CHRONIC INTRAVASCULAR COAGULATION IN ALEUTIAN DISEASE OF MINK

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The demonstration of fibrin and fibrin-like substances within the glomerular capillary loops of a variety of nephropathies, including lupus nephritis, glomerular lesions in rabbits produced by the infusion of thromboplastin, and the almost complete suppression of glomerular damage in Masugi nephritis by anticoagulation, has suggested disseminated intravascular coagulation as a common pathogenic mechanism in these renal alterations. Because the kidney lesions of Aleutian disease of mink have some similarity to those of lupus, it was thought that this animal disease might represent a model for diseases of low-grade, progressive, incomplete intravascular coagulation and offer an opportunity to study the hemostatic mechanism during the course of such a process. Therefore, a project was undertaken to investigate various coagulation parameters in a group of mink throughout the development of the disease. Particular attention has been focused on those components of the clotting system which alter during coagulation, including fibrinogen, platelets, and Factors II, V, and VIII.

MATERIALS AND METHODS

Blood was drawn for control coagulation studies from 20 Aleutian (symbol aa), or blue, mink by cardiac puncture. The mink were then inoculated with a potent preparation of Aleutian disease virus (ID$_{60}$ × 10$^4$). Three weeks following infection, blood was again drawn from all animals; thereafter, the mink were divided into groups so that blood samples could be obtained from representative animals each week. Bleedings of individual animals were spaced so as to prevent inordinate damage from blood loss or frequent cardiac punctures.

Control studies of an uninfected group of Aleutian mink were also started; but during the course of the experiment these animals all became spontaneously infected, invalidating the results. Five infected dark (symbol AA), or non-Aleutian, mink and 5 control dark mink were also studied simultaneously. The control dark mink did not show positive results to an iodine agglutination test, one of the early clinical indications of Aleutian disease. However, there may have been some spontaneous infection.


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even in these animals since the 2 groups of dark mink showed similar changes of many coagulation factors throughout the period of study.

Nine parts of blood were added to 1 part of 0.1 M sodium oxalate for determination of prothrombin time (PT),\(^6\) partial thromboplastin time (PPT),\(^9\) stypven time,\(^10\) and thrombin time (TT)\(^11\) using standard, commercially available reagents. Quantitative results of factor II,\(^12\) Factor V,\(^13\) and Factor VIII\(^14\) are reported in terms of percentage of normal human values. Aged human plasma was used as substrate for Factor V determination, while human hemophilic plasma was employed for Factor VIII. Homologous materials would have been preferable for some of these determinations, but were impractical or impossible to obtain. The changes noted should be valid, however, since the studies involved serial determinations using the same reagents.

Blood was placed in heparinized tubes for fibrinogen\(^15\) and cryofibrinogen\(^16\) determinations, and for measurement of platelet count\(^17\) and platelet adhesiveness. Platelet adhesiveness was calculated as a percentage of platelets removed from the whole blood after passing through a 15-in. length of plastic tubing (9/16-in. diameter) containing tightly packed No. 070 Superlite\(^\circledR\) glass beads (Minnesota Mining and Manufacturing Co.). The blood was forced up through the column of beads by steady hand pressure on a 2-mL plastic syringe. The first 10 drops were discarded, and the next 40 drops were collected over a period of approximately 20 sec. and used for comparison of platelet count with the sample before passage over the glass beads. This is a modification of Salzman's technique.\(^18\)

All of the above determinations were carried out immediately after the blood was drawn. Portions of the oxalated plasma were frozen for later measurement of fibrinolytic parameters. Active fibrinolysis was determined by casein hydrolysis\(^19\) using plasma treated with acid (and subsequently neutralized) to break up the enzyme inhibitor complex.\(^20\) Free and total profibrinolysin were determined by casein hydrolysis\(^19\) using plasma and acid-treated plasma, respectively, activated with streptokinase and a small quantity of highly purified human profibrinolysin.\(^21\) The latter was added to assure maximum activation with streptokinase by supplying proactivator. Mink plasma, however, does contain proactivator capable of reacting with streptokinase since the activation was approximately the same with and without the addition of human material. Nonspecific inhibitors to both the activation and hydrolytic processes were estimated by the difference between free (plasma) and total (acid-treated plasma) profibrinolysin.

