Pathological Changes in Virus Enteritis of Mink

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SUMMARY

The lesions which characterize viral enteritis of mink (VEM) were studied in twenty-six, ten-week-old mink which had been infected by force feeding a tissue suspension containing a Wisconsin strain of mink enteritis virus. The pathogenesis of the lesions was reconstructed from gross and histopathological changes observed in animals which were selected randomly from the group each day for necropsy during the course of the disease.

Alterations were observed in the tissues of all mink examined from post-inoculation day (PID) 4 through 13. The principal macroscopic lesions which consisted of fibrinous enteritis, enlargement and hemorrhage of the spleen and edema of mesenteric and hepatic lymph nodes were most conspicuous on PID 7 and 8. Histopathological changes including necrosis and desquamation of intestinal epithelium, depletion of mature lymphocytes in lymph nodes, thymus and spleen and loss of partly differentiated myeloid and erythroid cells from spleen and bone marrow also reached full development on PID 7 and 8. However, nuclear inclusion bodies which were presumed to be a product of the causative agent and, therefore, of diagnostic significance were most prevalent on PID 3, 4 and 5. The inclusions were observed in mucosal epithelial cells of the intestine, parenchymal cells of the liver and in lymphocyte precursor cells of the spleen, intestinal lymph nodules and mesenteric and hepatic lymph nodes.

RÉSUMÉ

On étudia les lésions caractéristiques de l'entérite à virus du vison (VEM) chez 26 animaux âgés de dix semaines, infectés en leur faisant ingérer de force une suspension tissulaire contenant une souche du virus Wisconsin. L'évolution des lésions fut observée macroscopiquement et microscopiquement en effectuant des nécropsies d'animaux choisis au hasard au cours de la maladie..

On remarqua des altérations tissulaires chez tous les visons examinés entre quatre et treize jours après l'inoculation (PID). Macroscopiquement, les principales lésions consistaient en une entérite fibrineuse, de la splénomégalie et de la splénorragie ainsi que de l'oedème des ganglions mésentériques et hépatiques, particulièrement les septième et huitième jour après l'inoculation (PID).

Histologiquement, on notait de la nécrose et de la desquamation de l'épithélium intestinal, de l'épuisement des ganglions lymphatiques, du thymus et de la rate en lymphocytes matures et la disparation de cellules myéloïdes et érythroïdes partiellement différenciées de la rate et de la moëlle osseuse. Ces caractéristiques étaient entièrement apparentes à partir des septième et huitième jour après l'inoculation (PID). On constata cependant que les corps d'inclusion nucléaires, présumément produits par l'agent causal et donc d'intérêt diagnostique, étaient plus abondants les troisième, quatrième et cinquième jour (PID). On trouva ces inclusions dans les cellules épithéliales de la muqueuse intestinale, le parenchyme hépatique et les pré-lymphocytes de la rate et des ganglions lymphatiques intestinaux, mésentériques et hépatiques.

INTRODUCTION

Macroscopic lesions characteristic of the advanced or terminal stages of viral enteritis of mink (VEM) have been described in several reports (5, 10, 16). Changes consistently observed in affected mink include: enteritis, enlargement of mesenteric lymph nodes, splenomegaly and splenic hemorrhage. Lesions apparently are similar both in naturally acquired and experimentally induced infections. Some histopathological alterations observed in the intestines of animals in the advanced stages

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Supported in part by a grant from the Mink Farmers Research Foundation. Animals used in the study were supplied by the Illinois Mink Farmers Research Association.

of the disease have also been described. According to reports by Schofield (16) and Myers and Fritz (11), intestinal lesions six to seven days after infection consist of necrosis and sloughing of the mucosal epithelium accompanied by pronounced swelling or "ballooning" of cells lining the crypts of Liberkühn. Myers and Fritz (11) also reported the occurrence of both nuclear and cytoplasmic inclusion bodies in intestinal epithelial cells. Both types of inclusions reportedly were Feulgen-negative and were observed only in the "proximal portion" of the small intestine. Cytoplasmic inclusions were seen only in greatly swollen cells within the crypts.

No studies which demonstrate the pathogenesis of the lesions or describe, in detail, microscopic changes in organs other than the intestine have been reported. Thus, criteria for pathological diagnosis of VEM and bases for assessment of pathological findings in suspected cases have not been established.

METHODS

The methods used for identification and inoculation of animals with mink enteritis virus (MEV) and the general design of the study have been described (12). In brief, two mink randomly selected from a group of twenty-six, ten-week-old, female mink were killed and examined every 24 hours from the second through the tenth day following oral inoculation of virus. Two additional mink, which apparently had survived the disease were killed and examined on post-inoculation day (PID) 13. With the exception of two mink which died on PID 8, all animals were examined immediately after having been killed by exsanguination.

