Studies on Ketosis in Dairy Cattle, XV: Response to Treatment with Cortisone and ACTH[1, 2]

J. C. Shaw, B. C. Hatziolos, and A. C. Chung

Department of Dairy Husbandry,
Maryland Agricultural Experiment Station, College Park

In 1947 Shaw (*1*) reported that an extract of the adrenal cortex was very effective for the treatment of ketosis in dairy cows. On the basis of this work, histopathologic and biochemical studies extending over a period of 4 years (*2–5*), and the effective use of cortisone in the treatment of ketosis, it was postulated (*4, 5*) that ketosis in dairy cows is due to an adrenal insufficiency involving the adrenal cortex and the anterior lobe of the pituitary gland. The gross and microscopic changes observed in the various organs showed a striking similarity to those seen in experimental animals exposed to a noxious agent, causing the alarm reaction phase of the so-called general adaptation syndrome (*6*). These include regressive changes of the anterior lobe of the pituitary gland, enlargement and degeneration of areas of the adrenal cortex, involution of the thymolymphatic system, acute involution of the pancreas, gastrointestinal inflammation and ulcers, nephrosis, and fatty changes in the liver. Seven out of 8 cows treated with cortisone recovered from ketosis. Later it was found that the cow which did not respond did not have "spontaneous" ketosis (*5*).

TABLE 1

EFFECT OF CORTISONE AND ACTH ON BLOOD GLUCOSE AND ACETONE BODIES OF COWS WITH KETOSIS*

Cow No.	Treatment with cortisone acetate (C) or ACTH	Blood glucose (G) and acetone bodies (AB) in mg/100 ml						Remarks
			Before treatment	Days after treatment				
				1	2	3	4–7	
1	0.9 g (C)	(G)	30.2	38.3	47.5			Complete recovery
		(AB)	23.1	13.6	7.5			
2	0.9 g (C)	(G)	20.3	23.8	45.5	32.9	31.5	Recovered slowly
		(AB)		33.2	14.1	17.0	10.0	
3	0.9 g (C) + 0.3 g next day	(G)	15.6	30.1	37.2	38.3	41.3	Complete recovery
		(AB)	54.8		58.4	39.6	13.1	
4	1.5 g (C) + 1.0 g on each of next 2 days	(G)	17.3	44.8	59.7	44.0	49.4	" "
		(AB)	59.5	46.6	30.3	24.5	5.1	
5	1.5 g (C) + 1.0 g next day	(G)	23.5	59.4	60.8	50.7		" "
		(AB)	56.0	43.0	32.2	6.5		
6	1.5 g (C)	(G)	34.3	44.3		51.0		" "
		(AB)	40.1	26.6		8.8		
7	1.5 g (C) + 1.0 g next day	(G)	30.8	59.1	51.6	38.3		" " †
		(AB)	37.8	29.2	25.9	20.1		
8	1.5 g (C)	(G)	18.1	41.0		41.9		" "
		(AB)	38.5	23.6		5.6		
9	1.5 g (C) + 1.0 g next day	(G)	15.4	68.0	56.1	—	52.4	" "
		(AB)	59.4	51.9	39.3	—	6.9	
10	1.5 g (C) + 1.0 g 7 hr later	(G)	23.8	89.6	69.8	55.4	50.8	" "
		(AB)	63.0	30.3	25.5	8.4		
11	1.5 g (C)	(G)	17.6	51.3	44.0	33.2	33.2	" "
		(AB)	13.5	11.2	3.5	5.6	4.2	
12	1.5 g (C)	(G)	35.1	40.5	45.6	48.3	40.0	" "
		(AB)	18.9	13.6	13.5	10.5	4.6	
13	1.5 g (C)	(G)	20.3	53.2	43.5	42.4	45.4	" "
		(AB)			26.8	4.4	3.9	
14	1.5 g (C)	(G)	32.1	43.7	44.8	45.9	45.0	" "
		(AB)	47.2	47.9	41.6	35.7	6.5	
15	1.0 g ACTH	(G)	27.3	61.3	32.7	43.9	34.3	Initial recovery‡
		(AB)	27.9	32.2	23.8	20.6	22.3	followed by relapse
16	1.0 g ACTH + 1.0 g (C) 3 days later	(G)	15.4	86.7	42.7	44.0	47.0	Complete recovery
		(AB)	38.4	32.4	23.8	29.7	9.9	

* All cows recovered appetite within 24 hr after treatment.
† Urine Rothera test negative on 5th day.
‡ Recovered following additional treatments with ACTH and cortisone.

