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HISTOPATHOLOGICAL STUDIES ON PARTURIENT HEMOGLOBINEMIA OF DAIRY COWS

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I. INTRODUCTION

A disease of unknown cause in dairy cows with hemoglobinuria recently came to the attention of the present writers. The disease occurs sporadically at the time of post-parturition in such eastern parts of Hokkaido as Nemuro, Kushiro and Obihiro districts. The disease is characterized by some outstanding clinical symptoms such as anemia, icterus, decrease of appetite and milk production, and cardiac palpitation; its course is so rapid that some animals die within a few days after the onset of illness. The dairymen and people concerned are, therefore, becoming subject to panic in respect to the disease.

Until relatively recent days, however, no literature as to the occurrence of this disease in Japan has been available except HIRAGA'S¹⁰⁾ first report.

It has been possible to identify the disease through the writer's investigations as similar to the serial disease which is distributed in Europe (Norway, Sweden, Finland, Denmark, Austria, Hungary, Estonia, Ireland) and Scotland and North America (Colorado, Utah and Idaho in the Rocky Mountain regions). The disease is named by investigators, each in his own way, such as "Parturient hemoglobinuria", "Puerperal hemoglobinemia", "Post-parturient hemoglobinuria", "Puerperal hemoglobinuria", "Parturient hemoglobinemia" and also as so-called "Red-water disease".

It is interesting that hitherto this disease has been often confused with piroplasmiasis and bovine hematuria (Stallrot), moreover EKELUND considered milk fever, ketosis and this disease as belonging to the

category of "lactation diseases". As the people of eastern Hokkaido areas are now believing this disease to be piroplasmosis, histopathological investigations were undertaken to establish the peculiarly characteristic diagnosis of this disease. It would be a great pleasure to the writers if their present study should contribute anything of value investigation of the causes of the disease.

II. OCCURRENCE AND SYMPTOMS

Parturient hemoglobinemia has been occurring sporadically mainly in Nemuro waste land situated in both Nemuro and Kushiro districts; that is in Nakashibetsu, Bekkai, Teshikaga, and Shibeche and sometimes in Tsurui (Kushiro district), and in Taiki and Toyokoro (Tokachi district). As a rule, many poor farmers are living in these districts; in Nemuro waste land known as the Mashu volcanic ashes region the soil is especially poor and the climate is severe. The occurrence of this disease has been conspicuously prevalent in the past 3 years. It is most frequent during the autumn and early winter; (September, October and November), and secondly from the later part of winter to early spring; (February, March and April).

The highest rate of affection occurs between the ages from 5 to 12 after the 3rd to 6th calving. The course of this disease is from one day to two weeks and most of victims die within a few days. As a rule, the disease attacks comparatively well-nourished cows with a good milk production in these areas, but whose food almost wholly consists of turnips and straw, lacking nourishing food.

The initial symptoms are anemia, icterus, failure of appetite, reduction in the milk yield, hemoglobinuria and often diarrhea. Anemia and icterus are so conspicuous that visible mucous membranes, mammary and internal thigh are pale and jaundiced. The body temperature is raised to 40°C to 41.5°C in some cases, but in general it is not greatly increased and it may become subnormal (35.4°C) in bad prognostic case. The pulse rate may vary between 160 to 180. An accelerated pulse is the dominant symptom. The heart beat is often tumultuous and loud. The blood shows remarkable reduction in erythrocytes which in acute cases may fall below 2.0 million. On the contrary, the leucocyte count is increased to 9,000~18,000; granulocytosis is often observed. In severe anemia cases with abnormal erythrocytes there appear such symptoms as anisocytosis, anisochromia, basic stippling of