Impression films of femoral and sternal bone marrow from each animal were air dried and stained with Wright's stain. Specimens of the lungs, liver, kidneys, spleen, heart, salivary glands, pancreas, thymus, adrenals, thyroids, parathyroids, gall bladder, urinary bladder, trachea, cerebrum, cerebellum, medulla, stomach, duodenum, jejunum, ileum, colon and mesenteric, hepatic, cervical mediastinal and iliac lymph nodes were collected from each animal for histopathological examination. At least five, and sometimes ten specimens were taken from each portion of the intestine listed.

The tissues were fixed in Zenkers fluid with acetic acid for eight hours, washed for two hours in running tap water, placed in 80 per cent ethanol for three to four hours and finally processed by the paraffin method. After sectioning, the tissues were stained with Harris' hematoxylin and eosin B. Selected duplicate sections also were stained by the Feulgen (7) or the May-Grunwald-Giemsa method. For assessment of pathological changes, each tissue specimen was compared with a corresponding specimen taken from uninfected mink of the same age.

Bacteriological studies which were described in an earlier report (12) were carried out on specimens of intestinal contents, kidneys, spleen, liver and lungs of each animal.

OBSERVATIONS

As reported previously (12), clinical signs of VEM appeared in all of the mink on PID 4 and regressed rapidly in all survivors, beginning on PID 10. On the basis of clinical observations, all of the mink appeared to be affected equally on any given day during the course of the disease.

The external appearance of mink killed for examination during the early stages of the disease was not altered substantially. However, on PID 7, 8, and 9, all mink subjected to necropsy appeared thin and had rough, unkempt fur. Dried mucus was observed at the inner canthus of the eyes and the conjunctivae were severely congested. When the bodies of such animals were opened, signs of dehydration and mild icterus were apparent. The mesenteric and serosal vessels were engorged with blood and strands of fibrin were often found overlying the liver, spleen and intestines.

The external appearance of mink examined on PID 10 through 13 was nearly normal. Mild congestion of the mesentery and intestinal serosa persisted, but signs of dehydration and icterus had virtually disappeared. Macroscopic and microscopic lesions which appeared in the intestinal tract, lymph nodes, spleen, bone marrow, liver and thymus during the course of the disease are described in the text which follows.

Intestinal Tract

Except for mild congestion, no gross changes were detected in the intestines of mink examined on PID 2 and 3. However, microscopic examination revealed an increased proportion of goblet cells in the

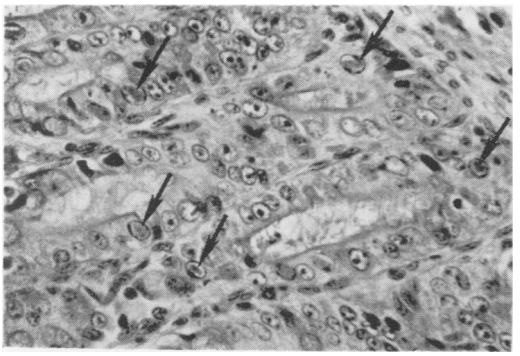

Fig. 1. Degeneration and nuclear inclusion body formation (arrows) in mucosal epithelium of lower ileum of mink killed on PID 4. H and E stain. X380.

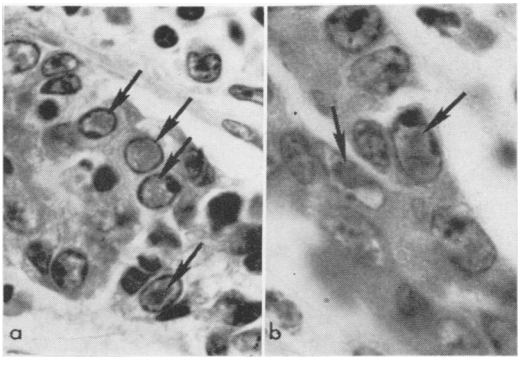

Fig. 2. Granular nuclear inclusion bodies (arrows) in mucosal epithelial cells of ileum of mink killed on PID. 5. H and E. stain. a. X700 b. X1110.

mucosal epithelium and increasing numbers of lymphocytes and other mononuclear leukocytes in the lamina propria. The changes were most marked in the distal two-thirds of the ileum.

