Viral kinetics and clinical outcome of FeLV infection in relation of the infectious challenge dose

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Introduction

Kittens inoculated with different doses of FeLV-induced tumor preparations showed a dose-dependent correlation with incidence of tumors, tumor regression, size of tumor, and rate of tumor growth [1]. In multicat households (specially in breeding colonies), where animals are kept in close contact and are exposed to very high doses of FeLV, up to 30% of the animals develop persistent viremia. In contrast, the incidence of persistent viremia in single cat households are very low (approximately 1%) [2]. To our knowledge, further experiments using varying FeLV-A inoculation instead of tumor preparations have not been performed. Although the data above suggest that virus doses may play an important role in the outcome post infection, it does not prove it.

With this study, we aimed to determine the influence of different virus doses on the resulting viral and proviral loads, the pathogenesis of infection and disease progression, and to define mechanisms that may be involved in the outcomes observed. We also studied the role of latently infected cats in the pathogenesis of FeLV and the clinical significance of such animals in perpetuating the infection in a determined population.

Materials and Methods

FeLV-A Glasgow strain
Intraperitoneal challenge

Group 1	Group 2	Group 3
n = 8	n = 10	n = 8
5 x 10^4 FFU	5 x 10^5 FFU	5 x 10^6 FFU

Blood collections, in weeks post-challenge

0 1 2 3 6 8 11 14 17 21 25 29 33 37 41 49 57 65 73 81 90 98 106 114 121 130

- **Quantitative real-time PCR:**
  Proviral load in blood cells and tissues
- **Quantitative real-time RT-PCR:**
  Cell-associated mRNA in leukocytes
  Vrial RNA in plasma and tissues
- **ELISA:**
  p27
  Anti-FeLV antibodies
- **Hematology**
- **Clinical examinations**

Results & Discussion

We observed that viral dose used for infection played a role in the establishment of early infection, namely active proviral integration (proviral DNA), viral transcription (cell-associated mRNA), production of virions (plasma RNA) and antigenemia (p27). However, in long-term infections, there was no association among infectious dose and levels of these parameters. Although no statistically significant difference among groups could be observed, cats challenged with the lowest dose harbored lower levels of viral associated parameters when compared to cats receiving the highest dose (fig. 1). These results indicate that cats exposed to high doses of FeLV might become infected more efficiently, but they still may be able to contain viral replication as well as cats exposed to lower virus doses.

Virus dose was not a major determinant of either outcome development or rate of disease progression. Only one cat in group 1 (12.5%, n=8) and one in group 2 (10%, n=10) became latently infected. All other cats became persistently infected. Cats receiving the middle dose fell sick more frequently, although there was no statistically significant difference among groups.

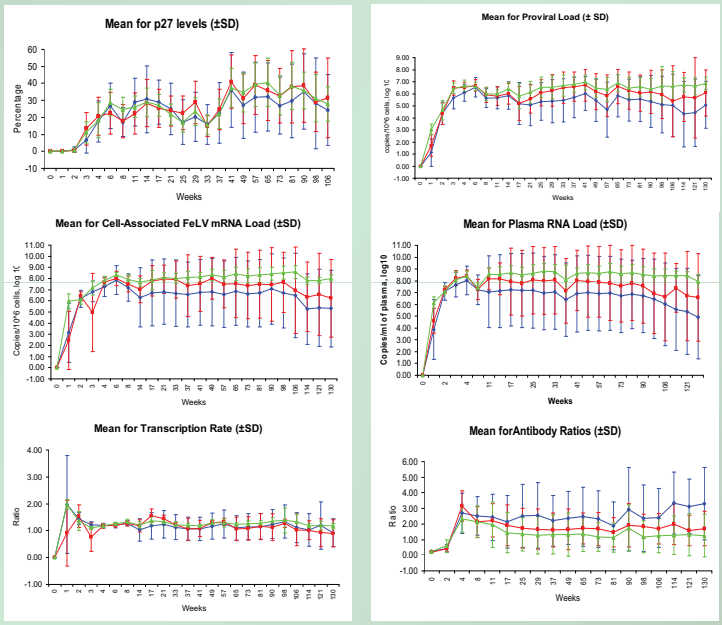

Fig. 1.: Different viral parameters presented as a function of time (in weeks) post-challenge. Group 1(♦), group 2 (■) and group 3 (▲).

However, viral dose influenced the production of cats actively shedding infectious FeLV in feces and saliva: 43% of cats in group 1 and 16.5% of cats in group 2 did not shed infectious virus either in saliva or feces. All cats from group 3 were shedders. Latently infected cats did not shed infectious virus and, therefore, mots likely do not pose a risk to susceptible cats.

There was no statistically significant difference among groups regarding the levels of anti-FeLV antibodies. However, we observed that cats, which lost the ability to produce high levels of FeLV-specific antibodies progressed more quickly to clinical disease. Cats with high levels of anti-FeLV antibodies had lower levels of plasma RNA, cell-associated mRNA and p27. This shows that cats displaying immune dysfunctions are more susceptible to uncontrolled viral replication.

Latently infected cats remained positive for the presence of provirus throughout the experiment. They also tested positive for the presence of FeLV DNA and RNA in several tissues examined, showing that virus most probably persists for the entire life of the host.

These results do not support the hypothesis that virus dose, thus infectious pressure, has an impact on the rate of disease progression and development of a certain outcome. However, regardless of the dose, reduced levels of viral transcription and replication (plasma RNA production) corresponded to clinical quiescence and retroviral persistence in a latent form, while increased viral expression and replication are associated to subsequent disease progression. Interestingly, levels of proviral DNA and p27 were not good predictors of disease progression and clinical outcome.

References

1.Snyder SP, Dungworth DL. Pathogenesis of feline viral fibrosarcomas: dose and age effects. J Natl Cancer Inst 1973;51(3):793-8.
2. Hardy WD, Jr. The feline leukemia virus. Journal of the American Animal Hospital Association 1981;17:951-980.