**Results**

The results of the coagulation and fibrinolytic determinations for the 9-week study of infected Aleutian mink are shown in Table I. These are expressed in terms of mean value plus or minus standard deviation (S.D.). Results of a simultaneous study carried out on smaller groups of infected and control dark mink are shown in Table II.

Since deposition of fibrin is the end product of coagulation, changes in fibrinogen levels are of key importance. Text-figure 1 shows the mean values and S.D.'s for fibrinogen obtained during the 9-week study of infected Aleutian mink. A significant drop (\(p < 0.001\)) was found between control levels and those of infected mink 3 weeks after infection. The levels at 4, 5, and 6 weeks were also lower. These levels indicate a period of the disease when intravascular coagulation was of particular importance. Between the fifth and seventh weeks, intravascular coagulation
TEXT-FIG. 1. Mean fibrinogen levels and S.D.'s of infected Aleutian mink.

TEXT-FIG. 2. Factor II, V, and VIII levels in mink with Aleutian disease.

TEXT-FIG. 3. Fibrinogen and Factor V levels in mink with Aleutian disease.

was either minimal or the animals were able to compensate for loss by overproduction of fibrinogen. The level at the seventh week was significantly higher than that found at Week 5 ($p < 0.01$). The high S.D.'s at Week 6 suggest that some animals were beginning to produce fibrinogen at a higher rate, while others were still having episodes of intravascular coagulation. Alternately decreasing and rising fibrinogen levels were found in the eighth and ninth weeks.

Changes in Factors II, V, and VIII levels in Aleutian disease are shown in Text-fig. 2. There is little variation in prothrombin concentration with maximum changes of $\pm 25\%$ of the original level. Factor V remained steady up to the fourth week, then showed a progressive rise for 3 weeks. There was a significant difference ($p < 0.01$) between the
### Table I

