | 418 | 428 | 434 | 451 | 455 | 458 | 469 | 517 |
| | 39 | 439 | 444 | 476 | 492 | 502 | 519 | 528 | 574 |
| Group 5 | 1 | 429 | -- | 465 | 470 | 488 | 501 | 524 | 554 |
| None | 7 | 429 | 473 | 471 | 465 | 493 | 503 | 546 | 580 |
| (infectious | 9 | 346 | 395 | 391 | 476 | 410 | 422 | 449 | 491 |
| control) | 10 | 450 | 484 | 476 | 415 | 479 | 478 | 509 | 536 |
| | 14 | 390 | 455 | 444 | 401 | 473 | 475 | 513 | 540 |
| | 29 | 449 | 470 | 460 | 489 | 494 | 498 | 524 | 535 |
| | 30 | 397 | 415 | 390 | 402 | 419 | 433 | 463 | 482 |
| | 33 | 380 | 402 | 390 | 472 | 413 | 423 | 460 | 484 |

Table A2. Temperature (degrees Fahrenheit)

| Group | Animal number | Weeks of chemical exposure: Period 1 | | Period 2 | | | Period 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 102.5 | 102.0 | 102.4 | 102.2 | 101.6 | 101.2 | 102.8 | 102.6 |
| Urea | 13 | 103.3 | 103.0 | 103.0 | 102.4 | 102.8 | 102.6 | -- | 102.2 |
| 0.1 lb/hd/dy | 15 | 102.7 | 103.0 | 102.0 | 102.8 | 101.0 | 102.0 | 102.8 | 102.0 |
| 8 weeks | 34 | 101.2 | 103.4 | 102.8 | 102.6 | 100.2 | 102.0 | 103.0 | 102.8 |
| | 35 | 101.4 | 103.0 | 102.2 | 102.8 | 102.4 | 102.6 | 102.0 | 102.0 |
| | 36 | 101.4 | 103.0 | 103.6 | 103.8 | 102.6 | 103.2 | 102.6 | 102.4 |
| | 38 | 103.6 | 103.0 | 103.0 | 102.2 | 102.0 | 102.0 | 102.8 | 102.6 |
| | 40 | 103.6 | 103.4 | 102.6 | 102.0 | 101.0 | 102.0 | 102.8 | 102.2 |
| Group 2 | 17 | 102.9 | 103.0 | 102.6 | 102.0 | 100.8 | 102.4 | 102.4 | 103.2 |
| EDDI | 18 | 103.6 | 104.6 | 102.8 | 102.8 | 101.0 | 103.0 | 104.4 | 102.8 |
| 500 mg/hd/dy | 19 | 102.3 | 102.8 | 102.6 | 103.2 | 102.4 | 101.2 | 103.4 | 101.6 |
| 3 weeks; | 25 | 102.8 | 104.0 | 103.4 | 103.8 | 101.8 | 102.0 | 102.8 | -- |
| 50 mg/hd/dy | 26 | 102.8 | 102.6 | 104.0 | 102.4 | 101.8 | 103.8 | 103.2 | 102.6 |
| 5 weeks | 28 | 102.8 | 103.0 | 103.2 | 105.4 | 102.0 | 101.0 | 102.6 | 103.0 |
| | 31 | 103.2 | 103.4 | 103.4 | 105.4 | 102.0 | 102.2 | 103.0 | 101.8 |
| | 32 | 103.8 | 104.0 | 103.8 | 103.8 | 102.0 | 103.6 | -- | 102.0 |
| Group 3 | 4 | 103.0 | 103.0 | 103.4 | 102.8 | 101.8 | 101.2 | 102.8 | -- |
| EDDI-Urea | 6 | 102.4 | 102.0 | -- | 103.0 | 102.0 | 100.6 | 102.0 | 103.0 |
| 50 mg EDDI/hd/dy- | 20 | 102.2 | 103.0 | 104.2 | 102.2 | 102.0 | 102.2 | 103.2 | 103.4 |
| 0.1 lb urea/hd/dy | 21 | 104.2 | 103.4 | 102.2 | 104.4 | 103.4 | 101.2 | 104.2 | 102.4 |
| 8 weeks | 22 | 102.5 | 102.0 | 102.2 | 100.8 | 100.8 | 106.6 | 103.0 | 101.6 |
| | 23 | -- | 102.0 | 103.4 | 103.5 | 102.6 | 100.8 | 103.0 | 102.8 |
| | 24 | -- | 102.6 | 103.4 | 103.2 | 100.4 | 102.8 | 103.8 | 100.8 |
| | 27 | 101.4 | 102.6 | 102.4 | 103.0 | 102.2 | 100.8 | 103.0 | 102.4 |

Table A2. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 | | Period 2 | | | Period 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 101.4 | 100.8 | 102.6 | 102.8 | 102.6 | 101.0 | 102.0 | 103.6 |
| None | 3 | 102.6 | 101.8 | 102.8 | 100.8 | 101.4 | 101.4 | 102.2 | 102.4 |
| (chemical | 5 | 102.8 | 102.2 | 102.2 | 101.8 | 101.0 | 101.6 | 101.8 | 102.0 |
| control) | 11 | -- | 102.6 | 102.8 | 102.6 | 102.4 | 102.4 | 102.6 | 102.6 |
| | 12 | 102.6 | 103.0 | 102.6 | 102.0 | 102.0 | 101.4 | 102.6 | 101.8 |
| | 16 | 103.0 | 102.8 | 102.6 | 102.4 | 102.2 | 101.6 | 102.4 | 102.0 |
| | 37 | 103.0 | 103.0 | 102.6 | 102.4 | 101.8 | 101.8 | 103.2 | 103.0 |
| | 39 | 103.1 | 102.0 | 104.0 | 102.7 | 101.4 | 101.0 | 102.4 | 101.8 |
| Group 5 | 1 | 102.6 | 103.2 | 101.8 | 102.8 | 101.8 | 101.5 | 102.2 | 101.2 |
| None | 7 | 102.5 | 102.8 | -- | 101.8 | 100.8 | 101.4 | 102.2 | 102.4 |
| (infectious | 9 | -- | 102.0 | 101.8 | 102.2 | 101.8 | 101.2 | 102.8 | 102.2 |
| control) | 10 | -- | 104.0 | 102.2 | 102.4 | 102.0 | 102.8 | 103.4 | 102.0 |
| | 14 | 103.6 | 102.0 | 102.8 | 102.4 | 102.0 | 101.6 | 102.4 | 102.2 |
| | 29 | 101.9 | 103.4 | 102.8 | 101.6 | 101.4 | 101.8 | 102.2 | 102.2 |
| | 30 | 103.2 | 102.2 | 102.6 | 102.8 | 102.8 | 101.8 | 102.8 | 102.0 |
| | 33 | 102.0 | 102.2 | 102.6 | 101.0 | 102.8 | 101.8 | 102.2 | 102.4 |

Table A3. Infectious bovine rhinotracheitis (IBR) antibody titers[a]

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Urea | 13 | 0 | 0 | 0 | 0 | 16 | 64 | -- | 0 |
| 0.1 lb/hd/dy | 15 | 0 | 0 | 0 | 0 | 16 | 16 | 32 | 16 |
| 8 weeks | 34 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 35 | 0 | 0 | 0 | 0 | 16 | 16 | 32 | 16 |
| | 36 | 0 | 0 | 0 | 0 | 16 | 16 | 64 | 32 |
| | 38 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40 | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 0 |
| Group 2 | 17 | 0 | 0 | 0 | 0 | 16 | 32 | 16 | 16 |
| EDDI | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 500 mg/hd/dy | 19 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 weeks; | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50 mg/hd/dy | 26 | 0 | 0 | 0 | 0 | 16 | 0 | 0 | 0 |
| 5 weeks | 28 | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 0 |
| | 31 | 0 | 0 | 0 | 0 | 16 | 32 | 16 | 0 |
| | 32 | 0 | 0 | 0 | 0 | 0 | 16 | -- | 0 |

[a]Titers expressed as reciprocal of highest serum dilution having a 50 percent reduction in plaques forming units (PFU).

