STUDIES ON KETOSIS IN DAIRY CATTLE. X. THE EFFECT OF A VITAMIN A DEFICIENCY[1]

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In earlier studies, it was observed that the blood plasma carotene and vitamin A of cows exhibiting spontaneous ketosis were quite normal, showing that the ketotic condition was not caused by a vitamin A deficiency. Likewise, these animals did not respond to massive oral doses of vitamin A (1). This latter observation was confirmed by Hayden *et al.* (2).

However, these studies did not answer the question as to whether a vitamin A deficiency in cows would produce ketosis. It appeared possible that the typical symptoms and blood picture associated with ketosis could be produced by a combination of a vitamin A deficiency and fasting immediately postpartum, since fasting during the early postpartal period usually results in a marked hypoglycemia and ketonemia (3), and the symptoms associated with a vitamin A deficiency resemble those frequently observed in ketosis. This report is believed to provide a rather conclusive answer to the above question.

EXPERIMENTAL METHODS

The data reported herein were obtained from an experiment designed to study the influence of quality and quantity of feed upon the incidence of ketosis. In the early part of the study, it was observed that the blood plasma carotene and vitamin A values were lower than was expected; so much so, in fact, that the decision was made to continue the animals on the same diet and study the influence of a vitamin A deficiency on ketosis. The variable factors planned in the beginning were protein, fat, soluble carbohydrate and energy intake. Timothy hay (U. S. no. 2) was used because of its relatively low protein content. Raw soybeans were used as a source of protein and fat and made up 40 per cent of the concentrate ration (K-3) which was fed to all three groups for 4 mo. prepartum and to groups 1 and 2 postpartum. In addition to the soybeans, the concentrate mixture consisted of beet pulp 30 per cent, molasses 20 per cent, crushed barley 5 per cent, ground wheat 3 per cent, steamed bone meal 1 per cent, and iodized salt 1 per cent. Group 3 received concentrate ration K-1 during the postpartal period. It consisted of beet pulp 50 per cent, crushed barley 30 per cent, ground wheat 18 per cent, steamed bone meal 1 per cent, and iodized salt 1 per cent.

Morrison's feeding standards (4) were used throughout the experiment for calculating the total digestible nutrient requirements. The cows were fed rather heavily during the prepartal period to get them in a relatively fat condition. Prior to being placed on experiment, all of the cows had received liberal amounts of corn silage and a good quality of lespedeza hay in addition to a concentrate.

Received for publication March 7, 1950.

[1] Paper no. A268, contribution no. 2211 of the Maryland Agricultural Experiment Station.

TABLE 1

Blood plasma carotene and vitamin A of cows in groups 1, 2, and 3

Cow		Vitamin A concentrate fed prepartum		Plasma carotene			Plasma Vitamin A			Remarks
				Day of parturition	5–7 d. postpartum	10–14 d. postpartum	Day of parturition	5–7 d. postpartum	10–14 d. postpartum	
		Days	Total I.U.	(μg./100 ml.)	(μg./100 ml.)	(μg./100 ml.)	(μg./100 ml.)	(μg./100 ml.)	(μg./100 ml.)	
					Group 1					
Becky	H[a]			.....	21.6	27.6	.....	5.7	6.0	
Lou	A			49.2	31.2	29.4	5.2	3.0	4.5	Retained placenta
Dita	H			27.0	33.6	24.0	5.4	3.9	3.9	
Viola	J			96.0	82.2	90.0	8.1	7.5	13.2	Milk fever
Av.				57.4	42.2	42.8	6.2	5.0	6.9	
					Group 2					
Lively	G			30.6	29.4	43.2	4.5	3.3	7.8[b]	Retained placenta
Matilda	H			31.8	26.4	29.4	2.7	4.8	4.5	Retained placenta
Lobelia	A			47.4	47.4	48.0	4.2	4.8	5.1	
Lizzie	G			42.6	37.8	56.4	3.3	5.1	8.1	Milk fever
Av.				38.1	35.3	44.3	3.7	4.5	5.9	
					Group 3					
Katrina	J	52	6,000,000	67.8	53.4	31.8	18.0	11.4	9.9	
Melanie	H	43	4,800,000	36.0	30.6	39.0	10.8	6.0	16.8	Milk fever
Burke	H	21	2,000,000	30.6	51.0	64.2	5.7	8.4	6.0	
Lorna	A	10	1,200,000	39.6	30.6	33.6	6.6	5.4	5.4	Milk fever
Maggie	H	26	2,800,000	30.0	45.6	33.0	8.4	7.2	7.2	Retained placenta
Av.				40.8	42.2	40.3	9.9	7.7	9.1	

[a] Letter denotes breed.

