Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Morphogenesis of a Virus in Cats with Experimental Feline Infectious Peritonitis

Preliminary ultrastructural and filtration studies have shown that feline infectious peritonitis (FIP) is probably caused by a virus although the virus could not be grown in tissue culture (*1*, *2*). Despite the fact that Hardy *et al.* (*3*) demonstrated that a feline leukemia virus antigen was present in 5 of 13 cats with spontaneous FIP and feline leukemia virus was found in electron micrographs from tissues of 1 of the 5 cats, in our study of various tissues from 25 cats with experimentally induced FIP, morphological forms of feline leukemia virus, as described by various workers (*4–6*), have never been seen. This paper reports the morphogenesis of a virus as detected in tissues from 12 of the 25 cats with experimental FIP.

The original source of the infectious material has been described (*7*). The 12 cats were killed on postinoculation days 3 to 19 (Table 1). They had been inoculated subcutaneously or intraperitoneally with bacteriologically sterile saline suspensions of kidney-, liver-, or omentum-containing lesions of FIP. Methods for the preparation of tissues for electron microscopic examination have been described (*8*). Thin sections were examined in a Philips EM-200, AEI EM 6B, or RCA EMU-3G electron microscope.

Viral particles were found most commonly in cells identified a macrophages in typical lesions of FIP in the omentum, spleen, liver, and subcutaneous site of inoculation. It could not be ascertained whether these macrophages originated from mesothelium, reticulum cells, blood monocytes, or tissue histiocytes. The impression was that they had originated from each of these sources. Viral particles were found in varying numbers in different cells. Cells containing viral particles were easily found in some sections, in others an extensive search was necessary. These cells were always in areas adjacent to the necrotizing lesions of FIP.

Most commonly, viral particles were usually seen in the Golgi area in vesicles and smooth-surfaced cysternae (Figs. 1, 2). Occasionally, phagosomes contained viral particles, sometimes in large numbers (Fig. 5). Extracellular particles were detected rarely. Occasionally, the virus was seen budding from smooth-surfaced vesicles or cysternae (Fig. 4). Budding from the plasma membrane was never detected. Double buds were rarely seen (Fig. 4b). Viral particles usually measured 70 to 80 mμ in diameter although some larger forms were seen (Figs. 2, 3). Most particles contained a donut-shaped nucleoid, 50 to 55 mμ in diameter, with a central lucent area of 20 to 30 mμ in diameter. The nucleoid was surrounded by a trilaminar unit membrane (Figs. 2, 3, 4). Other forms of viral particles,

TABLE 1

DETECTION OF VIRAL PARTICLES IN CATS WITH EXPERIMENTALLY INDUCED FELINE INFECTIOUS PERITONITIS

Cat number	Source of inoculum	Serial passage	Post-inoculation day	Tissue
1–3	Ref. (7)	1	12	Omentum
2–4	—	2	6	Omentum
2–5	—	2	7	Omentum
N-2	2–4, 2–5	3	6	Liver
4–8	—	4	17	Omentum
5–3	4–8	5	7	Omentum
6–6	5–3	6	19	Omentum, subq.
6–8	5–3	6	12	Omentum
6–30	5–3	6	11	Omentum
6–31	5–3	6	3	Omentum
7–2	6–6	7	5	Liver
7–5	6–6	7	9	Liver, spleen

