Effects of Acute Iodine Toxicity on Reproduction In a Dairy Herd

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Introduction

The manager for a 60 cow Guernsey herd in central Michigan contacted an extension veterinarian at Michigan State University because the herd was experiencing acute respiratory problems. The veterinarian and several veterinary students visited the farm to obtain a more complete history and to investigate the problem. Repeat visits were made at 7 to 10 day intervals for the next several months to monitor the herd health and reproductive performance. The objective of this paper is to report the effects of acute iodine toxicity on bovine reproduction performance in this 60 cow herd.

Herd History

The production level in this 60 cow Buernsey herd of 6545 kg (14,398 pounds) of milk and 321 kg (707 pounds) of butterfat was indicative of excellent management. The cows were housed in a stanchion barn and turned out twice daily for exercise, estrous detection and grazing in a pasture adjacent to the barn.

This herd was on a herd health program under the supervision of the local veterinarian and was relatively free of disease. All cows were vaccinated annually at approximately 30 days postpartum with a modified live virus strain of BVD and PI_3. All eligible cows were examined at monthly or more frequent intervals on the reproductive health program. Individual health and reproductive records were maintained on each cow in the herd.

Feeding Program

The daily forage feeding program consisted of 5.5 kg (12 lb) haylage, 6.8 kg (15 lb) corn silage and 3.6 kg (8 lb) hay in addition to pasture. A concentrate mix containing approximately 12 percent protein and 72 percent total digestible nutrients was prepared at the local elevator from home grown corn oats, and soybean meal. It was fed at the rate of 0.45 kg (1 lb) grain to .90 kg (2 lb) of milk. The average cow consumed approximately 11.5 kg (25 lb) of this ration daily which had been fed since May 1.

An organic iodide (EDDI)[a] was recommended by farm management to be mixed at the grain elevator with the concentrate mix at the rate of 0.9 kg (2 lb) per 910 kg (2000 lb) in response to an outbreak of foot rot in early June. The EDDI was added to the concentrate mix from June 13 to 23 and again from July 12 to August 1 for a total of 30 days.

The herdsman had collected information on the iodine supplement being added prior to our farm visit. It contained 99.5% active drug ingredients with the recommendations on the label indicating that adult cattle should receive 50 mg per head daily in the feed or salt continuously as an aid in the prevention of foot rot and lumpy jaw. The recommended dose for treatment of these conditions and respiratory infections was 500 to 500 mg daily for 2 to 3 weeks.

Clinical Signs

The initial farm visit revealed cows showing signs of partial anorexia, nasal and lacrimal discharge, salivation, rapid breathing, decreased milk production, and two cows had recently aborted.

The owners had made a presumptive diagnosis of IBR prior to the initial farm visit and treated the cows with antibiotics for several days without response.

Diagnostic Procedures

All available aborted fetuses and membranes were collected in a plastic bag, refrigerated, and transported to the diagnostic laboratory. Six of twelve aborted fetuses were submitted for a diagnosis. The other six consisted of two abortions which occurred before our arrival at the farm and four others which were undetected until four cows in the early stages of confirmed pregnance returned to estrus.

Blood for serologic analysis was collected via the tail vein from 12 cows which aborted. The serum titers for brucellosis, leptospirosis, IBR, BVD, and PI_3 were obtained. Paired samples were collected at three to four week intervals for IBR, BVD and PI_3.

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[a] *Ethylenediamine Dihydriodide (99.5% drug ingredient) Whitemore Laboratories, Inc., Myerstown, PA.*

Table. 1. Reproductive Profile on Cows Aborting Following Excessive Iodine Intake

Cow No.	Days lactation iodine feeding	Days gestation iodine feeding	Days iodine to abortion	Days gestation at abortion	Before Abortion		After Abortion		First estrus after abortion
					Days open	Services/ conception	Days open	Serices/ conception	
544	173	83	46	129	90	1	Sold open		23
564	181	40	80	120	141	4	65	3	19
613	201	64	61	125	137	4	22	1	22
615	216	57	73	130	159	2	Sold open		
618	213	148	73	221	65	1	Sold open		
644	178	72	76	148	106	1	19	1	19
647	156	45	72	117	111	2	44	1	22
709	141	72	34	106	69	1	21	1	21
762	156	94	66	160	62	1	Sold open		21
784	304	151	100	251	153	3	125	4	21
788	264	183	75	258	81	2	Sold open		
799	218	34	55	89	184	4	130	5	21
Total	2401	1043	811	1854	1358	26	426	16	189
Mean	200	87	68	155	113	2.2	61.9	2.3	21.0
St. Dev.	47.3	48.4	17.1	57.1	41.1	1.3	48.4	1.7	1.3
Range	141-264	34-183	46-100	89-258	62-184	1-4	19-130	1-5	19-23

Guarded culture tubes[b] were used for collecting uterine cultures from cows following abortion. Tubes containing Stuarts Transport Media[c] were used to transport the swabs to the laboratory. The same type swabs were used for collecting samples from the nasal passages for bacterial and viral isolation procedures.