Table A3. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 3 | 4 | 0 | 0 | 0 | 0 | 0 | 16 | 64 | 0 |
| EDDI-Urea | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 0 |
| 50 mg EDDI/hd/dy- | 20 | 0 | 0 | 0 | 0 | 16 | 16 | 16 | 0 |
| 0.1 lb urea hd/dy | 21 | 0 | - | 0 | 0 | 16 | 32 | 64 | 16 |
| 8 weeks | 22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 23 | 0 | 0 | 0 | 0 | 16 | 16 | 16 | 16 |
| | 24 | 0 | 0 | 0 | 0 | 32 | 32 | 32 | 32 |
| | 27 | 0 | 0 | 0 | 0 | 16 | 16 | 0 | 16 |
| Group 4 | 2 | 0 | 0 | 0 | 0 | 16 | 32 | 16 | 0 |
| None | 3 | 0 | 0 | 0 | 0 | 0 | 16 | 16 | 0 |
| (chemical | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 32 | 0 |
| control) | 11 | 0 | 0 | 0 | 0 | 0 | 0 | 32 | 0 |
| | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 16 | 0 | 0 | 0 | 0 | 16 | 64 | 128 | 64 |
| | 37 | 0 | 0 | 0 | 0 | 0 | 64 | 0 | 32 |
| | 39 | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 0 |
| Group 5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| None | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| (infectious | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| control) | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 16 |
| No IBR-H. somnus | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| challenge | 29 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 33 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Table A4. Bovine virus diarrhea (BVD) antibody screening results

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| Urea | 13 | 16 | 16 | 16 | 16 | 0 | 16 | -- | 0 |
| 0.1 lb/hd/dy | 15 | 16 | 16 | 0 | 16 | 0 | 16 | 0 | 0 |
| 8 weeks | 34 V[a] | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 35 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 36 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 38 | 0 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| | 40 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| Group 2 | 17 V | 0 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| EDDI | 18 | 0 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| 500 mg/hd/dy | 19 V | 0 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| 3 weeks; | 25 V | 16 | 16 | 0 | 16 | 16 | 16 | 16 | -- |
| 50 mg/hd/dy | 26 | 16 | 16 | 16 | 0 | 0 | 16 | 0 | 0 |
| 5 weeks | 28 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| | 31 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 32 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| Group 3 | 4 V | 0 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| EDDI-Urea | 6 V | 16 | 16 | -- | 16 | 16 | 16 | 16 | 16 |
| 50 mg EDDI/hd/dy- | 20 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| 0.1 lb urea/hd/dy | 21 | 16 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| 8 weeks | 22 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| | 23 V | 0 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 24 | 0 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| | 27 | 0 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |

[a]Indicates animals that were given BVD vaccine at the beginning of Week 1, Period 2.

Table A4. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 4 | 2 V | 0 | 16[b] | 16 | 16 | 16 | 16 | 16 | 16 |
| None | 3 | 0 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| (chemical | 5 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| control) | 11 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 12 | 16 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| | 16 | 16 | 16 | 16 | 16 | 16 | 0 | 0 | 0 |
| | 37 V | 0 | 0 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 39 V | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| Group 5 | 1 | 16 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| None | 7 | 16 | 16 | 16 | 16 | 16 | 16 | 0 | 16 |
| (infectious | 9 | 16 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| control) | 10 | 16 | 16 | 16 | 16 | 0 | 0 | 0 | 0 |
| | 14 | 16 | 16 | 16 | 16 | 16 | 0 | 0 | 0 |
| | 29 | 0 | 16 | 16 | 0 | 0 | 0 | 0 | 0 |
| | 30 | 0 | 16 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 33 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

[b]Sera were diluted 1:16 for BVD anitbody screening tests.

Table A5. Haemophilus somnus antibody titers[a]

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 8 | 32 | 32 | 32 | 64 | 64 | 32 | 32 |
| Urea | 13 | 16 | 4 | 32 | 16 | 128 | 256 | 64 | 32 |
| 0.1 lb/hd/dy | 15 | 4 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| 8 weeks | 34 | 16 | 32 | 8 | 8 | 8 | 16 | 16 | 8 |
| | 35 | 8 | 16 | 8 | 16 | 32 | 32 | 16 | 8 |
| | 36 | 16 | 32 | 16 | 64 | 128 | 64 | 64 | 16 |
| | 38 | 8 | 64 | 32 | 64 | 16 | 32 | 64 | 16 |
| | 40 | 16 | 16 | 16 | 32 | 128 | 32 | 32 | 32 |
| Group 2 | 17 | 16 | 128 | 32 | 64 | 32 | 32 | 32 | 16 |
| EDDI | 18 | 8 | 32 | 32 | 65 | 32 | 32 | 32 | 16 |
| 500 mg/hd/dy | 19 | 8 | 32 | 16 | 32 | 16 | 16 | 16 | 16 |
| 3 weeks; | 25 | 8 | 64 | 4 | 16 | 4 | 16 | 0 | 0 |
| 50 mg/hd/dy | 26 | 16 | 16 | 8 | 4 | 4 | 32 | 16 | 4 |
| 5 weeks | 28 | 16 | 32 | 64 | 128 | 32 | 32 | 16 | 16 |
| | 31 | 4 | 32 | 16 | 16 | 32 | 32 | 16 | 0 |
| | 32 | 16 | 32 | 16 | 16 | 8 | 0 | 0 | 64 |
| Group 3 | 4 | 16 | 32 | 64 | 128 | 64 | -- | 16 | 16 |
| EDDI-Urea | 6 | 8 | 16 | 16 | 8 | 64 | 32 | 16 | 8 |
| 50 mg EDDI/hd/dy- | 20 | 8 | 32 | 16 | 64 | 16 | 16 | 8 | 16 |
| 0.1 lb urea/hd/dy | 21 | 0 | 0 | 8 | 16 | 16 | 16 | 8 | 8 |
| 8 weeks | 22 | 8 | 32 | 16 | 16 | 16 | 8 | 8 | 16 |
| | 23 | 8 | 16 | 8 | 16 | 8 | 4 | 8 | 16 |
| | 24 | 4 | 16 | 8 | 32 | 16 | 16 | 16 | 16 |
| | 27 | 32 | 32 | 16 | 64 | 16 | 16 | 16 | 16 |

[a]Titers expressed as reciprocal of highest serum dilution having fixation of complement.

Table A5. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 4 | 32 | 64 | 128 | 64 | 128 | 64 | 64 |
| None | 3 | 4 | 16 | 32 | 32 | 16 | 32 | 8 | 16 |
| (chemical | 5 | 16 | 32 | 64 | 64 | 16 | 32 | 16 | 16 |
| control) | 11 | 16 | 32 | 64 | 128 | 128 | 128 | 32 | 32 |
| | 12 | 16 | 16 | 32 | 32 | 128 | 256 | 64 | 32 |
| | 16 | 16 | 32 | 16 | 128 | 128 | 64 | 32 | 16 |
| | 37 | 16 | 32 | 32 | 16 | 16 | 8 | 16 | 16 |
| | 39 | 8 | 16 | 16 | 32 | 256 | 64 | 32 | 32 |
| Group 5 | 1 | 32 | 64 | 32 | 64 | 32 | 32 | 16 | 8 |
| None | 7 | 32 | 0 | 64 | 32 | 64 | 32 | 8 | 16 |
| (infectious | 9 | 64 | 16 | 32 | 64 | 64 | 64 | 16 | 8 |
| control) | 10 | 32 | 32 | 16 | 16 | 16 | 16 | 16 | 16 |
| | 14 | 32 | 64 | 64 | 64 | 64 | 64 | 64 | 32 |
| | 29 | 8 | 64 | 32 | 64 | 64 | 64 | 16 | 16 |
| | 30 | 32 | 32 | 16 | 32 | 32 | 32 | 32 | 32 |
| | 33 | 32 | 16 | 16 | 32 | 128 | 64 | 64 | 64 |

