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PATHOLOGICAL STUDIES ON MERCURY POISONING IN CATTLE

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INTRODUCTION

In 1955, between early February and late May, a disease of unknown cause in dairy cows with dyspnea occurred sporadically in Monbetsu City, Hokkaido. The disease occurred in Kamishokotsu, Nakashokotsu, Shokotsu (in Monbetsu City) and Okoppe Town. The total affected cases were 29 of which 10 died or were slaughtered (Loss percentage: 34.48%).

The main symptoms were high fever (about 40°C) which continued for 2 or 3 weeks, severe dry cough, dyspnea, reduction of appetite and lactation, marked lachrymation and salivation, depilation and eczema which were often observed in every part of the body surface and petechiae in visible mucous membranes, etc.

As for the cause of the disease, infection and poisoning were suspected by practitioners and the authors consequently investigated these 2 points from every possible angle. However, the bacteriological and virological investigations conducted at the Laboratory of Veterinary Hygiene and Microbiology, Faculty of Veterinary Medicine, Hokkaido University concerning the former were negative in result. As for the latter suspected cause, linseed meal poisoning produced by linseed which had been treated with Ceresan (a mercurial fungicide) was suspected. Therefore, the animal experiments were carried out at the Monbetsu Animal Health Center and the Laboratory of Veterinary Internal Medicine, Faculty of Veterinary Medicine, Hokkaido University.

The present authors fortunately had the opportunity of conducting the pathological investigation on the disease and were able to confirm it as mercury poisoning. The following are the descriptions of the disease; any comment made on this report will be welcomed by the authors.

OCCURRENCE

Areas and the number of affected cases are as shown in table 1.

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TABLE 1. Occurrence in Each Area

AREA	AFFECTED		DIED OR SLAUGHTERED		CASES PATHO- LOGICALLY INVESTIGATED	
	Cases	Houses	Cases	Houses		
Monbetsu City	Kamishokotsu	12	6	5	4	4
	Nakashokotsu	6	3	2	1	2
	Shokotsu	8	5	0	0	0
	Total	26	14	7	5	6
Okoppe Town		3	3	3	3	2
Total		29	17	10	8	8

The sort of feeds was varied depending on the affected cows although linseed meal had been the common feed used by each farmer. The suspected linseed meal which is considered to be mixed with Ceresan, was brought into these areas between January 17 and February 2, 1955. One hundred seventy one cows (46 houses) were fed this linseed meal and 29 of them (17 houses) were affected. The duration of illness varied from 1~43 days in the 10 died or slaughtered cases.

MATERIALS AND METHODS

The investigated materials are listed in table 2. They comprised 10 cases in total: 8 natural (6 died, 2 slaughtered) and 2 experimental cases (1 died, 1 slaughtered).

After the post mortem examination was made, tissues were fixed in 10% formol solution and some of them were fixed with a mixture of alcohol, formol and acetic acid. Paraffin or frozen sections were prepared. Sections were subjected to various types of staining such as with hematoxylin-eosin stain, WEIGERT stain for elastic fiber, VAN GIESON stain

TABLE 2. Investigated Materials

CASE NO.	AUTOPSY NO.	SEX	AGE	NAME	DATE OF AUTOPSY MADE	TERMI-NATION	LOCALITY	MATERIAL
1	E1676	♀	4	W.N.	2/III	†	Monbetsu	Natural case
2	3615	"	5	B.K.	9/III	κ	"	"
3	E1679	"	10	Z.I.	10/III	†	Okoppe	"
4	E1684	"	8	N.S.	19/III	"	"	"
5	E1685	"	5	I.A.	24/III	"	Monbetsu	"
6	E1688	"	7	H.K.	26/III	κ	"	"
7	E1704	"	11	K.A.	11/IV	†	"	"
8	E1719	"	8	O.K.	12/V	"	"	"
9	3624	♂	7M.	Exp. 1	24/V	κ	Monbetsu Animal Health Center	Experi-mental case
10	3625	"	"	Exp. 2	7/VII	†	Lab. Vet. Int. Med., Hokkaido, Univ.	"

for collagen fiber, OKA's modification of BIELSCHOWSKY's silver impregnation for argyrophile fiber, Azan stain (HEIDENHEIN's modification), GIEMSA stain, thionine stain, Sudan III stain and MCMANUS's periodic acid SCHIFF reaction (PAS) for polysaccharides.

The dithizon method for detection of mercury was carried out in tissues, feed and body fluids. Materials were then measured by photoelectric colorimeter.

