CLINICAL AND BIOCHEMICAL STUDIES ON THE BASIS OF KETONE BODIES IN CATTLE

IV. OBSERVATIONS IN CATTLE AFFECTED WITH VARIOUS DISEASES

Tsukasa SAKAMOTO, Mitsuo SONODA
and Ryoichi NAKAMURA

Department of Internal Veterinary Medicine,
Faculty of Veterinary Medicine,
Hokkaido University, Sapporo, Japan

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INTRODUCTION

Recently, it has been thought that ketosis is one of the diseases belonging to the so-called "general adaptation syndrome" caused by the hormonal unbalance of the pituitary-adreno-cortical system resultant from some internal or external stress. The authors[12,18,19] have reported with special reference to the ketone bodies, blood sugar and eosinophile leucocytes in clinically healthy cows and compared between the various simplified tests for quantitative estimation of ketone bodies in urine. As a result of the investigations, a special group called "sub-normal group", so named by the authors, was pointed out; it was considered that this group coincided with the phase of the functional increase in the pituitary-adreno-cortical system caused by stress as reported by SELYE. In parallel with those studies, investigations on the basis of the ketone bodies in cattle affected with various diseases were conducted and the findings were compared with those of the normal cattle. In this paper, the results of the investigations are described.

MATERIALS AND METHODS

The cases were 171 cows affected with various diseases, which were brought to the veterinary clinic of this faculty. The experimental methods employed on the blood and urine were just the same as those described in a previous report.[17]

RESULTS OF THE INVESTIGATIONS

1. Values of the Blood Total Ketone

In comparison of the mean values of all affected groups with 3.11 mg/dl, the mean value of the normal group, the present ascertained values decreased only in mercurial poisoning but the value of the infertility group was 3.20 mg/dl, which is nearly approximately

TABLE 1. *Blood Ketone Values in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN VALUE OF KETONE (mg/dl)	RANGE (mg/dl)
Digestive	Enterocolitis	9	4.17	1.80～ 6.89
	Acute gastric dilatation	6	5.84	2.09～13.53
	Impaction of rumen	26	4.89	0.49～14.76
	Traumatic gastritis	13	3.93	2.58～ 6.89
	Acute tympanites	1	5.17	·
	Omasum atonia	11	12.30	2.75～25.83
	Total	66	5.94	0.49～25.83
Respiratory	Pneumonia	3	5.45	4.80～ 6.77
	Bronchial catarrh	8	15.95	13.24～66.42
	Total	11	13.08	4.80～66.42
Urinary	Bacterial pyelonephritis	9	9.43	2.21～23.53
	Bovine hematuria	4	9.42	1.35～30.75
	Total	13	9.43	1.35～30.75
Metabolic	Milk fever	7	8.08	2.83～20.91
	Postparturient unrising	3	43.34	4.55～68.88
	Parturient hemoglobinuria	7	9.31	3.08～28.29
	Ketosis	8	43.62	23.53～73.83
	Total	25	24.01	2.83～73.83
Infertility	Ovarial hypofunction	27	3.29	1.72～ 5.04
	Endometritis	6	3.48	2.95～ 4.31
	Ovarial cyst	3	1.80	1.60～ 2.21
	Total	36	3.20	1.60～ 5.04
Others	Mercurial poisoning	6	1.38	0.37～ 1.97
	Surgical operation	4	5.12	4.06～ 7.26

to the mean value of the normal group. In other affected groups, they were 5.12 to 24.01 mg/dl respectively, all showing increase by 65 to 672% over the value of the normal group. Especially, remarkable increase was found in the groups of metabolic, respiratory and urinary diseases. Furthermore, judging from the discrimination of the

diseases, the mean values of all diseases with the exception of ovarial cyst and mercurial poisoning increased than the mean value of the normal group. Notably, in omasum atonia of the digestive diseases, in bronchial catarrh of the respiratory diseases, in ketosis and postparturient paresis of the metabolic diseases, the mean blood ketone values were 12.30 to 43.62 mg/dl respectively, that is: they increased by 296 to 1,303% in comparison with the values of the normal group. Observing the range of the distribution of the ketones on the basis of 11.17 mg/dl, the value of the upper limit of the normal group, they showed apparent increases in omasum atonia, impaction of rumen and acute gastric dilatation, bronchial catarrh, bacterial pyelonephritis and bovine hematuria.