Table A6. Serum glutamic oxaloacetic transaminase (SGOT) (Reitman and Frankel units)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 21 | 138 | 110 | 132 | 100 | 116 | 138 | 114 |
| Urea | 13 | 150 | 128 | 95 | 116 | 110 | 106 | -- | 114 |
| 0.1 lb/hd/dy | 15 | 80 | 104 | 95 | 80 | 88 | 89 | 106 | 86 |
| 8 weeks | 34 | 116 | 94 | 132 | 46 | 78 | 106 | 120 | 60 |
| | 35 | 116 | 94 | 132 | 112 | 92 | 94 | 128 | 94 |
| | 36 | 138 | -- | 128 | 100 | 80 | 106 | 120 | 102 |
| | 38 | 134 | 94 | 100 | 88 | 80 | 106 | 128 | 102 |
| | 40 | 94 | 160 | 100 | 94 | 88 | 116 | 138 | 102 |
| Group 2 | 17 | 116 | 94 | 128 | 116 | 100 | 128 | 138 | 102 |
| EDDI | 18 | 72 | 146 | 122 | 106 | 94 | 119 | 128 | 130 |
| 500 mg/hd/dy | 19 | 158 | 116 | 88 | 100 | 94 | 138 | 138 | 102 |
| 3 weeks; | 25 | 138 | 116 | 138 | 106 | 128 | 116 | -- | -- |
| 50 mg/hd/dy | 26 | 106 | 104 | 164 | 116 | 106 | 128 | 122 | 102 |
| 5 weeks | 28 | 166 | 122 | 128 | 112 | 116 | 128 | 150 | 114 |
| | 31 | 128 | 88 | 138 | 88 | 92 | 94 | 110 | 94 |
| | 32 | 88 | 100 | 128 | 106 | 110 | 128 | -- | 130 |
| Group 3 | 4 | 200 | 138 | 116 | 110 | -- | 116 | 150 | -- |
| EDDI-Urea | 6 | 88 | 138 | -- | 118 | 94 | 128 | 128 | 130 |
| 50 mg EDDI/hd/dy- | 20 | 80 | 110 | 150 | 100 | 88 | 116 | 138 | 130 |
| 0.1 lb urea/hd/dy | 21 | 158 | 110 | 116 | 106 | 92 | 94 | 88 | 148 |
| 8 weeks | 22 | 150 | 174 | 150 | 116 | 128 | 128 | 80 | 102 |
| | 23 | 138 | 88 | 116 | 106 | 94 | 106 | 120 | 114 |
| | 24 | 166 | 100 | 132 | 118 | 72 | 94 | 120 | 86 |
| | 27 | 88 | 80 | 128 | 66 | 94 | 116 | 110 | 94 |

Table A6. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 4 | 2 | 106 | 128 | 106 | 95 | 94 | 106 | 106 | 114 |
| None | 3 | 116 | 94 | 116 | 116 | 100 | 106 | 106 | 94 |
| (chemical | 5 | 66 | 104 | 106 | 106 | 106 | 106 | 106 | 94 |
| control) | 11 | 138 | 116 | 128 | 95 | 84 | 106 | 128 | 86 |
| | 12 | 116 | 92 | 106 | 74 | 76 | 80 | 106 | 86 |
| | 16 | 106 | 94 | 95 | 106 | 84 | 89 | 110 | 86 |
| | 37 | 150 | 122 | 138 | 88 | 94 | 116 | 138 | 114 |
| | 39 | 52 | 94 | 95 | 92 | 74 | 88 | 106 | 40 |
| Group 5 | 1 | 52 | 50 | 88 | 76 | 58 | 106 | 95 | 78 |
| None | 7 | 88 | 138 | 106 | 100 | 106 | 116 | 128 | 102 |
| (infectious | 9 | 74 | 100 | 128 | 80 | 80 | 89 | 95 | 86 |
| control) | 10 | 215 | 116 | 84 | 84 | 94 | 106 | 128 | 86 |
| | 14 | 106 | 128 | 78 | 95 | 76 | 89 | 106 | 78 |
| | 29 | 94 | 94 | 106 | 88 | 88 | 106 | 106 | 86 |
| | 30 | 138 | 116 | 138 | 116 | 128 | 128 | 138 | 78 |
| | 33 | 88 | 110 | 128 | 40 | 84 | 80 | 106 | 78 |

Table A7. Blood urea nitrogen (BUN) -- mg/100 ml

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 19 | 18 | 14 | 14 | 18 | 8 | 15 | 21 |
| Urea | 13 | 16 | 22 | 18 | 20 | 21 | 21 | -- | 30 |
| 0.1 lb/hd/dy | 15 | 16 | 15 | 15 | 20 | 17 | 18 | 17 | 21 |
| 8 weeks | 34 | 18 | 18 | 10 | 15 | 15 | 14 | 16 | 20 |
| | 35 | 22 | -- | 15 | 40 | 21 | 22 | 17 | 28 |
| | 36 | 17 | -- | 13 | 16 | 15 | 12 | 15 | 22 |
| | 38 | 20 | 16 | 14 | 15 | 15 | 17 | 14 | 24 |
| | 40 | -- | 14 | 13 | 15 | 18 | 11 | 16 | 27 |
| Group 2 | 17 | 15 | 17 | 15 | 11 | 30 | 14 | 20 | 20 |
| EDDI | 18 | 19 | 15 | 12 | 17 | 16 | 19 | 17 | 17 |
| 500 mg/hd/dy | 19 | 28 | 14 | 13 | 20 | 18 | 15 | 15 | 20 |
| 3 weeks; | 25 | 20 | 40 | 18 | 26 | 23 | 25 | -- | -- |
| 50 mg/hd/dy | 26 | 15 | 14 | 14 | 19 | 14 | 18 | 8 | 17 |
| 5 weeks | 28 | 20 | 21 | 16 | 24 | 18 | 18 | 17 | 24 |
| | 31 | 16 | 18 | 11 | 27 | 16 | 21 | 21 | 18 |
| | 32 | 17 | 18 | 15 | 17 | 14 | 18 | 21 | 20 |
| Group 3 | 4 | 14 | 14 | 13 | 17 | 17 | 11 | 17 | -- |
| EDDI-Urea | 6 | 15 | 14 | -- | 20 | 14 | 10 | 15 | 20 |
| 50 mg EDDI/hd/dy- | 20 | 13 | 19 | 14 | 24 | 18 | 14 | 15 | 18 |
| 0.1 lb urea/hd/dy | 21 | 28 | 19 | 14 | 5 | 19 | 16 | 20 | 17 |
| 8 weeks | 22 | 23 | 16 | 11 | 11 | 17 | 18 | 14 | 22 |
| | 23 | 21 | 15 | 13 | 8 | 20 | 18 | 14 | 21 |
| | 24 | 20 | 17 | 14 | 18 | 19 | 21 | 13 | 25 |
| | 27 | 16 | 20 | 8 | 18 | 18 | 18 | 16 | 21 |

Table A7. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 15 | 18 | 16 | 15 | 17 | 6 | 18 | 17 |
| None | 3 | 16 | 13 | 17 | 17 | 16 | 11 | 19 | 16 |
| (chemical | 5 | 18 | 12 | 18 | 17 | 22 | 16 | 21 | 22 |
| control) | 11 | 17 | 14 | 16 | 11 | 19 | 16 | 20 | 17 |
| | 12 | 19 | 10 | 27 | 12 | 19 | 21 | 23 | 18 |
| | 16 | 16 | 17 | 14 | 17 | 17 | 18 | 23 | 13 |
| | 37 | 17 | 15 | 15 | 15 | 14 | 12 | 16 | 15 |
| | 39 | 18 | 15 | 16 | 17 | 17 | 15 | 19 | 20 |
| Group 5 | 1 | 13 | 16 | 15 | 16 | 19 | 8 | 18 | 19 |
| None | 7 | 17 | 9 | 13 | 16 | 16 | 8 | 19 | 22 |
| (infectious | 9 | 15 | 13 | 10 | 17 | 17 | 8 | 20 | 21 |
| control) | 10 | 16 | 14 | 15 | 11 | 17 | 10 | 15 | 17 |
| | 14 | 13 | 22 | 12 | 14 | 18 | 12 | 19 | 19 |
| | 29 | 20 | 17 | 13 | 18 | 14 | 16 | 21 | 22 |
| | 30 | 24 | 4 | 15 | 22 | 16 | 15 | 18 | 16 |
| | 33 | 18 | 16 | 14 | 15 | 20 | 20 | 21 | 20 |