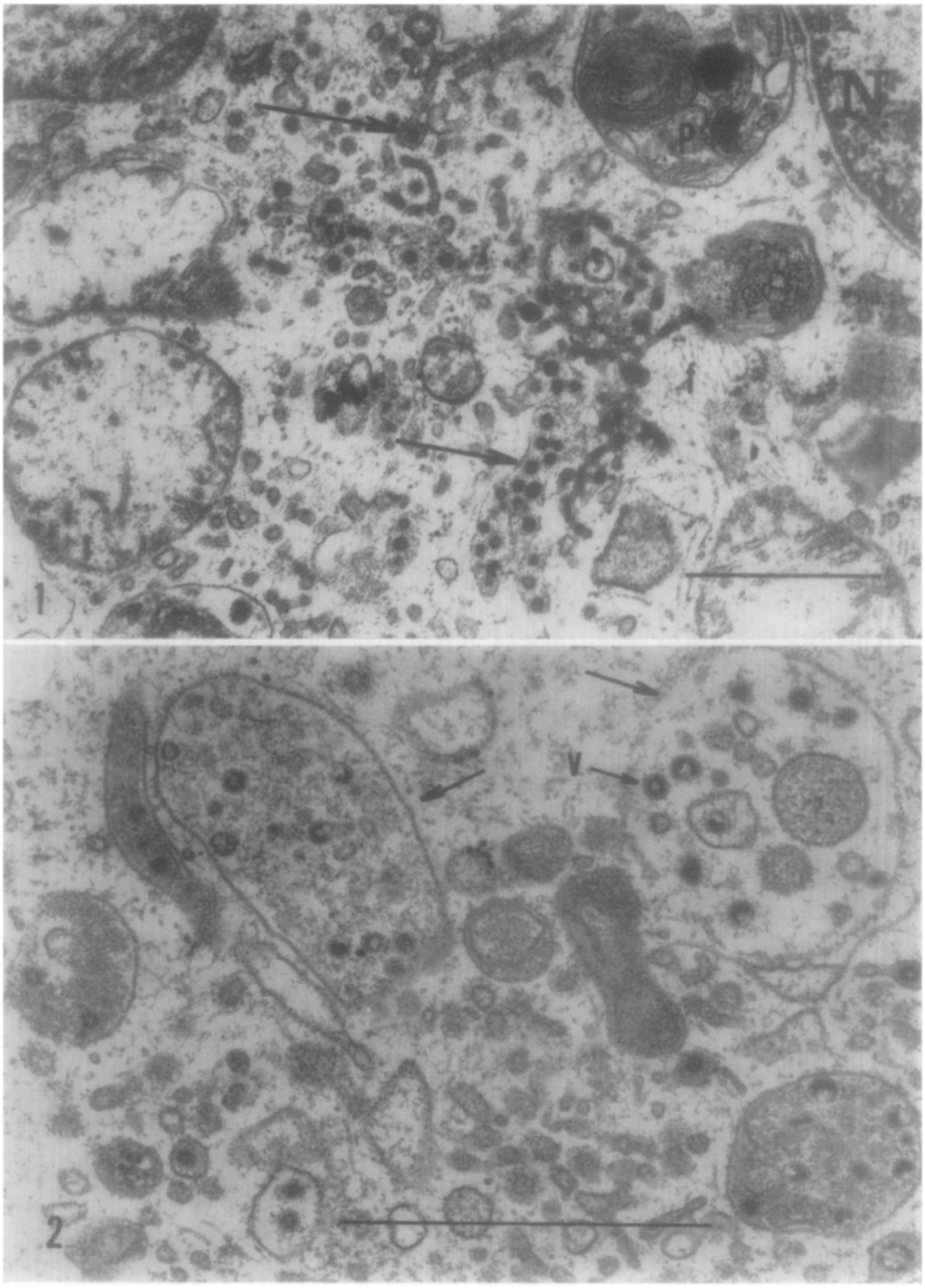

FIG. 1. Portion of a macrophage in the greater omentum of cat 2-4, 6 days after intraperitoneal inoculation. Many viral particles are visible in vesicles and smooth-surfaced cisternae (arrows). Phagosome (P), nucleus (N), microfibrils (f). ×28,000. Scale = 1 μ.

FIG. 2. Portion of a macrophage in the omentum of cat 2-5, 7 days after intraperitoneal inoculation. Many viral particles are seen in dilated smooth-surfaced cisternae (arrows) and smaller vesicles. Note the various forms including typical particles with donut-shaped nucleoid and a trilaminar unit membrane (arrow-v) and others with nucleoids appearing as solid spheres or crescents. ×53,800. Scale = 1 μ.

