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Immunopathogenesis of FIP

J. E. Barlough, D.V.M.

Ongoing research in several laboratories suggests that FIP is the result of complex immunologically-mediated phenomena involving antigen-antibody-complement interactions across vessel walls accompanied by virus persistence within mononuclear phagocytes. There are several lines of evidence supporting this hypothesis:

Hypergammaglobulinemia, which may or may not be specific for FIP virus, is characteristic of naturally-occurring FIP.

Differences in susceptibility to experimental infection with FIP virus between seropositive and seronegative cats imply that a process of immunologic sensitization has occurred previously in seropositive cats which predisposes them to the development of fulminating disease.

FIP virus-infected mononuclear phagocytes, IgG, and complement have all been demonstrated within typical FIP lesions.

Administration of serum containing antibodies to FIP virus to seronegative cats results in fulminating FIP following challenge with virus.

Circulating immune complexes and renal glomerular deposits of virus, IgG, and complement have been observed in both natural and experimental cases.

Hypocomplementemia and disseminated intravascular coagulation (DIC) have been associated with experimentally-induced FIP.

Temporary remissions may occasionally be achieved through the use of immunosuppressive drugs.

A positive FIP antibody test in an asymptomatic animal indicates neither clinical FIP, latent FIP, nor active viremia. This latter point is in direct contradistinction to the immunofluorescent test for feline leukemia virus (FeLV), in which a structural component of the virus, rather than antibody, is detected. Currently a practical laboratory test for detection of FIP virus analogous to the FeLV test is not commercially available. Research in our laboratory is aimed at developing such an antigen assay system. A serologic test for the presence of FIP virus would be especially useful for discriminating between cats with FIP and FIP-seropositive cats with other diseases. In addition, early identification of cats with the non-effusive form of FIP might be possible.

New insights in gastrointestinal viruses

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Viral gastroenteritis characterized by fever, anorexia, nausea, vomiting, vertigo, myalgia, abdominal cramps, diarrhea, and constitutional symptoms in varying combinations is one of the leading causes of morbidity and mortality in neonatal and young animals, birds, and man throughout the world.

In spite of the great importance of this problem, studies on the etiology of many diarrheal episodes failed to reveal an etiologic agent until recently. Traditional cell culture methods led to the discovery of hundreds of new viruses in feces but these viruses were not regularly implicated in cases of diarrhea, and only recently, with the use of direct electron microscopy (EM) on fecal preparation, have other viruses been detected in association with diarrhea. In general, most viruses detected by direct EM are difficult or impossible to cultivate in vitro.

The Cornell Feline Health Center

conducted a feline enteric virus screening survey from September, 1979, through August, 1980. One hundred eighty five (185) fecal samples were collected from hospitalized cats at the Small Animal Clinic of the Cornell Veterinary Teaching Hospital, were screened for enteric viruses by direct EM, and were examined for virus by isolation attempts in cell cultures.

The results are shown in Table 1 (page 3). Following are brief descriptions of the feline enteric viruses which were isolated during our one-year screening survey. Several of these viruses require further investigation in order to determine the extent of their involvement in feline viral gastroenteritis.

Feline Panleukopenia Virus

Only one feline panleukopenia virus (FPLV) isolate was obtained, that from the fecal sample of a cat with diarrhea. In unvaccinated cats, FPLV is the most
(Cont. on page 3)

Old friends with a new name

This issue of the Cornell Feline Health Center News officially announces our new name. When the Center began in 1974, it was called the Cornell Feline Research Laboratory. Since that time the scope of activities has broadened considerably.

Our new name more accurately represents the many facets of the program, which includes diagnostic and clinical services, public education, and consultation for practitioners, in addition to research on feline diseases.

Our name may be changed, but our goals are still the same: to improve the welfare of cats and to serve the community of those who care for cats.

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Gastrointestinal viruses (Cont. from page 2)

severe viral disease, often causing a fatal enteritis. Most cats admitted to the Small Animal Clinic were vaccinated against FPL, thus explaining the low incidence of FPLV in our study.

Feline Calicivirus

Three feline calicivirus (FCV) isolates out of 185 fecal samples were detected: two from cats with chronic diarrhea, and one from a cat diagnosed as "intestinal malabsorption." While FCV is a major cause of respiratory infections, it can be a cause of enteritis as well.