Table A8. White blood cells -- count/ml

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 8980 | 6700 | 8700 | 7700 | 7700 | 8600 | -- | 8400 |
| Urea | 13 | 17300 | 14200 | 14300 | 10700 | 13700 | 8800 | 7000 | 12800 |
| 0.1 lb/hd/dy | 15 | 6670 | 5700 | 7300 | 4900 | 7400 | 5400 | 4600 | 9490 |
| 8 weeks | 34 | 8100 | 7200 | 5400 | 5800 | 7800 | 12600 | 7000 | 8700 |
| | 35 | 7200 | 6700 | 5500 | 7800 | 5800 | 8700 | -- | 7500 |
| | 36 | 12600 | 8300 | 6800 | 9200 | 11500 | 13500 | 12600 | 11000 |
| | 38 | 8300 | 5100 | 6600 | 12700 | 8800 | 19600 | 5900 | 6500 |
| | 40 | 8100 | 9000 | 7700 | 8900 | -- | 9600 | 8000 | 9500 |
| Group 2 | 17 | 10750 | 11300 | 9400 | 10000 | 12700 | 12600 | 12000 | 13600 |
| EDDI | 18 | 11900 | 10700 | 8500 | 7700 | 5900 | 8400 | 11300 | 11900 |
| 50 mg/hd/dy | 19 | 8260 | 5600 | 6000 | 6000 | 5700 | 6700 | 6600 | 9100 |
| 3 weeks; | 25 | 13900 | 11000 | 9000 | 10000 | 11100 | 15200 | 11400 | -- |
| 50 mg/hd/dy | 26 | 8600 | 8200 | 8200 | 7400 | 7300 | 7700 | 8200 | 10850 |
| 5 weeks | 28 | 9150 | 7300 | 6200 | 9500 | 5200 | 9200 | 7800 | 10900 |
| | 31 | 11000 | 9200 | 8000 | 11000 | 1700 | 12400 | 10400 | 11600 |
| | 32 | 8200 | 6000 | 7300 | 5800 | 700 | 15600 | 9900 | 8600 |
| Group 3 | 4 | 9500 | 7700 | 8100 | 7700 | 11300 | 8500 | 12500 | -- |
| EDDI-Urea | 6 | 8700 | 8300 | -- | 6900 | 6700 | 8400 | 8300 | 10200 |
| 50 mg EDDI/hd/dy- | 20 | 8620 | 7000 | 6400 | 7700 | 6400 | 10100 | 6800 | 7850 |
| 0.1 lb urea/hd/dy | 21 | 7900 | 9100 | 10600 | 9200 | 7500 | 7000 | 9200 | 11800 |
| 8 weeks | 22 | 9700 | 8900 | 8500 | 11600 | 8100 | 7800 | -- | 14100 |
| | 23 | 7600 | 7000 | 9000 | 7800 | 9000 | 9100 | 6900 | 8150 |
| | 24 | 14800 | 10600 | 10300 | 9600 | 10600 | 11200 | 12400 | 11800 |
| | 27 | 8900 | 6700 | 8100 | 7500 | 8500 | 12200 | 8200 | 11200 |

Table A8. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 13800 | 11300 | 14200 | 12600 | 14300 | 18200 | 16200 | 14900 |
| None | 3 | 6690 | 5800 | 7900 | 5300 | 9000 | 7000 | 8400 | 7830 |
| (chemical | 5 | 13000 | 9600 | 11800 | 8800 | 10500 | 13200 | 11600 | 13200 |
| control) | 11 | 8690 | 8000 | 7400 | 6900 | 7800 | 7100 | 10800 | 9900 |
| | 12 | 9810 | 7200 | 7800 | 6300 | 7100 | 7100 | 10600 | 10800 |
| | 16 | 8095 | 7700 | 7900 | 5900 | 7200 | 7000 | 8900 | 9110 |
| | 37 | 9800 | 7600 | 9400 | 9000 | 8600 | 11600 | 10000 | 10400 |
| | 39 | 6900 | 6400 | 5000 | 5000 | 4800 | 6600 | 6400 | 6800 |
| Group 5 | 1 | 10050 | 7300 | 11200 | 14900 | 8900 | 10800 | 6700 | 12300 |
| None | 7 | 8410 | 8500 | 9300 | 6700 | 10500 | 9000 | 10800 | 11900 |
| (infectious | 9 | 10500 | 9000 | 7700 | 9500 | 8800 | 9300 | 9400 | 10300 |
| control) | 10 | 9220 | 6500 | 5600 | 7200 | 5500 | 7000 | 7300 | 7090 |
| | 14 | 7680 | 8500 | 9000 | 7600 | 7300 | 8300 | 8500 | 9490 |
| | 29 | 9750 | 6800 | 9900 | 8800 | 7600 | 13600 | 12500 | 11200 |
| | 30 | 8670 | 8500 | 10700 | 8500 | 6800 | 11600 | 12300 | 10300 |
| | 33 | 7300 | 7700 | 6900 | 9500 | 5300 | 10000 | 7900 | 7300 |

Table A9. Lymphocytes -- percent

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 65 | 75 | 65 | 53 | 69 | 64 | -- | 67 |
| Urea | 13 | 61 | 66 | 67 | 65 | 54 | 60 | -- | 77 |
| 0.1 lb/hd/dy | 15 | 68 | 58 | 71 | 88 | 73 | 68 | -- | 87 |
| 8 weeks | 34 | 59 | 63 | 80 | 65 | 61 | 50 | 70 | 37 |
| | 35 | 69 | 75 | 73 | 65 | 81 | 75 | -- | 73 |
| | 36 | 71 | 71 | 75 | 64 | 62 | 63 | -- | 57 |
| | 38 | 55 | 61 | 63 | 61 | 51 | 47 | -- | 67 |
| | 40 | 69 | 67 | 68 | 69 | -- | 76 | -- | 75 |
| Group 2 | 17 | 66 | 67 | 80 | 66 | 54 | 56 | 71 | 67 |
| EDDI | 18 | 60 | 67 | 76 | 79 | 82 | 57 | 54 | 75 |
| 500 mg/hd/dy | 19 | 69 | 59 | 76 | 64 | 45 | 56 | 78 | 75 |
| 3 weeks; | 25 | 66 | 61 | 78 | 81 | 74 | 70 | 76 | -- |
| 50 mg/hd/dy | 26 | 77 | 70 | 70 | 79 | 55 | 68 | 74 | 71 |
| 5 weeks | 28 | 70 | 68 | 82 | 44 | 72 | 69 | 70 | 81 |
| | 31 | 57 | 74 | 86 | 84 | 76 | 74 | 74 | 77 |
| | 32 | 87 | 73 | 73 | 93 | 66 | 56 | -- | 87 |
| Group 3 | 4 | 84 | 70 | 77 | 72 | 61 | 52 | 83 | -- |
| EDDI-Urea | 6 | 76 | 70 | -- | 58 | 63 | 65 | 74 | 81 |
| 50 mg EDDI/hd/dy- | 20 | 71 | 68 | 78 | 67 | 67 | 45 | 59 | 66 |
| 0.1 lb urea/hd/dy | 21 | 67 | 75 | 81 | 78 | 76 | 75 | 76 | 77 |
| 8 weeks | 22 | 87 | 69 | 79 | 73 | 79 | 75 | 83 | 78 |
| | 23 | 81 | 76 | 83 | 69 | 59 | 64 | 84 | 88 |
| | 24 | 72 | 66 | 63 | 79 | 64 | 71 | 60 | 70 |
| | 27 | 76 | 62 | 79 | 77 | 73 | 56 | 72 | 83 |

Table A9. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 79 | 71 | 86 | 77 | 59 | 75 | 70 | 86 |
| None | 3 | 72 | 83 | 84 | 81 | 65 | 80 | 85 | 74 |
| (chemical | 5 | 60 | 54 | 61 | 83 | 65 | 64 | 68 | 64 |
| control) | 11 | 80 | 67 | 74 | 69 | 74 | 56 | 73 | 60 |
| | 12 | 80 | 37 | 77 | 87 | 80 | 60 | 79 | 84 |
| | 16 | 84 | 76 | 79 | 87 | 75 | 72 | 85 | 59 |
| | 37 | 75 | 91 | 90 | 87 | 63 | 69 | 82 | 80 |
| | 39 | 74 | 62 | -- | 73 | 61 | 55 | 74 | 69 |
| Group 5 | 1 | 67 | 65 | 48 | 45 | 60 | 45 | 78 | 70 |
| None | 7 | 64 | 68 | 63 | 63 | 71 | 59 | 62 | 58 |
| (infectious | 9 | 71 | 95 | 66 | 60 | 59 | 60 | 73 | 72 |
| control) | 10 | 83 | 69 | 67 | 68 | 56 | 67 | 71 | 71 |
| | 14 | 67 | 70 | 76 | 60 | 71 | 73 | 58 | 76 |
| | 29 | 85 | 70 | 78 | 87 | 77 | 74 | 70 | 83 |
| | 30 | 72 | 69 | 68 | 80 | 73 | 77 | 83 | 66 |
| | 33 | 73 | 70 | 82 | 70 | 78 | 64 | 81 | 79 |