TABLE 1. *Investigated Materials*

| CASE NO. | AUTO-PSY NO. | BREED | SEX | AGE (YEARS) | LOCALITY | DATE OF AUTOPSY | PARTURITION | ONSET OF ILLNESS | DAYS FROM PARTURITION TO ONSET OF ILLNESS | COURSE (DAYS) | TERMINATION |
|----------|--------------|------------------|-----|-------------|-------------------------|-----------------|-------------|------------------|---|---------------|-------------|
| 1 | E. 563 | Holstein | ♀ | 12 | Nishishunbetsu (Nemuro) | 6/XI '51 | /X | /XI | 26 | 2~3 | † |
| 2 | O. 665 | Holstein Bastard | " | 12 | Taiki (Tokachi) | 29/XII '51 | 7/XII | 27/XII | 20 | 3 | † |
| 3 | O. 682 | " | " | 6 | Toyokoro (Tokachi) | 18/II '52 | 11/II | 17/II | 6 | 1 | † |
| 4 | E. 701 | " | " | 8 | Bekkai (Nemuro) | 26/IX '52 | — | — | — | — | † |
| 5 | E. 702 | " | " | 11 | Nakashibetsu (Nemuro) | 1/XI '52 | — | 28/X | — | 5 | † |
| 6 | E. 764 | " | " | 11 | " " | 27/XII '52 | 12/XI | 25/XI | 13 | 2 | † |
| 7 | O. 666 | " | " | 12 | — (Tokachi) | 13/XII '52 | — | — | 14 | — | † |
| 8 | E. 805 | " | " | 6 | Bekkai (Nemuro) | 1/IV '53 | 18/III | 28/III | 10 | 3 | † |
| 9 | E. 814 | " | " | 9 | Hororo (Kushiro) | 15/IV '53 | 24/III | 30/III | 6 | 16 | † |
| 10 | E. 816 | " | " | 9 | Osobetsu (Kushiro) | 22/IV '53 | — | 20/IV | — | 3 | † |
| 11 | 3398 | " | " | 5 | Satsutomonai (Kushiro) | 26/IV '53 | 9/IV | 19/IV | 10 | 3 | † |
| 12 | — | " | " | 12 | Kyosei (Kushiro) | — | 5/IV | 25/IV | 20 | — | Recovery |

Case No. 1 is the same case as HIRAGA's¹⁰⁾ case No. 4.

the erythrocyte and appearance of normoblasts. The urine is usually dark red or a port-wine colour. The sediment in the form of *stroma remnants* of destroyed erythrocytes does not contain complete red cells. The reaction was highly alkaline, and benzidin test showed distinctly positive results. Protein content was remarkable and sugar in the urine showed only traces of reducing substances. *Piroplasma* could not be found in the blood preparation.

III. MATERIALS AND METHODS

Investigated materials are collected from a total eleven cases within the years 1951 to 1953 inclusive. Most of the materials were sent from these areas for investigation; in some cases complete autopsies were performed by the present writers. Moreover for reference, data are added on one case of biochemically investigated result. Investigated materials are listed in Table 1.

After macroscopical observations, in some of the autopsy cases bacteriological investigation was carried out. All tissues were fixed in 10% formol solution and embedded in paraffin. Sections were stained as a routine with hematoxylin-eosin. Frozen sections were also prepared and stained with Sudan III for the detection of fat.

IV. RESULTS

The outline of each case is presented as follows:

Case 1. This animal was well-nourished with a good milk yield and fed with dent corn and pumpkins. A blood count showed R.B.C. 3,940,000, leucocytes 18,240 (lymphocytes 26.87, monocytes 7.05, polymorphonuclears (seg.) 14.10, (non seg.) 38.77, eosinophiles 13.22%). Anisocytosis, anisochromia, basophilic stippling and normoblasts presented. Hemoglobin, protein and sugar were highly positive in urine.

Histologically the liver showed characteristic demarcated necrotic foci in the center of hepatic lobules. Especially around the foci the nuclear degeneration of hepatic cells such as wall hyperchromatosis, then karyorrhexis, anisonucleosis were diffusely noted. In the foci a large number of rounded naked endothelia survived and around the foci many polymorphonuclears and naked endothelia were accumulated. In general R.E.S. cells were slightly swollen and in the sinusoid polymorphonuclears, eosinophiles and lymphocytes were recognized. In the GLISSON'S sheath, its size being normal, lymphocytes and eosinophiles were slightly accumulated. Remarkable fatty infiltration throughout the liver lobules was seen. Numerous fine granular orange yellowish fat droplets were confirmed in the parenchyma by Sudan III staining. Endothelia and KUPFFER'S cells take gross fat independently. Lial sinuses dilated and abundant in blood content. Spleen

showed marked hemosiderosis. Glomeruli were enlarged and edematous in kidney. In the space of BOWMAN'S capsule hyalinous, sometimes fibrinous serous substances were exuded. A parenchymatous degeneration was remarkable in *pars recta* of HENLE'S loop and somewhat in the convoluted tubules. In a part of the epithelial cells of renal tubules hemosiderin deposit was noted.