RESULTS

Natural Cases

Case 1

Clinical History

A cow, aged 4, had an attack of dyspnea, dry cough, lachrymation and high fever (40.5 C) on February 16, 1955. On February 26, purulent nasal discharge and continued high fever were noted. Two days later she rapidly become worse while accelerated heart beat and weak pulse were observed. Pulse rate was 110 and respiratory count was 80. Milk yield was gradually decreased until her death after another 2 days.

Anatomical Diagnosis

1) *Bronchitis catarrhalis subacuta*. 2) *Nephritis interstitialis subacuta*. 3) Medullary swelling and edema of general lymph nodes. 4) Enlargement of splenic follicles. 5) Slight hepatic cirrhosis. 6) General venous congestion and edema.

Histological Appearances

Multiple focal necroses, passive hyperemia and peripheral fatty infiltration were observed in the liver. Endothelia were swollen and increased. Sometimes karyorrhexis and PAS positive granules of these cells were noted. GLISSON's sheath tissues were proliferated and eosinophils, lymphocytes and histiocytes were accumulated. Sometimes PAS positive multinucleated giant cells appeared. At the same time *endophlebitis obliterans et productiva chronica* was present. In the spleen, Malpighian corpuscles were enlarged and multinucleated giant cells were proliferated. Hemosiderosis was noted. Cellular infiltration was conspicuous in the renal interstitial tissue. The infiltrating cells were composed mainly of histiocytes with included giant cells, lymphocytes, eosinophils and neutrophils. Marked congestion, hemorrhage and edema were noted in the renal interstitium. A protein deposit filled BOWMAN's capsular spaces. Necrobioses and marked infiltration were found in the convoluted tubules and HENLE's loop (*Pars recta*). In the lung, congestive edema, hemorrhage and subacute catarrhal bronchiolitis and bronchitis were observed. The lymph nodes showed blood resorption, *lymphadenitis catarrhalis* and sometimes giant cells in the follicles.

Case 2

Clinical History

A cow, aged 5, was afflicted by high fever (40.1°C), dyspnea, dry cough, severe lachrymation and salivation on February 16, 1955. High fever continued. Appetite and lactation were decreased. Eczema appeared in the lower part of the abdomen and udder. On March 3, the body temperature showed 38.4 C, pulse rate was 100 and respiratory count was 28. The animal then showed a marked loss of appetite and could hardly stand.

Depilation in back regions and eczema in udder were recognized. Hemorrhagic diarrhea, serous nasal discharge, petechiae, dyspnea and accelerated heart beat were noted. A blood count showed erythrocytes 1.45 mill., leucocytes 9,400.

Anatomical Diagnosis

- 1) Multiple petechiae in general serous and mucous membranes.
- 2) Subendocardial hemorrhage and increased pericardial fluid.
- 3) *Bronchitis catarrhalis subacuta*.
- 4) Medullary swelling and edema in general lymph nodes.
- 5) Enlargement and multiple petechiae in the liver.
- 7) Gelatinous infiltration and hematoma in cervical and thoracic regions.
- 8) Petechiae in the small intestine and hemorrhage in gastric subserosa and submucosa.
- 9) General anemia and yellowish bone marrow.

Histological Appearances

The liver showed venous congestion with focal hemorrhages and multiple focal necroses of the parenchyma, most marked around the central veins. Marked hepatic fatty infiltration was present especially in the necrotic and their peripheral regions. Red pulp was congested, showed bleeding. The follicles were enlarged and giant cells were often found in them. Scattered focal interstitial accumulation consisting mainly of histiocytes accompanied by lymphocytes were present especially in the perivascular and periglomerular areas of the kidneys. Fatty infiltration was noted in the convoluted tubules and HENLE'S loop. Marked hemorrhages had occurred in the subepicardium, subendocardium and myocardium. Particularly the auricles were extensive. A large number of eosinophils was found throughout these lesions, in which histiocytes were also present as well as scattered neutrophil polymorphonuclears. Moreover, subacute catarrhal bronchitis, catarrhal lymphadenitis, congestion and hemorrhages in the alimentary canal were noted. In the eczematous skin lesions, keratinization of epidermis was shown and neutrophils were infiltrated. Hemorrhage, hyperemia and perivascular histiocytic infiltration were conspicuous in the subcutaneous tissue. Submeningeal and parenchymatous hyperemia and hemorrhages were noted in the central nervous system.

Case 3

Clinical History

A cow, aged 10, lost appetite and its milk production was decreased from February 2, 1955. On February 18, the temperature showed 38.7°C, pulse rate was 63~70 and respiratory count was 32. Depression, depilation in the pelvis, back elbow and face regions, paleness in conjunctivae, enlargement of submaxillary lymph nodes and a visible venous pulse were noted. Increased respiratory sounds and irregular heart beat were likewise noted. The temperature began to rise starting from February 2 following such a course as 39.1°C (20/II), 40.3°C (22/II), 39.1°C (23/II), 38.9°C (25/II) and 39.1°C (4/III). On March 8th, the temperature showed 39.1°C, pulse rate was 98 and respiratory count was 49. The pulse rate was irregular and heart noise was increased. The animal became weak, unable to stand. Severe anemia and loss of appetite were manifested. She died on March 9.