Table A10. Segmented neutrophils -- percent

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 25 | 23 | 30 | 38 | 17 | 25 | -- | 29 |
| Urea | 13 | 23 | 20 | 21 | 28 | 30 | 33 | -- | 19 |
| 0.1 lb/hd/dy | 15 | 25 | 35 | 21 | 11 | 13 | 21 | -- | 12 |
| 8 weeks | 34 | 33 | 35 | 14 | 30 | 21 | 40 | 24 | 37 |
| | 35 | 20 | 15 | 18 | 28 | 12 | 22 | -- | 24 |
| | 36 | 6 | 12 | 18 | 32 | 12 | 15 | -- | 33 |
| | 38 | 27 | 26 | 28 | 37 | 40 | 45 | -- | 26 |
| | 40 | 27 | 22 | 29 | 26 | -- | 16 | -- | 22 |
| Group 2 | 17 | 26 | 13 | 13 | 11 | 13 | 20 | 19 | 12 |
| EDDI | 18 | 31 | 9 | 17 | 16 | 9 | 31 | 42 | 20 |
| 500 mg/hd/dy | 19 | 21 | 22 | 11 | 17 | 39 | 22 | 17 | 23 |
| 3 weeks; | 25 | 26 | 33 | 21 | 18 | 18 | 26 | 18 | -- |
| 50 mg/hd/dy | 26 | 10 | 25 | 22 | 15 | 25 | 22 | 20 | 20 |
| 5 weeks | 28 | 24 | 24 | 10 | 47 | 17 | 20 | 26 | 12 |
| | 31 | 37 | 17 | 10 | 12 | 16 | 21 | 23 | 21 |
| | 32 | 0 | 17 | 18 | 6 | 20 | 33 | -- | 13 |
| Group 3 | 4 | 11 | 26 | 20 | 26 | 21 | 28 | 10 | -- |
| EDDI-Urea | 6 | 18 | 24 | -- | 34 | 21 | 20 | 24 | 18 |
| 50 mg EDDI/hd/dy- | 20 | 17 | 18 | 18 | 27 | 22 | 39 | 36 | 24 |
| 0.1 lb urea/hd/dy | 21 | 26 | 16 | 16 | 18 | 13 | 18 | 16 | 12 |
| 8 weeks | 22 | 10 | 17 | 13 | 22 | 10 | 18 | 13 | 18 |
| | 23 | 12 | 13 | 14 | 28 | 17 | 24 | 12 | 10 |
| | 24 | 19 | 24 | 26 | 18 | 12 | 14 | 17 | 21 |
| | 27 | 16 | 27 | 21 | 20 | 21 | 32 | 21 | 15 |

Table A10. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 10 | 17 | 9 | 20 | 23 | 10 | 23 | 11 |
| None | 3 | 22 | 5 | 12 | 19 | 20 | 15 | 12 | 22 |
| (chemical | 5 | 25 | 41 | 27 | 14 | 51 | 20 | 22 | 30 |
| control) | 11 | 8 | 25 | 22 | 29 | 7 | 23 | 22 | 30 |
| | 12 | 10 | 43 | 17 | 11 | 8 | 19 | 19 | 15 |
| | 16 | 11 | 19 | 18 | 0 | 8 | 23 | 13 | 35 |
| | 37 | 16 | 6 | 8 | 12 | 21 | 12 | 13 | 14 |
| | 39 | 19 | 29 | -- | 21 | 33 | 38 | 21 | 23 |
| Group 5 | 1 | 18 | 24 | 40 | 39 | 27 | 43 | 18 | 23 |
| None | 7 | 29 | 27 | 31 | 28 | 19 | 20 | 31 | 24 |
| (infectious | 9 | 16 | 23 | 20 | 36 | 25 | 19 | 23 | 24 |
| control) | 10 | 11 | 27 | 29 | 31 | 22 | 12 | 23 | 35 |
| | 14 | 24 | 20 | 17 | 18 | 13 | 12 | 40 | 22 |
| | 29 | 11 | 25 | 19 | 13 | 19 | 20 | 25 | 15 |
| | 30 | 15 | 19 | 21 | 17 | 19 | 11 | 18 | 28 |
| | 33 | 19 | 25 | 15 | 27 | 18 | 34 | 16 | 20 |

Table A11. Band neutrophils -- percent

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 0 | 0 | 0 | 1 | 10 | 4 | - | 0 |
| Urea | 13 | 0 | 0 | 0 | 0 | 7 | 2 | - | 0 |
| 0.1 lb/hd/dy | 15 | 0 | 0 | 1 | 0 | 3 | 6 | - | 0 |
| 8 weeks | 34 | 0 | 0 | 0 | 0 | 12 | 4 | 1 | 0 |
| | 35 | 0 | 0 | 0 | 0 | 2 | 0 | - | 0 |
| | 36 | 0 | 0 | 1 | 0 | 10 | 5 | - | 0 |
| | 38 | 0 | 0 | 2 | 0 | 4 | 2 | - | 6 |
| | 40 | 0 | 0 | 0 | 1 | -- | 3 | - | 0 |
| Group 2 | 17 | 0 | 0 | 0 | 1 | 11 | 6 | 0 | 1 |
| EDDI | 18 | 0 | 0 | 0 | 1 | 1 | 3 | 1 | 0 |
| 500 mg/hd/dy | 19 | 0 | 2 | 1 | 1 | 3 | 14 | 0 | 0 |
| 3 weeks; | 25 | 0 | 1 | 0 | 0 | 2 | 1 | 3 | - |
| 50 mg/hd/dy | 26 | 0 | 0 | 1 | 0 | 5 | 4 | 3 | 0 |
| 5 weeks | 28 | 0 | 0 | 0 | 6 | 4 | 2 | 3 | 0 |
| | 31 | 0 | 0 | 0 | 0 | 4 | 1 | 0 | 0 |
| | 32 | 0 | 0 | 1 | 0 | 0 | 1 | - | 0 |
| Group 3 | 4 | 0 | 1 | 0 | 0 | 14 | 13 | 0 | - |
| EDDI-Urea | 6 | 0 | 0 | - | 2 | 13 | 9 | 0 | 0 |
| 50 mg EDDI/hd/dy- | 20 | 0 | 0 | 0 | 3 | 0 | 3 | 0 | 6 |
| 0.1 lb urea/hd/dy | 21 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 |
| 8 weeks | 22 | 0 | 3 | 0 | 0 | 3 | 6 | 1 | 0 |
| | 23 | 0 | 0 | 0 | 0 | 8 | 6 | 0 | 0 |
| | 24 | 0 | 1 | 0 | 0 | 3 | 4 | 0 | 0 |
| | 27 | 0 | 1 | 0 | 0 | 0 | 3 | 5 | 0 |

Table A11. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 4 | 2 | 0 | 1 | 0 | 0 | 12 | 1 | 0 | 0 |
| None | 3 | 0 | 0 | 0 | 0 | 12 | 0 | 1 | 0 |
| (chemical | 5 | 0 | 0 | 0 | 0 | 6 | 6 | 2 | 0 |
| control) | 11 | 0 | 0 | 0 | 0 | 10 | 0 | 2 | 0 |
| | 12 | 0 | 0 | 1 | 0 | 9 | 6 | 0 | 0 |
| | 16 | 0 | 0 | 1 | 8 | 7 | 9 | 0 | 0 |
| | 37 | 0 | 0 | 0 | 0 | 6 | 4 | 1 | 0 |
| | 39 | 2 | 0 | - | 0 | 2 | 6 | 0 | 0 |
| Group 5 | 1 | 0 | 2 | 3 | 2 | 8 | 2 | 0 | 6 |
| None | 7 | 0 | 0 | 1 | 0 | 5 | 15 | 2 | 0 |
| (infectious | 9 | 0 | 0 | 2 | 6 | 7 | 14 | 1 | 0 |
| control) | 10 | 0 | 0 | 0 | 0 | 17 | 12 | 1 | 0 |
| | 14 | 0 | 2 | 1 | 0 | 6 | 11 | 2 | 0 |
| | 29 | 0 | 0 | 0 | 0 | 2 | 2 | 4 | 0 |
| | 30 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | 33 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |

