COMPARATIVE CHANGES IN LABORATORY PARAMETERS OF SPECIFIED PATHOGEN FREE (SPF) AND NON-SPECIFIED PATHOGEN FREE (NON-SPF) LABORATORY CATS INFECTED WITH FELINE IMMUNODEFICIENCY VIRUS (FIV)

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Background: Studies using non-SPF laboratory cats as a model for testing putative immune modulating drugs, were reported earlier. This study was performed to determine if FIV+, SPF cats housed in a barrier unit would be a superior model.
Methods: A group of 8 purpose bred SPF cats housed in a barrier unit was infected with blood from a FIV+, SPF donor cat. Blood samples were taken weekly for 6 weeks and then 6 weekly for 200 weeks. A similar group of 16 non-SPF cats was used for comparison. Sero conversion was confirmed with an Elisa test. Routine, standardised full blood count, differential white cell counts and lymphocyte subsets were recorded and plotted on the same graphs. Mean trend lines for all parameters were compared and changes within groups and between groups were statistically analysed using the SAS procedure for mixed models and a 5% confidence interval.
Results: Large variations in individual as well as group means and medians were noted in both groups. Many changes in and between groups reached statistical significance, but were not clinically relevant. Highly significant and potentially clinically relevant differences between the groups were: Eosinophil count decreased in the SPF group and increased in the non-SPF group. CD3 and CD8 percentage decreased more rapidly in the non-SPF group. CD4 absolute count and CD4/CD8 ratio decreased more rapidly in the SPF group. Several cats in the non-SPF group died during the study period, while none in the SPF group died.
Conclusions: Apart from a few selected parameters, the changes in standard laboratory tests of FIV+, SPF and non-SPF cats are similar and the SPF model is not superior. Differences can probably be explained by infective immune stimulation in the non-SPF cats. The use of a sophisticated and expensive SPF model in long term studies using standard laboratory parameters is not essential. Survival remains the most important parameter in non-SPF cats.

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IMMUNOLOGICAL MEMORY AND ACTIVATION STATUS OF HIV POSITIVE PATIENTS: NON-TREATED VERSUS MODUCARE™ TREATED PATIENT GROUPS

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Background: Memory immune responses are very important in protecting the host against invading pathogens including those that are common causes of disease in HIV positive and AIDS patients. Moducare™ is a natural immune modulator shown to have efficacy in several chronic conditions (tuberculosis, HIV, RA) as well as in vitro. The aim of this study was to investigate the effect of Moducare™ on CD4 memory cells and immune activity in HIV positive patients and to compare the responses in untreated patients with similar absolute CD4 numbers.
Methods: Patients enrolled in a clinical study of Moducare™ were compared to a comparative group not included in the study (comparable baseline CD4 cell numbers). Memory and naïve CD4's were analysed for CD3, CD4, CD45RA (naïve) and CD45RO (memory) expression by flow cytometry. Activation: CD4+ and CD8+ cells were activated with Ionomycin and TPA and analysed for CD 69 expression.
Results: This cross-sectional study reveal that the Moducare™ treated patient group (n=28) has a higher absolute numbers of CD8+ cells ($p < 0.05$) and higher numbers of CD4+CD45RO+ cells ($p < 0.05$) when compared to the same markers in the untreated patients (n=26). Furthermore, the treated patients demonstrated better responses to the activation stimuli (CD8+CD69+, $p < 0.01$).
Conclusions: Based on these results, the patients who are being treated with Moducare™ have a better CD4 memory status and immune activation than do those that are not receiving therapy. This confirms that long term use of the immune modulator may provide protection against opportunistic infections and slow down the loss of immunological memory to pathogens. This observation is important in a country where anti-retroviral drugs are not routinely prescribed to infected patients.

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ENHANCED SPONTANEOUS APOPTOSIS OF CD4+ LYMPHOCYTES IN FELINE IMMUNODEFICIENCY VIRUS INFECTED (FIV+), SPECIFIED PATHOGEN FREE (SPF) CATS, TREATED WITH THE IMMUNE MODULATOR, BETASITOSTEROL/BETASITOSTEROL GLUCOSIDE (MODUCARE ™)

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Background: The effects of FIV infection and drugs on the immune system can be studied in the absence of infective stimuli in a SPF cat colony. A comparative, single measurement study in FIV+, SPF cats, reporting on the correlation between spontaneous apoptosis and other parameters was recently presented. This study was extended to include more time points and an uninfected (FIV-) control group.
Methods: Three groups of FIV+, SPF cats, housed in a barrier unit, were used. One group of 9 cats was treated with a once daily MODUCARETM capsule. A second group of 8 was the untreated FIV+ control and a third group of 28 the FIV- control. Blood sampling was done 6 weekly for 320 weeks. Spontaneous CD4+ lymphocyte apoptosis was measured by annexin V binding to CD4+ gated lymphocytes for the last 4 specimens of the FIV+ cats and the last 2 of the FIV- cats. Total white cell and absolute lymphocyte counts and lymphocyte subsets were also measured. The means of these were statistically analyzed, using the Kolmogorov-Smirnov (non-parametric) method and a 5% confidence interval.
Results: The mean percentage of spontaneous apoptosis in the treated group was significantly higher ($p < 0.001$) than in the non treated group, although not as high as in the FIV- group (39% vs 19% vs 81%). The total white cell count in the FIV+ treated group and the FIV- group was the same, but was significantly lower ($p<0.05$) in the FIV+ non-treated group. Total lymphocyte count, CD3+, CD4+ and CD8+ percentages were significantly lower ($p<0.001$) in the FIV+ treated group than the other two groups.
Conclusions: The results confirm the correlation between apoptosis and the other parameters noted during the previous study and allows a comparison with FIV- cats. Spontaneous CD4+ apoptosis possibly protects the FIV+ cat by reducing the number of virus producing cells. This phenomenon was enhanced in the group treated with the immune modulator.

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