Particulary, great increases were found in such metabolic disorders as milk fever, postparturient unrising, parturient hemoglobinuria and ketosis respectively. However, in enterocolitis, acute tympanites and traumatic gastritis in the digestive disorders, all diseases belonging to the infertility group, mercurial poisoning and surgical operation, the ascertained values ranged under the upper limit of the normal group.

From the above results, it may be generalized that the blood total ketone values increased in the various diseases not only in the mean values but in the range of the distribution excepting mercurial poisoning, infertility, and certain diseases of the digestive system.

TABLE 2. *Blood Acetone Values in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN VALUE OF ACETONE (mg/dl)	RANGE (mg/dl)
Digestive	Enterocolitis	4	1.61	0.53~ 2.70
	Acute gastric dilatation	1	2.70	·
	Impaction of rumen	4	1.02	0.18~ 1.58
	Traumatic gastritis	5	1.45	0.90~ 1.89
	Omasum atonia	1	3.15	·
	Total	15	1.57	0.18~ 2.70
Urinary	Bacterial pyelonephritis	2	2.37	1.60~ 3.15
Metabolic	Parturient hemoglobinuria	2	2.38	0.81~ 3.94
	Ketosis	4	18.51	16.50~23.37
	Total	6	13.30	0.81~23.37
Infertility	Ovarial hypofunction	1	0.60	·
	Endometritis	2	0.77	0.67~ 0.90
	Total	3	0.72	0.60~ 0.90

2. Values of the Blood Acetone

On the basis of the classification of the disease groups, the mean values of 3 groups, with the exception of the value of the infertility group, were 1.57 to 13.30 mg/dl, which show increases by 99 to 1,584% in comparison with 0.79 mg/dl, which is the mean value of the normal group; especially the increase was marked in the group of the metabolic disorders. Also, in the differentiation of the disease, the values of all diseases excepting the infertility group were increased; especially in ketosis the rate of increase was marked. But examining the range on the basis of the upper limit of the normal group or 4.53 mg/dl, one may see that all of the values of the 4 cases of ketosis increased over the upper limit but in other diseases all of the maximum values of the range showed under the upper limit of the normal group.

From the above results, it may be seen that the blood acetone mean values increased in all diseases excepting infertility group, and all the values of ketosis cases were over the upper limit but in other diseases, they fluctuated within the range of the normal group.

3. Values of the Urine Total Ketone

Examining the mean values of the disease groups on the basis of 6.19 mg/dl, the mean value of the normal group, they increased by 11 to 1,511% in all groups excepting mercurial poisoning, especially they increased markedly in metabolic, respiratory and urinary disease groups. Next, regarding the rise and fall of the ketone values in discrimination of the disease, they decreased in endometritis and ovarial cyst out of the infertility group and also in mercurial poisoning, but in all other diseases they increased. After that, in comparison of the range of the distribution on the standard of the upper limit of the normal group, namely 43.41 mg/dl, the range of each of the cases of enterocolitis, traumatic gastritis, pneumonia, infertility, mercurial poisoning and surgical operation showed values less than the upper limit but in other diseases, the values of the urine ketones showed a distribution over the upper limit.

From the above observations, it may be seen that the urine ketone values increased in all disease groups excepting infertility and mercurial poisoning. Especially the rate of the increases were marked in the metabolic, respiratory and urinary diseases.

4. Values of the Urine Acetone

As a result of the comparison of the urine acetone values of the disease groups on the basis of the mean urine acetone value of the normal group, which showed 1.25 mg/dl, the mean values of each group with the exception of 2 groups such as infertility and surgical operation may be stated to range between 3.09 to 28.23 mg/dl, that is; in all disease groups, especially in the metabolic and urinary diseases increased prominently. Secondly, observing from the discrimination of the disease in each disease group, the mean values of the enterocolitis from among the digestive diseases and of the endometritis from among