A Yoeman biopsy punch[d] was used to collect the endometrial specimens which were fixed in formalin immediately. The biopsy sections were paraffin embedded, cut at 6 μm and stained with hematoxylin and eosin.

The data on occurrence of abortions were analyzed by Chi square to determine if there was a significant difference between the trimester of pregnancy when the initial feeding began and the occurrence of abortion.

Results and Discussion

Abortions

The aborted fetuses and membranes were submitted to the diagnostic laboratory from six cows. The fetuses were in various stages of decomposition and appeared to have been dead in the uterus for an unknown time prior to delivery. The two which aborted nearest to term were in early stages of fetal mummification which has been reported to occur most frequently in Guernsey's duirng the last trimester of pregnancy.[13] These two Guernsey cows were at 251 and 258 days of gestation when the abortion occurred. Fetal mummification has been reported to follow infectious causes of fetal death due to vibriosis, mycotic agents, IBR, BVD and leptospirosis.[13] The role which iodine may have played in causing the mummification is not known.

Abortions eventually occurred in 12 cows within a 68 day period following the initial date of iodine feeding (Table 1). They had a mean lactation length of 200 days and 87 day gestation length at the time of initial feeding. The mean interval to the time of abortion was 68 days at 155 days of gestation.

Serum samples collected for brucellosis and leptospirosis titers at the first farm visit following each abortion were negative for brucellosis and leptospirosis. Paired serum samples were collected at the first visit following each abortion and convalescent samples were collected approximately one month later for IBR, BVD, and PI_3 from the remaining 9 cows. They were negative for IBR antibodies on the hemagglutination test except for a purchased cow which had a titer of 1:32 on the initial test before being sold. BVD and PI_3 virus neutralizing antibodies were present in all acute and convalescent samples; however, the changes in titers were not considered diagnostic. All of these cows had been vaccinated during the current lactation at

[b] *Tiegland Swabs (Modified) Haver-Lockhart Laboratories, Shawnee, Kansas.*

[c] *Culturettes, Scientific Products Co., Romulus, Michigan.*

[d] *United Surgical Supplies Co., Inc., Post Chester, NY.*

approximately 30 days postpartum for BVD and PI_3 but not IBR. The results of these tests conducted for brucellosis, leptospirosis, IBR, BVD and PI_3 helped to eliminate these pathogens from consideration as the etiological agent causing the abortions.

The nasal swabs did not contain any bacterial or viral pathogens.

Uterine cultures and endometrial tissue were collected from 10 of 12 cows following abortion for microbiologic and histopathologic procedures. *C. pyogenes* was cultured from two cows and hemolytes *E. coli* from two other cows. The cultures on the other six cows were negative.

The four cows with positive cultures also had an endometritis based on histopathologic examination while the other six were normal. Post-partum cows frequently have uterine infection[2] and endometritis.[4]

A specific etiological diagnosis was not determined in any of the 12 cows which aborted; however, only 20 to 25% of bovine abortions commonly yield a definitive etiological diagnosis.[13]

Iodine Feeding

The actual amount of supplemental iodine being fed for therapeutic purposes in this herd was calculated to be approximately 12,170 mg per day for the cow consuming 11.5 kg (25 lb) concentrate daily. Trace mineralized salt which contained .007% iodine was also available free choice with variable individual consumption.

The therapeutic recommendation on the label was to administer 400 to 500 mg per head daily for two to three weeks as an aid in the treatment of foot rot caused by *Spherophorus necrophorus*, lumpy jaw caused by *Actinobacillosis lignieresi*, and respiratory infections by acting as an expectorant. This latter usage for respiratory infections is not recommended by some clinical researchers[8] [9] and the highest intake recommended by the National Research Council (NRC) for dairy cattle is 0.5 ppm or about 12 mg per day.[12]

Possible sources of organic and inorganic iodine frequently observed on farms with iodine toxicity include EDDI in the salt, commercial mineral supplements fed both free choice and included in the concentrate, and commercial protein supplements prepared for addition to the concentrate.

