Some Clinical and Hematological Features
of Virus Enteritis of Mink

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SUMMARY

Twenty-six, ten-week-old mink were infected by force feeding by pipette 2 ml of a tissue suspension containing a Wisconsin strain of mink enteritis virus. Four days later, diarrhea and partial or complete loss of appetite developed simultaneously in all of the animals. Squinting and occasional vomiting were also observed. By the sixth day after inoculation, all of the mink were anorectic and weak. Anorexia persisted for 48 to 96 hours. Diarrhea and vomiting continued until the eighth to ninth day after exposure. For the first two days after the appearance of diarrhea, the feces contained large quantities of mucus and intestinal casts were seen frequently in the droppings. Thereafter, the feces consisted mostly of yellowish green, watery fluid and contained no casts. Some of the animals died on the eighth day after infection. Those which survived were severely dehydrated and debilitated, but resumed eating and achieved complete clinical recovery within the next five to six days.

Leukopenia, i.e., total leukocyte count of less than 5,000 cells per mm^3 of blood, was found in seven of nine mink examined during the height of the disease. Leukopenic animals were deficient in both lymphocytes and neutrophils.

INTRODUCTION

Virus enteritis of mink (VEM) was recognized first in 1947 when epizootics occurred among ranch mink in southern Canada (8). The disease subsequently spread to the United States and threatened the mink industry of the midwestern and northwestern parts of the country during the early part of the past decade.

Clinical signs of VEM include anorexia, vomiting and severe diarrhea (3, 8). Stools of affected animals usually contain large quantities of mucus and intestinal casts or "plugs" composed of fibrin, mucus and desquamated intestinal mucosa. In immature animals, anorexia and diarrhea usually occur about four days after exposure to infectious material and persist for four to seven days (9). However, peracute infections have been reported in which anorexia was followed by death in 12 to 24 hours without the occurrence of diarrhea (4). Mortality of 80 percent or more is possible in newly-weaned kits. Mature mink often survive the disease after a period of sickness which may last several weeks (8).

In addition to the overt signs of VEM, a reduction of the number of leukocytes in the blood may be found in affected animals (1, 6, 7). Despite its frequent occurrence, however, neither the cause nor the diagnostic importance of leukopenia in VEM has been established.

Several types of vaccine have proved effective in controlling VEM among ranch mink. However, should outbreaks of the disease occur, definite criteria for clinical and pathological diagnosis would be helpful in avoiding serious losses. Some observations on clinical and hematological features of VEM made in the course of a pathological study of the disease are reported in this paper.

MATERIALS AND METHODS

Thirty 10-to-12-week-old, female mink of various types were used in the study. The animals were examined individually and observed closely for two weeks in order to assure that they were free of disease. Blood samples were obtained twice from each animal to establish normal hematological values. At the end of the observation period, 26 of the mink were infected with a Wisconsin strain of mink enteritis virus

TABLE I. Appetite and Stool Record of Mink after Infection with Mink Enteritis Virus

Mink No.	Days after Infection										
	1	2	3	4	5	6	7	8	9	10	11
3	N/N	N/N									
5	N/N	N/N									
8	N/N	N/N	N/N								
25	N/N	N/N	N/Mu								
16	N/N	N/N	N/N	N/MuF							
9	N/N	N/N	N/N	P/MuF							
10	N/N	N/N	N/N	F/Mu	O/Mu						
11	N/N	N/N	N/N	O/MuC	O/MuC						
29	N/N	N/N	N/N	F/Mu	P/Mu	O/MuC					
15	N/N	N/N	N/N	F/N	P/Mu	O/MuC					
27	N/N	N/N	N/N	P/Mu	P/MuF	O/MuF	O/MuB				
26	N/N	N/N	N/N	O/MuC	O/MuF	O/MuF	O/F				
1	N/N	N/N	N/N	N/N	O/MuC	O/Mu	O/MuC	O/MuF			
4	N/N	N/N	N/N	N/N	O/MuC	O/Mu	O/MuF	O/MuF			
7	N/N	N/N	N/N	N/N	F/MuF	O/MuC	O/MuC	O/F	O/FB		
13	N/N	N/N	N/N	N/N	P/Mu	P/Mu	O/MuF	O/FB	O/MuF		
12	N/N	N/N	N/N	N/N	O/Mu	O/Mu	O/MuF	O/F	O/F	O/FPf	
28	N/N	N/N	N/N	N/N	N/F	P/MuB	O/MuF	O/MuF	O/MuF	F/None	
6	N/N	N/N	N/N	N/N	N/N	P/MuC	O/MuC	O/MuF	O/F	O/F	F/FPf
14	N/N	N/N	N/N	N/N	P/Mu	O/MuF	O/MuF	O/F	O/F	F/None	N/FPf
18	N/N	N/N	N/N	F/N	F/Mu	O/MuC	O/MuF	O/F	F/FPf	N/FPf	N/N
17	N/N	N/N	N/N	F/Mu	P/Mu	O/MuF	O/MuF	O/F	O/F	F/F	N/N
30	N/N	N/N	N/N	F/Mu	F/Mu	O/MuC	O/F	F/F	F/F	N/N	N/N
24	N/N	N/N	N/N	P/Mu	P/MuB	O/MuF	O/MuF	O/MuF	F/FPf	F/N	N/N
21	N/N	N/N	N/N	F/MuB	O/MuB	O/MuC	O/F	F/F	F/FPf	N/N	N/N
23	N/N	N/N	N/N	F/MuB	P/MuB	O/Mu	O/F	O/F	F/None	F/N	N/N