[b] Vitamin A concentrate given *per os* a few days previously; value not included in average.

Beginning approximately 4 mo. prepartum, the cows were changed to timothy hay and the 40 per cent soybean ration. During the fourth and third months prepartum, the cows were fed all they would eat up to 140 per cent of requirements. During the 2-mo. dry period this was increased to 180 per cent.

In the postpartal period, the cows in group 1 received a rather high level of energy intake, whereas the cows in groups 2 and 3 were limited to approximately 50 per cent of their total digestible nutrient requirements for 3 wk. and then put on full feed as rapidly as possible. The hay was fed at the rate of 1.5 lb. per 100 lb. live weight to all cows during the prepartal period and to the cows in group 1 during the postpartal period. The cows in groups 2 and 3, which were maintained on a low level of energy intake postpartum, received 0.8 lb. of hay per 100 lb. weight during the first 3 wk. postpartum and 1.5 lb. thereafter. The concentrate mixture constituted the remainder of the total digestible nutrients. In addition, the cows in group 3 received 400,000 I. U. of a vitamin A concentrate twice per week for varying periods prepartum as indicated in table 1. The dosage was kept relatively low because of the opportunity afforded by this study to determine whether a relatively small intake of vitamin A over short periods would suffice to prevent the injury to the fetus which otherwise was certain to occur. Two additional cows were included in group 2 in the original study, but they calved before the vitamin A analyses were initiated and so are not included in this report.

Blood samples for carotene, vitamin A and glucose determinations were drawn at frequent intervals prepartum, on the day of parturition and twice per week thereafter.

A modification of the procedure of Moore (5) and of Kimble (6) was used for plasma vitamin A and carotene. Somogyi's (7) modification of the Shaffer and Somogyi method was used for blood glucose.

RESULTS

In table 1 the plasma carotene and vitamin A values of 13 cows are shown for the period immediately postpartum. The cows in groups 1 and 2 exhibited marked vitamin A depletion, as will be observed from the plasma vitamin A values. The cows in group 3, which received the vitamin A concentrate, exhibited a somewhat higher level of plasma vitamin A during the postpartal period.

An even better estimation of the degree of vitamin A depletion of these cows may be obtained from the data presented in table 2 on their calves. All of the calves from the cows in groups 1 and 2 showed evidences, usually marked, of vitamin A deficiency. At 5 days of age, only one of the calves from these eight cows was normal in appearance, even though the calves were allowed free access to the colostrum of their dams for the first 3 days. The one calf (Viola's) which was normal in appearance at 5 days, received 500,000 I. U. of vitamin A concentrate on the day of birth. Additional evidence of the degree of vitamin A depletion in these cows was the low level of vitamin A in the colostrum, which was indicated by the relatively small increase in the plasma vitamin A of the calves by the fifth day after birth.

TABLE 2

Blood plasma carotene and vitamin A of calves from cows in groups 1, 2, and 3

Dam of Calf	At birth			5 d. after birth[a]		
	Carotene	Vitamin A	General condition	Carotene	Vitamin A	General condition
	(μg./100 ml.)	(μg./100 ml.)		(μg./100 ml.)	(μg./100 ml.)	
			Group 1			
Becky	.....	.....	Weak, eye hemorrhage	1.8	7.8	Weak, died of scours at 2 wk.
Lou	1.8	2.1	Eye hemorrhage	3.6	3.6	Scours
Dita	0.0	1.2	Eye hemorrhage, paralyzed, rapid respiration	.....	.....	Did not recover from paralysis
Viola	1.8	6.0[b]	Eye hemorrhage	2.4	5.4[c]	Good
Av.	1.2	1.7		2.6	5.7[b]	
			Group 2			
Lively	1.2	2.4	Eye hemorrhage, blind, paralyzed	.....	.....	Killed on 2nd day
Matilda	.....	.....	Twins, born dead	.....	.....	Dead at birth
Lobelia	1.2	3.6	Eye hemorrhage, rapid respiration	2.4	5.4	Weak
Lizzie	2.4	2.7	Eye hemorrhage	8.4	8.7	Scours
Av.	1.6	2.9		2.4	5.4	
			Group 3			
Katrina	0.6	3.0	Good	6.0	14.1	Good
Melanie	0.6	2.4	Good	2.4	14.4	Good
Burke	0.6	1.5	Good	3.6	8.1	Good
Lorna	0.0	1.2	Weak	.....	.....	Died of bacteremia
Maggie	0.6	2.7	Good	1.8	6.6	Good
Av.	0.5	2.2		3.5	10.8	