Histological Appearances

Central focal necroses, passive hyperemia and hemorrhage were observed in the liver.

In GLISSON's sheath, the connective tissues were proliferated. Malpighian corpuscles in the spleen were enlarged and reticulum cells were proliferated. Red pulp was congested. Marked histiocytic cellular infiltration was noted in the renal interstitium and sometimes multinucleated giant cells were detected in it. Necrobioses, calcification, hemosiderin deposit and regeneration were observed in the convoluted renal tubules. Fatty infiltration was observed in a part of the HENLE's loop. The heart showed venous congestion and histiocytic cellular interstitial proliferation. Otherwise subacute catarrhal bronchopneumonia, catarrhal lymphadenitis and subacute non-specific diffuse mastitis were also noted. In the central nervous system, circulatory disturbances were demonstrated.

Case 4

Clinical History

A cow, aged 8, lost appetite from 10 days before parturition. Eczema was recognized in face and cervical regions. The temperature rose to 40°C and pulse rate was 90. Visible mucous membrane were markedly anemic. Lachrymation, salivation, eczema and edema in extremities were noted. She died on March 19.

Histological Appearances

Multiple central focal hepatic necroses were recognized. Fine fat droplets and PAS positive granules were recognized in and around the necrotic lesions. Vascular endothelia were swollen and increased. Karyorrhexis was often noted and PAS positive granules were deposited in the endothelia. In GLISSON's sheath the connective tissues were proliferated. Malpighian corpuscles in the spleen were enlarged and giant cells were detected in them. Red pulp was congested. Massive histiocytic cellular accumulation, edema, hyperemia and hemorrhages were demonstrated in the renal interstitium. Necrobioses of renal convoluted tubules, protein droplets and degenerated cell masses in the tubular cavities were also recognized. Fatty infiltration was also detected in the renal tubules (*Pars recta*) and HENLE's loop. The heart showed marked hemorrhages in the subendocardium, subepicardium and myocardium. Marked eosinophilic infiltration was accompanied by histiocytic cellular proliferation. Sometimes giant cells appeared in the alveolar wall. Catarrhal lymphadenitis with giant cells was also found. In the alimentary canal, subacute eosinophilic catarrhal enteritis was noted. Congestion and hemorrhages were observed in the central nervous system.

Case 5

Clinical History

A cow, aged 5, was affected on March 21. Slight cough, reduction in appetite and milk yield, congestive conjunctivae, hemorrhagic diarrhea and bloody milk were observed. The temperature rose to 39.8°C, pulse rate was 72 and respiratory count was 24. Erythrocyte count was 5.09 mill. The body temperature went up to 40.2°C, pulse was 100 and respiratory count was 28 on the next day. Hemorrhagic lachrymation and epistaxis were noted. On March 23, the temperature showed 39.5 C and at 3 p. m. she died.

Histological Appearances

Multiple focal necroses were seen in the center of the hepatic lobules. Passive

hyperemia and focal hemorrhages were also present. Vascular endothelia were activated. Cellular accumulation was found in GLISSON's sheath. Malpighian corpuscles in the spleen were enlarged and multinucleated giant cells were present. Red pulp was congested. The kidneys showed perivascular interstitial cellular infiltration. Necrobioses and hemosiderin deposit were noted in the convoluted tubules. Hemorrhages were present in the peripelvic tissues. Slight fine granular fat droplets were seen in HENLE's loop. The heart showed much extensive hemorrhage. Large number of eosinophils were present in the heart interstitium; they comprised histiocytes, polymorphonuclear leucocytes and lymphocytes. Subacute catarrhal bronchitis, peribronchial hemorrhage and catarrhal lymphadenitis were found. In the central nervous system, sometimes perivascular eosinophilic and histiocytic cellular infiltration were involved.

Case 6

Clinical History

A cow, aged 7, suffered from dyspnea, dry cough, lachrymation and salivation on February 16, 1955. The temperature went up to 40.1°C. Maxillary lymph nodes were enlarged. Depilation and eczema were noted in her face. On March 19, temperature showed 40.1°C, pulse rate was 100 and respiratory count was 21. Depression, petechiae in nasal mucous membrane, accelerated heart beat were noted. Depilation in abdomen, shoulder and vulva, eczema in udder and congested conjunctivae with petechiae were found. Petechiae in vaginal mucous membrane were noted. On March 26, she died.