On PID 4 and 5, the intestines of all mink examined contained large quantities of mucus. Moderate congestion of the intestinal mucosa was also observed, but no other changes were apparent. Microscopic examination revealed that half to two-thirds of the epithelial cells lining the crypts and covering the sides of the villi had undergone necrosis. Many of the remaining epithelial cells contained nuclear inclusion bodies (Fig. 1, 2). Some of the inclusions completely filled the nucleus of affected cells while others were separated from the nuclear chromatin by a clear zone or halo. The former were slightly basophilic and Feulgen-positive; the latter were entirely eosinophilic and Feulgen-negative. In addition, the latter type of inclusion body often did not constitute a single discrete intranuclear mass, but consisted of loose aggregates of granular material occupying the central portion of the nucleus. Inclusions similar to both types seen in the intestinal epithelium were also observed in the nuclei of a few large lymphocytes or reticular cells in submucosal lymph nodules (Fig. 3). The lamina propria of the intestine contained large numbers of mononuclear and polymorphonuclear leukocytes.

The intestines of mink examined on PID 6 were severely congested and edematous. A readily visible layer of fibrin covered the mucosa throughout the entire small intestine, but was especially prominent in the lower two-thirds of the ileum. The intestinal contents consisted of mucus and yellowish-green, watery fluid.

Additional accumulation of fibrin on the mucosa and an increasing fluid content of the intestine were observed in animals examined on PID 7 and 8. Concurrently, the intestine became distended and flaccid, but the walls remained thickened as a result of persisting edema. Scattered petechial hemorrhages appeared on both the mucosa and serosa.

Microscopic examination of the intestines of mink killed on PID 6, 7, and 8 disclosed progressive necrosis of the mucosal epithelium, increasing edema of the submucosa and increasing accumulation of leukocytes, especially neutrophils, in the lamina propria. Destruction of epithelium covering the sides of the villi and lining the crypts was so rapidly progressive and so extensive in the ileum that even by PID 6, few cells containing inclusion bodies remained. In the duodenum and jejunum, however, loss of epithelium occurred more gradually and

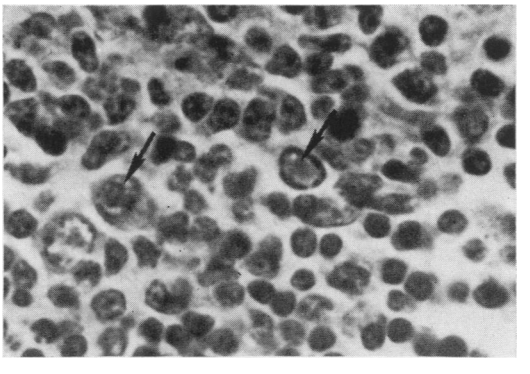

Fig. 3. Nuclear inclusion bodies (arrows) in transitional lymphocytes in submucosal lymph nodule of ileum of mink killed on PID 5. H and E stain. X1110.

was incomplete in many areas. For those reasons, inclusion bodies, although not prevalent, could be found in the upper portion of the intestine with relative ease through PID 7 and 8. Both the cytoplasm and nuclei of epithelial cells underwent marked swelling in the process of degeneration which preceded necrosis and sloughing. Such swelling occurred both in cells which contained inclusions and in those which did not.

By PID 8, the only intact mucosal epithelium remaining in the lower ileum was found in crypts overlying submucosal lymph nodules. In the duodenum and jejunum, meanwhile, foci of regenerating cells developed adjacent to areas in which necrosis was still progressive.

The intestines of mink examined on PID 9 were virtually empty. Fibrin coating the mucosa had sloughed in a few areas exposing deeply reddened tissue beneath. In such areas, which were most prevalent in the ileum, microscopic examination revealed that the villi were completely denuded and greatly shortened. In intervening parts of the intestine, evidence of epithelial cell regeneration was prominent. Replacement of cells had progressed most in the duodenum and jejunum, but had also begun in the ileum. Inclusion bodies were rare in all parts of the tract.

On PID 10, the intestines had nearly normal tone and contents. Mild congestion and edema persisted, but the layer of fibrin which coated the mucosa was quite thin. Areas where sloughing of fibrin and epithelium had occurred were neither numerous nor distinct. Microscopic examination revealed that regeneration of epithelium was nearly complete in the duodenum and jejunum and was well advanced in the ileum. Numerous lymphocytes, plasma cells, macrophages and neutrophils remained in the lamina propria throughout the intestines.

On PID 13, both the serosal and mucosal surfaces of the intestine had a yellowish-tan cast when examined at necropsy. A few scattered fibrin deposits still adhered to the mucosa; the rest presumably had undergone lysis or had sloughed without serious disturbance to the underlying tissue. Tone and contents of the intestines were normal. Microscopic examination revealed almost complete regeneration of mucosal epithelieum in all portions of the intestine. However, cell debris remained in many of the crypts and leukocytes were still conspicuous in the lamina propria.