COAGULATION AND FIBRINOLYTIC DETERMINATIONS * FOR ALEUTIAN (AR) MINK INFECTED WITH ALEUTIAN DISEASE

<table>
<thead>
<tr>
<th>Determination</th>
<th>20/0</th>
<th>10/3</th>
<th>3/4</th>
<th>4/5</th>
<th>6/6</th>
<th>4/7</th>
<th>4/8</th>
<th>2/9</th>
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</thead>
<tbody>
<tr>
<td>PT (sec.)</td>
<td>12.1 ± 0.8</td>
<td>11.6 ± 0.8</td>
<td>12.3 ± 1.1</td>
<td>11.5 ± 0.3</td>
<td>12.0 ± 1.3</td>
<td>12.3 ± 0.7</td>
<td>12.0 ± 0.9</td>
<td>11.7 ± 0.7</td>
</tr>
<tr>
<td>PTT (sec.)</td>
<td>36.3 ± 3.7</td>
<td>32.3 ± 4.1</td>
<td>32.0 ± 4.4</td>
<td>29.5 ± 4.8</td>
<td>32.0 ± 1.8</td>
<td>30.3 ± 1.7</td>
<td>28.3 ± 1.4</td>
<td>30.5 ± 0.5</td>
</tr>
<tr>
<td>Factor II (%)</td>
<td>199 ± 59</td>
<td>200 ± 87</td>
<td>173 ± 57</td>
<td>192 ± 26</td>
<td>211 ± 17</td>
<td>255 ± 69</td>
<td>183 ± 15</td>
<td>166 ± 18</td>
</tr>
<tr>
<td>Factor V (%)</td>
<td>419 ± 121</td>
<td>454 ± 151</td>
<td>407 ± 255</td>
<td>578 ± 271</td>
<td>670 ± 142</td>
<td>850 ± 295</td>
<td>588 ± 134</td>
<td>1800 ± 170</td>
</tr>
<tr>
<td>Factor VIII (%)</td>
<td>781 ± 348</td>
<td>1269 ± 587</td>
<td>800 ± 135</td>
<td>985 ± 253</td>
<td>867 ± 306</td>
<td>1190 ± 1074</td>
<td>835 ± 117</td>
<td>660 ± 198</td>
</tr>
<tr>
<td>Plat. (X 10^-4)</td>
<td>748 ± 128</td>
<td>564 ± 183</td>
<td>376 ± 138</td>
<td>385 ± 188</td>
<td>349 ± 94</td>
<td>221 ± 35</td>
<td>283 ± 57</td>
<td>216 ± 114</td>
</tr>
<tr>
<td>Stygven time (sec.)</td>
<td>22.8 ± 2.3</td>
<td>25.1 ± 4.4</td>
<td>13.4 ± 6.9</td>
<td>25.6 ± 6.5</td>
<td>16.9 ± 2.9</td>
<td>19.5 ± 2.0</td>
<td>34.7 ± 3.6</td>
<td>32.2 ± 10</td>
</tr>
<tr>
<td>Plat. adh. (%)</td>
<td>57 ± 25</td>
<td>88 ± 5</td>
<td>34 ± 48</td>
<td>47.0 ± 54</td>
<td>88 ± 3</td>
<td>64 ± 36</td>
<td>58 ± 13</td>
<td>—</td>
</tr>
<tr>
<td>Fib. (mg./100 ml.)</td>
<td>338 ± 34</td>
<td>267 ± 43</td>
<td>201 ± 64</td>
<td>223 ± 31</td>
<td>228 ± 87</td>
<td>310 ± 25</td>
<td>187 ± 69</td>
<td>250 ± 49</td>
</tr>
<tr>
<td>Cryop. (mg./100 ml.)</td>
<td>9 ± 5.0</td>
<td>35 ± 17</td>
<td>45 ± 1</td>
<td>32 ± 9.6</td>
<td>59 ± 12</td>
<td>35 ± 9.5</td>
<td>26.0 ± 6.2</td>
<td>28 ± 5</td>
</tr>
<tr>
<td>Free profib.</td>
<td>5.05 ± 0.9</td>
<td>6.6 ± 1.34</td>
<td>5.1 ± 1.4</td>
<td>12.5 ± 1.6</td>
<td>9.1 ± 2.8</td>
<td>10.3 ± 1.8</td>
<td>6.2 ± 0.54</td>
<td>7.3 ± 1.4</td>
</tr>
<tr>
<td>Total profib.</td>
<td>12.57 ± 1.7</td>
<td>14.6 ± 1.76</td>
<td>12.9 ± 5.3</td>
<td>18.6 ± 3.3</td>
<td>15.1 ± 1.6</td>
<td>16.2 ± 1.6</td>
<td>13.8 ± 3.3</td>
<td>17.2 ± 4.8</td>
</tr>
<tr>
<td>Active fib.</td>
<td>1.0 ± 0.57</td>
<td>0.5 ± 0.62</td>
<td>0.0</td>
<td>0.3 ± 0.58</td>
<td>0.3 ± 0.6</td>
<td>1.6 ± 0.8</td>
<td>0.0</td>
<td>0.3 ± 0.36</td>
</tr>
<tr>
<td>Inhibitor</td>
<td>8.52 ± 1.6</td>
<td>8.4 ± 3.05</td>
<td>7.7 ± 3.9</td>
<td>6.3 ± 1.9</td>
<td>6.3 ± 1.5</td>
<td>7.6 ± 1.2</td>
<td>7.7 ± 3.1</td>
<td>10.1 ± 3.3</td>
</tr>
<tr>
<td>TT (sec.)</td>
<td>17.6 ± 1.8</td>
<td>20.2 ± 3.6</td>
<td>25.7 ± 5.1</td>
<td>28.0 ± 9.0</td>
<td>25.2 ± 3.4</td>
<td>36.0 ± 9.0</td>
<td>32.3 ± 5.1</td>
<td>23.9 ± 2.9</td>
</tr>
</tbody>
</table>

*Expressed in terms of mean value plus or minus S. D.
### Table II

COAGULATION AND FIBRINOLYTIC DETERMINATIONS* FOR DARK MINK (AA)