[a] All calves were allowed to remain with dams for 3 d.
[b] Obtained colostrum before sample was taken
[c] Received 500,000 I.U. of vitamin A *per os* on day of birth } not included in averages.

TABLE 3

Blood glucose level and general condition of cows depleted of vitamin A and on varying levels of energy intake postpartum

Cow	Blood glucose in mg./100 ml.									Comments on symptoms of ketosis
	Days prepartum		Day of parturition	Days postpartum						
	15–13	8–6		3–4	7–8	10–11	13–14	17–18	20–21	23–24	
					Group 1						
Becky	.....	43.6	52.4	34.1	43.6	39.2	36.0	43.4	44.1	45.6	Negative
Lou	39.0	39.9	57.3	29.9	38.6	37.8	33.5	42.6	38.1	40.0	Negative
Dita	.....	45.1	63.5	33.6	42.1	27.9	39.4	30.5	38.6	38.6	Negative
Viola	46.3	45.6	.....	38.1	39.4	41.9	38.6	35.4	37.5	41.9	Negative
Av.	42.7	43.6	57.7	33.9	40.9	36.7	36.9	38.0	39.6	41.5	
					Group 2						
Lively	50.0	46.4	65.6	25.7	38.1	33.8	31.1	35.1	28.1	39.4	See table 4
Matilda	47.3	45.1	62.1	41.0	33.2	38.1	35.8	34.6	30.2	49.1	Negative
Lobelia	41.2	38.0	.....	34.8	32.7	37.8	38.1	34.0	28.5	38.6	Negative
Lizzie	38.1	46.4	71.8	33.3	29.2	25.9	21.4	17.6	20.3	37.0	Negative
Av.	46.7	44.0	66.5	33.7	33.3	33.9	31.6	30.3	26.5	41.0	
					Group 3						
Katrina	41.9	43.5	61.8	44.6	38.3	29.2	44.6	38.1	.....	.....	Negative
Melanie	42.6	36.7	92.6	31.1	22.4	17.0	18.6	35.4	35.9	.....	Negative
Burke	40.3	48.6	88.0	36.7	31.3	21.1	21.9	21.9	25.4	49.4	Negative
Lorna	41.7	47.0	.....	36.2	.....	31.3	27.3	34.6	33.5	38.6	Negative
Maggie	45.4	48.1	67.8	27.8	37.8	27.3	33.2	24.0	26.5	41.3	Negative
Av.	42.4	44.8	62.0	35.3	32.5	31.5	29.1	30.8	30.3	43.1	

The relatively small amount of vitamin A concentrate administered to the cows in group 3 protected four of the five calves from showing symptoms of a vitamin A deficiency at birth. The one calf in this group which showed evidence of a vitamin A deficiency was from the cow Lorna, which did not receive any vitamin A supplement until 10 days before parturition. On the other hand, the feeding of a small amount of vitamin A supplement to the cows Maggie and Burke, beginning with the 26th and 21st days prepartum, was sufficient to prevent the development of any external signs of a vitamin A deficiency in their calves.

An analysis of the hay showed that the cows were receiving approximately 35 μg. of carotene per pound of body weight from this feed. Since the concentrate mixture supplied very little vitamin A, the cows apparently were just at or slightly below their minimum requirements for carotene intake (8). However, the very low blood plasma vitamin A levels of the cows at time of parturition and the marked symptoms of vitamin A deficiency observed in the calves at birth suggested that the vitamin A depletion of the cows was greater than could be explained on the basis of the carotene intake. It was suspected that the high proportion of soybeans in the ration was responsible inasmuch as Hilton *et al.* (9) had observed that the feeding of soybeans to cows depressed the vitamin A content of the butter obtained from these cows. A carefully controlled experiment then was conducted with calves in which it was found (11) that the feeding of soybeans did indeed exert a very marked depressing effect upon both the plasma and liver vitamin A.