Table A12. Eosinophils -- percent

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 2 | 2 | 3 | 8 | 3 | 4 | - | 3 |
| Urea | 13 | 15 | 11 | 10 | 7 | 9 | 5 | - | 4 |
| 0.1 lb/hd/dy | 15 | 6 | 4 | 6 | 1 | 9 | 3 | - | 2 |
| 8 weeks | 34 | 6 | 4 | 5 | 5 | 5 | 5 | 3 | 26 |
| | 35 | 9 | 8 | 7 | 4 | 4 | 3 | - | 3 |
| | 36 | 3 | 15 | 6 | 3 | 16 | 16 | - | 9 |
| | 38 | 6 | 5 | 7 | 2 | 4 | 6 | - | 6 |
| | 40 | 3 | 7 | 3 | 2 | 0 | 3 | - | 2 |
| Group 2 | 17 | 5 | 19 | 7 | 22 | 21 | 8 | 2 | 17 |
| EDDI | 18 | 7 | 8 | 5 | 4 | 7 | 8 | 3 | 4 |
| 500 mg/hd/dy | 19 | 8 | 15 | 11 | 16 | 12 | 7 | 5 | 1 |
| 3 weeks; | 25 | 6 | 1 | 0 | 1 | 3 | 1 | 3 | 0 |
| 50 mg/hd/dy | 26 | 2 | 3 | 6 | 5 | 11 | 5 | 3 | 7 |
| 5 weeks | 28 | 5 | 6 | 8 | 2 | 6 | 6 | 4 | 3 |
| | 31 | 1 | 4 | 3 | 2 | 3 | 4 | 3 | 2 |
| | 32 | 7 | 5 | 5 | 0 | 9 | 7 | - | 0 |
| Group 3 | 4 | 1 | 0 | 2 | 2 | 3 | 7 | 5 | -- |
| EDDI-Urea | 6 | 2 | 4 | 0 | 6 | 2 | 5 | 2 | 0 |
| 50 mg EDDI/hd/dy- | 20 | 11 | 12 | 4 | 3 | 10 | 12 | 5 | 10 |
| 0.1 lb urea/hd/dy | 21 | 6 | 5 | 3 | 4 | 10 | 1 | 5 | 6 |
| 8 weeks | 22 | 2 | 10 | 1 | 5 | 6 | 1 | 3 | 2 |
| | 23 | 7 | 9 | 2 | 2 | 7 | 6 | 1 | 1 |
| | 24 | 6 | 6 | 3 | 3 | 17 | 7 | 3 | 7 |
| | 27 | 6 | 5 | 0 | 3 | 6 | 6 | 2 | 2 |

Table A12. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 4 | 7 | 3 | 2 | 4 | 13 | 3 | 1 |
| None | 3 | 6 | 5 | 4 | 6 | 2 | 5 | 2 | 4 |
| (chemical | 5 | 10 | 3 | 8 | 2 | 8 | 10 | 7 | 5 |
| control) | 11 | 10 | 5 | 3 | 2 | 7 | 9 | 3 | 10 |
| | 12 | 5 | 14 | 3 | 1 | 3 | 4 | 1 | 1 |
| | 16 | 4 | 4 | 2 | 4 | 8 | 5 | 2 | 3 |
| | 37 | 8 | 0 | 1 | 0 | 9 | 4 | 4 | 6 |
| | 39 | 4 | 10 | 0 | 3 | 3 | 1 | 3 | 8 |
| Group 5 | 1 | 12 | 4 | 6 | 3 | 4 | 10 | 3 | 7 |
| None | 7 | 6 | 4 | 3 | 2 | 4 | 6 | 5 | 17 |
| (infectious | 9 | 8 | 2 | 9 | 4 | 9 | 7 | 3 | 2 |
| control) | 10 | 1 | 4 | 4 | 0 | 2 | 4 | 5 | 5 |
| | 14 | 3 | 2 | 3 | 2 | 9 | 4 | 0 | 2 |
| | 29 | 4 | 3 | 1 | 0 | 2 | 2 | 1 | 2 |
| | 30 | 10 | 7 | 1 | 3 | 6 | 9 | 1 | 4 |
| | 33 | 6 | 3 | 3 | 1 | 2 | 1 | 1 | 1 |

Table A13. Monocytes -- percent

| Group | Animal number | Weeks of chemical exposure: Period 1 | | Period 2 | | | Period 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 6 | 0 | 1 | 0 | 1 | 3 | - | 2 |
| Urea | 13 | 1 | 3 | 1 | 0 | 0 | 0 | - | 0 |
| 0.1 lb/hd/dy | 15 | 1 | 3 | 0 | 0 | 2 | 2 | - | 0 |
| 8 weeks | 34 | 2 | 0 | 1 | 0 | 1 | 1 | 2 | 0 |
| | 35 | 2 | 2 | 2 | 0 | 0 | 0 | - | 0 |
| | 36 | 0 | 2 | 0 | 1 | 0 | 1 | - | 0 |
| | 38 | 2 | 8 | 0 | 0 | 1 | 0 | - | 1 |
| | 40 | 0 | 4 | 0 | 2 | - | 2 | - | 1 |
| Group 2 | 17 | 3 | 1 | 0 | 1 | 1 | 0 | 2 | 0 |
| EDDI | 18 | 2 | 4 | 1 | 0 | 1 | 1 | 0 | 1 |
| 500 mg/hd/dy | 19 | 2 | 2 | 1 | 2 | 1 | 1 | 0 | 1 |
| 3 weeks; | 25 | 2 | 4 | 1 | 0 | 3 | 2 | 0 | - |
| 50 mg/hd/dy | 26 | 1 | 2 | 1 | 0 | 4 | 1 | 0 | 2 |
| 5 weeks | 28 | 1 | 2 | 0 | 1 | 1 | 2 | 0 | 3 |
| | 31 | 5 | 5 | 1 | 2 | 1 | 0 | 1 | 0 |
| | 32 | 0 | 5 | 3 | 1 | 5 | 2 | - | 0 |
| Group 3 | 4 | 4 | 3 | 1 | 0 | 1 | 0 | 2 | - |
| EDDI-Urea | 6 | 4 | 2 | - | 0 | 1 | 1 | 0 | 1 |
| 50 mg EDDI/hd/dy- | 20 | 1 | 2 | 0 | 0 | 1 | 1 | 0 | 0 |
| 0.1 lb urea/hd/dy | 21 | 1 | 4 | 0 | 0 | 1 | 0 | 3 | 5 |
| 8 weeks | 22 | 1 | 0 | 1 | 0 | 2 | 0 | 0 | 2 |
| | 23 | 0 | 2 | 0 | 1 | 0 | 0 | 3 | 1 |
| | 24 | 3 | 3 | 3 | 0 | 4 | 4 | 0 | 2 |
| | 27 | 2 | 5 | 0 | 0 | 0 | 3 | 0 | 0 |

Table A13. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 7 | 4 | 2 | 1 | 2 | 0 | 4 | 2 |
| None | 3 | 0 | 7 | 0 | 0 | 1 | 0 | 0 | 0 |
| (chemical | 5 | 5 | 2 | 3 | 1 | 0 | 0 | 0 | 1 |
| control) | 11 | 2 | 3 | 1 | 0 | 2 | 2 | 0 | 6 |
| | 12 | 5 | 6 | 2 | 1 | 0 | 1 | 1 | 0 |
| | 16 | 1 | 1 | 0 | 1 | 2 | 1 | 0 | 3 |
| | 37 | 1 | 3 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 39 | 1 | 3 | - | 3 | 1 | 0 | 2 | 6 |
| Group 5 | 1 | 3 | 5 | 2 | 1 | 1 | 0 | 1 | 0 |
| None | 7 | 1 | 1 | 2 | 0 | 1 | 0 | 0 | 1 |
| (infectious | 9 | 5 | 0 | 3 | 0 | 0 | 0 | 0 | 2 |
| control) | 10 | 5 | 0 | 0 | 1 | 4 | 5 | 0 | 1 |
| | 14 | 6 | 6 | 3 | 0 | 1 | 0 | 0 | 0 |
| | 29 | 0 | 2 | 1 | 0 | 0 | 2 | 0 | 6 |
| | 30 | 3 | 5 | 0 | 0 | 6 | 1 | 0 | 0 |
| | 33 | 2 | 2 | 0 | 2 | 0 | 4 | 2 | 0 |