TABLE 3. *Urine Ketone Values in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN VALUE OF KETONE (mg/dl)	RANGE (mg/dl)
Digestive	Enterocolitis	9	7.60	4.61～ 14.76
	Acute gastric dilatation	6	28.22	6.52～135.00
	Impaction of rumen	26	12.10	2.46～ 60.27
	Traumatic gastritis	13	6.28	3.20～ 12.30
	Acute tympanites	1	9.84	·
	Omasum atonia	11	27.90	3.08～ 58.04
	Total	66	10.11	2.46～135.00
Respiratory	Pneumonia	3	8.82	7.26～ 11.07
	Bronchial catarrh	8	57.65	5.29～233.00
	Total	11	44.33	5.29～233.00
Urinary	Bacterial pyelonephritis	9	39.56	3.03～147.60
	Bovine hematuria	4	22.21	3.33～ 72.60
	Total	13	34.22	3.03～147.60
Metabolic	Milk fever	7	37.09	3.36～123.00
	Postparturient unrising	3	171.39	7.29～274.60
	Parturient hemoglobinuria	7	21.86	3.24～ 89.79
	Ketosis	8	199.33	104.55～282.90
	Total	25	99.75	3.24～282.90
Infertility	Ovarial hypofunction	30	8.22	2.71～ 15.99
	Endometritis	8	5.38	3.08～ 9.84
	Ovarial cyst	4	4.52	2.95～ 5.90
	Total	42	7.32	2.71～ 15.99
Others	Mercurial poisoning	6	2.51	1.60～ 3.32
	Surgical operation	4	7.13	5.41～ 11.68

the infertility group were 1.11 mg/dl and 0.94 mg/dl respectively; they decreased by 11.2 and 24.8% in comparison to the mean value of the normal group, but in other diseases, all of the mean values increased. On the other hand, in a comparison of the upper limit of the normal group or 24.95 mg/dl, in the diseases such as enterocolitis, traumatic

TABLE 4. *Urine Acetone Values in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN VALUE OF ACETONE (mg/dl)	RANGE (mg/dl)
Digestive	Enterocolitis	6	1.11	0.60～ 2.18
	Acute gastric dilatation	1	29.50	•
	Impaction of rumen	12	5.04	0.42～ 33.21
	Traumatic gastritis	6	3.32	0.90～ 6.53
	Omasum atonia	4	6.85	2.41～ 11.80
	Total	29	3.09	0.42～ 33.21
Respiratory	Pneumonia	3	6.32	6.30～ 6.50
	Bronchial catarrh	4	16.26	2.40～ 52.50
	Total	7	12.07	2.40～ 52.50
Urinary	Bacterial pyelonephritis	3	29.34	10.08～ 38.61
	Bovine hematuria	3	5.75	0.60～ 15.30
	Total	6	17.54	0.60～ 38.61
Metabolic	Milk fever	7	11.28	0.82～ 50.25
	Postparturient unrising	3	23.37	0.90～ 36.00
	Parturient hemoglobinuria	5	7.45	0.92～ 17.64
	Ketosis	8	57.85	24.00～150.00
	Total	23	28.23	0.82～150.00
Infertility	Ovarial hypofunction	2	1.38	0.90～ 1.86
	Endometritis	4	0.94	0.45～ 0.95
	Total	6	1.08	0.45～ 1.86
Other	Surgical operation	4	1.25	0.39～ 3.38

gastritis, omasum atonia, pneumonia, bovine hematuria, parturient hemoglobinuria, ovarial hypofunction, endometritis and surgical operation, the rise and fall of the urine acetone ranged under the upper limit of the normal group, but in other diseases they all exceeded the upper limit.

From the above results, it was clear that urine acetone values showed increasing tendencies in the various diseases excepting the 2 groups of infertility and surgical operation.

TABLE 5. *Blood Sugar Levels in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN VALUE OF BLOOD SUGAR (mg/dl)	RANGE (mg/dl)
Digestive	Enterocolitis	9	62	29～ 80
	Acute gastric dilatation	6	68	55～ 85
	Impaction of rumen	26	68	42～110
	Traumatic gastritis	13	80	50～142
	Acute tympanites	1	62	·
	Omasum atonia	11	67	23～120
	Total	66	69	23～142
Respiratory	Pneumonia	3	65	60～ 70
	Bronchial catarrh	8	69	45～ 80
	Total	11	66	45～ 80
Urinary	Bacterial pyelonephritis	9	67	58～102
	Bovine hematuria	4	92	29～185
	Total	13	75	29～185
Metabolic	Milk fever	7	90	80～103
	Postparturient unrising	3	60	52～ 68
	Parturient hemoglobinuria	7	53	42～ 70
	Ketosis	8	44	20～ 57
	Total	25	64	20～103
Infertility	Ovarial hypofunction	26	68	32～106
	Endometritis	7	60	27～105
	Ovarial cyst	3	80	30～133
	Total	36	67	27～133
Others	Mercurial poisoning	6	96	60～144
	Surgical operation	4	66	43～103

5. Values of the Blood Sugar

The mean values of the blood sugar for the groups in the various diseases ranged between 64 to 96 mg/dl. They were highest in mercurial poisoning and were lowest in