Feline Astrovirus

Astroviruses were visualized by EM in the feces of a four-month-old kitten with diarrhea. Astroviruses are isometric, approximately 28nm in diameter, and when negatively stained, give the

impression of a white, five- or six-pointed star superimposed on the virus particle.

Astroviruses have been visualized in the feces of humans, calves, lambs and turkeys with diarrhea. Experimental transmission experiments of mammalian astroviruses indicate they induce mild and constitutional symptoms. Studies on the pathogenesis of astrovirus infection in lambs have shown the site of virus multiplication to be the mature villous epithelial cell of the small intestine. There is a clinical impression that astrovirus-associated gastroenteritis in man and animals is generally milder than that associated with rotaviruses. Asymptomatic excretions of astroviral particles have been reported in humans, calves and

(Cont. on page 4)

Table 1. Viruses detected in 185 fecal samples from hospitalized cats.

Virus	Virus Group	No. of Positive Samples (%)	Clinical Signs
Feline panleukopenia virus	Parvoviridae	1 (0.5)	diarrhea
Feline calicivirus	Caliciviridae	3 (1.6)	2 with diarrhea 1 with intestinal malabsorption
Feline astrovirus	Picornaviridae ?	1 (0.5)	diarrhea
Non-cultivable feline enteric virus	Picornaviridae ?	1 (0.5)	no diarrheal signs
Feline rotavirus	Reoviridae	5 (2.7)	no diarrheal signs 1 with arthritis
Feline reovirus (Type III)	Reoviridae	1 (0.5)	no diarrheal signs
Feline enteric coronavirus	Coronaviridae	20 (10.8)	with/without diarrhea

Gastrointestinal viruses (Cont. from page 3)

lambs. Attempts to propagate both mammalian (including feline) and avian astroviruses in cell cultures have been unsuccessful.

Non-cultivable Feline Enteric Virus

Non-cultivable enteric virus was detected by EM in a fecal sample of a one-year-old male cat. This virus (approximately 29nm in diameter) is larger than feline panleukopenia virus but smaller than feline calicivirus. The virion is spherical and has no characteristic surface configurations on it. Attempts to propagate this virus in cell cultures have been unsuccessful so far.

A 28-29nm non-cultivable enteric virus has been detected in feces from babies with or without diarrhea. As this is the first report on non-cultivable feline enteric virus, it is unknown how widespread and how important it is.

Feline Rotavirus

Rotaviruses, medium-sized viruses approximately 72nm in diameter containing double-stranded RNA, are common causes of gastroenteritis in the young of many, if not all, mammalian and avian species. We confirmed the existence of a feline rotavirus and determined that it was distinct from human, canine, bovine, porcine and simian rotaviruses. Pathogenesis studies are in progress in our laboratory.

Feline Reovirus

Reovirus was visualized by EM in the fecal sample of a cat with no gastrointestinal signs. Reoviruses may be associated with asymptomatic or mild respiratory or enteric infections in many species, including the cat.

Feline Enteric Coronavirus

Feline enteric coronavirus (FECV) was isolated from 20 of the 185 fecal samples examined (approximately 10%).

The cat has at least two which are morphologically distinct: FECV and feline infectious peritonitis (FIP) virus. The disease producing potential of FECV is unknown, but it is known that infected cats become persistent carriers and shedders of this virus. FIP virus, although not detected in this survey, can be shed in feces of infected cats.

Update on ELISA test for FeLV

J. E. Barlough, D.V.M.

Reports have recently appeared that suggest modifications, under certain circumstances, in interpretation of antigen detection tests (ELISA and IFA) for FeLV.

Researchers at Glasgow have indicated that of about 500 blood samples submitted for routine FeLV examination, approximately one-third more have been positive with the ELISA test kit (Leukassay F[®], Pitman-Moore) than by virus isolation. Concurrently, comparison studies of IFA and ELISA methods carried out at the University of California, Davis, have identified a previously undetected group of cats--those with persistence of soluble FeLV antigen (ELISA-positive) for extended periods of time without expression of cell-associated antigen (IFA-negative), or with only transient (one week or less) expression.

