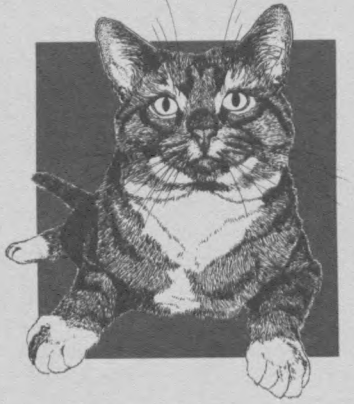

Feline Health Topics

for veterinarians

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Vaccine Associated Sarcomas

Dennis Macy, D.V.M., M.S., D.A.C.V.I.M.

Feline rabies has been increasing in the United States since 1979. For the last 10 years, more cases of rabies have been reported in cats than in dogs. The increase in rabid cats is attributed to the low number of cats vaccinated for rabies and the recent outbreak of wildlife rabies in the United States. More postexposure prophylaxis in humans are related to exposure to rabid cats than exposure to rabid dogs. These factors, along with the approval for subcutaneous administration of rabies vaccines in the mid 1980s, have increased subcutaneous rabies vaccination in cats in the United States. Several recent reports have linked subcutaneous administration of rabies vaccination with subsequent development of fibrosarcoma at the injection sites in cats.

The Laboratory of Pathology at the University of Pennsylvania (LPUP) School of Veterinary Medicine has provided pathology services to practicing veterinarians for more than two decades. Twenty to thirty percent of approximately 18,000 specimens received each year are obtained from cats at this facility. Prior to 1987, postvaccinal reactions were seldom seen at LPUP; however an increase in these reactions has since been recognized, and more than 75 postvaccinal reactions have been identified since 1987 (1987-1991). LPUP has also experienced a 61% increase in the number of fibrosarcomas in the feline biopsy specimens since 1987. Vaccine injection sites such as hind limbs, dorsal neck, dorsal lumbar area, flank and dorsolateral thorax accounted for the vast majority of increase in reported fibrosarcomas ($P < 0.0007$), while noninjection sites showed no increase in fibrosarcoma incidence during this same period of time.

Histologic Studies Suggest Cause

Histologic evaluation of these specimens found that 51% (101/198) of feline fibrosarcomas to be partially infiltrated by lymphocytes and macrophages. Forty-two percent of these contained a gray-brown granular to crystalline foreign material in the macrophages within the lesion. These lesions were further evaluated by x-ray microanalysis and the material was shown to be aluminum and oxygen. The results of this study suggest the material is an aluminum salt (either aluminum hydroxide or aluminum phosphate compounds) used as adjuvants in killed vaccines.

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Most inactivated vaccines, including rabies, use adjuvants to enhance the immune response of the host. One report has indicated approximately 20% of feline vaccine products contain aluminum salts either in the form of aluminum hydroxide or aluminum phosphate. Killed vaccines used in humans may only contain aluminum salts as adjuvants. However, veterinary vaccines may contain a variety of substances as adjuvants (i.e. bacterial fractions, surface-active agents, complex carbohydrates, etc.). Unfortunately, the precise makeup of an adjuvant in a veterinary vaccine is considered proprietary information. Aluminum-containing adjuvants have been previously reported to produce granulomas in cats and dogs. One sarcoma has been attributed to an aluminum oxide ceramic hip prosthesis in man. Despite the literature suggesting that aluminum hydroxide and aluminum-hydroxide-containing-rabies vaccine in particular, are responsible for fibrosarcoma development in cats, the evidence presented in these studies has been inconclusive. Many cats evaluated in the study received other subcutaneously administered vaccines, such as feline leukemia vaccines which also are adjuvanted.

Feline Health Topics

A publication for veterinary professionals
The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats everywhere, by developing methods to prevent or cure feline diseases, and by providing continuing education to veterinarians and cat owners. All contributions are tax-deductible.

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Many veterinarians use more than one inactivated vaccine in cats presented for routine immunization. Early reports singled out rabies vaccination in the association of postvaccinal granuloma and sarcoma production, but failed to include feline leukemia vaccination as a possible source of these adverse reactions. Feline leukemia vaccines are all inactivated and all but one are adjuvanted. They were first introduced in 1985, about the same time the rabies vaccine received a subcutaneous label, and thus fit the time frame consistent with the increased incidence of fibrosarcoma development. Some feline-leukemia-virus (FeLV) vaccines contain substances that may be equally or more responsible for postvaccinal reactions and subsequent fibrosarcomas than that of aluminum hydroxide.

