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Short Papers

Effect of diethylcarbamazine on serum antibodies to feline infectious peritonitis in cats

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In preceding studies by the author, use of the immunomodulator drug diethylcarbamazine resulted in the detection of antibodies to feline oncornavirus-associated cell membrane antigen in nine feline leukaemia virus infected cats that had previously given negative results to this antibody. In the present report, seven diethylcarbamazine-treated cats developed higher serum antibody titres to feline infectious peritonitis more frequently than did seven untreated controls. Since feline infectious peritonitis is caused by a coronavirus, these results suggest that diethylcarbamazine treatment could be exploited for vaccination and treatment strategies for non-retroviral in addition to retroviral infections.

Keywords: Feline infectious peritonitis; diethylcarbamazine; immunomodulator drugs

Diethylcarbamazine (DEC) has long been used in the treatment of filariasis in humans. The anti-infective action of DEC in filarial infections has been attributed to immunomodulation[1,2]. Previous investigators have suggested that one possible mode of action of DEC is to 'opsonize' microfilariae[1]. Other studies showed that DEC increased adherence of microfilariae to peripheral white blood cells *in vitro* in the presence of human serum containing high titres of antibody to microfilarial sheaths[3]. Although recent research indicates that killing of microfilariae results from DEC-induced platelet-derived free radicals[4], there is also evidence that an 'opsonic' activity of DEC may promote peripheral white blood cell/antigen interactions, and that this may in part account for the immune responses to filarial antigens noted after successful DEC treatment of human filariasis[2].

That DEC treatment resulted in development of serum antibodies to feline oncornavirus-associated cell membrane antigen (FOCMA) in nine FeLV-infected cats previously giving negative results for this antibody suggested that DEC might increase antibody titres to a wide variety of infectious agents. Antibody to FOCMA in FeLV-infected cats has been associated with resistance to FeLV-related neoplasias[5]. DEC treatment given with FeLV vaccine has resulted in increased titres and duration of antibody to FOCMA in two FeLV-naive cats in comparison to two FeLV-naive cats given vaccine without DEC. In addition, DEC treatment of cats with household exposure to FeLV giving negative results for FeLV antigens in peripheral blood leucocytes resulted in increased titres of antibody to FOCMA in such cats[6,7].

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DEC generally causes little toxicity (gastrointestinal irritation in humans in oral doses >10 mg kg^{-1} day^{-1}), but can result in serious reactions in hosts with heavy nematode infections because of untoward immune responses following rapid death of the worms[8].

The present report examines the effect of DEC treatment on serum antibodies to feline infectious peritonitis (FIP). FIP, caused by a coronavirus, is a common and often fatal opportunistic infection in FeLV-infected cats. Approximately 50% of clinically evident FIP infections occur in FeLV-infected cats[9]. The effect of DEC treatment on serum antibodies to toxoplasmosis, which rarely causes clinical disease in FeLV cats, was also investigated.

Fourteen cats were studied; seven of these 14 were treated with DEC and seven were untreated. Each group of seven consisted of three FeLV leucocyte antigen negative cats given 1 ml Leukocell FeLV vaccine i.m. (Norden Laboratories, Lincoln, NE, USA) and four FeLV-infected cats. All four FeLV-infected cats gave positive results for FeLV antigens in peripheral blood leucocytes (determined by Dr W.D. Hardy, Jr and coworkers, Laboratory of Veterinary Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA). All 14 cats were tested for FeLV leucocyte antigens twice, at 0 and 8 weeks, when serum samples were drawn for FIP antibody titres. Details regarding the mode of infection of the FeLV-infected cats are given in *Table 1*. Results of studies regarding the effect of DEC on FeLV infection in these cats have been described[6,10]. DEC was given orally at 10 mg kg^{-1} day^{-1} as a single daily dose for courses ranging from 2 weeks to continuous treatment, as stated in *Table 1*. All 14 cats were housed at the Harvard School of Public Health. Serum samples were drawn before DEC treatment and 8 weeks later. Titres of serum antibody to feline infectious peritonitis and toxoplasmosis were determined under code via indirect

Table 1 Effect of diethylcarbamazine (DEC) on titres of serum antibody to feline infectious peritonitis in domestic cats as determined by indirect membrane immunofluorescence[a]