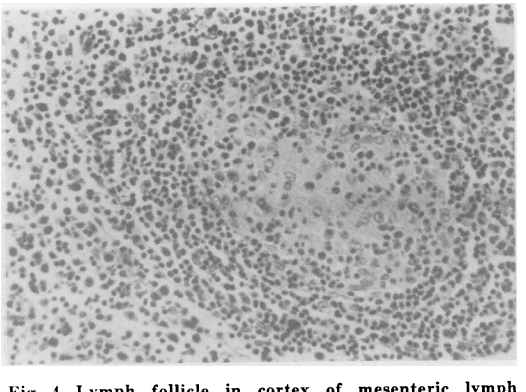

Fig. 4. Lymph follicle in cortex of mesenteric lymph node of mink killed on PID 6. Most of the small lymphocytes have been lost from the periphery of the follicle and an amorphous, eosinophilic substance fills the germinal center. H and E stain. X180.

Lymph Nodes

No significant gross alterations were observed in the lymph nodes of any of the mink examined through PID 5. However, beginning on PID 2, microscopic examination of the mesenteric and hepatic nodes revealed increasing evidence of accelerated lymphopoiesis in the follicles and hyperplasia of macrophages in the sinuses. Concurrently, there was increasing evidence of lymphocyte necrosis, both in the follicles and medullary cords. Similar, but much less striking changes were observed in the cervical, mediastinal and iliac nodes. On PID 4 and 5, nuclear inclusion bodies like those seen in the intestine and submucosal lymph nodules were observed in a few of the large lymphocytes or reticular cells in the germinal centers. Cells containing inclusions were less frequently observed in the medullary pulp.

On PID 6, the mesenteric and hepatic nodes of both mink examined were enlarged as much as five times their normal size. Cervical, mediastinal and iliac nodes were enlarged only slightly. The mesenteric nodes had a soft consistency and exuded large quantities of clear fluid when incised. Microscopic examination revealed evidence of marked edema and lymphocyte necrosis. The population of small lymphocytes had been reduced by half or more and the germinal centers contained varying quantities of amorphous, eosinophilic material in which only a few reticular cells and transitional lymphocytes persisted (Fig. 4). No cells containing inclusion bodies were seen

and there was virtually no mitotic activity among the lymphoid cells. Large (12 to 20 microns dia). round or oval undifferentiated cells were conspicuous throughout the nodes, but especially in the medullary cords. Morphological and tinctorial features of such cells varied to some extent, but most were round or oval with deeply eosinophilic cytoplasm and hyperchromatic nuclei. The nuclei were often eccentric in position and occasionally bore an identation. Cervical, mediastinal and iliac nodes were slightly edematous and contained some evidence of lymphocyte necrosis, but the alterations were not outstanding.

The population of undifferentiated cells in the mesenteric and hepatic nodes increased markedly while loss of small lymphocytes continued through PID 8. Severe edema, evident both on macroscopic and microscopic examination of the nodes, persisted.

Enlargement or fusion of some of the undifferentiated cells gave rise to moderate numbers of multinucleate giant cells which were conspicuous in the mesenteric and hepatic nodes of mink killed on PID 9 (Fig. 5). Evidence of renewed lymphopoiesis was also observed on PID 9. Much of the eosinophilic material which had accumulated in the germinal centers during earlier stages of the disease had been replaced by reticular cells and transitional lymphocytes. Miotic figures were prevalent among the new cells and the zone of small lymphocytes normally present around the germinal centers was again evident.

On PID 10, the mesenteric and hepatic nodes were still slightly enlarged and moderately edematous. However, evidence of active lymphopoiesis was present in nearly every follicle and it was apparent that the population of small lymphocytes in both cortex and medulla had been partially restored. Because of this, the undifferentiated cells which had constituted almost the entire cell population of the cords on PID 8 and 9 were less conspicuous. Giant cells also appeared to be less numerous.

By PID 13, proliferation of lymphocytes in the mesenteric and hepatic nodes had resulted in enlargement (Fig. 6) and blending of adjacent follicles in the cortices and complete restoration of lymphocyte populations in the medullary cords. Similar, but less prominent signs of accelerated lymphopoiesis were observed in the cervical, mediastinal and iliac nodes. Signs of edema were no longer evident in any of the nodes.