A commentary in the AVMA Journal reported the experience of a private diagnostic lab in the Rocky Mountain region with 176 vaccine-associated sarcomas. This further supported the Pennsylvania study finding of an association between vaccination and subsequent tumor development. This report identified fibrosarcomas, fibrous histiocytomas and osteosarcomas at injection sites. Subsequent investigations have added chondrosarcomas to the list of tumors associated with vaccination. The vaccine-associated-soft-tissue sarcomas are often anaplastic and grow rapidly. Although vaccine-induced sarcomas frequently recur following surgery, they do not frequently metastasize to distant sites.

Epidemiologic Study

Despite these reports, the evidence for the development of vaccine-induced sarcomas has been based on subjective assessment of a causal link between vaccination sites and sarcoma location until an epidemiologic study from the University of California was published in the AVMA Journal in August of 1993. The study included the participation of over 200 veterinarians in private practice in California and Hawaii, with a population of 345 cats with fibrosarcomas.

In addition to confirming the temporal increase in the incidence of sarcomas with tumors found in cervical/ interscapular and femoral regions, the study quantified the increase in risk and incidence associated with both rabies and feline leukemia vaccines. The findings of this research include : (1) postvaccination fibrosarcoma occurrence is principally related to feline leukemia and rabies vaccines, both of which are generally killed product vaccines, rather than the modified-live vaccines;(2) the risk of a fibrosarcoma rose as the number of different vaccines given at the same body site rose as well; (3) no brand of vaccine appeared to be associated with a higher or lower risk of tumor development; (4) the tumors appear to be a response to a profound localized inflammation that occurs following vaccination. The inflammation may occur in part as a result of the presence of vaccine adjuvants or of large quantities of vaccine antigen; (5) postvaccination fibrosarcomas are not restricted to vaccines that contain aluminum salts as adjuvants; (6) tumors were found following both subcutaneous and intramuscular vaccination; (7) concurrent FeLV or FIV status did not affect the risk of fibrosarcoma development; and (8) the incidence of postvaccination sarcomas is low, approximately 10 to 12 cases for every 100,000 FeLV or rabies vaccines given.

AAFP Vaccination Recommendations

The American Association of Feline Practitioners and the Academy of Feline Medicine have actively participated in efforts to investigate the causal link of vaccinations to the development of tumors and have established two general guidelines for vaccine administration.

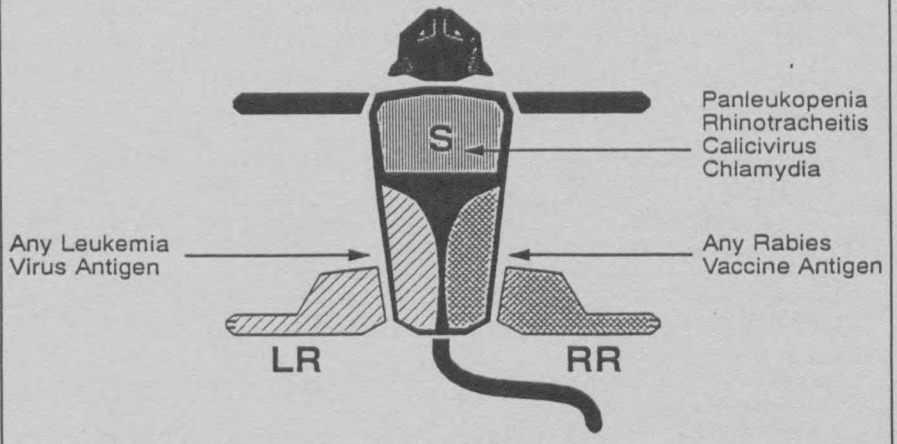
1. Veterinarians should standardize vaccination protocols within their practice and document the location of the vaccination, the type of vaccine administered, and the manufacturer of the vaccine in the patient's permanent record.

2. The following vaccine sites are recommended:

a) Vaccines containing antigens panleukopenia, feline herpesvirus I, feline calicivirus (+/- Chlamydia) should be administered in the scapular region(s).

b) Vaccines containing leukemia virus antigen (+/- other antigens) should be administered in the left rear region (LR) according to manufacturer's recommendations. Leukemia=Left

c) Vaccines containing rabies antigen (+/- other antigens) should be administered in the right rear region (RR) according to the manufacturer's recommendations. Rabies=Right.