The data in tables 1 and 2 show that the cows in groups 1 and 2 were depleted of vitamin A to such an extent that not only were the plasma vitamin A values of the cows extremely low, but most of the calves showed evidences of vitamin A deficiency of considerable severity at birth.

The blood glucose values and observations on possible symptoms of ketosis in these cows during the postpartal period are presented in table 3. The cows in group 1 had blood glucose levels which are in the normal range for well-fed cows during the postpartal period, on the basis of a very large volume of data (unpublished) which has been accumulated in this laboratory. Some decrease usually occurs during this period. No symptoms of ketosis were observed.

The cows in groups 2 and 3 which received a lower level of energy intake postpartum (approximately 50 per cent of requirements) exhibited a lower level of blood glucose than the cows in group 1. However, the decrease in blood glucose was of the same magnitude in the cows in group 3, which received a vitamin A supplement, as in the cows in group 2 which were depleted of vitamin A. No symptoms of ketosis were observed in any of the animals.

One of the cows (Lively) in group 2 showed marked symptoms of a vitamin A deficiency. The blood plasma carotene and vitamin A and the blood glucose values obtained on this cow are presented in some detail in table 4. It will be noted that the plasma vitamin A values were very low immediately prepartum and postpartum. The calf was completely blind and paralyzed at birth. On the fourth, fifth and sixth days following parturition, this cow exhibited night

TABLE 4

The effect of low energy intake postpartum on the blood glucose level of a cow exhibiting a marked vitamin A deficiency

Date	Plasma carotene	Plasma vitamin A	Blood glucose	Per cent of T.D.N. requirements consumed	Remarks
	(μg./100 ml.)	(μg./100 ml.)	(mg./100 ml.)		
7/25	189.6	14.7	41.9	126	
8/8	132.0	18.0	41.6	135	
8/22	90.6	13.5	46.5	136	
8/28	.....	.....	.....	163	Beginning of dry period
9/19	60.6	11.7	46.4	161	
10/14	45.6	9.9	38.3	138	
10/17	46.2	5.1	46.4	151	
10/21	27.0	5.4	44.8	91	
10/22	30.6	4.5	65.6	66	Calved, calf blind and paralyzed, cow retained placenta
10/23	.....	.....	.....	55	Calf died
10/24	.....	.....	.....	55	Placenta removed
10/25	30.0	1.5	25.7	42	
10/26	.....	.....	.....	31	
10/27	.....	.....	.....	55	Cow exhibited slight incoordination and night blindness
10/28	29.4	3.3	25.4	55	Cow exhibited marked incoordination and night blindness
10/29 A.M.	34.8	4.8	38.1	60	Cow exhibited marked incoordination and night blindness
P.M.	.....	.....	.....	.....	1,000,000 I. U. vitamin A *per os*
10/30	30.6	14.1	43.5	57	1,000,000 I. U. vitamin A *per os*, marked incoordination
10/31	.....	.....	.....	45	1,000,000 I. U. vitamin A *per os*, slight improvement
11/1	38.4	16.2	33.8	44	1,000,000 I. U. vitamin A *per os*, definite improvement
11/2	.....	.....	.....	50	1,000,000 I. U. vitamin A *per os*, definite improvement
11/3	.....	.....	.....	52	
11/4	43.2	7.8	31.0	51	1,000,000 I. U. vitamin A *per os*
11/5	.....	.....	.....	53	Still showed some night blindness and slight incoordination
11/6	.....	.....	.....	47	1,000,000 I. U. vitamin A *per os*
11/7	40.8	12.6	35.1	47	Appeared almost normal
11/11	39.0	8.1	28.1	55	Put on full feed
11/13	.....	.....	.....	95	
11/14	23.4	5.1	39.4	95	
11/18	30.0	6.3	42.7	104	

blindness and incoordination. On the sixth day, the incoordination was so marked that the cow had considerable difficulty maintaining her equilibrium. A careful study of the blood glucose values fails to show any evidence that the hypoglycemia of ketosis is associated with a vitamin A deficiency. On the day that the general incoordination of the animal was most severe and might have been assumed to compare with the incoordination often associated with ketosis, the blood glucose value had risen to an almost normal level of 38.1 mg. per cent. With the oral administration of large doses of vitamin A, the cow improved rapidly but the blood glucose again decreased. When the cow was put on "full feed," the blood glucose returned to normal very quickly, indicating that the low postpartal blood glucose was due to a lack of sufficient energy and not to a vitamin A deficiency.