Symbols for Appetite (left)
N — Normal   P — Poor
F — Fair   O — Anorectic

Symbols for Stool (right)
N — Normal   B — Blood
F — Fluid   Pf — Partly Formed
Mu— Mucus Content   C — Intestinal Casts

(MEV). Infection was accomplished by force feeding each animal by pipette with two ml of a 20 percent suspension prepared from the pooled macerated spleens and intestines from five, freshly killed, six-week-old mink kits. The kits had been infected by a similar method seven days before and had overt signs of VEM.

Beginning 48 hours after administration of infectious material, two mink were selected at random from the group of 26 for examination of blood and necropsy. Two additional mink were removed for examination each succeeding day through the 10th day when all remaining animals appeared to have recovered from the disease. Two of the surviving mink were killed and examined on the 13th day after inoculation; the rest were observed through day 27.

Four mink served as controls. Two were given 2 ml of homologous antiserum by subcutaneous injection 24 hours before administration of infectious material. The other two animals were kept in isolation and subsequently killed without exposure to MEV.

All mink were housed and fed in the manner described by Myers et al (7). The animals were observed several times daily, but to avoid unusual stress, they were not handled or unduly disturbed. Variations in appetite, alterations in the character of stools, and the occurrence of vomiting and other signs of abnormal function were recorded.

Mink to be examined each day were rendered unconscious by a sharp blow on the head. After obtaining unclotted blood samples from the heart in the manner described by Myers et al (7), the mink were killed by exsanguination. The bodies were opened aseptically and samples of kidney, spleen, liver, lung and intestine were collected for bacteriological examination. All samples of organs except the intestine were cultured on blood agar and McConkey's agar. Intestinal contents were incubated in selenite broth for 18 hours and then placed on Bacto-SS agar[1] for isolation of *Salmonella* and *Shigella sp.*

TABLE II.   Changes in the Blood of 12-week-old Mink During the Course of Viral Enteritis

	Normal Values Established Prior to Infection			Value on the 5th through 9th Days after Infection			Leukopenic Mink WBC < 5000 per mm3
	Mean	Range	St. Dev.	Mean	Range	St. Dev.	Mean
Etythrocytes x 10⁶ /mm³ blood	7.28	6.10 – 9.01	2.2	7.88	6.41 – 9.61	1.1	6.64
Hematocrit (%)	45.2	3ℝ – 55	5.1	63.2ᵉ	48 – 80	12.3	57.9ᵉ
Hemoglobin (gms/ 100 cc blood)	14.9	12 – 16	1.2	16.1	11.5 – 18	4.8	16.2
Leukocytes x 10³ /mm³ blood	9.43	6.2 – 13.9	2.2	4.43ᵈ	2.8 – 6.6	1.1	3.90ᵈ
Neutrophils x 10³	4.24	3.0 – 6.9	1.0	2.94ᵈ	1.9 – 3.6	0.5	2.77ᵈ
Neutrophils (%)	43.8	35 – 60	7.8	68.3ᵉ	54 – 84	9.8	68.9ᵉ
Lymphocytes x 10³ /mm³ blood	4.56	2.4 – 8.1	0.5	1.52ᵈ	0.7 – 3.0	0.7	1.23ᵈ
Lymphocytes(%)	53.2	41 – 60	6.1	29.2ᵈ	16 – 46	9.6	28.1ᵈ

ᵉSignificantly higher than mean before infection (p < .01).
ᵈSignificantly lower than mean before infection (p < .01).

RESULTS

CLINICAL OBSERVATIONS

Individual records of appetite and stool variation are given in Table I. Environmental conditions prevented the procurement of accurate records of water consumption.

Day 1 and 2. None of the 26 mink given infectious material manifested any signs of disease during the first two days after inoculation.

Day 3. A small quantity of mucus was seen in the feces of one mink, but the affected animal ate normally and had no other signs of sickness.

Day 4. Nineteen of 22 mink had soft, watery stools which contained copious, greyish-white, sometimes blood-stained mucus. In addition, intestinal casts were observed in the feces of four animals. Only three mink had normal appetites and all were inactive. Many of the animals sat in hunched positions with eyes partly closed but reacted violently when disturbed.