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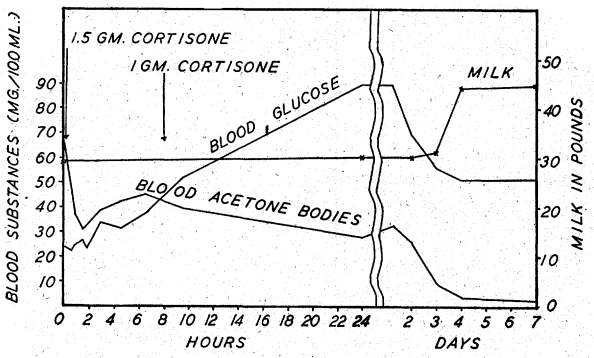

FIG. 1. Response of a cow with "spontaneous" ketosis to cortisone.

In the diagnosis of "spontaneous" ketosis the following criteria were used: hypoglycemia, ketonemia, refusal of feed, rapid loss in body weight, decreased milk production, incoordination, and either marked lethargy or high excitability. In addition, total leucocyte counts were made, and the rectal temperature was taken as an aid in detecting infections such as metritis. This report deals only with uncomplicated cases of ketosis. Blood glucose and acetone bodies were determined before treatment and at varying intervals after treatment. The methods used were the same as given previously (*7*).

The data on 14 cows with ketosis treated with a saline suspension of cortisone acetate (Cortone—Merck) and 2 cows treated with ACTH are given in Table 1. Both preparations were injected intramuscularly. In most cases there was a marked improvement in appetite within 18–20 hr. Within 48 hr the appetite was usually quite normal. Signs of incoordination and paresis always disappeared within 24 hr. The blood glucose usually increased to a level considerably above normal within 24 hr and frequently was above normal for 2 or 3 days. The blood acetone bodies returned to normal more slowly. The usual pattern was for the acetone bodies to continue at a high level for 2 or 3 days followed by a sharp drop to normal on the fourth or fifth day. The intramuscular injection of 1.5 g of cortisone was sufficient to produce complete recovery in the 6 cases so treated and recorded in Table 1. The administration of an additional gram a few hours later to Cow 10 and one day later to Cows 5, 7, and 9 appeared to be the most effective treatment. Cow 4 received 1 g/day for 2 additional days because the response was not marked until the second day after treatment.

In one case the blood glucose and acetone bodies were determined at frequent intervals following the injection of 1.5 g of cortisone with an additional gram being injected 7 hr later. It will be noted from Fig. 1 that the blood glucose increased markedly within 3 hr and was almost normal within 7 hr, when an additional gram was injected. On the following day the blood glucose was almost twice normal as a result of the rather large total dosage (2½ g) given during the first day. The blood acetone bodies did not return to normal until the fourth day after the initial treatment. Milk production likewise did not change appreciably until the fourth day, when a marked increase was noted. To date 25 cases of uncomplicated "spontaneous" ketosis have been treated with cortisone, and all have recovered completely, although it was necessary to administer cortisone as many as three to four times where relapses occurred.

Two cases were treated with 1 g of corticotropin (ACTH). Recovery of appetite, increase in milk production, and increase in blood glucose was similar to that obtained with cortisone. Additional treatment was required in each case before recovery was complete. Both cows had histories of previous attacks and had responded to dextrose treatment very slowly, so it cannot be concluded on the basis of these results that cortisone is any more effective than ACTH.

Some observations of considerable interest were made on normal and fasted lactating cows. Cortisone acetate was administered intramuscularly to 3 normal cows on an adequate energy intake and to 2 cows receiving 30% of the calculated net energy requirements for 5 days prior to and 1 day following injection (Table 2). Cortisone had little effect on the blood

TABLE 2

EFFECT OF CORTISONE ON THE BLOOD GLUCOSE LEVEL OF COWS NOT EXHIBITING "SPONTANEOUS" KETOSIS

Cow	Cortisone acetate injected	Blood glucose in mg/100 ml											
		Days before injection				Day of injection	Days after injection						
		4	3	2	1	0	1	2	3	4	5	6	7
Full-fed cows													
A	1.5 g					52.7	60.8	58.3					
B	1.0 g + 1.0 g next day			52.4	53.2	40.8	38.9	51.5					
C	3.0 g			50.0	55.8	45.1	55.9	55.4					
*Cows fasted before injection**													
D	1.5 g	59.1	55.6	34.6		36.5	93.4	78.8	69.7	60.2	57.5	52.1	58.6
E	1.5 g	44.0	36.2	27.0	31.3	27.3	79.1	64.8	62.1	54.8	52.1	52.1	53.2