SPLEEN

No significant macroscopic changes were observed in the spleens of mink examined during the first five days after inoculation of virus. However, on PID 6, the spleens of both mink examined were slightly enlarged and on PID 7, 8 and 9, the spleens of all mink killed were enlarged three to four times normal size. The affected spleens were excessively soft and had a dull red to tannish-pink color with dark red mottling. The dark red areas were large and irregular and were ascribed to intense focal congestion or hemorrhage. Splenomegaly was less pronounced in mink examined on PID 10, but the abnormal color and consistency persisted. On PID 13, the spleens appeared normal except for slight enlargement and excessive friability.

Some of the histopathological changes in the spleen were difficult to detect. The difficulty was attributable mainly to the fact that the red pulp of the mink spleen is

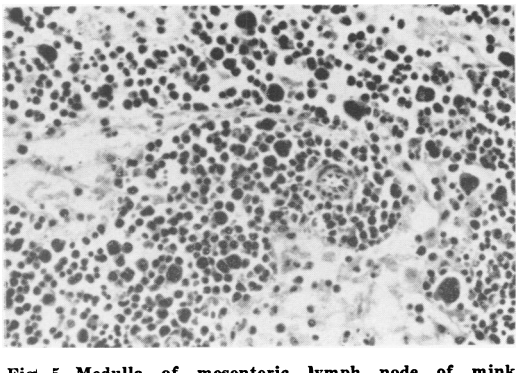

Fig. 5. Medulla of mesenteric lymph node of mink killed on PID 9. Cords are filled with hyperchromatic undifferentiated cells and giant cells. H and E stain. X180.

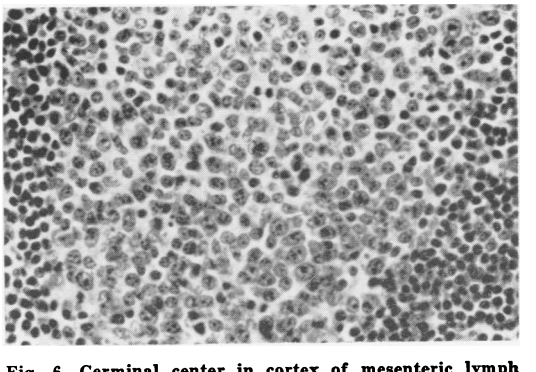

Fig. 6. Germinal center in cortex of mesenteric lymph node of mink killed on PID 13. Precursor cells, large lymphocytes and cells in mitosis are numerous. H and E stain. X380.

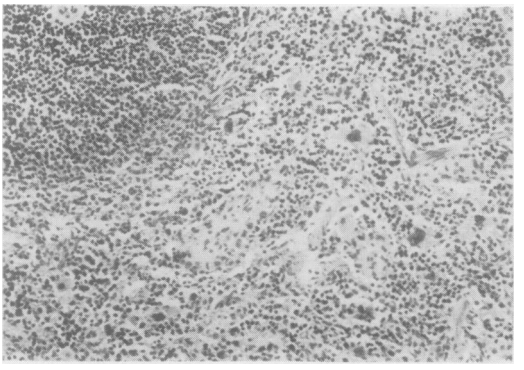

Fig. 7. Spleen of uninfected mink with normal follicle (upper left) and red pulp containing myelopoietic and erythropoietic cells. H and E stain. X70.

Fig. 8. Spleen of mink which died on PID 8. Cell populations in red pulp are reduced and focal hemorrhages (arrow) are present. H and E stain. X70.

populated in part by erythropoietic and myelopoietic cells with all stages of development represented. The classification of undifferentiated cells within such a mixed population presented many difficulties.

There were no signs of accelerated lymphopoiesis in the splenic follicles during early stages of the disease. In other respects, changes affecting the lymphoid elements of the spleen were less striking, but generally similar to changes observed in the lymph nodes. Nuclear inclusion bodies were seen in a few transitional lymphocytes or reticular cells in the germinal centers on PID 4 and 5. On PID 6, loss of small lymphocytes from the periphery of the follicles was apparent and evidence of lymphopoietic activity was reduced. Necrosis and loss of mature lymphocytes continued through PID 7 and 8. However, the population of precursor cells and transitional lymphocytes in the center of the follicles appeared to increase while the amorphous eosinophilic substance which had accumulated in the germinal centers practically disappeared from most of the follicles. Loss of lymphocytes from the follicles was accompanied by loss of some of the myeloid and erythroid cells as well as most of the lymphocytes from the red pulp. By PID 8, the red pulp contained virtually no lymphocytes and less than half the normal number of metarubricytes, metamyelocytes, band cells and fully differentiated granulocytes. Focal congestion, hemorrhage and mild proliferation of macrophages accompanied the loss of such cells. Degeneration and loss of megakaryocytes were observed only in the spleens of mink which died on the eighth day (Figs. 7 and 8).