Anatomical Diagnosis

1) Focal hepatic necroses. 2) Anemic edema and petechiae in the kidneys. 3) *Bronchitis purulenta subacuta*. 4) Enlargement of splenic follicles. 5) Medullary swelling and edema in lymph nodes. 6) Multiple petechiae in general serous and mucous membranes. 7) Remarkable hemorrhage in the subendocardium, subepicardium and heart muscles. 8) Petechiae in the small intestine.

Histological Appearances

Multiple focal necroses were seen in the liver. Around the foci, fatty infiltration was conspicuous and PAS positive granules were found. Endothelia were proliferated with PAS granules. Cellular infiltration was also observed in GLISSON's sheath. Malpighian corpuscles on the spleen were enlarged and contained multinucleated giant cells, red pulp was congested. The kidneys showed marked histiocytic cellular infiltration in the interstitium and sometimes giant cells were present in it. There were degeneration, hyalinization and fat infiltration in the convoluted tubules and HENLE's loop. Protein droplets were contained in the lumen of the tubules and BOWMAN's capsulae. Marked hemorrhages were noticeable in the subendocardium, subepicardium and heart muscles. Histiocytic cellular proliferation was noted in the heart interstitium and sometimes giant cells were present. Sometimes myodegeneration and figure of *myocarditis interstitialis* were observed. Otherwise subacute catarrhal bronchitis, catarrhal lymphadenitis, hemorrhages in the gastric intermuscles and subacute catarrhal enteritis were shown. In the central nervous system, there were congestion, hemorrhage and sometimes perivascular cuffs. In the occipital lobe, there were fresh degenerated foci. Microglia cell foci and proliferation

were detected at the same time.

Case 7

Clinical History

A cow, aged 11, manifested lachrymation, salivation and eczema in her face on March 18, 1955. On March 21, the temperature showed 39.1°C, pulse rate was 59 and respiratory count was 20. Erythrocyte count was 5.45 mill. and leucocyte count was 7,200. On April 9, petechiae in the various mucous membranes and bloody feces were noted. The temperature showed 38.8°C, pulse rate was 90 and respiratory count was 20. On April 10, she lost appetite completely and discharged dark reddish urine. On April 11, it becomes difficult for her to stand and she fell in collapse. She died at 11.15 a. m.

Anatomical Diagnosis

1) Multiple petechiae in general subserosa and submucosa. 2) Enlargement of general lymph nodes. 3) Edema of the large intestine. 4) Anemia in the parenchymatous organs. 5) Fascioliasis.

Histological Appearances

The liver showed congestive edema and proliferation of R. E. S. The connective tissues in GLISSON's sheath were proliferated. Malpighian corpuscles of the spleen were enlarged and the sinuses of the red pulp were congested. Peritrabecular and subcapsular hemorrhages were also noted. The kidneys showed focal interstitial cellular accumulation and marked congestive edema. Necrobioses and fatty infiltration in the convoluted tubules were noted. The heart showed much extensive hemorrhage in the valve, subepicardium subendocardium and myocardium. Remarkable eosinophilic cellular infiltration was found in the heart interstitium. The lung showed peribronchial hemorrhages and bronchoectasia. Moreover, catarrhal lymphadenitis, chronic eosinophilic obliterated endoarteritis, acute hemorrhagic catarrhal gastritis, subacute catarrhal enteritis with hemorrhage and chronic catarrhal cystitis, etc. were noted. In the central nervous system, congestion and hemorrhages and sometimes slight perivascular cuffs were observed.

Case 8

Clinical History

A cow, aged 8, manifested dry cough on March 9, 1955. The body temperature showed 38.5°C, pulse rate was 50 and respiratory count was 20. On March 10, erythrocyte count was 5.34 mill. and leucocyte was 9,600. On April 7, the animal showed a decreased appetite and a temperature of 39.2°C. On April 11, the temperature showed 38.2°C, pulse rate was 140 and respiratory count was 40. She struggled and discharged dark reddish urine. Appetite was completely lost. On the next day, she found difficulty in standing and collapsed. She died at 11.00 a. m.

Anatomical Diagnosis

1) Petechiae in every part of the body. 2) *Bronchitis catarrhalis subacuta*. 3) General venous congestion. 4) Renal calculi.

