CANINE CORONAVIRUS INFECTION IN CATS; A POSSIBLE ROLE IN FELINE INFECTIOUS PERITONITIS

F. McArdle*, M. Bennett*†, R.M. Gaskell*, B. Tennant*,
D.F. Kelly* and C.J.Gaskell†

Departments of Veterinary Pathology* and Veterinary
Clinical Science†, University of Liverpool
'Leahurst', Neston, Wirral, L64 7TE, U.K.

INTRODUCTION

Feline infectious peritonitis virus (FIPV) and canine coronavirus (CCV) are serologically closely related viruses with at least some genome sequence homology (Pedersen et al, 1978; Horzinek et al, 1982; Shockley et al, 1987). They are distinguished mainly by their host species of origin, and there are also some accounts of minor or one-way serological differences between the two groups (e.g. Pedersen et al, 1978). However some strains, at least, of CCV can infect cats (Barlough et al, 1984; Stoddart et al, 1988) and it is not known how consistent the serological differences are when applied to a large number of canine and feline isolates.

Antibody to FIPV, whether actively or passively acquired, is known to enhance the development of disease in most cats upon subsequent FIPV infection (Pedersen and Boyle, 1980; Weiss and Scott, 1981). However, enhancement of FIP by previous infection with CCV has not been found (Barlough et al, 1984; Stoddart et al, 1988). In this paper we describe some preliminary experiments in which previous exposure to two strains of CCV appeared to cause enhancement of FIP, and, furthermore, sequential systemic inoculation of two cats with a further strain of CCV caused FIP without exposure to FIPV.

MATERIALS AND METHODS

The CCV isolates used in this study were CCV-171, the original American strain (Binn et al, 1974) with unknown passage history, CCV-C54 and CCV-INSAVC-1, geographically distinct UK strains at sixth and fifth passage respectively, and CCV-INSAVC-

1/c, a ninth passage clone of CCV-INSAVC-1. The feline isolate used was FIPV-CVR1036, originally isolated from the faeces of an adult British cat with acute diarrhoea and kindly supplied by Dr DA Harbour, University of Bristol. Except where stated, CCV isolates were grown in A-72 (canine) cells (Binn et al, 1980) and FIPV isolates in FEA (feline) cells (Jarrett et al, 1973). Virus neutralisation (VN) tests were as described by Stoddart et al (1988b).

The overall design of the experiments is shown in Table 1. Briefly, eight six-months-old, specific pathogen free cats, with no detectable antibody to CCV and FIPV, were divided into four groups of two (A, B, C and D) and housed in separate, barrier maintained rooms within an isolation unit. Groups A to C were inoculated orally with $10^{6.8}$ TCID₅₀ CCV-171, CCV-C54 or $10^{7.3}$ CCV-INSAVC-1/c respectively, and group D inoculated orally with uninfected A-72 cells and media as controls. After 26 days, cats in groups A-C were again inoculated orally with homologous virus in an attempt to increase serum VN antibody.

On day 57, cats in groups A, B and D were inoculated orally with 10^6 TCID₅₀ FIPV-CVR1036. As the cats in group C still had not developed antibody to CCV, they were inoculated with 10^7 TCID₅₀ CCV-INSAVC-1/c, this time intramuscularly and intraperitoneally, and intramuscularly again on day 78. All the cats were examined for clinical signs, and samples were taken regularly for attempted virus isolation and VN antibody assays.

Table 1

Summary of experimental design; Cats were inoculated orally with CCV or FIPV on the days indicated, except * indicates intramuscular and † indicates intraperitoneal inoculation.