By day 10, there was evidence of renewed lymphopoiesis in the splenic follicles, but the population of lymphocytes and of developing erythrocytes and granulocytes in the red pulp remained low. On PID 13, the splenic follicles were slightly larger than normal because of the prevalence of transitional lymphocytes and lymphoblasts in the germinal centers and broadening of the zones of small lymphocytes which surrounded them. Cell populations in the red pulp appeared to be nearly normal.

Bone Marrow

The myeloid-erythroid ratios obtained from cell counts of the marrow of uninfected mink in this and preliminary studies were so highly variable that a range of values useful for comparison with cell counts in the bone marrow of infected animals was not established. However, changes in the cellular constitutents of the marrow during the course of the disease appeared to be similar to alterations in the myeloid and erythroid elements of the spleen. A considerable reduction in numbers of myeloid and erythroid cells in advanced stages of differentiation was apparent in marrow specimens from mink examined on PID 7 through 10. Undifferentiated cells and megakaryocytes were not substantially reduced in number except in animals which died on the eighth day.

Liver

Nuclear inclusion bodies were observed in hepatic cells of all mink killed on PID 4 and 5 (Fig. 9). The inclusions were not numerous. Only rarely was it possible to

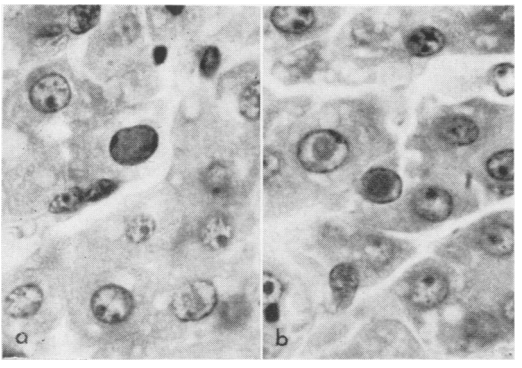

Fig. 9. Nuclear inclusion bodies in hepatic cells of mink killed on PID 4. Some of the inclusions completely fill the nucleus (a) while others (b) are surrounded by clear zones. H and E stain. X700.

find areas in the liver specimens which contained more than three or four inclusion-bearing cells per high power field. Some inclusions filled the nuclei; most were separated from the marginated nuclear chromatin by a clear zone. Like the inclusions observed in the intestine, the former tended to be finely granular, slightly basophilic and Feulgen positive while the latter were coarsely granular, entirely eosinophilic and Feulgen negative.

The affected livers were not otherwise altered except for moderate parenchymatous degeneration. No inclusion bodies were found in the livers of any of the mink examined after PID 5; however, parenchymatous degeneration of gradually increasing severity was observed through PID 10.

THYMUS

Loss of small lymphocytes from the cortex of the thymus occurred beginning on PID 6 and 7. As a result, the histological distinction between cortex and medulla was soon lost and the thymic lobules were reduced in size. Reticular cells persisted and appeared to proliferate to some extent, but the cortex remained almost devoid of lymphocytes through PID 13 (Figs. 10 and 11).

Changes in tissues other than those described in the preceding text were mild and appeared to be wholly non-specific. Parenchymatous degeneration and congestion developed in the kidneys and myocardium of the mink, beginning on PID 5 and 6. The changes gradually increased in severity through PID 10. Excessive storage of zymogen granules was observed in the pancreas and moderate inspissation with retention of bile in the gall bladder were observed in mink examined on PID 6 through 8. No significant changes were detected in the other organs examined.

DISCUSSION

A relationship between the formation of nuclear inclusion bodies and necrosis of intestinal epithelium in the infected mink appeared to be clear. However, until it has been demonstrated that such inclusions contain specific antigens or are related to the development or replication of mink enteritis virus, their significance can only be

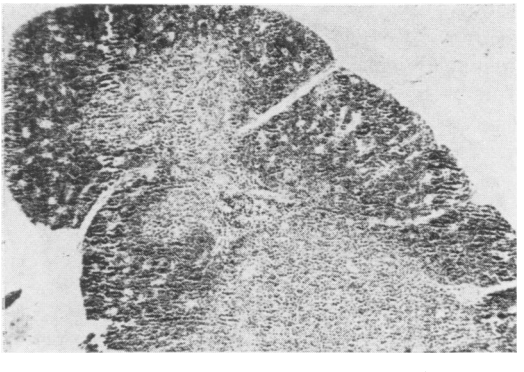

Fig. 10. Thymus of uninfected mink with typical, dense population of small lymphocytes in cortex. H and E stain. X70.