Table A14. Packed cell volume -- percent

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 31 | 36 | 36 | 38 | 38 | 33 | 35 | 38 |
| Urea | 13 | 42 | 40 | 40 | 45 | 39 | 40 | 41 | 36 |
| 0.1 lb/hd/dy | 15 | 36 | 38 | 39 | 34 | 38 | 37 | 40 | 41 |
| 8 weeks | 34 | 40 | 39 | 38 | 40 | 39 | 39 | 44 | 40 |
| | 35 | 40 | 35 | 42 | 37 | 38 | 37 | -- | 39 |
| | 36 | 33 | 32 | 40 | 36 | 33 | 34 | 35 | 35 |
| | 38 | 39 | 39 | 38 | 33 | 38 | 32 | 33 | 40 |
| | 40 | 36 | 35 | 37 | 35 | -- | 35 | 38 | 40 |
| Group 2 | 17 | 40 | 37 | 39 | 33 | 38 | 38 | 45 | 39 |
| EDDI | 18 | 36 | 42 | 40 | 36 | 42 | 42 | 45 | 43 |
| 500 mg/hd/dy | 19 | 40 | 39 | 36 | 35 | 37 | 37 | 38 | 38 |
| 3 weeks; | 25 | 38 | 37 | 39 | 34 | 35 | 35 | 35 | -- |
| 50 mg/hd/dy | 26 | 36 | 40 | 36 | 40 | 39 | 39 | 43 | 41 |
| 5 weeks | 28 | 31 | 35 | 34 | 35 | 35 | 39 | 41 | 38 |
| | 31 | 39 | 37 | 40 | 27 | 26 | 31 | 36 | 38 |
| | 32 | 35 | 34 | 33 | 37 | 37 | 34 | 38 | 41 |
| Group 3 | 4 | 39 | 42 | 39 | 33 | 37 | 36 | 43 | -- |
| EDDI-Urea | 6 | 37 | 40 | -- | 27 | 38 | 33 | 43 | 38 |
| 50 mg EDDI/hd/dy- | 20 | 33 | 38 | 40 | 36 | 41 | 36 | 39 | 43 |
| 0.1 lb urea/hd/dy | 21 | 33 | 35 | 37 | 42 | 37 | 40 | 43 | 35 |
| 8 weeks | 22 | 41 | 35 | 35 | 36 | 37 | 39 | -- | 39 |
| | 23 | 38 | 39 | 40 | 35 | 41 | 39 | 39 | 36 |
| | 24 | 38 | 37 | 39 | 33 | 42 | 37 | 43 | 40 |
| | 27 | 34 | 35 | 39 | 38 | 26 | 38 | 41 | 43 |

Table A14. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 39 | 39 | 36 | 35 | 36 | 33 | 31 | 39 |
| None | 3 | 31 | 35 | 35 | 29 | 34 | 33 | 33 | 39 |
| (chemical | 5 | 39 | 40 | 36 | 32 | 35 | 34 | 34 | 40 |
| control) | 11 | 38 | 38 | 39 | 38 | 37 | 34 | 36 | 37 |
| | 12 | 44 | 42 | 38 | 40 | 37 | 35 | 41 | 40 |
| | 16 | 35 | 35 | 35 | 37 | 37 | 36 | 41 | 39 |
| | 37 | 38 | 33 | 35 | 37 | 39 | 33 | 34 | 41 |
| | 39 | 38 | 34 | 39 | 36 | 36 | 36 | 30 | 38 |
| Group 5 | 1 | 38 | 39 | 34 | 35 | 36 | 34 | 34 | 38 |
| None | 7 | 38 | 40 | 39 | 39 | 42 | 40 | 39 | 45 |
| (infectious | 9 | 41 | 37 | 38 | 40 | 41 | 38 | 40 | 44 |
| control) | 10 | 47 | 48 | 43 | 39 | 42 | 36 | 43 | 48 |
| | 14 | 35 | 35 | 37 | 35 | 38 | 39 | 35 | 38 |
| | 29 | 37 | 33 | 38 | 36 | 39 | 39 | 36 | 43 |
| | 30 | 34 | 38 | 39 | 38 | 41 | 37 | 40 | 41 |
| | 33 | 39 | 24 | 38 | 37 | 38 | 39 | 37 | 44 |

Table A15. Fibrinogen -- mg/100 ml

| Group | Animal number | Weeks of chemical exposure: Period 1 | | Period 2 | | | Period 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 1 | 8 | 100 | 300 | 300 | 300 | 500 | 100 | -- | 100 |
| Urea | 13 | 500 | 700 | 400 | 1300 | 700 | 200 | 1800 | 200 |
| 0.1 lb/hd/dy | 15 | 200 | 400 | 100 | 700 | 300 | 300 | 100 | 100 |
| 8 weeks | 34 | 100 | 400 | 200 | 400 | 400 | 300 | 800 | 200 |
| | 35 | 400 | 400 | -- | 600 | 600 | 200 | -- | 100 |
| | 36 | 200 | -- | 200 | 400 | 700 | 100 | 1700 | 300 |
| | 38 | 100 | 200 | 200 | 800 | 600 | 300 | 1300 | 200 |
| | 40 | 300 | 400 | 400 | 400 | -- | 100 | 900 | 300 |
| Group 2 | 17 | 200 | 400 | 300 | 600 | 500 | 300 | 3300 | 200 |
| EDDI | 18 | 300 | 400 | 200 | 400 | 500 | 300 | 1200 | 100 |
| 500 mg/hd/dy | 19 | 200 | 500 | 400 | 600 | 400 | 500 | 900 | 100 |
| 3 weeks; | 25 | 300 | 400 | 300 | 300 | 400 | 300 | 500 | -- |
| 50 mg/hd/dy | 26 | 200 | 500 | 200 | 600 | 600 | 200 | 700 | 200 |
| 5 weeks | 28 | 100 | 400 | 300 | 600 | 600 | 200 | 900 | 100 |
| | 31 | 400 | 500 | 300 | 800 | 800 | 200 | 400 | 100 |
| | 32 | 300 | 500 | 300 | 600 | 600 | 100 | -- | 300 |
| Group 3 | 4 | 300 | 400 | 300 | 900 | 600 | 100 | 1600 | -- |
| EDDI-Urea | 6 | 100 | 300 | -- | 400 | 500 | 200 | 500 | 100 |
| 50 mg EDDI/hd/dy- | 20 | 300 | 300 | 200 | 600 | 400 | 200 | 300 | 100 |
| 0.1 lb urea/hd/dy | 21 | 300 | 300 | 200 | 200 | 500 | 100 | 1200 | 300 |
| 8 weeks | 22 | 200 | 400 | 300 | 300 | 300 | 400 | -- | 200 |
| | 23 | 300 | 200 | 200 | 700 | 700 | 300 | 300 | 100 |
| | 24 | 200 | 200 | 200 | 200 | 500 | 700 | 1400 | 100 |
| | 27 | 200 | 300 | 200 | 500 | 300 | 300 | 1000 | 200 |

Table A15. (Continued)

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 4 | 2 | 300 | 500 | 300 | 100 | 600 | 100 | 500 | 200 |
| None | 3 | 300 | 400 | 400 | 100 | 500 | 100 | 200 | 100 |
| (chemical | 5 | 200 | 500 | 400 | 600 | 500 | 200 | 300 | 200 |
| control) | 11 | 500 | 400 | 300 | 500 | 600 | 100 | 400 | 300 |
| | 12 | 400 | 200 | 300 | 100 | 400 | 200 | 100 | 300 |
| | 16 | 400 | 400 | 200 | 500 | 500 | 200 | 300 | 200 |
| | 37 | 100 | 700 | 200 | 800 | 500 | 100 | 200 | 300 |
| | 39 | 100 | 400 | 300 | 500 | 400 | 300 | 400 | 200 |
| Group 5 | 1 | 300 | 200 | 300 | 800 | 600 | 100 | 300 | 300 |
| None | 7 | 900 | 400 | 200 | 200 | 500 | 200 | 400 | 200 |
| (infectious | 9 | 300 | 300 | 200 | 500 | 500 | 100 | 400 | 200 |
| control) | 10 | 200 | 300 | 200 | 400 | 500 | 100 | 100 | 100 |
| | 14 | 200 | 300 | 200 | 300 | 400 | 600 | 100 | 200 |
| | 29 | 500 | 100 | 300 | 400 | 300 | 100 | 300 | 200 |
| | 30 | 300 | 400 | 200 | 600 | 600 | 200 | 200 | 300 |
| | 33 | 100 | 300 | 300 | 500 | 700 | 200 | 600 | 300 |