Cat group	Untreated			DEC-treated		
	day 0	8 weeks	Effect	day 0	8 weeks	Effect
	Serum antibody			Serum antibody		
FeLV naive/FeLV-vaccinated[b]	8 192	8 192	NC	256	512	2-fold inc
(FeLV leucocyte antigen negative)	2 048	2 048	NC	1 024	4 096	4-fold inc
FeLV-exposed/FeLV-vaccinated[c]	4 096	8 192	2-fold inc	512	512	NC
(FeLV leucocyte antigen negative)						
FeLV-infected offspring of FeLV queen[d]	512	2 048	4-fold inc	128	2 048	16-fold inc
(FeLV leucocyte antigen positive)	512	2 048	4-fold inc	256	512	2-fold inc
FeLV Rickard-inoculated cats[e]	8 192	16 384	2-fold inc	16 384	8 192	2-fold dec
(FeLV leucocyte antigen positive)[f]	4 096	2 048	2-fold dec	4 096	16 384	4-fold inc

NC, no change; inc, increase; dec, decrease. [a]Performed under code by Tufts Diagnostic Veterinary Laboratory, Jamaica Plain, MA; result given is reciprocal of highest dilution scored positive. [b]Four FeLV-naive cats from a specific pathogen free breeding colony; two treated with DEC 10 mg kg^{-1} day^{-1} p.o. for 2 weeks after one 1 ml dose i.m. of Leukocell FeLV vaccine, two untreated. [c]Outbred cats with known epidemiologic exposure to FeLV; one treated with DEC 10 mg kg^{-1} day^{-1} p.o. for 2 weeks after one 1 ml dose i.m. of Leukocell; one untreated. [d]Littermates first positive for FeLV leukocyte antigen at age 2 months; two treated with DEC 10 mg kg^{-1} day^{-1} p.o. on a continuous basis; two untreated. [e]Littermates inoculated with the Rickard strain of FeLV in the post-weanling period; two were treated with DEC 10 mg kg^{-1} day^{-1} p.o. for 1 month at 9 months of age; two untreated. [f]FeLV viral antigen in peripheral blood leucocytes was tested at the Laboratory of Veterinary Oncology, Memorial Sloan-Kettering Cancer Center, New York City

membrane immunofluorescence on infected acetone-fixed target cells by Tufts Diagnostic Veterinary Laboratory, Jamaica Plain, MA, USA. The ATCC VR-867 Dahlberg strain of FIP and the RH strain of toxoplasmosis were used for these studies. All 14 cats remained healthy throughout the study period.

In the DEC-untreated group, the serum antibody titre to FIP increased fourfold in two FeLV-infected cats. In the treated group, three cats showed significant rises in serum antibody titres to FIP. Such titres increased fourfold in two treated cats. Of these, one cat was FeLV-infected and one was FeLV-vaccinated/previously FeLV-naive. Serum antibodies to FIP increased 16-fold (repeated to ensure accuracy) in an additional DEC-treated FeLV-infected cat. Furthermore, some increases in serum antibody titres to FIP were noted in both DEC-treated, FeLV-vaccinated cats that were previously FeLV-naive, whereas no titre increases were observed in the DEC-untreated vaccinated controls (see *Table 1*). Thirteen of the 14 observed cats gave negative results (<1:16 titre) for serum antibody to toxoplasmosis. The one cat giving positive results (1:64 titre) for toxoplasmosis antibody was treated with DEC; the titre did not change after treatment. These data may reflect lack of evidence for active toxoplasmosis infection in the 14 cats.

Adequate titres of serum antibody to FIP have not been proved to protect cats from FIP infection or FIP-related disease. However, the data presented in this report suggest that DEC treatment results in higher titres of serum antibodies to non-retroviral infectious agents such as FIP, in addition to retroviral agents such as FeLV.

This action of DEC could be exploited for vaccination and treatment strategies for a variety of pathogens infecting humans as well as cats and other animal species. In addition, diagnoses of active infections based on rapid, striking rises in serum antibody titres during DEC therapy should ideally be supported by pathogen isolation or conclusive clinical signs.

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Note added in proof

An untreated offspring of an FeLV-infected queen (see footnote *d* in *Table 1*) was killed ≈12 months after first giving positive results for FeLV leucocyte antigens because of fever, vomiting and diarrhoea unresponsive to antibiotics and supportive care. Findings at necropsy were consistent with feline infectious peritonitis (FIP). This is the only cat of the 14 study animals that has developed evidence of FIP disease.

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