<table>
<thead>
<tr>
<th>Determination</th>
<th>Injured (No. of mink/wk. post injection)</th>
<th>Control (No. of mink/wk. post injection)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>s/0</td>
<td>s/3</td>
</tr>
<tr>
<td>PT (sec.)</td>
<td>11.1 ± 0.85</td>
<td>11.4 ± 0.92</td>
</tr>
<tr>
<td>PTT (sec.)</td>
<td>38.2 ± 4.4</td>
<td>39.2 ± 3.9</td>
</tr>
<tr>
<td>Factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II (%)</td>
<td>175 ± 17</td>
<td>173 ± 32</td>
</tr>
<tr>
<td>V (%)</td>
<td>328 ± 128</td>
<td>342 ± 121</td>
</tr>
<tr>
<td>VIII (%)</td>
<td>948 ± 390</td>
<td>652 ± 206</td>
</tr>
<tr>
<td>Plat. (× 10^-3)</td>
<td>599 ± 254</td>
<td>681 ± 339</td>
</tr>
<tr>
<td>Stypven time (sec.)</td>
<td>29.2 ± 1.8</td>
<td>25.2 ± 4.7</td>
</tr>
<tr>
<td>Plot. adh. (%)</td>
<td>72 ± 7</td>
<td>89 ± 13</td>
</tr>
<tr>
<td>Fib. (mg./100 ml.)</td>
<td>340 ± 42</td>
<td>341 ± 93</td>
</tr>
<tr>
<td>Cryop. (mg./100 ml.)</td>
<td>20 ± 22</td>
<td>55 ± 15</td>
</tr>
<tr>
<td>Free profib.</td>
<td>5.1 ± 0.27</td>
<td>7.8 ± 1.8</td>
</tr>
<tr>
<td>Total profib.</td>
<td>12.3 ± 1.7</td>
<td>15.0 ± 0.7</td>
</tr>
<tr>
<td>Active fib.</td>
<td>1.1 ± 0.7</td>
<td>0.76 ± 0.64</td>
</tr>
<tr>
<td>Inhibitor</td>
<td>8.0 ± 0.91</td>
<td>8.0 ± 0.80</td>
</tr>
<tr>
<td>TT (sec.)</td>
<td>16.4 ± 1.6</td>
<td>17.0 ± 2.8</td>
</tr>
</tbody>
</table>

* Expressed in terms of mean value plus or minus S.D.
control levels and those of infected mink for the seventh week. A 30\% drop at 8 weeks was followed by a tremendous increase showing a vast overproduction of Factor V—perhaps as a response to previous utilization. Again this increase is significant \((p < 0.001)\). Factor VIII, after an initial sharp rise, showed cyclical variations suggestive of alternate phases of utilization and overproduction. The rise at Week 3 is significant \((p = 0.001)\), while the drop between Weeks 3 and 4 is also significant \((p = 0.02)\).

When fibrinogen and Factor V are compared (Text-fig. 3), it is evident that changes in these 2 substances parallel each other after the initial decrease in fibrinogen level. This parallelism is strong evidence for repeated utilization of both of these factors by a process of intravascular coagulation, and suggests that the rate of production of the 2 proteins may be similar.

Shainoff and Page\textsuperscript{22} have suggested that levels of cryoprotein equivalent to 26\% of the fibrinogen are necessary before fibrin itself can be de-
posited in the tissues. A comparison of fibrinogen and cryofibrinogen are shown in Text-fig. 4. At 4 weeks and again at 6 weeks the condition for fibrin deposition has been fulfilled.

Changes in the fibrinolytic enzyme system are shown in Text-fig. 5. While no obvious correlation can be found between these changes and

**TEXT-FIG. 6.** Fibrinogen levels and platelet counts in mink with Aleutian disease.

**TEXT-FIG. 7.** Platelet count and stypven times in mink with Aleutian disease.

**TEXT-FIG. 8.** Platelet adhesiveness and platelet count in mink with Aleutian disease.

those of the coagulation factors, the variations suggest that there are periods of fibrinolytic activation resulting in decreased levels of pro-fibrinolysin and inhibitors, followed by periods of regeneration of these substances. The rates of production of profibrinolysin and inhibitors and of fibrinogen are obviously different. The mink is interesting in that it
is the only animal studied in this laboratory which consistently shows the presence of an active fibrinolysin.

A comparison of fibrinogen levels and platelet counts is shown in Text-fig. 6. Here, the changes are similar during the first 6 weeks of the disease. After this, whereas the fibrinogen levels alternately rise and fall suggesting periods of production followed by additional episodes of intravascular fibrin deposition, the production of platelets is apparently unable to keep up with the destructive effects of intravascular coagulation. This occurs in spite of megakaryocytes in the spleen and bone marrow and maintenance of hematocrit (Hct) levels of approximately 50%. Anemia is a late manifestation of Aleutian disease but is seldom seen during the early stages which have been studied here. Statistically significant differences are found between the control platelet count and that of infected mink at 7 weeks \( (p < 0.001) \).