Histological Appearances

The liver showed central passive hyperemia and focal hemorrhages. Endothelial cells were swollen. Hepatic fatty infiltration was remarkable. Red pulp in the spleen was congested and follicles were hyperplastic but the size was normal. Macrophagocytes were accumulated in the secondary follicles of the spleen. Histiocytic, plasmacytic and lymphocytic cellular infiltration were also discovered in the renal interstitium. Epithelial cells of the convoluted tubules and HENLE'S loop showed fatty infiltration. Hemorrhages were also detected in the subendocardium, subepicardium, myocardium and epicardial fat tissues. Fatty infiltration was noted in the heart muscles. The lung showed venous congestive edema, bronchoectasia and circumscribed acinous pneumonia. Catarrhal lymphadenitis was generally confirmed. In the central nervous system, meningeal hyperemia and hemorrhage were remarkable. Destroyed foci in the medulla oblongata were demonstrated.

Experimental Cases

Case 9

Animal...Holstein cross-bred, bull calf, weight 82.5 kg, 7 months old, which had not been fed with linseed meal was used.

Place...Monbetsu Animal Health Center.

Duration...30 days, from April 25 to May 24.

Rations...Linseed was sterilized with Ceresan (a mercurial fungicide) adopting the standard procedure of the linen-producing company which distributed the material to the farmers in this district as a seed. According to this method, the rate of linseed to Ceresan is 240 : 1. Experimentally obtained linseed meal was produced using this sterilized linseed.

Method...Feeding the animal with 1.3 kg of the experimental linseed meal, 0.3 kg rice-bran and 7 kg ensilage per day.

Control...Holstein cross-bred, bull calf, weight 150 kg, 15 months old, which had not been fed with linseed meal was used. This animal was fed with 2.5 kg of linseed meal which did not contain Ceresan and common feed per day. No symptom was observed in this animal.

Clinical History

Sixteen days after beginning of the ration, lachrymation appeared. On the 17th day, depilation at the root of the tail was manifested. From the 18th day, depression, eczema in breast and abdomen and swelling in *Lnn. poplitei* were noted. Four days later, a slight cough appeared and the temperature rose to 39.8°C. On the next day, the animal was depressed. Cough and salivation became worse. The temperature showed 40.2°C. On the 27th, severe cough, petechiae in the left conjunctiva, salivation and albuminuria were noted. The temperature rose to 40.5°C, erythrocyte count was 6.62 mill. and leucocyte was 2,400. On the 28th, the animal staggered. The temperature showed 39.5°C. On the 29th, eczema appeared around the eye regions and albuminuria occurred. On the 30th, the body temperature showed 38.4°C. The animal was killed.

Anatomical Diagnosis

1) Enlargement of general lymph nodes. 2) Slight interstitial hepatitis. 3) Enlargement of splenic follicles. 4) Focal interstitial nephritis.

Histological Appearances

GLISSON's sheath showed histiocytic cellular infiltration and *endophlebitis obliterans et productiva chronica*. Intimagramulomatous cellular accumulation was also seen in the vessels. The spleen was congested. Focal cellular accumulation was noted in the renal interstitium. Hemorrhages were seen in the subendocardium, myocardium and valve in the heart. Fatty infiltration was detected in the heart muscles. The lung showed venous congestion, peribronchial cellular accumulation and bronchoectasia. *Lymphadenitis catarrhalis* was confirmed. Passive hyperemia and congestion was remarkable in various organs. The central nervous system was also congested.

Case 10

Animal...Holstein cross-bred, bull calf, weight 85 kg, 7 months old, which had not been fed with linseed meal was used.

Place...Laboratory of Veterinary Internal Medicine, Faculty of Veterinary Medicine, Hokkaido University, Sapporo.

Duration...60 days, from May 8 to July 6.

Rations and Methods...The first experiment, 8/V~16/VI, 40 days. The animal was given the same feed as in case 9. The animal received this diet consisting of 1.5 kg linseed meal, 0.7 kg rice-bran and 5.0 kg hay per day. The second experiment, 17/VI~6/VII, 20 days. The animal was fed with Ceresan.

Clinical History

Twenty-three days after beginning the special feeding, the animal showed a high fever of 41.5°C and 2 days later, crisis occurred. Some clinical symptoms such as the temporal pyrexia, anorexia, depression and laboured breathing, etc. were observed (The first experiment). From the 41st day, the animal was fed with 8.5~85 g of Ceresan per day for 20 days, and dieting this linseed meal was discontinued (The second experiment). On the 8th day after the beginning of the second experiment, the animal manifested a decreased appetite and diarrhea. Diarrhea became worse. Three days before the death, erythrocytes numbers were extremely decreased. The animal died on the 20th day.

Anatomical Diagnosis

1) *Gastritis hemorrhagica et necroticans superficialis acuta*. 2) *Enteritis catarrhalis hemorrhagica acuta*. 3) Multiple greyish-white spot in the kidneys (Calcification). 4) Subepicardial hemorrhages and slight right side dilatation of the heart ventricle. 5) Edema of the general lymph nodes.