Table A16. Total protein -- g/100 ml

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 1 | 8 | 6.7 | 6.4 | 6.7 | 6.9 | 6.9 | 6.6 | 9.5 | 6.5 |
| Urea | 13 | 6.3 | 6.5 | 6.5 | 6.6 | 6.9 | 7.0 | 9.5 | 6.9 |
| 0.1 lb/hd/dy | 15 | 6.7 | 7.2 | 7.2 | 7.0 | 6.9 | 6.8 | 9.5 | 7.0 |
| 8 weeks | 34 | 8.3 | 7.1 | 7.0 | 7.3 | 6.9 | 7.3 | 10.0 | 6.0 |
| | 35 | 8.8 | 7.3 | 7.4 | 7.7 | 7.8 | 7.5 | -- | 7.2 |
| | 36 | 7.8 | -- | 7.3 | 7.0 | 7.3 | 7.4 | 12.0 | 7.1 |
| | 38 | 7.1 | 7.0 | 7.4 | 7.9 | 6.9 | 7.2 | 10.0 | 7.0 |
| | 40 | 7.1 | 7.1 | 6.7 | 6.9 | 6.3 | 7.1 | 10.0 | 7.5 |
| Group 2 | 17 | 6.8 | 7.0 | 7.2 | 7.1 | 7.3 | 7.0 | 10.0 | 7.0 |
| EDDI | 18 | 7.4 | 7.5 | 7.4 | 7.4 | 7.7 | 7.5 | 8.9 | 6.6 |
| 500 mg/hd/dy | 19 | 7.3 | 7.1 | 6.9 | 6.8 | 6.3 | 6.4 | 8.2 | 6.2 |
| 3 weeks; | 25 | 7.0 | 7.3 | 7.3 | 6.5 | 6.4 | 6.5 | 7.3 | -- |
| 50 mg/hd/dy | 26 | 6.9 | 7.2 | 6.9 | 7.4 | 7.4 | 7.2 | 10.0 | 7.0 |
| 5 weeks | 28 | 6.6 | 7.0 | 6.5 | 6.6 | 6.5 | 6.5 | 9.2 | 6.6 |
| | 31 | 6.8 | 7.3 | 7.2 | 6.5 | 6.6 | 6.6 | 7.9 | 7.3 |
| | 32 | 7.8 | 7.0 | 6.5 | 6.8 | 6.8 | 6.5 | -- | 6.8 |
| Group 3 | 4 | 6.8 | 7.5 | 7.1 | 7.2 | 7.1 | 6.6 | 8.9 | -- |
| EDDI-Urea | 6 | 6.4 | 7.0 | -- | 6.7 | 6.8 | 6.6 | 9.8 | 6.3 |
| 50 mg EDDI/hd/dy- | 20 | 7.2 | 7.1 | 7.2 | 7.2 | 7.2 | 6.8 | 8.4 | 6.4 |
| 0.1 lb urea/hd/dy | 21 | 6.3 | 7.1 | 6.7 | 6.8 | 7.2 | 6.3 | 11.0 | 7.4 |
| 8 weeks | 22 | 7.3 | 7.0 | 6.9 | 6.4 | 6.2 | 6.8 | -- | 7.0 |
| | 23 | 7.3 | 7.2 | 7.1 | 7.4 | 7.0 | 7.1 | 7.8 | 6.7 |
| | 24 | 6.6 | 6.8 | 7.1 | 6.8 | 7.3 | 6.8 | 10.0 | 7.2 |
| | 27 | 6.7 | 6.8 | 7.4 | 6.7 | 6.3 | 6.0 | 10.0 | 6.9 |

Table A16. (Continued)

| Group | Animal number | Weeks of chemical exposure | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Period 1 | | Period 2 | | | Period 3 | | |
| | | -1 | 0 | 1 | 2 | 3 | 4 | 6 | 8 |
| Group 4 | 2 | 7.1 | 7.5 | 6.9 | 6.5 | 7.0 | 6.7 | 7.1 | 7.1 |
| None | 3 | 6.9 | 7.2 | 6.8 | 6.5 | 7.0 | 6.8 | 6.9 | 7.2 |
| (chemical | 5 | 6.8 | 7.5 | 6.8 | 6.8 | 6.8 | 6.8 | 6.5 | 7.5 |
| control) | 11 | 7.2 | 6.9 | 6.9 | 6.8 | 6.4 | 6.2 | 7.1 | 7.1 |
| | 12 | 1.2 | 7.0 | 7.0 | 6.4 | 6.5 | 6.7 | 6.5 | 7.3 |
| | 16 | 7.1 | 7.0 | 7.0 | 7.0 | 7.3 | 6.6 | 6.5 | 7.1 |
| | 37 | 7.8 | 8.1 | 7.5 | 7.8 | 7.3 | 6.8 | 6.5 | 7.1 |
| | 39 | 7.4 | 7.4 | 7.0 | 6.9 | 6.6 | 6.8 | 6.4 | 6.8 |
| Group 5 | 1 | 6.3 | 6.5 | 6.3 | 7.0 | 6.4 | 6.1 | 7.2 | 6.4 |
| None | 7 | 7.3 | 7.4 | 7.0 | 6.2 | 7.1 | 7.1 | 7.1 | 7.5 |
| (infectious | 9 | 6.5 | 6.4 | 6.4 | 6.6 | 6.7 | 6.4 | 6.6 | 6.2 |
| control) | 10 | 7.8 | 7.6 | 7.5 | 7.7 | 7.7 | 6.7 | 6.8 | 6.9 |
| | 14 | 7.3 | 6.6 | 7.1 | 6.6 | 7.0 | 6.9 | 6.7 | 6.7 |
| | 29 | 7.5 | 7.5 | 7.0 | 6.5 | 6.6 | 6.5 | 7.6 | 6.9 |
| | 30 | 6.9 | 6.8 | 7.4 | 6.9 | 6.7 | 6.5 | 7.0 | 7.0 |
| | 33 | 8.1 | 6.6 | 7.2 | 7.3 | 7.5 | 7.0 | 6.8 | 7.6 |

Table A17. Total blood iodine -- ng/100 ml

| Group | Animal number | Weeks of chemical exposure: Period 1 -1 | Period 1 0 | Period 2 1 | Period 2 2 | Period 2 3 | Period 3 4 | Period 3 6 | Period 3 8 |
|---|---|---|---|---|---|---|---|---|---|
| Group 2 | 17 | 95 | 156 | 860 | 1259 | 954 | 274 | 281 | 284 |
| EDDI | 18 | 191 | 216 | 1477 | 1243 | 938 | 282 | 263 | 280 |
| 500 mg/hd/dy | 19 | 156 | 184 | 1544 | 1480 | 1212 | 276 | 297 | 291 |
| 3 weeks | 25 | 126 | 161 | 1290 | 1497 | 928 | 235 | 273 | -- |
| 50 mg/hd/dy | 26 | 117 | 141 | 1420 | 1554 | 1114 | 294 | 273 | 270 |
| 5 weeks | 28 | 115 | 159 | 1389 | 1393 | 922 | 274 | 280 | 252 |
| | 31 | 108 | 107 | 989 | 1580 | 1248 | 302 | 264 | 266 |
| | 32 | 160 | 171 | 1424 | 1404 | 932 | 279 | -- | 288 |
| Group 3 | 4 | 106 | 144 | 260 | 310 | 326 | 261 | 176 | -- |
| EDDI-Urea | 6 | 110 | 142 | -- | 300 | 268 | 346 | 295 | 310 |
| 50 mg EDDI/hd/dy- | 20 | 72 | 96 | 248 | 296 | 330 | 244 | 244 | 244 |
| 0.1 lb urea/hd/dy | 21 | 182 | 181 | 314 | 248 | 334 | 294 | 341 | 237 |
| 8 weeks | 22 | 177 | 165 | 202 | 300 | 309 | 246 | -- | 284 |
| | 23 | 110 | 156 | 298 | 322 | 321 | 297 | 342 | 324 |
| | 24 | 61 | 140 | 292 | 280 | -- | 214 | 149 | 198 |
| | 27 | 102 | 104 | 264 | 296 | 298 | 281 | 241 | 282 |
| Group 5 | 1 | 160 | 173 | 186 | 166 | 156 | 169 | 176 | 177 |
| None | 7 | 79 | 113 | 119 | 117 | 107 | 113 | 110 | 115 |
| (infectious | 9 | 173 | 161 | 167 | 169 | 160 | 156 | 154 | 158 |
| control) | 10 | 128 | 148 | 164 | 164 | 163 | 162 | 166 | 149 |
| | 14 | 112 | 154 | 144 | 125 | 132 | 142 | 135 | 116 |
| | 29 | 134 | 144 | 144 | 150 | 132 | 146 | 128 | 126 |
| | 30 | 100 | 128 | 137 | 124 | 121 | 140 | 134 | 130 |
| | 33 | 110 | 111 | 130 | 112 | 134 | 108 | -- | 180 |