Case 2. Red urine, anemia and icterus were so conspicuous that this animal was killed in order to ascertain the cause of the sickness. Body temperature showed 39.8°C, 41.2°C, pulse was counted 95.

Autopsical diagnosis: 1) multiple *nephritis purulenta parenchymatosa*, 2) multiple hepatic focal necrosis, 3) anemia, 4) subendocardial hemorrhages of the heart and *myodegeneratio cordis*, 5) slight enlargement of the spleen, 6) enlargement of the lymphnodes, and 7) *enteritis catarrhalis*.

Bacteriologically, *Corynebacterium renalis* was confirmed in liver, spleen, kidneys, lung and lymphnodes. Also *Corynebacterium pyogenes* was detected in liver abscess.

Histologically, necrotic and necrobiotic foci were present in the center of liver lobules. Fatty infiltration was remarkable throughout the liver lobules. Lial sinuses were remarkably dilated and congested. Splenic pulp showed marked hemosiderosis. Right kidney showed pyelitis and *nephritis purulenta* with interstitial nephritis. Left kidney showed vacuolar and fatty degeneration in convoluted tubules and HENLE'S loop. Subendocardial and intermuscular hemorrhages and congestion were remarkable in heart. Lung showed congestive edema. *Enteritis catarrhalis*, *cystitis simplex subacuta* and *lymphadenitis catarrhalis* were also detected.

Case 3. This animal had fever 40.5°C and exhibited hemoglobinuria on the 6th day after parturition and died next day.

Histologically, multiple central focal necrosis was visible in liver lobules. Fatty infiltration of liver and kidneys was remarkable. BOWMAN'S capsules were dilated and some of them filled with serous exudation. Spleen showed marked hyperemia, collections of numerous eosinophiles. Multiple necrobiotic foci were scattered in and hyalinous thrombi were recognized in splenic pulp. Siderocytes were comparatively few. Subendocardial and intermuscular hemorrhages and edema of the heart were confirmed. Proliferation of histiocytes was remarkable in the interstitial tissues of the heart. Lymphnodes were edematous and sinuses were dilated. Endothelia and reticulum cells were proliferated.

Case 4. This material was sent from Nemuro Branch of Hokkaido Agricultural Experiment Station. Details were indistinct.

Histologically, central liver cell cord had become atrophic and remarkable biliary stasis was confirmed. R.E.S. cells were activated, swollen and increased. Fatty infiltration of liver parenchyma was also recognized in the lobule center. In spleen, perivascular accumulations of basophilic dark nuclear round cells (so-called L-cells by YAMAGIWA) were visible. Abundant siderocytes and L-cells were markedly proliferated in splenic pulp which was edematous. Hemosiderin deposits were re-

cognized in convoluted renal tubules. *Lymphadenitis catarrhalis* was remarkable.

Case 5. Clinical description is the same as the above.

Histologically, large hepatic focal necrosis was confirmed with hemorrhages in lobular center. Fatty infiltration of liver parenchyma was also detected. Congestive edema, trabecular hemorrhages and severe hemosiderosis were seen in spleen. Vacuolar and fatty degeneration was conspicuous in the renal tubules. Especially hyaline drop degeneration was confirmed in the *pars recta* of HENLE'S loop. BOWMAN'S capsules were dilated and sometimes filled with serous exudation. Histiocytic proliferation was conspicuous in the interstitial tissues of the heart. *Pericarditis subacuta* and deposit of fat granules in the muscular fibers were confirmed.

Case 6. This animal was a good milk producer giving an average of 40 lbs of milk daily. She bore a female calf on November 12, 1952 (7th calving). After parturition mother and child were both in good health condition and milk yield was 30 lbs daily. On the 13th day after parturition, the first symptom noted in the morning was decrease in appetite but milk yield was not decreased. At noon appetite was completely lost and hemoglobinuria followed abruptly at 2.00 p. m. In the evening, she could not stand, body temperature rose to 39.8°C and pulse was counted 60. Next day body temperature showed 35.4°C and pulse was 160, and then she died in the evening. She was fed daily on cornstalk (6 kg), beet top and rutabaga (45 kg), a liberal amount of grass and small amount of salt. This ration is extremely lacking in calorific and protein values.