Histological Appearances

The liver was congested and endothelia were swollen. The red pulp of the spleen was congested. Follicles were atrophic and karyorrhexis was remarkable. The kidneys showed congestion and degeneration with marked necroses, calcification, basophilic homogenization and eosinophilic granulization of the epithelial cells of the convoluted tubules and HENLE's loop. In the intestitium, reparation was so conspicuous that histiocytic cells were reactively proliferated. The heart showed venous congestion. In the stomach, hemorrhages were extensive. The surface of the mucous membrane showed necrosis and was covered with

fibrinous pseudomembranes. Submucous edema was remarkably observed. The lesions of the duodenum and the beginning of the jejunum were like those of the stomach. The large intestine showed congestion, hemorrhages and catarrh. The other organs showed congestion and hemorrhages. The only abnormality in the central nervous system was focal cellular infiltration in the part of the cerebellar meninges without congestion.

Detection for Mercury

Detection for mercury on various organs and tissues were carried out in the natural and experimental cases. On the other hand, mercury detection on body fluids, feces and feed of cows in the endemic areas were also performed. The results obtained are listed in tables 3 and 4.

TABLE 3. *Mercury Contents in the Tissue of Various Organs (ppm).
Detection on 10 g (Wet Weight) of Tissue*

MATERIAL	CASE NO.	TERMI-NATION	KIDNEY	LIVER	ABOMA-SUM	LUNG	HEART MUSCLES	SPLEEN	CUTIS
Natural Cases	1	†	8.40	0	.	.	.	0.00	.
	2	κ	71.62	0.70	0.01	0.05	0.00	0.02	0.00
	3	†	3.56	0.32
	4	†	13.60	0.56	0.25	0.12	0.15	.	.
	5	†	6.56	0.10
	6	κ	20.80	1.40	0.00	0.15	0.20	.	.
	7	†	2.26	0.04
	8	†	11.52	0.02
Experimental	9	κ	47.50	0.00
	10	†	86.00	0.52
Control Cases	11	κ	0.0	0.0
	12	κ	.	.	0.0	.	0.0	.	.
	13	κ	0.0	0.0	0.0	.	0.0	.	.

TABLE 4. *Mercury Contents (ppm) in Body Fluids, Feces and Feed of Cows in the Endemic Areas*

COWS	CASES	BLOOD	URINE	MILK	FECES	FEED
Affected	7	0.0	0.02	0.01	0.01	0.003
Non Affected	8	0.0	0.0	.	.	.
Control	5	0.0	0.0	0.0	.	.

DISCUSSION

Characteristic post mortem changes which were commonly observed in the natural cases were as follows:

Subacute interstitial nephritis, subacute catarrhal bronchitis, enlargement and edema of general lymph nodes, enlargement of splenic follicles, subendocardial and subepicardial hemorrhages, multiple petechiae in general subserosa and submucosa, catarrh and hemorrhages in the alimentary canal, hepatic focal necrosis and general circulatory disturbances such as hyperemia and hemorrhages were anatomically noted.

Histologically, the main lesions of this disease may be arranged as follows: 1) Interstitial reaction, 2) Activities of the reticuloendothelial system in a wide sense, 3) Parenchymatous degeneration, 4) Respiratory changes, 5) Vascular changes, 6) Circulatory disturbances, 7) Changes in the alimentary canal, 8) Skin lesions.

As to interstitial reaction and activities of the reticuloendothelial system in a wide sense, the lesions were conspicuous in the renal interstitium, GLISSON's sheath and heart interstitium. The renal interstitium showed marked histiocytic proliferation sometimes accompanying multinucleated giant cells. In GLISSON's sheath, remarkable histiocytic proliferation which was often accompanied by giant cells was noted. At the same time, the connective tissues were also proliferated. In the heart interstitium, histiocytic cellular proliferation and eosinophilic infiltration were remarkable and giant cells were often noted. Moreover, general reticuloendothelial cells were reactively proliferated. Such effects as catarrhal lymphadenitis, hyperplasia of Malpighian corpuscles with giant cells in the spleen and alveolar histiocytic cellular proliferation sometimes with giant cells in the lung were observed. Parenchymatous degeneration was an important change in this disease. Multiple central focal necroses in the hepatic lobules were frequently noted. Vascular endothelia often showed degeneration and fat droplets and PAS positive granules were in it. The degeneration of renal tubules was normally slight except in one case (Case 6), but fatty infiltration was detected in all cases excepting one (Case 3). Fatty infiltration was conspicuous in the convoluted tubules and HENLE's proximal loops. Respiratory changes which prove the clinical symptoms, such as severe dry cough and dyspnea, were noted. Subacute catarrhal bronchiolitis and bronchitis (6 in 8 cases) were confirmed. Besides, bronchoectasia, emphysema and pulmonary hemorrhages were frequently observed. Circumscribed acinous pneumonia was also detected in one case (Case 8). *Endophlebitis obliterans et productiva chronica* was shown as vascular changes. There were such circulatory disturbances as venous congestion and hemorrhage; especially hemorrhages in the submucosa and catarrh were also seen in the stomach and small intestine. As skin lesions, depilation and eczema were macroscopically observed. Microscopically keratinization of the skin surface, hyperemia and hemorrhages in the subepidermic layer and perivascular histiocytic cellular cuffs were demonstrated. In the central nervous system, no encephalitic change was found and circulatory disturbances such as hyperemia and hemorrhages