Trace mineral salt was the only one of these products available on this farm. Soybean oil meal was the primary protein supplement added to the concentrate mix on this farm. This product has been shown to be goitrogenic and may increase the need for additional iodine.[6] Soybean meal was included in the ration of this herd both before and after the abortion problem without evidence of goiter due to an iodine deficiency.

Herd Reproductive Performance Summary

The effects of iodine toxicity on reproductive performance for three years before, during and after the time the feed contamination occurred are illustrated (Table 3). Desirable goals are also indicated. Although the days open, services per conception and repeat breeding exceeded desired goals, annual improvement occurred in each of these categories except services per conception in the year of the outbreak. The primary effect which the iodine toxicity had on reproductive performance was to increase the occurrence of abortions in the herd from approximately 3 to 16 percent and the cows subsequently culled for infertility increased from 2 to 11 percent (Table 3).

Table 2. Relationship Between Stage of Gestation on Date of Initial Exposure to Excessive Iodine Intake and Time of Abortions in a Dairy Herd

Stage of Gestation	No. Cows	Pregnant (%)	No. Cows Aborting	Cows Aborting (%)
1-90	20	45	9	66
91-180	7	38	2	25
181-term	11	9	1	9
	38	100%	12	100%

Five open cows were sold after aborting because they were in late lactation and milk production was not at an economical level. The days open and services per conception in the 12 cows which aborted were 113 and 2.2, respectively, while after abortion they were 61 and 2.3, respectively in the 7 which conceived again (Table 1). These 7 cows conceived more rapidly after the abortion than prior to the abortions, suggesting that the acute iodine toxicity did not have a residual effect on subsequent fertility.

There were 20 open postpartum cows on the first day the excessive iodine feeding began. These cows averaged 137 days open and 3.25 services per conception compared to 113 days and 2.7 respectively for the entire group. Anestrus was not a problem in these cows. The iodine toxicity appeared to increase days open and services per conception in cows being bred and abortions in pregnant cows during the time being fed; however, residual effects on reproduction following

Table 3. Effects of Iodine Toxicity on Reproductive Performance in a Guernsey Herd

Criteria	Before	During	After	Goal
Total cows	71	75	72	
Days open	118	113	108	<100
Services/conception	2.5	2.7	2.2	<1.5
Abortions (%)	3	16	3	<3%
Repeat breeding (%)	27	23	18	<10%
Cows sold	20	20	18	
Culling percentage (%)	28	26	25	<25%
Reasons for Disposal (%)				
Dairy purposes	20	11	12	>10%
Low production	3	1	8	<10%
Infertility	2	11	3	<2
Mastitis	2	0	0	<2
Injury	0	1	1	<2
Death	2	2	1	<2

withdrawal from the feed could not be detected. Reproductive efficiency was reduced in cows continuously fed thyroprotein, an exogenous source of thyroxine.[14]

The mean interval to the first observed estrus after the abortion was 21 days in 9 cows (Table 1). The other 3 cows were sold within 10 days after the abortion. Examination per rectum following the abortions revealed a recent ovulation or developing corpus luteum in these cows, indicating that an estrus had occurred at the same approximate time as the abortion. These findings were consistent with the occurrence of the first observed estrus 21 days after the abortions.

When the relationship between stage of gestation on date of initial exposure to excessive iodine intake and rate of abortions was analyzed, more abortions occurred in cows during the first trimester of pregnancy (Table 2). Although only 53% of the pregnant cows were in the first trimester of pregnancy, 75% of the abortions occurred in this group ($P < 0.1$). A possible explanation for a majority of the abortions occurring in cows which were in the first trimester of pregnancy at the time of initial iodine feeding is that these cows were producing more milk and receiving more concentrate containing the supplementation iodine than cows in later gestation. It is also possible that the fetus is more susceptible to iodine during the first trimester of pregnancy. When radioiodine was administered to 21 pregnant cows at 7 days before expected parturition, the iodine concentration in the circulation of the fetus was over five times that found in the dam's plasma.[11] The amniotic fluid contained more iodine than fetal plasma, with the chorionic fluid iodine concentration midway between maternal and fetal plasma.[11] The high fetal iodine concentrations were attributed to the inability of the fetus to excrete iodine in the urine.