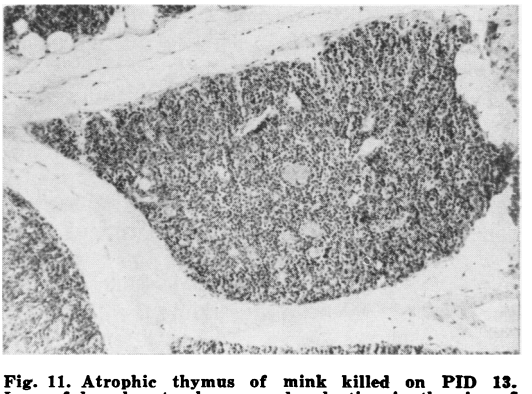

Fig. 11. Atrophic thymus of mink killed on PID 13. Loss of lymphocytes has caused reduction in the size of lobules and loss of distinctive appearance of cortex. H and E stain. X70.

surmised. Should the inclusions prove to be pathognomonic of the disease, the results of this study indicate that in order to demonstrate them, the diagnostic pathologist must seek animals still in early stages of the disease. Inclusions were numerous in the intestinal epithelium of all mink examined during the first three to four days after the appearance of clinical signs of VEM. As is often true in cases of infectious feline enteritis in fully susceptible kittens, however, destruction of intestinal epithelium was so far advanced by the time the animals approached a moribund state that inclusions could rarely be demonstrated. The likelihood that inclusion bodies would be observed in the liver and lymphoid tissues in naturally occurring VEM is greatly reduced by the apparent paucity of inclusions, as well as their early and transient occurrence in those sites. Cytoplasmic inclusions which were observed by Myers and Fritz (11) in the intestinal mucosa in VEM were not observed in any of the mink examined in the course of the study.

The nuclear inclusions observed in the intestines, lymph nodes and liver could be placed into one of two general categories based on their structure and staining qualities. One form of inclusion was eosinophilic, Feulgen negative, distinctly granular and separated from the marginated chromatin and nucleolus by a clear zone or halo; the other type was moderately basophilic, Feulgen positive, finely granular or homogenous and filled the entire nucleus. Actually, many minor structural and tinctorial variations were represented among inclusions within each category. Forms resembling several of the developmental stages of feline panleukopenia inclusion bodies depicted in a report by Johnson (4) were seen. The nuclear inclusion observed by Myers and Fritz (11) in the intestines of mink with VEM reportedly were all of the Cowdry (1) type A, Feulgen negative form. Intestinal inclusion bodies observed in most early studies on feline panleukopenia have also been described as type A (2, 3, 6) and Feulgen negative (8). More recently, however, Lust, Gorham and Sato (9) demonstrated that the fully developed nuclear inclusion bodies, produced by a variant of feline panleukopenia virus in tissue cultures, were DNA positive.

The destruction of lyphocytes in the lymph nodes, intestinal lymph nodules, spleen and thymus during the course of VEM is an intriguing aspect of the disease. Although perhaps a non-specific phenomenon, this effect almost certainly contributed to the occurrence of lymphopenia in the mink (12) and warrants additional study. Similar changes have been observed in the lymphatic organs of germfree cats following inoculation with feline enteritis virus (15). The consistent finding of such changes in the absence of intestinal lesions led the authors to speculate that "lymphocytes may be the target cells for the virus." Repeated observation of lymphocyte depletion (8, 14) and of the occurrence of inclusion bodies in the lymphatic tissues of cats infected with infectious enteritis virus (2, 3, 6, 8) lends considerable support to such a hypothesis. The paucity of inclusions observed in sites of lymphocyte destruction is not incongruous considering the variety of factors which may influence viral cytopathic effects. In attempting to discover the cause or causes of lymphocyte destruction in both VEM and feline enteritis, consideration must be given to influence of the diseases on adrenal secretions as well as to the possible action of a lymphocytolytic product derived from virus infected cells.

Since little evidence of necrosis in progress was observed among erythropoietic and myelopoietic cells in the spleen or bone marrow of the mink, the mode of cell depletion in those elements would seem to differ from that which resulted in loss of cells from the lymphatic organs. Large numbers of immature myeloid cells have been observed in the blood of mink seven to nine days after infection with mink enteritis virus (13). Whether this occurrence bears any relationship to the disappearance of partially differentiated blood cells from the spleen and bone marrow which begins around the sixth day after infection is not known. However, maturation arrest in the hematopoietic tissues could be responsible for both phenomena.