If platelet count and stypten time are compared (Text-fig. 7), it is

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**TEXT-FIG. 9.** Thrombin time in mink with Aleutian disease.

**TEXT-FIG. 10.** Fibrinogen and platelet changes in infected Aleutian mink and in uninfected dark mink.

**TEXT-FIG. 11.** Prothrombin and partial thromboplastin times in mink with Aleutian disease.
evident that at most times there is an inverse relationship between changes in these 2 parameters. As the platelet count goes down, the stypven time increases. The use of Russell’s viper venom without cephalin, as in this series, requires the presence of platelet phospholipid dissociated from intact platelets. At 4 weeks and more dramatically at 7 weeks, there is a shortening of the stypven time suggesting that there has been a recent destruction of platelets with release of platelet Factor 3.

The stypven time for infected mink is significantly higher than the control level at 6 weeks (p = 0.001), while it is significantly lower at Week 7 (p = 0.01). Changes in platelet adhesiveness contrasted with platelet count are shown in Text-fig. 8. The primary effect seems to be an increase in platelet adhesiveness followed by a sharp drop which lasts 2 weeks. It may be that at this time the more adhesive platelets have been removed from circulation. During this period of low adhesiveness there is even a slight rise in platelet count, while an increase in adhesiveness is again followed by a drop in both count and adhesiveness.

A progressive increase in TT, indicating the presence of an antithrombin, is shown in Text-fig. 9. Whether this antithrombin is the result of thromboplastin release or fibrinolytic activity, or perhaps a component of the increasing gamma globulin concentration (as seen in some cases of multiple myeloma) is not clear from these results.

A comparison of fibrinogen and platelet changes in control dark mink and infected Aleutian mink is shown in Text-fig. 10. The changes observed in the dark mink were not statistically significant for these determinations.

Prothrombin time remained relatively constant throughout the experiment (Text-fig. 11). Partial thromboplastin time, on the other hand, shortened significantly. These short PTT’s are difficult to interpret, particularly since both infected and control dark mink showed similar trends. They may represent formation and prolonged circulation of procoagulants as a part of the disease process; or they may be the result, in some unrecognized way, of repeat cardiac punctures.

Deaths immediately following cardiac puncture are indicative of an increased sensitivity to trauma. During the third and fourth week after infection, 5 Aleutian mink out of a total of 19 died shortly after cardiac puncture. In 2 of the 5, a hemopericardium was present, perhaps reflecting a hypocoagulable state. Throughout the rest of the experiment there were only 2 deaths following a total of 41 cardiac punctures.

With light microscopy, the kidneys of Aleutian-disease-infected animals showed a progressive, irregular, eosinophilic thickening of the glomerular basement membranes, predominantly in a mesangial pattern.
with an eventual glomerular obliteration. Electron-microscopic study of these glomeruli also showed a predominantly mesangial pattern of change. There were a swelling of the mesangium and irregular, electron-dense, granular subendothelial deposits on the basement membrane (Fig. 1). These deposits are seen most often at the junction of mesangial and endothelial cells (Fig. 2 and 3). A light granular deposit was observed between swollen mesangial cells (Fig. 4). Electron-dense subendothelial deposits in Aleutian-disease-affected kidneys have also been described by Kindig, Spargo, and Kirsten.26 Porter, Dixon, and Larsen,27 by immunochromic techniques, have demonstrated fibrin deposition together with globulin and albumin in a mesangial pattern in kidneys of mink with Aleutian disease. The granular deposits seen by electron microscopy may represent a mixture of incompletely polymerized fibrin, albumin, and globulin. The globulin and albumin are trapped within the interstices of the fibrin aggregates wherever they are deposited. It is of interest that the glomerular subendothelial deposits of fibrin in preeclampsia and in lupus nephritis also lack the typical periodicity of fibrin when studied by electron microscopy and, similarly, can be identified only by immunochromic methods.

**DISCUSSION**

Aleutian, or blue, mink are a genotype characterized by light pelts ranging in color from gunmetal through violet to pearl. This gene is an autosomal recessive trait and carries with it the Chediak-Higashi syndrome which is common to man, mink, and cattle.28 Animals of this genotype also differ from the standard dark mink in their greater susceptibility to Aleutian disease virus and to the lethal effects of the disease.

