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# Immunosuppression in a Comparative Study of Feline Leukemia Virus Vaccines

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We read with interest the paper on the comparative efficacy of feline leukemia virus (FeLV) inactivated whole-virus vaccine and canarypox virus-vectored vaccine during virulent FeLV challenge and immunosuppression by Patel et al. (1).

Although the title mentions that the challenge was conducted with immunosuppressed animals, immunosuppression and its impact on the results and conclusions of the study were not discussed by the authors. As a consequence, the conclusions of this study are misleading and inconsistent with previous publications on the efficacy of canarypox-FeLV vaccine (2–5).

Concurrent corticosteroid administration has been used at the early age of research on FeLV vaccines because some scientists had difficulties in getting cats infected with FeLV. It may, however, introduce a severe bias in the conclusions of the study. This concern can be overcome by using virulent FeLV strains, making immunosuppression not anymore required to infect cats. We and others have been successfully using the same challenge strain as Patel and colleagues (FeLV 61E) without concurrent immunosuppressive treatment (6–9). The good practice in veterinary vaccinology is to use a challenge model as close as possible to the natural conditions of infection. For FeLV, oronasal or contact challenge (without immunosuppression) is therefore the method of choice to test vaccines. In this context, it is surprising that the rationale for immunosuppression of the cats was not explained by the authors.

In this study, the 10-mg/kg dose of methylprednisolone acetate (MPA) administered to the cats was significantly greater than that usually recommended (2 to 4 mg/kg), as was the frequency of administration, at the time of the challenge and 1 week postchallenge (the recommended interval for a second dose of MPA is usually 2 to 3 weeks). This dose and regimen were not only immunosuppressive; they also resulted in clinical signs in some animals. Indeed, three cats had to be euthanized "due to weight loss, dehydration, and lethargy secondary to MPA administration." Two of them belonged to the canarypox-FeLV vaccine group, and the third one belonged to the control group. Beyond the ethical concerns it raises, we may expect a treatment with adverse effects on the general body condition to interfere with the results of the study. No justification of the MPA dose and regimen used was provided by the authors. The possible impact of those side effects on the quality of the results and the conclusion of the study was not discussed.

It would be tempting to reply that all of the animals were subjected to the same treatment and thus MPA administration did not affect the conclusions of the study. However, corticosteroid-induced immunosuppression more specifically affects T-cell-mediated immunity through both genomic and nongenomic pathways (10, 11). Glucocorticoids' "actions on the adaptive immune response are to suppress cellular (Th1) immunity and promote humoral (Th2) immunity" (10). As a consequence, the impact of this immunosuppression may be different, depending on the mode of action of the vaccine. This study compared an adjuvanted whole-virus inactivated vaccine and a canarypox-vectored vaccine, which have different modes of action (12). Although the mechanism of action of the whole inactivated FeLV vaccine is not clearly documented, antibodies are expected to play a role through virus neutralization and/or antibody-dependent cytotoxicity. Anti-FeLV antibodies induced by the Nobivac vaccine were still present at the time of challenge. For the canarypox-FeLV vaccine, protection is not mediated by antibodies and the FeLV-specific T-cell response plays a key role (2, 5, 12). Administration of large doses of MPA at the time of challenge is expected to affect the recall response to FeLV, especially the T-cell response. We therefore cannot reject the hypothesis that glucocorticoid-induced immunosuppression had a stronger impact on the efficacy of canarypox-FeLV vaccine than on that of Nobivac vaccine. This aspect was not discussed by the authors.

Surprisingly, the proviral loads in controls and persistently infected cats in general were on the order of $10^{10}$ DNA copies/ml, which gives an average of 1,000 DNA copies/cell. This order of magnitude is 100 to 1,000 times as great as the proviral loads usually reported in experimentally or naturally infected cats (13–15). Are those great proviral loads a consequence of immunosuppression? They confirm that this challenge experiment was very artificial and not representative of FeLV infection in nonimmunosuppressed cats. This should also be clearly stated in the conclusions of the study.

In conclusion, the efficacy of the vaccines was compared in a very artificial model not representative of their conditions of use and with a probable bias associated with the massive administration of glucocorticoids. Unless the concerns and questions listed in this letter are clearly discussed by the authors, the conclusions of the study are misleading and do not contribute to the progress of veterinary vaccinology.

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