Group of cats		Days into experiment			
		0	26	57	78
A	CCV-171		CCV-171	FIPV-CVR1036	-
B	CCV-C54		CCV-C54	FIPV-CVR1036	-
C	CCV-INSAVC -1/c		CCV-INSAVC -1/c	CCV-INSAVC -1/c*†	CCV-INSAVC -1/c*
D	cells/media		-	FIPV-CVR1036	-

RESULTS

Following the first inoculation with CCV, no clinical signs were observed in any cats apart from mild diarrhoea in cats in group B (C54 virus) at 4-12 days post-inoculation (dpi). Virus was isolated sporadically between 4-20 dpi from oropharyngeal

and rectal swabs of all cats, except one cat in group A and the uninfected cats in group D. Homologous VN antibody titres at 21 dpi were 64 in groups A and B, and <2 in groups C and D. Further oral inoculation with CCV on day 21 was not associated with any clinical signs. On day 57, cats in groups A and B had VN titres to homologous viruses of 128, but cats in groups C and D did not have antibody to any CCV strain.

After oral inoculation with FIPV on day 57, cats in groups A and B rapidly developed severe disease, and by 5-7 days after challenge serum VN titres had reached a mean of 1024. Virus was isolated four days after challenge from oropharyngeal swabs from cats in group B only. Clinical signs such as inappetence, neurological signs and jaundice became apparent on days 6-12, and cats were killed as soon as they became ill. Cats in groups A and B had minimal gross lesions at necropsy, but histological lesions consistent with FIP. In contrast, cats in group D, which had not been previously exposed to CCV, remained healthy for much longer. One cat in group D developed 'wet' FIP at 30 days post-challenge; 100mls of abdominal fluid were collected at necropsy and microscopic examination revealed typical granulomatous lesions in the serosa. The other cat in group D did not become ill, apart from mild pyrexia at 12-18 days post-challenge, but microscopic focal lymphocytic accumulations were found in the mesentery and peritoneum at necropsy 94 days post-challenge. Virus was isolated post-mortem from one cat in each of groups A, B and D. Virus was isolated on FEA cells mostly from the gut, but also occasionally from other tissues including lung, spleen and peritoneum.

No clinical signs were observed in the cats in group C but by 35 days after the first intramuscular and intraperitoneal inoculations the cats had mean serum VN antibody titres to CCV-INSAVC-1/c of 768. Both cats were killed, and gross lesions of 'wet' FIP were found in both at necropsy. Twenty and 75 mls abdominal fluid were collected from each cat, and both cats had a fibrinous serositis. Microscopic examination confirmed an exudative serositis typical of 'wet' FIP. Virus was isolated from both cats mainly from the gut and tonsils. Virus was isolated on A-72 cells, but not high passage FEA cells.

Aliquots of the viruses used to inoculate cats and samples of viruses isolated from the cats post-mortem were compared in VN assays using cat antisera to FIPV-CVR1036 and CCV-171 and dog antisera to CCV-INSAVC-1. The two CCV antisera did not distinguish between any of the viruses. However, the FIPV antiserum had a significantly higher titre against FIPV and viruses isolated from cats in groups A, B and D than against CCV-INSAVC-1/c and virus isolated from cats in group C.

DISCUSSION

Infection of cats with CCV isolates has been demonstrated previously (Barlough et al 1984, Stoddart et al 1988), although we do not know of any previous report of diarrhoea in cats associated with CCV infection. There is some evidence of natural dog-to-cat transmission of CCV via contaminated faeces (Dr W Baxendale, personal communication). Thus it is possible that dogs may be a source of coronavirus infection to cats in the field, and some cases of symptomatic feline enteric coronavirus (FECV) infection may, in reality, be due to CCV infection.

Furthermore, although only preliminary in nature, these studies show that infection with at least some strains of CCV can predispose cats to enhanced development of FIP upon subsequent exposure to FIPV. These findings contrast with those of Barlough et al (1984) and Stoddart et al (1988), who found that previous infection with one strain of CCV did not predispose cats to enhanced FIP. This may be because of differences in the strains of CCV and FIPV used in the various studies, or due to differences in route of virus inoculation.