Day 5. All of the mink had severe diarrhea as well as partial or complete loss of appetite. The stools generally contained larger quantities of mucus than on the preceding day and in a few instances contained traces of blood; however, the incidence of casts was not increased. Vomiting was observed for the first time. The vomitus consisted of yellowish-green, watery fluid admixed with small quantities of clear mucus.

Day 6. All of the mink were anorectic and appeared to be extremely weak. Instead of assuming the hunched, sitting position previously described, most of the mink now sprawled on sternum and abdomen with their limbs extended. Squinting and occasional vomiting continued. The feces were more fluid in character and generally contained smaller quantities of mucus than on day five. Intestinal casts were observed in the stools of nearly half of the animals.

Day 7. Anorexia continued and all mink remained in about the same state as that observed on the previous day. However, the feces were entirely fluid, containing only traces of mucus or blood; no intestinal casts were observed.

Day 8. Two mink died on the eighth day. All of the remaining animals had rough, unkempt fur and for the first time, appeared to be dehydrated. The stools were scanty and consisted of yellowish-green, watery fluid. Some of the mink continued to retch or vomit occasionally. Two animals ate sparingly despite pronounced debility.

Day 9. Seven of the 10 surviving mink resumed eating, but consumed only about half of their normal ration. The stools remained excessively fluid but, in a few instances, were partly formed. Three animals passed no feces at all. Mink with returning appetites appeared to be stronger than on day eight; they still were inactive but irritable when disturbed.

Day 10. All of the mink ate at least part of their food and were more active than on the previous day. Most of them had partly formed or normal stools.

Day 11. Clinical recovery appeared to be complete on the 11th day. Both appetite and stools were normal and the animals were active. Two of the survivors were killed for examination on day 13. The remaining mink continued to be clinically normal during a further two weeks observation period.

Neither of the mink which received homologous antiserum prior to the administration of infectious material had any change in appetite during the entire period of observation. However, small quantities of mucus and fluid were seen in the feces of both animals on day seven. This slight aberration continued intermittently for a ten-day period. No other signs of disease could be detected in either of the mink.

BLOOD CHANGES

The most striking changes in the blood during the course of the disease were variations in leukocyte count. Seven of the nine animals examined on the fifth through the ninth days after infection were leukopenic, i.e., had total leukocyte counts less than 5,000 cells per mm^3 of blood (Table II). Blood from the tenth animal killed during that interval could not be examined because of clotting. The proportion of neutrophils in the blood of the leukopenic mink was elevated, but absolute cell counts indicated that the animals were both neutropenic and lymphopenic. Lymphopenia was also found in animals which had normal total leukocyte counts and appeared to be a feature of the disease throughout its course. Absolute neutrophil counts were generally within the normal range or only slightly elevated in non-leukopenic mink.

No changes in the total red blood cell count or hemoglobin content of the blood were detected; however, hematocrit values were significantly elevated on the fifth through the ninth days after infection.

BACTERIOLOGICAL FINDINGS

No pathogenic, aerobic bacteria were recovered from the organs of any of the mink during any stage of the disease.

PATHOLOGICAL CHANGES

Fibrinonecrotic enteritis splenomegaly and enlargement of mesenteric lymph nodes were observed in all mink examined on the fifth through the tenth day after infection. Gross and microscopic changes will be described in detail in a subsequent report.

DISCUSSION

Due to individual constitutional differences and possible variations in susceptibility, it would be presumptuous to expect all mink exposed to MEV to react in the same degree. However, signs of the disease developed almost simultaneously in all exposed animals and regressed on the tenth day after infection in all of the survivors. Moreover, all of the mink appeared to be equally affected on any given day during the course of the disease. These circumstances tend to support the premise that the time of occurrence and sequence of changes in the blood and tissues could be deduced from examination of a small number of animals killed at successive stages of the disease.

In general, the time of onset, the duration and the character of the clinical signs of VEM observed were similar to those reported previously for both the experimentally induced and naturally occurring disease (8, 9, 10). However, intestinal casts were seen in the stool of only about half of the animals which is perhaps a lower incidence than one might expect, judging from earlier reports. Also, casts were observed only during the first three days after diarrhea began. In later stages of the disease, the feces consisted mostly of yellowish-green watery fluid and contained relatively small quantities of mucus. Such changes in the stool likely resulted from progressive damage of the intestinal mucosa followed by inflammation and exudation of fluid.

Anorexia and fluid loss from vomiting and diarrhea would be expected to cause dehydration of affected animals. However, although a slight elevation of hematocrit was detectable beginning on the fifth day after infection, dehydration was not suggested by the appearance of the animals or by necropsy findings until the seventh and eighth day. Hematocrit values returned to normal and normal appearance was rapidly regained by surviving animals which resumed eating.