were forming the main lesions.

In the two experimental cases, experimental methods and lesions were different respectively. The first experimental case (Case 9) was poisoned by the linseed meal produced from linseed which had been treated with Ceresan (a mercurial fungicide). This experimental condition was identical with the natural cases. In the second experimental case (Case 10), the first half of the experiments revealed the same condition as the first case but no remarkable symptom was detected except temporal pyrexia. In the latter half of the experiments, animal was fed only with a large amount of Ceresan. Therefore, the quantity of the mercury contents of the former was small but the latter was large. The clinical symptoms and pathological changes of the former (Case 9) were similar to those of the natural cases. This case was considered to be chronic mercury poisoning. No symptom was found in the latter (Case 10), similar to those in the former. The latter showed marked renal parenchymatous degeneration with an extensive calcification. Hemorrhagic and necrotic gastroenteritis, catarrhal lymphadenitis and general circulatory disturbances were also noted. These lesions of the latter case were considered to be due to subacute mercury poisoning.

With regard to the cause of the disease, infection or poisoning was suspected by practitioners as mentioned above. With respect to infection, bacteriological and virological investigations showed negative result. No pathological evidence for infection, especially psittacosis which was suspected throughout the investigation, was demonstrated.

With respect to the poisoning, as the natural cases were all commonly fed with linseed meal, so linseed meal poisoning caused by linseed which had been treated with Ceresan was suspected by clinicians. As cattle have a high sensitivity to mercury, investigators, from the beginning, suspected that the clinical symptoms of this disease are like to those of mercurialism. According to FRÖHNER,⁴⁾ indication such as dyspnea, cough, nasal discharge, salivation, catarrhal gastroenteritis, eczema, depilation, petechiae in visible mucous membranes, albuminuria, anuria and sometimes paralytic symptoms are emphasized. STEVENS¹⁴⁾ also described the similar symptoms and the present cases manifested remarkably resemblant symptoms to the above. DEKIEWIET²⁾ & MCENTEE⁹⁾ reported the occurrence of mercury poisoning caused by oat seeds which had been treated with fungicide. The conditions of the present cases were similar to those of the above cases. Poisoning through the inhalation of mercury vapour is also reported by RICKER et al.,¹²⁾ KULKOW et al.⁷⁾ and PETRELIUS.¹¹⁾ From old times, it is known that many workers have pathologically described the renal changes of mercurialism as "sublimate kidney". On calcification, SAIKOWSKY¹³⁾ and NEUBERGER¹⁰⁾ demonstrated it as a characteristic change, but the occurrence varies with the course of disease. KLEMPER⁶⁾, in the chronic cases, recognized that the necrotic parenchymatous inflammation was slight, there were no calcificated lesions in the kidney and interstitial inflammation was extensive. These lesions were similar to those in the present case 9. The authors, however, are unable to state immediately that these renal lesions are characteristic to the mercury poisoning. LEMKE⁸⁾ considered that the calcification in renal convoluted tubules and regeneration of epithelium are not characteristic to the mercurialism. Nevertheless the present disease was deeply suspected as mercury poisoning considering the other changes. In other words, in mercury poisoning, the respiratory changes, such as glottis edema, bronchitis, pulmonary edema and focal

pneumonia, etc. have already been described by many workers (HENKE et al.,⁵⁾ FRÖHNER⁴⁾ and PETRELIUS¹¹⁾). Bronchitis was frequently observed in the present cases. As vascular changes, FELLINGER et al.³⁾ and SCHENKEN et al.¹³⁾ also reported various changes caused by endoarteritis. As for the skin changes, ALMKVIST¹⁾ reported that in the first stadium, vascular dilatation and edema are noted as indirect mercury action upon the blood vessels. In the second stadium, hyperemia and edema present culture fluid to bacterial infection and remain dermatitis. The chronic cases in this study all indicated eczema and depilation which originated in local hyperemia and gradually became worse. With respect to the central nervous system, some workers such as KULKOW et al.,⁷⁾ had noted the severe lesions but the present authors recognized mainly such the circulatory disturbances as hyperemia and hemorrhages.