In table 5, similar blood data are presented on a cow which was depleted of vitamin A but was maintained on a relatively high energy intake postpartum. The blood glucose level was quite normal for a cow receiving from 70 to 90 per cent of the required total digestible nutrient intake. No symptoms of ketosis were observed.

DISCUSSION

It is evident from the low levels of blood plasma carotene and vitamin A and the marked signs and symptoms of vitamin A deficiency in one of the cows postpartum and several of the calves at birth, that a very marked depletion of vitamin A was effected in a number of the cows during the parturient period. The fact that no symptoms of ketosis were observed and that there was no apparent relationship between vitamin A depletion and deficiency and the level of blood glucose shows that a vitamin A deficiency *per se* does not produce ketosis in cows. Superimposing fasting upon vitamin A depletion did not change this relationship. While it is preferable to determine blood ketone bodies in such studies, the fact that a hypoglycemia and typical symptoms of ketosis must exist (11) for an adequate diagnosis of ketosis makes it possible to rule out ketosis when such data do not exist. Since the degree of vitamin A depletion effected in this study seldom is observed under field conditions, it appears quite clear that the incidence of ketosis in dairy cattle is much too high to be explained on this basis even if a vitamin A deficiency did produce ketosis. It must be concluded that not only is ketosis in dairy cows, as it occurs under field conditions, not due to a vitamin A deficiency as has been reported by Patton (7) but that a vitamin A deficiency does not produce ketosis in dairy cows.

SUMMARY

Detailed observations were made on 13 cows which were maintained on a low carotene diet for approximately 4 mo. prepartum and 3 wk. postpartum. The vitamin A depletion of these cows was accentuated by the feeding of a concentrate ration containing 40 per cent soybeans which was later shown to exert a marked depressing action on blood plasma and liver vitamin A. Five of the cows received a vitamin A supplement prepartum which resulted in the birth of four normal-appearing calves. The other eight cows dropped calves which

TABLE 5

The blood glucose level of a vitamin A depleted cow on a relatively high energy intake postpartum

Date	Plasma carotene	Plasma vitamin A	Blood glucose	Per cent of T. D. N. requirements consumed	Comments
	(μg./100 ml.)	(μg./100 ml.)	(mg./100 ml.)		
6/27	38.4	7.2	45.1	159	
7/1	16.8	7.5	43.6	158	
7/4	27.0	5.4	63.5	41	Calved, calf exhibited general paralysis, extensive eye
7/5	24.6	4.2	47.5	58	hemorrhage, rapid respiration
7/8	33.6	6.9	33.6	70	Calf given vitamin A supplement
7/11	33.6	3.9	42.1	78	
7/15	24.6	4.5	27.9	80	Respiration of calf normal and eye more clear but paresis not improved
7/18	24.0	3.9	39.4	82	Calf was killed
7/22	27.0	4.8	30.5	89	
7/25	27.0	5.1	38.6	81	Cow exhibited no symptoms of ketosis
7/29	25.8	4.5	38.6	87	
8/1	30.0	6.0	41.6	86	
8/5	28.8	6.3	34.6	89	
8/8	33.6	7.2	47.8	88	

showed marked signs and/or symptoms of a vitamin A deficiency. The blood plasma vitamin A values of these eight cows were extremely low during the postpartal period and one cow exhibited marked symptoms of a vitamin A deficiency. Of the eight cows, four were maintained on a low level of energy intake for 3 wk. postpartum (50 per cent of requirements). The five cows receiving the vitamin A supplement prepartum were on the same low level of energy intake postpartum. In spite of the severe vitamin A depletion and deficiency produced in these cows, none showed symptoms of ketosis and the degree of hypoglycemia produced by partial fasting was as large in the case of the vitamin A-supplemented cows as in the vitamin A-depleted cows. The cows exhibiting a marked vitamin A depletion but receiving higher levels of energy intake postpartum exhibited normal levels of glucose during the postpartal period. None of the cows showed symptoms of ketosis. It is concluded that not only is spontaneous ketosis, as it is observed under field conditions, not due to a vitamin A deficiency but that a vitamin A deficiency *per se* does not produce ketosis in dairy cows in the postpartal period.

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