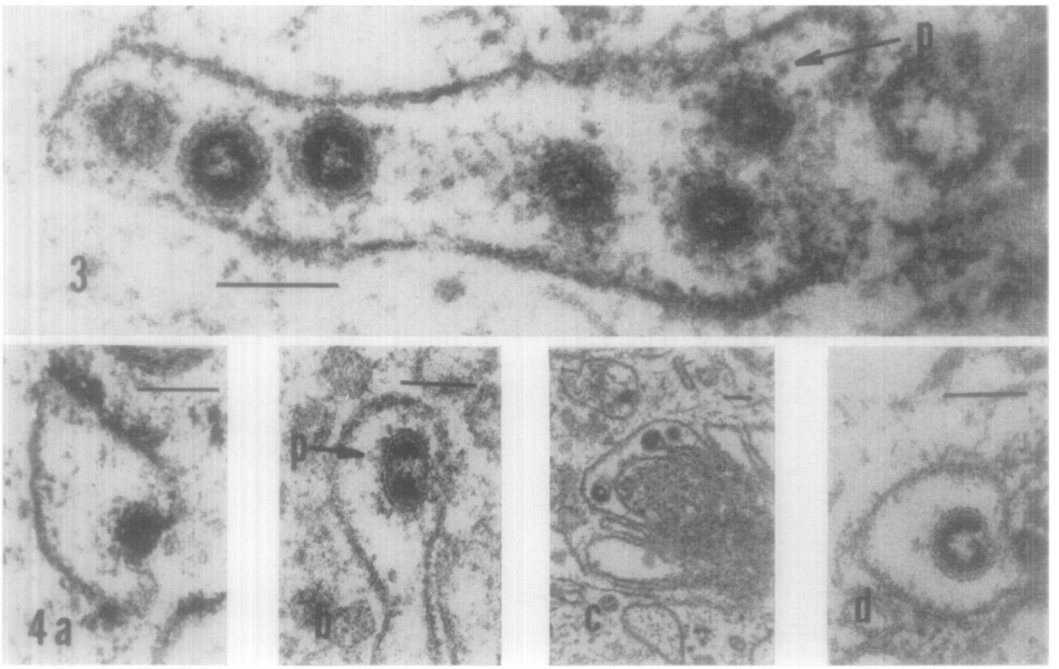

FIG. 3. Omentum of cat 2–5. The size and structure of the typical viral particle in smooth-surfaced cisternae can be seen. The donut-shaped nucleoid is surrounded by a trilaminar unit membrane. Club-shaped projections (arrow-p) are seen associated with some viral particles. ×160,000. Scale = 100 mμ.

FIG. 4. Portions of macrophages showing stages of budding. (a) and (b) are from the liver of a 7-day-old cat, 6 days after subcutaneous inoculation. The trilaminar unit membrane is prominent in (b). It appears to be continuous with the membrane of the vesicle in (a). Club-shaped projections (arrow-p) are associated with the particles in (b). In (c) and (d), from the omentum of cat 2–5, the final stages of the budding process is observed. (a), (b), and (d) ×107,600. (c) ×36,400. Scale = 100 mμ.

which appeared to be degenerating forms, were frequently seen, especially in cysternae and phagosomes. Their nucleoid took various forms from solid spheres to crescentic shapes, and their unit membranes were intact or appeared as ingle slines (Figs. 2, 5).

Club-shaped projections were occasionally seen associated with viral particles (Figs. 3, 4b). No other viruses or microorganisms could be identified in electron micrographs of the 25 cats studied, except for the viral particles described above.

The morphogenesis and morphology in thin sections of the virus reported above is similar to that of the human coronavirus 224-E and mouse hepatitis virus (*9*, *11*). If the club-shaped projections noted in some electron micrographs of the virus reported above are, indeed, viral structures, a further similarity to coronaviruses is evident (*10*).

Though similarities to feline leukemia virus (FLV) are apparent, the virus in cats with experimental FIP appears somewhat different in electron micrographs because: (a) FLV is larger in size. This consistent difference in average size has been demonstrated using the same electron microscope and identical techniques in one laboratory (*2*, *4*, *8*); (b) FLV buds from the plasma membrane, and the virus in cats with FIP does not (*4*–6); and (c) FLV may have an intermediate shell or ring (*4*, *6*, *8*). A morphological comparison of FLV to the virus in cats with FIP appears similar to one of mouse hepatitis virus and 224-E to murine leukemia viruses.