Autopsical diagnosis: 1) multiple focal necrosis and fatty infiltration of liver, 2) slight enlargement of spleen, 3) cloudy swelling of kidneys and urinary stone formation, 4) dilatation of the ventricles and endocardial hemorrhages of the heart, 5) hemoglobinuria.

Histologically, multiple focal necrosis was confirmable in the center of liver lobules and the necrosis was irregular in shape. Atrophy of liver cell cord and high degree of fatty infiltration of liver parenchyma were found. Severe hemosiderosis, congestion, multiple necrobiotic foci and fibrin-thrombi were noted in spleen. Vacuolar degeneration in the renal tubules and serous exudation in BOWMAN'S capsules were remarkable. Myodegeneration and scar formation of the heart were detected, especially fat droplets were deposited in the muscular fibers.

Case 7. Two weeks after parturition, the animal had fever 41°C and manifested anemia and hemoglobinuria. Soon death occurred.

Autopsical diagnosis: 1) multiple hepatic necrosis, 2) congested spleen, 3) anemia.

Histologically, liver cell cords were irregularly arranged and atrophic. Also central liver necrosis was confirmed in liver lobules. Spleen showed marked hemosiderosis and congestion. Vacuolar degeneration, karyorrhexis and karyolysis were found in the convoluted renal tubules.

Case 8. This animal bore a calf on 18 March 1953 and had milk production 30 lbs daily. She manifested hemoglobinuria in the evening of March 28, and died

after 4 days.

Histologically, also multiple central liver necrosis was confirmed. Liver parenchyma were markedly fat-infiltrated. Biliary emboli were detected. Degeneration of renal tubules was remarkable, such condition as karyolysis, picnosis, granular and hyaline drop degeneration were recognized. Pigment granules were deposited in some parts of the renal tubules.

Case 9. This animal gave birth to a male calf on March 24. Six days after parturition, she developed a severe lacrimation. On April 11, appetite, drinking and milk production showed no remarkable changes. Next day she rapidly became worse and manifested severe icterus and hemoglobinemia. Body temperature showed 39.6°C, pulse rate was 121 and respiratory count was 46. The first heart sound was irregular and she died on April 15.

Histologically, multiple central demarcated liver necrosis and fatty infiltration were remarkable. Hemorrhagic infarct, fibrin-thrombi in the sinus and severe hemosiderosis of spleen were recognized. Fatty infiltration of renal tubules, enlarged glomeruli and in the space of BOWMAN's capsules hyalinous serous exudation were ascertained. Interstitial cell proliferation, some myodegeneration and scar formation were recognized in the heart.

Case 10. This animal was once affected by so-called "tick fever". She fell down on April 20 and next day body temperature was 35.4°C. Anemia was remarkable but icterus was not recognized and tremor occurred. She died in the early morning of April 22.

Biochemical examination of urine showed, acetone (-), sugar (+), kreatinin (+), Ca 2.7 mg/dl, Mg 0.9 mg/dl, inorg. phosphorus 4.1 mg/dl, total phosphorus 4.3 mg/dl, total protein 0.7 g/dl.

Histologically, multiple central liver necrosis was found. Around foci anisonucleosis and biliary emboli were detected. Parenchymatous fatty infiltration was remarkable. Marked hemosiderosis and congestion were visible. Glomeruli were congested and in the space of BOWMAN's capsules serous exudation was seen. Numerous vacuoles and fatty infiltration were remarkable in the renal tubules. Pigment deposit was also found in the renal tubules. Intermuscular and subepicardial hemorrhages and congestion of the heart were noted. Also interstitial cell proliferation of the heart was conspicuous. Congestive edema and edema of the interlobular connective tissues of the lung were remarkable. Lymphoid tissue of lymphnodes were abundant in cellular elements, and reticulocytes and macrophages were proliferated.