As above described, this disease was deeply suspected clinicopathologically as having been caused by mercury poisoning. So the authors performed mercury detection of tissues, body fluids and feed in the natural and experimental cases. As in tables 3 and 4, all cases showed positive. It was confirmed that this disease is mercury poisoning.

SUMMARY

The authors pathologically investigated 10 cases (8 natural and 2 experimental cases) concerning a disease of unknown cause in dairy cows in Monbetsu City, Hokkaido.

The results obtained were as follows.

1. Natural cases were considered to be chronic mercury poisoning and all cases showed mercury in tissues.
2. The clinical and pathological changes in the first experimental case (Case 9) were considerably similar to those of the natural cases and were considered to be due to chronic mercury poisoning.
3. The second experimental cases (Case 10) was considered to be subacute mercury poisoning.
4. In the natural cases, subacute interstitial nephritis, subacute catarrhal bronchitis, enlargement and edema of general lymph nodes, enlargement of splenic follicles, subendocardial and subepicardial hemorrhages, depilation and circumscribed dermatitis, general hyperemia and hemorrhages, sometimes focal hepatic necroses and slight liver cirrhosis were anatomically noticeable.
5. Histopathologically, the activities of the reticuloendothelial system in a wide sense, such as general histiocytic cellular proliferation and giant cell formation were observed. Interstitial cellular reaction in the kidneys, connective tissue proliferation with cellular accumulation in GLISSON'S sheath, catarrhal lymphadenitis, the enlargement of Malpighian corpuscles in the spleen, focal hepatic necroses, degeneration of epithelial cells in the renal convoluted tubules, subacute

catarrhal bronchitis, *endophlebitis obliterans et productiva*, subendocardial and subepicardial hemorrhages, catarrh, congestion and hemorrhages in the alimentary canal and circumscribed dermatitis were noted.

6. The disease was considered to be a chronic mercury poisoning caused by linseed meal produced from linseed which had been treated with Ceresan (a mercurial fungicide).

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EXPLANATION OF PLATES

PLATE I.

- Fig. 1. Case 3. Kidney: Marked histiocytic proliferation accompanying multinucleated giant cell.
Hematoxylin-eosin stain (H.-E.). × 100
- Fig. 2. Case 1. Kidney: Multinucleated giant cell and histiocytic proliferation.
H.-E. × 400
- Fig. 3. Case 9. Kidney: Interstitial cellular accumulation.
H.-E. × 100
- Figs. 4 & 5. Case 10. Kidney: Degeneration with marked necroses, calcification, basophilic homogenization and eosinophilic granulization of the epithelial cells of the convoluted tubules and HENLE'S loop. Histiocytic proliferation in the interstitium.
H.-E. × 100 (Fig. 4), × 400 (Fig. 5)
- Fig. 6. Case 2. Lymph node: *Lymphadenitis catarrhalis*.
H.-E. × 400

PLATE II.

- Fig. 7. Case 6. Spleen: Multinucleated giant cells in the Malpighian corpuscles.
H.-E. × 200
- Figs. 8 & 9. Cases 4 & 2. Liver: Focal central necrosis.
H.-E. × 100 (Fig. 8), × 400 (Fig. 9)
- Fig. 10. Case 9. Liver: *Endophlebitis obliterans*.
VAN GIESON stain. × 200
- Fig. 11. Case 7. Heart: Marked hemorrhage in the heart muscles.
H.-E. × 100
- Fig. 12. Case 7. Heart: Marked eosinophilic cellular infiltration in the heart interstitium.
H.-E. × 400

PLATE III.

- Figs. 13 & 14. Cases 1 & 6. Lung: *Bronchitis catarrhalis subacuta*.
H.-E. × 100 (Fig. 13), × 45 (Fig. 14)
- Fig. 15. Case 10. Stomach: *Gastritis necroticans superficialis*. Karyorrhexis and pycnosis are conspicuous.
H.-E. × 400
- Fig. 16. Case 10. Stomach: The surface of the mucous membrane showed necrosis and was covered with fibrinous pseudomembranes. Submucous edema, hemorrhages and hyperemia are conspicuous.
H.-E. × 45
- Fig. 17. Case 10. Skin: Keratinization of epidermis, neutrophilic infiltration and perivascular histiocytic proliferation are conspicuous.
H.-E. × 45
- Fig. 18. Case 4. Thalamus: Hemorrhage.
H.-E. × 45