Pathogenesis

The trace element iodine is an essential constituent of the hormone thyroxin which controls the rate of cellular oxidation and energy metabolism.[15] A deficiency leads to endemic goiter. An iodine deficiency and associated hypothyroidism in cattle has been reported to cause aboritons and the birth of weak or dead calves. It was reported that abortions in cattle were caused by the intravenous administration of sodium iodide at the rate of 1 g/15 kg of body weight.[3] Ten normal cows ranging from 320 to 455 kg in body weight and 4 to 7 months pregnant were treated intravenously with 50 g (20% solution) of sodium iodide, but abortions did not occur.[10]

The exact mechanism by which iodine toxicity causes fetal death is unknown. When calves with an initial weight of 120 kg received 1250 mg of iodine daily for six months, there was an interference with titer maintenance to some antigens, with lymphocyte DNA synthesis, and with phagocyte activity of white blood cells.[5] In a field study of chronic iodine toxicity in dairy cattle[7] depressed immune mechanisms accompanied by changes in metabolic and adrenal function were reported.

Diagnosis

The diagnosis of iodine toxicity was based on an intake of organic and inorganic iodine of approximately 1000 times daily requirements for 30 days during a 45 day period. Clinicals signs were characteristic for the condition.[12] The clinical signs did not respond to antibiotic therapy and disappeared following removal of the EDDI from the ration except for abortions. The pathogenic organisms responsible for vibriosis, trichomoniasis, brucellosis, leptospirosis, BVD, and IBR were not detected which helped to elinimate the common infectious causes of abortion from consideration.

Serum and milk or urine iodine concentrations would have been helpful to confirm the diagnosis but were not available. The iodine excreted in milk is dose dependent in the usual supplemental ranges with dietary iodine the principal source of iodine in milk.[15]

Treatment

No treatment was necessary after the *excess* iodine was removed from the ration. Cows with uterine infection following abortions received and responded to symptomatic antibiotic therapy.

Prevention

The fact that acute iodine toxicity occurred in one Michigan herd and chronic iodine toxicity was reported in 10 other dairy herds[7] indicates a need for guidelines to prevent further problems.

The following recommendations should prove hlepful to nutritionists, dairymen and veterinarians in preventing errors in general feed formulation and in providing the proper dietary intake of iodine and other trace minerals.

1. Read the labels of all feed ingredients to determine the presence and concentration of iodine.
2. Follow directions carefully.
3. Be aware of all possible sources of iodine such as salt, minerals, and protein supplements. Iodized salt containing 0.01% iodine included at 1% in the concentrate mix is equivalent to 1 ppm iodine. A forage to concentrate ratio of 2:1 will add .33 ppm iodine plus the iodine in feed will supply 0.5 ppm in diet recommended for lactating cows.[12]
4. Avoid adding additional ingredients to balance an existing ration. Start with the basic grains and then add the correct amount of protein supplement, vitamins and minerals.
5. Calculate the average daily iodine intake for the highest producing cows before making the proposed recommendations of iodine supplementation as follows:
   a. Identify all sources of iodine in the ration.
   b. Convert weight of all feeds in pounds to kg (lbs ÷ 2.2 = kg).
   c. Convert iodine concentration to mg/kg. Move decimal point four places to right (0.01% = 0100.0 = 100 mg/kg = 100ppm).
   d. Calculate mg of iodine from each source.

e. Total the iodine intake in mg/day. The highest recommended daily intake for dairy cattle is 12 mg/day.

6. Balance the total ration for all nutrients and feed according to National Research Council requirements.

Conclusions

The feeding of supplemental iodine at approximately 1000 times the daily requirement to 60 high producing Guernsey cows for 30 days resulted in 12 abortions within a 68 day period following the initial date of iodine feeding. These 12 cows which aborted had a mean lactation length of 200 days and 87 day gestation length at the time of initial feeding. The annual abortion rate in the herd increased from 3% to 16% following the excessive iodine intake. The majority of the abortions occurred in cows which were in the first trimester of pregnancy when feeding began. The subsequent fertility was normal. The number of days open and services per conception were increased in the 20 open cows which were being bred during the period when the iodine intake was excessive.

The infectious agents considered to be abortifacients in cattle were eliminated from consideration by submitting aborted fetuses, placenta membranes, uterine cultures and tissue, nasal swabs and blood samples to the diagnostic laboratory for evaluation and testing.

The maximum iodine intake recommended for lactating dairy cattle is 12 mg/day. This level of iodine supplementation is beneficial for optimum health and productivity. The feeding of excessive iodine levels may have an adverse effect on health and will increase the iodine content of milk in proportion to the content in the ration. Dietary iodide should be limited to nutritional requirements with prophylactic and therapeutic amounts avoided until efficacy is documented by controlled research.

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