Case 11. This animal gave birth to a female calf on April 9, 1953 and after the 10th day from parturition, she manifested loss of appetite and hemoglobinuria. Next day she died with severe heart beat and sudation.

Autopsical diagnosis: 1) multiple liver necrosis, 2) anemia, 3) right side dilatation of the heart, 4) subendocardial and pericardial petechiae of the heart, 5) interstitial pulmonal edema, 6) hemoglobinuria.

Histologically, multiple central slightly demarcated liver necrosis with cellular

reaction were detected. Liver parenchyma contained numerous gross and fine fat droplets. Sinuses were dilated and blood content increased in spleen. Spleen showed also marked hemosiderosis. In general, kidneys were edematous and congestion was conspicuous in the medulla. High degree of fatty infiltration, partial hemosiderin deposit were recognized in the renal tubules. Glomeruli were enlarged and in the cavity of BOWMAN'S capsules serous exudation was contained. Valvular edema, endocardial and intermuscular hemorrhages of the heart were remarkable.

Case 12. This animal had been affected with similar symptom three years before. Visible mucous membranes were anemic and body temperature showed 39.5°C, pulse was counted 92, hemoglobin content was 26%, R. B. C. was 1,852,000, leucocytes was 9,400 and discharged hemoglobinuria.

Results of biochemical investigation were as follows:

Serum: total protein 8.5 g/dl, albumin 32.9%, globulin 67.1% (α -globulin 21.3, β -gl. 29.7, γ -gl. 16.1%), A/G 0.62, inorg. phosphorus 4.7 mg/dl, total phosph. 11.2 mg/dl, Ca 4.65 mg/dl, Mg 1.2 mg/dl, K 9.8 mg/dl. Milk: casein 1.8 g/dl, albumin and globulin 0.7 g/dl, sugar 2.5 g/dl, fat 3.7 g/dl, Ca 72.5 mg/dl, Mg 24.8 mg/dl, P 89.4 mg/dl. Urine: acetone (-), sugar (+), kreatinin (+), Ca trace, Mg trace, inorg. phosph. 1.5 mg/dl, total phosph. 1.6 mg/dl, total protein 0.8 g/dl.

V. DISCUSSION

The lesions of this disease take the forms, chiefly, of parenchymatous degeneration such as hepatic necrosis, degeneration of epithelial cells of kidney, myodegeneration, hemolytic changes and fatty degeneration of liver and kidney. Second in importance are circulatory disturbances such as congestion, hemorrhages, edema and thrombi in addition to proliferative changes which are accompanied by reactive changes in the reticuloendothelial system. The present writers consider that inflammatory changes such as *nephritis purulenta* have a secondary meaning. Findings made in connection with the present study are similar to the descriptions which have been published by many investigators such as WALLACE (1926), EKELEND (1928), HJÄRRE (1928, 1930), HAUPT (1930), FARQHARSON and SMITH (1938), HUTYRA, MAREK and MANNINGER (1938), MADSEN and NIELSEN (1939). But it is still doubtful whether ulceration of abomasum is a characteristic change of this disease as reported by EKELEND and HJÄRRE. HJÄRRE explained that the characteristic liver necrosis is a secondary symptom of the hemolysis and is produced by thrombosis. But the writers cannot agree with his opinion; it is considered by them that a certain toxic substance which is produced by metabolic disturbances provokes the hepatic intoxicative necrosis.

Differentiations could be made indicating that the diseases of piroplasmosis, bovine hematuria (Stallrot), bacillary hemoglobinuria, leptospirosis, bacillary pyelonephritis and puerperal sepsis differ from parturient hemoglobinemia.

As piroplasmosis is characterized by hemoglobinuria, hydremia, oligocythemia, icterus and prostration, it is similar to this disease. Many people in these Hokkaido areas are now believing this disease to be piroplasmosis as WALLACE experienced in England. They consider an acute exacerbation of a latent piroplasmosis, as do also many other observers, to be a recrudescence of a pre-existing latent piroplasmic infection.