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Suggested Procedures

In a yet to be published prospective evaluation of postvaccinal reactions, we compared the vaccine reactions of the three largest selling rabies and FeLV vaccines 21 days postadministration. Based on this preliminary data, we can make a few observations and conclusions: (1) FeLV vaccines, including the one tested that contained aluminum hydroxide, produce significantly less reaction than the three largest-selling three-year rabies vaccines used in the United States. (2) The postvaccinal reactions were most severe for vaccines that contained aluminum hydroxide, whether it be rabies or FeLV vaccines. Non-adjuvanted FeLV vaccines had the least postvaccinal

reactions. (3)The reaction rates were qualitative and quantitatively more severe than has been previously reported by the manufacturer(s) of the vaccines (i.e. the reaction rate reported by one manufacturer at 21 days postvaccination for its rabies vaccine was 0.5% in cats). This study found the postvaccinal reaction rate to be 100%. Some postvaccinal reactions following rabies vaccination were found to be as large as 1.4 cm in diameter.

The Veterinarian's Responsibility

In our clinical experience, postvaccinal sarcomas are usually very aggressive, and because of their invasiveness and interscapular location they are difficult, if not impossible, to successfully remove by surgery. Although most masses that develop at vaccine sites three weeks following vaccination are granulomas and resolve within one to two months, some lead to soft-tissue sarcoma development.

Practicing veterinarians should attempt to reduce the risk of soft tissue sarcoma development, and develop practices that increase the chances of successful treatment of these tumors when sarcomas develop. In addition to these goals, we need to try to determine the vaccine products that may be most responsible for this often fatal complication following a routine veterinary procedure.

Several relatively simple changes in routine vaccine procedures may allow us to meet these goals. First, cats should not be unnecessarily vaccinated (i.e. annual vaccination for rabies with a three-year rabies product should be discouraged). None of the killed vaccines, either FeLV or rabies, should be given in the interscapular space. It is suggested that rabies vaccination be given subcutaneously on the right side of the body of the cat and that feline leukemia virus be given on the left side, and that the location, vaccine manufacturer, vaccine type and serial number be recorded in the medical record. When giving booster vaccinations, previous vaccine sites should be avoided. Vaccines administered subcutaneously on a limb may be preferable because they may allow for amputation of a tumorous site with potentially a higher rate of cure than we are now experiencing with surgery in the interscapular space. Although intramuscular administration of vaccine has been suggested as a means of curbing fibrosarcoma development, it appears that it only results in tumors that are more difficult to detect, thus reducing the chances of early diagnosis and surgical cure.

If the veterinarian suspects that a mass is a vaccine-induced sarcoma, we recommend that the veterinarian do a Tru-cut biopsy or another type of incisional biopsy of the mass to confirm that it is a tumor and not a postvaccinal granuloma. Do not excise the mass prior to biopsy; attempts at simple excision of these tumors is seldom curative and ultimately leads to local recurrence with a more difficult second attempt at surgical excision. Even attempts at aggressive wide surgical excision are often incomplete. Our current recommendation is to include radiation therapy either before or after wide excision in the management of vaccine-induced tumors. ■

Additional Reading:

1. Dubielzig RR: Ocular sarcoma following trauma in three cats. J Am Vet Med Assoc 184(5):578-581, 1984.

2. Dubielzig RR, Haukins KL, Miller PE: Myofibroblastic sarcoma associated with rabies vaccination in a cat. Vet Pathol 29(5):438, 1992.

3. Esplin DG, MCGill LD, Meininger AG, Wilson SR: Postvaccination sarcomas in cats. J Am Vet Med Assoc 202(8):1245-1247, 1993.

4. Hendrick MJ, Brooks JJ: Postvaccinal sarcomas in the cat: histology and immunohistochemistry. Vet Pathol 31: 126- 129, 1994.

5. Hendrick MJ, Dunagan C: Focal necrotizing granulomatous panniculitis associated with subcutaneous injection of rabies vaccine in cats and dogs: 10 cases (1988- 1989). J Am Vet Med Assoc 198(2):304-305, 1991.

6. Hendrick MJ, Goldschmidt MH: Do injection site reactions induce fibrosarcomas in cats? [letter] J Am Vet Med Assoc 199:968, 1991.

7. Kass PH, Barnes WG, Spangler WL, Chomel BB, Culbertson MR: Epidemiologic evidence for a causal relation between vaccination and fibrosarcoma tumorigenesis in cats. J Am Vet Med Assoc 203(3):396-405, 1993.

This article has been reprinted from the 12th Proceedings of the ACVIM Forum, 1994, with permission of the author. Dr. Dennis Macy is employed by the School of Veterinary Medicine at Colorado State University.

Research Briefs

Risk of FIP in cats naturally infected with feline coronavirus

Researchers at the University of Glasgow, United Kingdom conducted a longitudinal study of 820 cats in 73 households over a period of 6 years to establish the fate of pet cats that were seropositive after natural exposure to feline coronavirus (FCoV). In particular, their risk of developing feline infectious peritonitis (FIP) was determined. The seropositive cats were assigned to 1 of 3 groups: cats from households in which FIP had recently been diagnosed; cats from households in which FIP had not been diagnosed, but from which kittens had been relocated and subsequently died of FIP; and cats from households in which FIP had not been diagnosed.