Comparisons of FIP and mouse hepatitis reveal further similarities. Recent studies have shown a possible pathological interrelationship of FIP and feline leukemia (*3*, *4*, *7*). Earlier, mouse hepatitis virus was found complicating studies with mouse

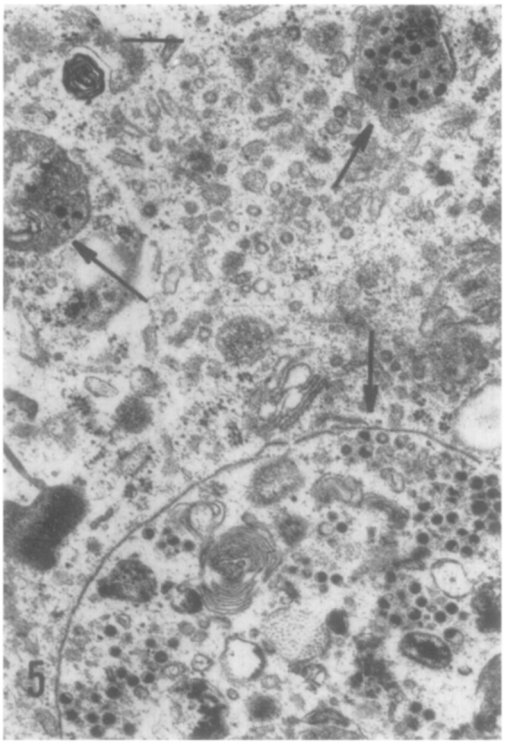

FIG. 5. Omentum of cat 2-5. A large phagocytic structure and two smaller dilated cysternae (arrows) are observed containing numerous viral particles with dense nucleoids. × 16,100. Scale = 0.5 μ.

leukemia (12). Vasculitis, peritonitis, and lymphoid necrosis are seen in mice with mouse hepatitis and in cats with FIP (*2*, *7*, *13*).

ACKNOWLEDGMENTS

The author thanks Dr. G. H. Theilen, Dr. D. L. Dungworth, R. J. Munn, R. P. Smith, J. Pangborn, H. Moles, and S. Huang for their contributions to this study. This work was supported in part by USDA 529-15-1, USPHS Grant No. 1 SO 1 FR-05457-06 and the Chancellor's Patent Fund for graduate student research.

REFERENCES

1. ZOOK, B. C., KING, N. W., ROBISON, R. L., and MCCOMBS, H. L., *Pathol. Vet.* **5**, 91–95 (1968).
2. WARD, J. M., MUNN, R. J., GRIBBLE, D. H., and DUNGWORTH, D. L., *Vet. Rec.* **83**, 416–417 (1968).
3. HARDY, W. D., GEERING, G., OLD, L. J., DE HARVEN, E., BRODEY, R. S., and MCDONOUGH, S., *Science* **166**, 1019–1021 (1969).
4. THEILEN, G. H., KAWAKAMI, T. G., DUNGWORTH, D. L., SWITZER, J. W., MUNN, R. J., and HARROLD, J. B., *J. Amer. Vet. Med. Ass.* **153**, 1864–1872 (1968).
5. RICKARD, C. G., POST, J. E., NORONHA, F., and BARR, L. M., *J. Nat. Cancer Inst.* **42**, 987–1014 (1969).
6. LAIRD, H. M., JARRETT, W. F. H., CRIGHTON, G. W., and HAY, D., *J. Nat. Cancer Inst.* **41**, 879–893 (1968).
7. WARD, J. M., and THEILEN, G. H., *Vet. Med. Small Anim. Clin.* **64**, 1052–1056 (1969).
8. THEILEN, G. H., DUNGWORTH, D. L., KAWAKAMI, T. G., MUNN, R. J., WARD, J. M., and HARROLD, J. B., *Cancer Res.*, in press (1970).
9. BECKER, W. B., MCINTOSH, K., DEES, J. H., and CHANOCK, R. M., *J. Virol.* **1**, 1019–1027 (1967).
10. *Nature London* **220**, 650 (1968).
11. WATANABE, K., *J. Electronmicrosc.* **18**, 158–188 (1969).
12. MANAKER, R. A., PICZAK, C. V., MILLER, A. A., and STANTON, M. F., *J. Nat. Cancer Inst.* **27**, 29–51 (1961).
13. GLEDHILL, A. W., DICK, G. W. A., and NIVEN, J. S. F., *J. Pathol. Bacteriol.* **69**, 299–309 (1955).

JERROLD M. WARD

Department of Pathology
School of Veterinary Medicine
University of California
Davis, California 95616

Accepted March 9, 1970