Indeed, piroplasmosis in these districts has been of very frequent occurrence. But it is a small type as is revealed by the reports of HIRAGA¹¹⁾, SASAKI, KAME and others. Small type of *Piroplasma* in Japan corresponds to *Theileria (Babesia) mutans* in other countries. It is known that this type of *Piroplasma* is almost harmless, although sometimes manifesting the weak clinical symptoms which were reported by HIRAGA¹¹⁾, SASAKI¹⁸⁾ and ISHII et al.¹⁴⁾ Unfortunately the present writers could not yet have any opportunity to make autopsy of this type of piroplasmosis. But according to GILBERT⁶⁾ and DOYLE'S¹⁾ anatomical findings, it is different from the parturient hemoglobinemia. No *Piroplasma* was detected in the blood preparation of this investigation. But even if piroplasma does exist in the blood of this disease, it will not play any important role in the cause of this disease, for the majority of the normal cows of these areas have this parasite; its pathogenicity is extremely weak and the anatomical findings connected with its activity are different from those of this disease.

The bovine hematuria (Stallrot) of these districts has already been reported by two of the present authors. The lesions of the hematuria are limited to the urinary bladder while the other internal organs are normal except for anemia caused by the hemorrhages of bladder. It is easily differentiated from parturient hemoglobinemia.

Bacillary hemoglobinuria, or ictero-hemoglobinuria, is similar to parturient hemoglobinemia. The cause of this disease is the anaerobic bacillus, *Clostridium hemolyticus bovis*, according to VAWTER and RECORDS'S²⁰⁾ investigations. The disease occurs most frequently in swampy, poorly-drained areas and in excessively irrigated pastures, being most prevalent during the summer and early fall. The disease, geographically, is found in the mountain valleys or in regions of low to moderate

elevation of the Sierra Nevada and Coast ranges in the U.S.A. and also among the Andes in Chile. This disease is characterized by sudden onset, rapid course, high temperature, hemoglobinuria and occasionally bowel hemorrhages. Death usually occurs in 24 to 36 hours after the first appearance of definite symptoms. Postmortem examination reveals bloody discharges from the natural body openings. A profusion of hemorrhages occurs on the mucous membranes, subcutis and serous surfaces of the viscera and pleura. Hemoglobinuria is constantly observed. One large hemorrhagic infarct is invariably found in the liver, usually located on the upper or lower extremities. In this respect, liver findings and hemorrhagic septicemic changes of this disease are different from those of parturient hemoglobinemia.

Leptospirosis is characterized by anemia, icterus and hemoglobinuria, but the writers are not aware of any occurrence of this disease in eastern Hokkaido areas. It is easily differentiated without serological investigation, for findings in parturient hemoglobinemia do not include interstitial nephritis and leptospira.

One case of bacillary pyelonephritis affected with parturient hemoglobinemia has come to the writer's attention. But this disease is easily differentiated, for it presents suppurative inflammations of urinary organs caused by bacillus.

Puerperal sepsis is caused by metritis in puerperium. It is easily differentiated from parturient hemoglobinemia, by non-existence of septic changes and by abnormality of genital organs.

No distinct differentiation could be made between the disease of milk fever and ketosis (acetonemia) on the one hand and the present disease on the other except that the hepatic fatty infiltration of ketosis is similar to that observed in this disease, because there are no detailed reports on histopathological studies and the writers have no experience of the disease. However, MADSEN and NIELSEN¹⁵⁾ reported that samples of the blood plasma of parturient hemoglobinemia cases were found to be extremely low in inorganic phosphorus content. Certainly, in the available only one biochemically investigated case, the inorganic phosphorus values of the blood plasma were quite low. It indicated about one-tenth of normal values (4.7 mg/dl). Also FISH⁴⁾ reported that there was a decrease of 25.5% in inorganic blood phosphorus in normal cows immediately after calving and that there was an additional decrease of 38% in cows suffering from milk fever. It is natural that EKELUND²⁾ emphasized the relationship between milk fever, parturient hemo-

globinemia and ketosis, and re-stated it as belonging in the category of "lactation diseases". So it seems that some relationship between milk fever, ketosis, aphosphorosis and parturient hemoglobinemia do exist.