TABLE 6. *Numbers of Eosinophile Leucocytes in Various Diseases*

GROUP	DIAGNOSIS	NO. OF CASES	MEAN NO. OF EOSINOPHILE LEUC.	RANGE
Digestive	Enterocolitis	3	497	320～ 630
	Acute gastric dilatation	5	300	0～ 600
	Impaction of rumen	10	267	25～ 800
	Traumatic gastritis	13	340	0～ 400
	Omasum atonia	11	259	50～ 800
	Total	42	308	0～ 800
Respiratory	Pneumonia	2	200	200
	Bronchial catarrh	6	713	120～1,250
	Total	8	585	120～1,250
Urinary	Bacterial pyelonephritis	3	513	180～ 800
	Bovine hematuria	2	660	660
	Total	5	572	180～ 800
Metabolic	Milk fever	2	95	51～ 140
	Postparturient unrising	3	1,017	400～1,150
	Parturient hemoglobinuria	2	800	0～1,600
	Ketosis	8	1,270	800～1,800
	Total	15	750	0～1,800
Infertility	Ovarial hypofunction	35	504	45～1,440
	Endometritis	3	515	310～ 888
	Ovarial cyst	3	1,062	288～1,960
	Total	41	549	45～1,960
Others	Mercurial poisoning	6	631	0～2,016
	Surgical operation	4	82	0～ 120

the metabolic diseases but they were all higher than the mean value of the blood sugar in the normal group or 60.6 mg/dl. But in the observations under the discrimination of the disease, in the cases of postparturient unrising, parturient hemoglobinuria and ketosis from among the metabolic disease, especially in ketosis, the rate of the decrease was extreme. The distribution of the blood sugar values in the various diseases extended above

mean value very widely, but in ketosis, the values of the blood sugar ranged less than the mean value for the normal group; they fluctuated between 20 to 57 mg/dl.

From the above observation, it may be stated that the values of the blood sugar in ketosis showed a tendency to marked decrease.

6. Number of Eosinophile Leucocytes

Observing the classification of the disease groups, one sees that the mean numbers of the eosinophile leucocytes ranged between 82 to 750 per 1 mm^3 of blood. Namely, in the 2 groups of the digestive diseases and surgical operation, the numbers of the eosinophile leucocytes showed markedly less than 485, the mean values of the normal group. But in other disease groups, the numbers all increased. From amongst them, the values of the metabolic disease group were much the largest. In addition, in comparing the discrimination of the disease, the mean values of the digestive diseases excepting enterocolitis, of pneumonia, of milk fever and of surgical operation showed less than those of normal group but in all other diseases, they showed increase. The rate of increase was by far the largest in ketosis. In the range of the distribution, the values fluctuated within a very wide range. But in ketosis, the numbers of the eosinophile leucocytes ranged between 800 to 1,800; the values of all ketosis cases were over the mean value of the normal group.

From the above data, it may be said that the number of eosinophile leucocytes in the various diseases rose and fell within a very wide range, but in ketosis all cases revealed a tendency of increase in eosinophile leucocytes.

Discussion

In these experiments, it was clarified that the total ketone and also free acetone contents of blood and urine in cases of cattle affected with various diseases presented very wide variations from disease to disease. Already, Bailey and others[2,5~8,11,13~15] have reported that the ketone bodies in the blood or urine, increased in such diseases e. g., chronic indigestion, traumatic gastritis, endoparasitic diseases, peritonitis, pneumonia, pyelonephritis, mastitis, metritis, retained placenta, hydrops of the allantois, milk fever and cobalt-, vitamin A-and B-deficiencies. Also the increases of the ketone bodies were found in Johne's disease by Glenny[5] and in anaplasmosis by Lopez-Pacheco. Considering from the authors' data and the references, the differential diagnosis between clinical ketosis and the diseases complicated by ketonemia or ketonuria was very difficult but clinically, such differential diagnosis is very important. Especially, amongst these complicated diseases, the digestive disorders and milk fever may come into question, because their respective syndromes resemble that of ketosis. Fox and McAuliff reported that in the differentiation between ketosis and milk fever in regular practice, the pupillary reaction to light is very important. There is a reflex reaction in ketosis, but this reflex is absent in milk fever. By Sampson[13] acetonemia was