REFERENCES

1. **COWDRY, E. V.** The problem of intranuclear inclusions in virus diseases. Archs. Path. **18**: 527-542. 1934.
2. **HAMMON, W. D. and J. F. ENDERS.** A virus disease of cats, principally characterized by aleukocytosis, enteric lesions and the presence of intranuclear inclusion bodies. J. exp. Med. **69**: 327-351. 1939.
3. **HAMMON, W. D. and J. F. ENDERS.** Further studies on the blood and hematopoietic tissues in malignant panleukopenia of cats. J. exp. Med. **70**: 557-564. 1939.

4. **JOHNSON, R. H.** Feline panleukopenia virus. II. Some features of the cytopathic effects in feline kidney monolayers. Res. vet. Sci. **6**: 472-481. 1965.

5. **KNOX, B.** Virus enteritis of mink in Denmark. Nord. Vet. Med. **12**: 145-169. 1960.

6. **LAWRENCE, J. S., J. T. SYLVERTON, J. S. SHAW and F. P. SMITH.** Infectious feline agranulocytosis. Am. J. Path. **16**: 333-335. 1940.

7. **LILLIE, R. D.** Histopathologic Technic and Practical Histochemistry. pp. 132-133. New York and Toronto: The Blakiston Co., Inc. 1954.

8. **LUCAS, A. M. and W. H. RISER.** Intranuclear inclusions in panleukopenia of cats. Am. J. Path. **21**: 435-465. 1945.

9. **LUST, S. J., J. R. GORHAM and N. SATO.** Occurrence of intranuclear inclusions in cell cultures infected with infectious feline enteritis virus. Am. J. vet. Res. **26**: 1163-1166. 1965.

10. **MACPHERSON, L. W.** Feline enteritis virus — its transmission to mink under natural and experimental conditions. Can. J. comp. Med. **20**: 197-202. 1956.

11. **MYERS, W. L. and T. E. FRITZ.** Histopathologic changes in virus enteritis of mink. Can. J. comp. Med. **23**: 246-249. 1959.

12. **REYNOLDS, H. A.** Some clinical and hematological features of virus enteritis of mink. Can. J. comp. Med. **33**: 155-159. 1969.

13. **REYNOLDS, H. A.** Unpublished data.

14. **RISER, W. H.** The histopathology of panleukopenia in the domestic cat. Am. J. vet. Res. **7**: 455-465. 1946.

15. **ROHOVSKY, M. W. and R. A. GRIESMER.** Experimental feline infectious enteritis in the germfree cat. Pathologia vet. **4**: 391-410. 1967.

16. **SCHOFIELD, F. W.** Virus enteritis in mink. N. Am. Vet. **30**: 651-654. 1949.

Book Review

EXPERIMENTAL MEDICINE AND SURGERY IN PRIMATES. *Annals of the New York Academy of Sciences, Volume 162, Article 1, June 3, 1969. Editor-in-Chief: Marc Krauss. Consulting Editors: Edward I. Goldsmith and J. Moor-Jankowski. Published by the New York Academy of Sciences, 704 pages. Price $32.50.*

This publication reports the proceedings of a conference entitled "Experimental Medicine and Surgery in Primates" held in New York in September, 1967.

The conference was the first of two such gatherings in which investigators utilizing primates in biomedical research assembled to report their results and observations.

The more than 70 papers presented are grouped into eight categories, namely: Taxonomy and Comparative Biology, Cardiovascular Studies, Phylogenetics, Perinatal and Related Problems, Procurement and Maintenance, Experimental Surgery, Infectious Disease and Toxicology.

Specific topics receiving detailed coverage include: atherosclerosis and transplantation immunology and the role of immmunoglobulins in determining the phylogenetic relationships between man and the lower primates.

The six papers discussing atherosclerosis provide an excellent summary of the then current situation with respect to the experimental production of this disease in the subhuman primate. The data reported would be necessary reading for one embarking on research into this field. The same may be said of the papers discussing transplantation immunology; however, research is progressing so rapidly in this area that much of what was then reported must now be reassessed.

One hundred and thirty-two authors have contributed to this work, most of them leading authorities in their respective fields; consequently, many of the papers are highly specific and are of interest only to individuals engaged in investigations into the specific subjects covered.

The preponderance of papers are oriented towards medical research; however, two sections which may be of interest to the veterinarian are those discussing procurement and maintenance of nonhuman primates and infectious disease. These, however, provide minimal new information for the individual familiar with primates and insufficient for the unindoctrinated.

In summary it may be said that this publication offers little to the veterinarian seeking only to familiarize himself with primates and the problems associated with their maintenance and care in the laboratory. However, the investigator intending to use these animals in any study in the biomedical sphere will find the book both a useful and valuable addition to his library. — *M. J. Walcroft.*