These findings suggest that a persistent antigenemia, possibly due to release of soluble FeLV antigen from an as yet unidentified focus outside the bone marrow, may be responsible for positive ELISA results on IFA-negative blood samples. It is probable that cats only transiently

(Cont. on page 5)

Herpesvirus induced atherosclerosis

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Atherosclerosis is a serious disease of arteries in which the blood flow may be slowed or blocked as a result of fatty and mineralized deposits in arterial walls. Several high risk factors have been implicated as causing the disease: high cholesterol levels, hypertension, smoking, diabetes and obesity. However, a group of scientists concluded in 1974 that other factors should be sought and investigated since these high risk factors could not account for all the atherosclerosis seen. Research at Cornell on a new feline herpesvirus was the impetus for an entirely new concept of the possible cause of atherosclerosis.

In 1973, the senior author reported that a feline herpesvirus induced cholesterol and fat droplet accumulations in infected cell cultures. Further observations of the induction of intracellular and extracellular chemical crystals were thought to be cytopathic effects caused by the cell associated herpesvirus. It was hypothesized that this virus caused feline urolithiasis.

This was substantiated by experimental studies in specific pathogen free cats. Following inoculation with herpesvirus alone, cats developed urolithiasis in all its manifestations: hematuria, straining to urinate, urethral obstruction and cystitis.

Viral-induced cholesterol and fat droplet accumulations in infected cell cultures led the author to speculate that herpesviruses might cause atherosclerosis. This resulted in the experiments in which it was shown that Marek's disease (MDV) infection caused atherosclerosis even in chickens

having normal levels of blood cholesterol. Further research showed that MDV infection alters the fat metabolism of arterial smooth muscle cells (SMC) in tissue culture. These results suggest a mechanism by which the herpesvirus can cause fat deposits in artery walls.

These findings may be of particular significance and relevance to human atherosclerosis since humans are known to be persistently infected with up to five herpesviruses. This is a prime example of how discoveries in feline health research may prove directly applicable and extremely important to human health.

Bequest to aid feline health

The Cornell Feline Health Center has received a bequest from the estate of Mrs. Sarah H. Swits of Ballston Spa, N.Y.

Mrs. Swits was a true lover of cats and carried on a long-term correspondence with the Center prior to her death. Her bequest will greatly aid current and future research in feline diseases. It is received with the utmost respect and gratitude for her loyalty.

ELISA (Cont. from page 4)

ELISA-positive represent those animals only transiently viremic with FeLV; because bone marrow cells are not infected in transiently viremic cats, it is expected that such animals would be IFA-negative. The reasons for persistent antigenemia, however, are still unclear at present.

Feline Health Symposium set for July 12-17

Cornell's Adult University will host a Feline Health Symposium July 12-17, 1981, geared to meet the needs of cat breeders and fanciers.

Topics presented by the staff of the Cornell Feline Health Center will include nutrition; general health management; medical and surgical problems; viral, reproductive, respiratory, and skin diseases; and infant kitten mortality.

Field trips are scheduled to the Agway Nutrition Research Laboratory, the Specific Pathogen Free Cat Colony, the Small Animal Clinic, and the Diagnostic Laboratory.

Those interested in obtaining information on registration, tuition and housing for the week-long symposium should contact Mary K. Gloster, Cornell's Adult University, 626B Thurston Ave., Ithaca, NY 14853, telephone (607) 256-6240.

Personnel news

Leo A. Wuori, D.V.M., joined the CFHC in November, 1980, as Assistant Director/Extension Associate.

A Cornell graduate ('42) and former small animal practitioner, he has served on the N.Y.S. College of Veterinary Medicine Advisory Council and Alumni Council. In addition, he has served as executive board member of the N.Y.S.V.M.S. for 16 years, and as president in 1977.

Dr. Wuori's private hospital received honorable mention as the Veterinary Economics Magazine Hospital of the Year in 1966, and he was chosen as N.Y.S.V.M.S. Veterinarian of the Year in 1979.

Dr. Wuori's responsibilities at the CFHC will include public relations; interacting with veterinarians, cat owners and researchers; coordinating all publications; and a major effort toward raising funds to support the research on feline diseases.