* Beginning 3 weeks postpartum received 30% of net energy requirements for 5 days before and for 1 day after injection of cortisone acetate.

glucose of the normal cows even when as much as 3 g was administered in one dose. However, the injection of 1.5 g of cortisone into each of the 2 fasted cows resulted in a marked increase in blood glucose. This increase in the glucose was greater and was maintained at a higher level for a longer period of time than that observed in most cows with "spontaneous" ketosis that received the same amount of cortisone. A fasting ketosis was evident in these 2 cases, but the cows appeared to be quite normal otherwise. This was to be expected, since much more severe fasting has resulted in a marked hypoglycemia and ketonemia but has failed to produce the signs and symptoms typical of "spontaneous" ketosis (*8*).

It might be postulated that cortisone cures ketosis in cows purely because of the marked hyperglycemic effect of cortisone on fasted cows. The gross and histopathologic changes observed in cows with ketosis indicate a pituitary and adrenal involvement, however. Also, when smaller doses of cortisone have been used, the physical appearance of the cow has shown definite improvement before blood glucose increased. For example, Cow 2 in Table 1 exhibited a complete recovery of appetite and disapperance of incoordination within 20 hr after treatment with 900 mg of cortisone, even though blood glucose did not increase appreciably until the following day.

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Parthenogenetic Reproduction in *Phytomyza plantaginis* R.-D., the Second Reported Case in the Family Agromyzidae (Diptera)

Kenneth E. Frick

Irrigation Experiment Station,
The State College of Washington, Prosser

Hering (*1*) reported reproduction without males in *Phytomyza crassiseta* Zett., having caged unfertilized females with their host plant, *Veronica* sp. From these he obtained more females. He pointed out that it is exceptional to find a male in north Germany, whereas in south Europe the natural population consists of about 50% males.

Hering found it difficult to explain why parthenogenesis had not been found in the closely related *P. plantaginis* in Europe. Frost (*2*) mentions both sexes in describing the species from eastern North America. However, when the writer found that 125 adults reared from larvae mining the leaves of *Plantago lanceolata* L. in central California proved to be females, he set up a laboratory experiment to test the possibility of parthenogenetic reproduction in this species.

A specimen of plantain, free of larvae of the leaf miner, was transplanted into a gallon jar. Forty-six females, all reared from pupae obtained from Santa Cruz, Calif., and examined for sex, immediately upon emergence were introduced into the jar. After about 10 days a large number of mines appeared on the leaves. From these, 13 females were obtained, in addition to numerous larvae and pupae that were killed and preserved. The 13 females were then introduced into another jar containing plantain, from which 8 larvae were obtained. The experiment had to be terminated at this point.

A preliminary study of the reproductive system of those females producing viable eggs has shown the spermotheca to be present, indicating the possibility of fertilization in the presence of males. A study of the morphological basis for this phenomenon will be reported in another paper.

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Observations on the Apparent Failure of Beer's Law Near the Transmission Limit of a Solvent

J. M. Vandenbelt, Carola Henrich, and Shirley L. Bash

The Research Laboratories,
Parke, Davis & Company, Detroit, Michigan

A recent paper by Ungnade, Kerr, and Youse (*1*) reports variations in the extinction coefficient of phenol with change in solute concentration, which the authors ascribe to a failure of Beer's law. They obtained log ε values of 3.00 to 3.68 (ε = 1,000 to 4,790) for the 218–219 mμ primary (*2*) band, and a shift in the maximum to 225 mμ at the highest concentration. Since deviations of this magnitude are not usual in spectrophotometric practice, observations were made on the compound to investigate the response of our own Beckman spectrophotometer under the given conditions.

Solutions of phenol in 95% ethanol were prepared over the concentration range employed by Ungnade, Kerr, and Youse, and the absorption curves were determined, using a constant slit width of 1.0 mm through the maximum of the primary band. Variations in the absorption of this band were generally like those observed by Ungnade, Kerr and Youse—namely, a substantial decrease in intensity and an apparent shift of the maximum to 222 mμ. However, the extinction coefficient of the secondary band maxi-