It is interesting that hemolytic anemia with jaundice in sheep, and kale anemia in cattle are similar to this disease. Anemia with jaundice in sheep which was reported by STAMP et al.¹⁹⁾ shows extremely low in inorganic phosphorus, but kale anemia according to ROSENBERGER'S¹⁷⁾ reports indicates normal values of inorganic phosphorus. The cause of parturient hemoglobinemia is still unknown. But STAMP et al.¹⁹⁾ consider that anemia in sheep is due to kale and rape feeding. Also MADSEN and NIELSEN¹⁵⁾ consider that puerperal hemoglobinemia most commonly occurs when cows are fed rations including sugar-beet by-products. But the authors considered it as a kind of disease which is produced by disturbances of metabolism. On the etiological features of this disease, therefore, great results may be expected from further investigation by biochemical and other methods in the future.

VI. SUMMARY AND CONCLUSION

Histopathological investigation was made of eleven cases affected with parturient hemoglobinemia.

1) Anatomically the outstanding changes found were an anemia, icterus, and edema in general. The blood was watery and dark. Especially the liver had undergone the most extensive changes. The livers of all cases were brownish-yellow or orange-yellow in colour due to fatty infiltration, sometimes slightly swollen and usually showed multiple necrotic patches. The spleen was usually congested on section of the pulp bulges and presented dark red, hemorrhagic appearance. Moreover, cloudiness of kidney, right side dilatation of the heart with subendo- and subepicardial hemorrhages, congestive edema of the lung, and enlargement and edema of the lymphnodes were found. A general diffuse catarrhal inflammation of the small intestine was recognized, but no changes were noted in the abomasum. The urinary bladder was always filled with dark red urine caused by presence of hemoglobin.

2) Histologically the most characteristic changes were observed in the liver; namely, necrotic and necrobiotic foci in the central area of liver lobules. Fatty infiltration was general throughout the lobules in almost all of the cases and endothelial cells took fat independently.

A parenchymatous degeneration, such as hyaline drop degeneration and vacuolar degeneration were conspicuous in the kidney, especially fatty infiltrations were remarkable in *pars recta* of HENLE'S loop and in some parts of the convoluted tubules. In some stages, hemosiderin deposits were noted in the epithelial cells of kidney. Some cases showed *glomerulonephritis serosa acuta* and most cases contained serous exudation in the cavity of BOWMAN'S capsule. The spleen of all cases was abundant in blood content and pulp showed high hemosiderosis. Sometimes, fibrin-thrombi were recognized in the sinus of the spleen. Subendo- and subepicardial hemorrhages and congestion of the heart were recognized and especially proliferated histiocytes in the interstitium were conspicuous. Some cases showed cardiac myodegeneration, and fine granular fat deposits in the muscular fiber. Moreover, *enteritis catarrhalis*, *lymphadenitis catarrhalis* and edema were found.

3) It was concluded that the main changes of this disease are parenchymatous degeneration and secondly circulatory disturbances in addition to proliferative changes which accompanied with reactive changes in R.E.S.

4) The authors differentiated the disease of piroplasmosis, bovine hematuria (Stallrot), bacillary hemoglobinuria, leptospirosis, bacillary pyelonephritis and puerperal sepsis from parturient hemoglobinemia.

5) It is considered that some relationship exists between milk fever, ketosis, aphosphorosis and parturient hemoglobinemia.

6) This disease is considered to be a sort which is produced by disturbances of metabolism.

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EXPLANATION OF PLATES

- Fig. 1.** Case No. 9. Liver: Central necrotic foci and marked hepatic fatty infiltration. Hematoxylin and eosin. $\times 130$.
- Fig. 2.** Case No. 1. Liver: Central necrotic foci and hyaline thrombi in the hepatic central vein. Hematoxylin and eosin. $\times 130$.
- Fig. 3.** Case No. 9. Spleen: Fibrin thrombi in the sinus and marked hemosiderosis in pulp. Hematoxylin and eosin. $\times 130$.
- Fig. 4.** Case No. 9. Heart: *Myodegeneratio cordis* and cellular infiltration in the interstitium. Hematoxylin and eosin. $\times 130$.
- Fig. 5.** Case No. 1. Kidney: Degeneration of renal tubules. Hematoxylin and eosin. $\times 530$.
- Fig. 6.** Case No. 1. Kidney: Hyaline drop degeneration of renal tubules. Hematoxylin and eosin. $\times 530$.