Several investigators have reported that leukopenia is a common feature of VEM (1, 6, 7). However, the reports differ with respect to the total leukocyte count below which the mink were considered leukopenic. The range of the normal white blood cell (WBC) count for mink given by Coffin (2) is 5,700 to 9,300 cells per mm^3 of blood. Myers *et al* (7) found that 93 percent of WBC counts carried out on healthy mink kits fell within this range and obtained no

counts less than 6,000 cells mm³. On this basis, they regarded a total WBC count less than 5,000 cells per mm³ to be indicative of leukopenia and found that leukopenia consistently developed in susceptible 10 to 16-week-old mink by the sixth day after infection with MEV. Burger and Gorham (1) considered a WBC count less than 3,000 leukocytes per mm³ of blood to indicate leukopenia. They observed a "transient" leukopenia in some mink on the fifth through the ninth day after exposure to MEV.

In the present study, 58 WBC counts made prior to infection ranged from 6,100 to 13,900 cells per mm³ with a mean of 9,430 and a standard deviation of ± 2,197. Since these findings were similar to those of Myers *et al.* (7), mink which had total WBC counts less than 5,000 cells mm³ were considered to be leukopenic. With this criterion, leukopenia was found in seven of nine mink examined on the fifth through the ninth day after infection with MEV. Since multiple examinations of the blood of individual animals were not carried out, it is not known whether leukopenia developed gradually or suddenly or how long it persisted. Judging by data obtained from different animals examined on successive days, it appears that leukopenia developed rapidly, but not precipitously, and was maintained for about 72 hours.

Absolute lymphopenia was observed in all mink within 48 hours after inoculation with MEV, and, although most marked at the height of the disease, persisted in all infected animals examined through the 11th day. Neutropenia, however, was found only in leukopenic mink. While the latter finding suggests that leukopenia in VEM results from loss of circulating neutrophils, comparison of mean lymphocyte and neutrophil counts of infected mink with those of uninfected mink reveals that the proportionate decrease in total lymphocytes was much greater than the decrease in total neutrophils. Thus, although neutropenia may have provided the final impellent, leukopenia was attributed largely to a decrease of circulating lymphocytes. The deficiency of lymphocytes was further emphasized by the relative neutrophilia observed in leukopenic mink while such animals were, in fact, neutropenic. It is interesting that lymphopenia is also a feature of viral enteritis of cats (FVE), however, leukopenia in affected cats is attributable primarily to a decrease in circulating neutrophils. Furthermore, neutropenia in FVE-infected cats is usually so marked that relative lymphocytosis results. (5, 8).

Elevation of the mean of the hematocrit values observed in mink on the fifth through the ninth days after infection suggests that there was some degree of hemoconcentration during the height of the disease. Slight, concurrent alterations in red cell count and hemoglobin content of the blood, were noted but did not prove to be statistically significant.

REFERENCES

1. BURGER, D. and J. R. GORHAM, State College of Washington. Progress Reports. Mink Farmers Res. Found. 1960.
2. COFFIN, D. L. Manual of Veterinary Clinical Pathology. 3rd edition. pp. 156-157. Ithaca, New York: Comstock Pub. Assoc. 1953.
3. GORHAM, F. R. and G. R. HARTSOUGH. Virus diseases of mink. Proc. Bk. Am. vet. med. Ass. 91: 244-247. 1954.
4. KNOX, B. Virus enteritis of mink in Denmark. Nord. Vet. Med. 12: 145-169. 1960.
5. LAWRENCE, J. S., J. T. SYLVERTON, J. S. SHAW and F. P. SMITH. Infectious feline agranulocytosis. Am. J. Path. 16: 333-335. 1940.
6. MACPHERSON, L. W. Feline enteritis virus — its transmission to mink under natural and experimental conditions. Can. J. comp. Med. 20: 197-202. 1956.
7. MYERS, W. L., J. O. ALBERTS and C. A. BRANDLY. Certain characteristics of the virus of infectious enteritis of mink and observations on the pathogenesis of the disease: Preliminary report. Can. J. comp. Med. 23: 282-287. 1959.
8. SCHALM, O. W. Veterinary hematology, 2nd Ed. pp. 530-531. Philadelphia Pa: Lea and Febiger. 1965.
9. SCHOFIELD, F. W. Virus enteritis in mink. N. Am. Vet. 30: 651-654. 1949.
10. WILLS, C. G. Notes on infectious enteritis of mink and its relationship to feline enteritis. Can. J. comp. Med. 16: 419-420. 1952.
11. WILLS, D. G. and J. BELCHER. The prevention of virus enteritis of mink with commercial feline panleukopenia vaccine. J. Am. vet med. Ass. 128: 559-560. 1956.