classified into 2 groups such as complicated and uncomplicated ones and he said if hypoglycemia and ketonemia are corrected by suitable carbohydrate therapy and the cow does not recover, it is usually safe to conclude that the animal either is in an advanced stage of acetonemia or, what is more probable, that she is also affected with one or more complicating conditions. Also CRAIGE stated in the differential diagnosis among true acetonemia and other diseases resemblant to ketosis in clinical syndromes, the cases which respond to intravenous injection of 50% dextrose for as long as 24 hours may be diagnosed as true acetonemia. ROEPKE proposed that a 1 : 10 dilution of the urine before using it in the Ross test would help eliminate the cases which are not primary ketosis. On the other hand, SHOW[16] said that the urine test alone is not infallible in diagnosing ketosis. To judge from only the increase in the ketone values of blood or urine in diagnosing of ketosis is very dangerous because there is a special group such as "sub-normal group" which showed increase of the ketone bodies in clinically healthy cattle, and also the ketone values for cattle affected with various diseases displayed a very wide range. In ketosis from the present data, comparing with other diseases, not only increases of the ketone bodies in the blood or urine but decrease of the blood sugar and increase of eosinophile leucocytes were noteworthy. Conjecturing from the reports of PUNTRIANO and SHOW et al.,[17] it will be thought that in the sub-normal group, the function of the adrenal cortex is increasing, but in ketosis it is decreasing, and the results obtained in the various diseases is due to the hormonal unbalance in the various degree of the pituitary-adreno-cortical system. In other words, it may be seen that ketosis is one of the diseases situated in the stage of exhaustion in the general adaptation syndrome, and the "sub-normal group" which showed not only increase of ketone bodies but also increase of the blood sugar and marked decrease in number of eosinophile leucocytes situated in the stage of resistance, namely it is in a condition one step before ketosis. These mutual relations are summarized as shown in table 7. Up to this time, in this country as a result of attaching great importance to only the rise and fall of the ketone bodies in diagnosing ketosis veterinarians may have often fallen in to great confusion in the differential diagnosis of the cattle diseases.

From the above described data, the authors think that in diagnosing ketosis, not only the rise and fall of the values of the ketone bodies but the estimation of blood sugar values and the eosinophile leucocytes and also the clinical inspections are indispensable factors.

Furthermore, considering the internal and external factors which exert an influence upon the rise and fall of the ketone value, so-called pathological ketonemia or ketonuria, namely, true clinical ketosis and physiological or

TABLE 7. *Differential Diagnosis in Various Diseases*

GROUP		CLINICAL SYMPTOM	VALUE OF KETONE BODY	LEVEL OF BLOOD SUGAR	NO. OF EOSINOPHILE LEUCOCYTE
Clinically healthy cow	normal	−	Normal	Normal	Normal
	sub-normal	−	Increase	Increase	Decrease
Ketosis		+	Increase	Decrease	Increase
Various diseases		+	Normal~Increase	Decrease~Increase	Decrease~Increase

Note { +……indicates the presence of symptoms.
−……indicates lack of symptoms.

complicated ketonemia or ketonuria, must be exactly differentiated.

SUMMARY

A study was made by the authors on the basis of the ketone bodies in 171 cases affected with various diseases, and the results thus obtained may be summarized as follows.

1. The blood total ketone values increased in the various diseases not only in mean values but also in the range of the distribution with the exception of some diseases such as mercurial poisoning and infertility.

2. The blood acetone mean values increased in all diseases excepting infertility group; but in the range of the acetone values of all diseases excepting ketosis which were all over the upper limit of the normal group, the blood acetone values fluctuated within the range of the normal group.

3. The urine total ketone values increased in all of the disease groups, especially in metabolic, respiratory and urinary diseases but with the exception of infertility and mercurial poisoning.

4. The urine acetone values showed increasing tendencies in the various diseases excepting 2 groups, viz., infertility and surgical operation.

5. The blood sugar levels for the various diseases ranged so widely that they fluctuated between 20 to 185 mg/dl; their mean values were within 53 to 96 mg/dl. In ketosis they ranged between 20 and 57 mg/dl and their mean value was 44 mg/dl. That is blood sugar levels decreased markedly.

6. The numbers of eosinophile leucocytes in the various diseases rose and fell within a very wide range but in ketosis all cases showed tendencies to increase.

7. Considering from the authors' results, examinations of the blood sugar values, of the number of eosinophile leucocytes and cilinical inspection as well as estimation of the ketone bodies of the blood or urine are to be considered indispensable factors in the differential diagnosis of ketosis and other diseases.

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