During the course of Aleutian disease, the mink show an increasing hypergammaglobulinemia which can be detected by the iodine agglutination test8 when the gamma globulin concentration reaches approximately 2 gm./100 ml. and the A/G ratio is 1. This usually occurs 3–4 weeks after infection and may be positive when other symptoms are still at a subclinical level. As clinical symptoms develop (with loss of weight being among the first) melena may be present, and 10–20% of those visibly sick bleed at the mouth. Ragged ulcers at the gingival border bleed when the mink are handled. For this reason ranchers frequently have called these mink "bleeders."29 Since a tendency toward bleeding is a characteristic of Chediak-Higashi syndrome in the 3 species studied, the bleeding may be an effect of the genotype as well as the disease.28 It has been shown, however, that the bleeding is not due to congenital coagulation defects.80

By the sixth or seventh week there is a severe infiltration of plasma
cells into the tissues. Depending on the stage of the disease the kidneys are enlarged and reddened or swollen, pale, and pitted.\textsuperscript{29} Enlargement of spleen and lymph nodes and occasional yellowish brown mottling of the liver are other signs of the disease.

The blue mink commonly die of Aleutian disease within 4 months of infection, while dark mink may live 9–12 months following the initial rise in gamma globulin. The latter have even been known to show remissions, at least so far as gamma globulin levels are concerned.

The work reported here indicates that this viral disease induces chronic intravascular coagulation. The incompletely polymerized fibrin which is formed is filtered on the glomerular basement membrane and is phagocytized by the mesangial cells of the renal glomerulus. The mechanism by which the intravascular coagulation is mediated in this disease is not known. It may be a result of formation of antigen-antibody complexes, the effect of the virus on endothelium, or a direct effect of the virus on the coagulation mechanism. Whatever the cause or causes of coagulation, the indications for such a process are numerous and in this study were as follows:

1. Decrease in fibrinogen and platelets in the circulating blood
2. Cyclical changes in Factor V and Factor VIII
3. Increase in cryoprotein to within 26\% of the fibrinogen level on at least 2 occasions
4. Variations of the fibrinolytic system suggesting alternate periods of activation and regeneration
5. Inverse relationship between platelet count and stypven time except for 2 occasions of short stypven time suggesting recent destruction of platelets with release of platelet Factor III
6. Increase in TT showing the presence of an anticoagulant due to gamma globulin production, thromboplastin formation, or fibrinolytic activity
7. Decrease in PTT suggesting formation and circulation of procoagulants
8. Demonstration of subendothelial deposits, probably representing a form of fibrin, on the glomerular basement membranes

While some variation was observed in both the infected and control dark mink, the changes were much more pronounced in animals of the Aleutian genotype.

In addition, Karstad\textsuperscript{31} has demonstrated that mink infected with Aleutian disease are "prepared" for the generalized Shwartzman reaction and that actual glomerular thrombi occurred spontaneously in a few cases of Aleutian disease. This represents a clear histologic demonstration of disseminated intravascular coagulation.
Summary

Studies of coagulation and fibrinolytic changes in the plasma of mink during the course of Aleutian disease indicated a process of episodic, incomplete intravascular coagulation with considerable removal of fibrinogen and platelets from the circulation. These episodes were followed by increased levels of some factors, probably due to a stimulation of production. Platelet formation, however, did not keep up with the processes of destruction. It is suggested that intravascular coagulation is an intermediate mechanism for the development of some of the lesions observed in animals with Aleutian disease.

References


31. Karstad, L. Personal communication.

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[ Illustrations follow ]
**Legends for Figures**

**Key:**

CAP = capillary lumen  
M = mesangial cell  
E = endothelial cell  
LG = light granular deposit  
G = granular deposit  
MC = cytoplasm of mesangial cell

**Fig. 1.** Kidney section from mink infected with Aleutian disease showing subendothelial granular deposit on glomerular basement membrane. × 21,600.
FIG. 2. Glomerular capillary from mink infected with Aleutian disease for 9 weeks. Mesangial cell is swollen and active; there is a dark granular deposit at its junction with endothelium. $\times$ 10,800.
Fig. 3. Higher magnification of Fig. 2 showing granular deposit at junction of mesangial cell and endothelium. × 22,000.
Fig. 4. Glomerular capillary from mink infected with Aleutian disease showing light granular deposit in mesangial region surrounding cytoplasmic extensions of mesangial cells. $\times$ 13,500.