It is interesting that the FIPV strain used in these experiments was originally isolated from a cat with enteritis, and might therefore have been described as a feline enteric coronavirus (FECV). That one cat without CCV antibody developed clinical 'wet' FIP after inoculation with FIPV-CVR1036 and the other had only mild FIP-like lesions post-mortem, might suggest that FIPV-CVR1036 is of relatively low pathogenicity. However, it is well-known that some cats can be resistant to some FIPV strains (Pedersen and Floyd, 1985), and age may also play a role in susceptibility to disease.

CCV-INSAVC-1/c did not appear to be infectious to kittens by oral inoculation, but two intraperitoneal and intramuscular inoculations did produce 'wet' FIP in both cats. That the lesions in these cats were due to infection with CCV-INSAVC-1/c and not contamination with FIPV is borne out by the ability of the virus isolated from the cats in group C to grow on A-72 cells only, and by VN assays using FIPV-CVR1036 antisera.

To ascertain whether some CCV strains can cause FIP in cats following oral inoculation will require further research. However, we believe that these studies, albeit involving only small numbers of animals, suggest a closer relationship between FIPV and CCV than is generally assumed and have considerable epidemiological implications. Further studies, probably involving sequencing of several canine and feline coronavirus isolates, are required in order to better understand the taxonomic relationship of FIPV and CCV. Further work is required to discover how frequently coronaviruses are transmitted from dogs to cats in the field. The ability of CCV to infect cats obviously may have a bearing on the use of serology to diagnose FIPV infection, on measures for controlling FIP in cat colonies and may also affect the use of live CCV vaccines in dogs.

REFERENCES

Barlough, JE., Stoddart, CA., Sorresso, GP., Jacobson, RH & Scott, FW. (1984) Experimental inoculation of cats with canine coronavirus and subsequent challenge with feline infectious peritonitis virus. *Laboratory Animal Science* 34: 592-597.

Binn, LN., Lazar, EC., Keenan, KP., Huxsoll, DL., Marchwicki, RH. and Strano, AJ. (1974) Recovery and characterisation of a coronavirus from military dogs with diarrhoea. *Proceedings of the Annual Meeting of the U.S. Animal Health Association*, 78: 359-366.

Binn, LN., Marchwicki, RH. and Stephenson EH (1980) Establishment of a canine cell line: Derivation, characterisation and viral spectrum. *American Journal of Veterinary Research* 41: 855-860.

Horzinek, MC., Lutz, H. and Pedersen, N. (1982) Antigenic relationships among homologous structural polypeptides of porcine, feline and canine coronaviruses. *Infection and Immunity* 37: 1148-1155.

Jarrett, O., Laird, HM. and Hay, D. (1973) Determinants of the host range of feline leukaemia viruses. *Journal of General Virology* 20: 169-175.

Pedersen, NC. and Floyd, K. (1985) Experimental studies with three new strains of feline infectious peritonitis virus: FIPV-UCD2, FIPV-UCD3 and FIPV-UCD4. *Compendium on Continuing Education* 7: 1001-1011.

Pedersen, NC., Ward, J. and Mengeling, WL. (1978) Antigenic relationship of feline infectious peritonitis virus to coronaviruses of other species. *Archives of Virology* 58: 45-53.

Shockley, LJ., Kapke, PA., Lapps, W., Brian, DA., Potgeiter, LND. and Wodds, R. (1987) Diagnosis of porcine and bovine enteric coronavirus infections using cloned cDNA probes. *Journal of Clinical Microbiology* 25: 1591-1596.

Stoddart, CA., Barlough, JE., Baldwin, CA. and Scott, FW. (1988) Attempted immunisation of cats against feline infectious peritonitis using canine coronavirus. *Research in Veterinary Science* 45: 383-388.

Stoddart, ME., Gaskell, RM., Harbour, DA. and Gaskell, CJ. (1988b) Virus shedding and immune responses in cats inoculated with cell-culture-adapted feline infectious peritonitis virus. *Veterinary Microbiology* 16: 145-158.