Cats in the first group were not at greater risk of developing FIP than were cats in the other 2 groups. Consequently, any household in which seropositive cats live must be considered a potential source of FCoV that can cause FIP. There was no evidence that the enhanced disease, which has been described after experimentally induced infection of seropositive cats, exists in nature. Thus, analysis of the survival of the seropositive cats over periods of up to 36 months indicated that their risk of developing FIP decreased with time, suggesting the development of immunity rather than increased susceptibility to disease. In addition, of 56 cats deemed to have been naturally reinfected because their anti-FCoV antibody titers decreased and subsequently increased, only 3 developed FIP.—*(Resource: Am J Vet Res, 56 (4): 429-434, 1995)*

Antiproliferation and colony-forming inhibition activities of recombinant feline interferon (rFelFN) on various cells in vitro

The antiproliferative and colony inhibiting activities of recombinant feline interferon (rFelFN type I) against various cells in vitro were examined. Feline and canine cells were both sensitive to rFelFN. To inhibit the growth of feline cells by 5o% approximately 5×10^2 to 1×10^3 U/mL rFelFN was required and maximum activity was achieved at a concentration of 1×10^5 U/mL. Approximately 5×10^3 to 5×10^4 U/mL rFelFN was necessary to inhibit the growth of cannine cells by 50%. The antipro-liferative and colony inhibiting activities of rFelFN on canine cells appeared to be cell-specific and dose-dependent. However, human, monkey and hamster cells were resistant to rFelFN. We suggest that fFelFN might be useful for treatment of feline and some canine neoplastic conditions.—*(Resource: Can J Vet Res 59:67-69, 1995)*

Comparison of PCR detection of Bartonella and Afipia felis DNA with serology and skin tests

Two polymerase chain reaction (PCR) hybridization assays were developed to determine the role of *Bartonella* (formerly *Rochalimaea*) in cat scratch disease (CSD). These assays were applied on 89 pus aspirates from skin test-positive CSD patients (group 1) and on 137 pus and lymph node specimens from CSD suspects (group 2). *Bartonella* DNA was detected in 96% of the samples from group 1 patients and in 60% of group 2 samples; however, *A. felis* DNA could not be detected in any clinical samples. These results suggest that CSD is caused by *Bartonellae* and that *A. felis* does not play a significant role in this zoonosis. A strong correlation between *Bartonella* PCR positivity and *Bartonella henselae* antibody titer was found. Comparison of CSD skin test results with those obtained by *Bartonella* PCR suggests a low sensitivity of the skin test.—*(Resource: J Infect Dis, 171:916-923, 1995)*

(continued on next page)

Other Research Articles of Interest:

Brown DC and Holt D: Subcutaneous emphysema, pneumothorax, pneumomediastinum, and pneumopericardium associated with positive-pressure ventilation in a cat. JAVMA 206:997-999, 1995.

Christopher M, Broussard JD, Peterson ME: Heinz-body formation associated with ketoacidosis in diabetic cats. J Vet Int Med 9:24-31, 1995.

Day DG: Feline cholangiohepatitis complex. Vet Clin N Am Sm Anim Pract 25:375-385, 1995.

Dhein CR and Barbee DD: Use of bone marrow serum for biochemical analysis in healthy cats. JAVMA 206:487-490, 1995.

Dimski DS and Taboada J: Feline idiopathic hepatic lipidosis. Vet Clin N Am Small Anim Pract 25:357-373, 1995.

Fyfe JC: Glycogen storage disease in cats. JAVMA 206:286-287, 1995.

Sale of Stamp Collection Will Benefit Feline Health Center

The Cornell Feline Health Center recently received a stamp collection from an anonymous donor in memory of his cats. The collection is being sold in its entirety, and is valued at $17,000. The condition of the stamps are rated fine to extra-fine quality. The oldest stamp dates to 1908. The collection includes such valuable stamps as the Presidential set (32 stamps), dated 1938; Famous Americans series, dated 1940; and the Library series, dated 1954-61.

Interested philatelists should contact Dr. Jim Richards, Assistant Director, Cornell Feline Health Center, College of Veterinary Medicine, Ithaca, NY 14853 for a complete listing of the stamps in the collection.

Glaus TM, Jacobs GJ, Rawlings ED, et. al.: Surgical removal of heartworms from a cat with caval syndrome. JAVMA 206:663-666, 1995.

Greene RT and Troy GC: Coccidioidomycosis in 48 cats: A retrospective study. J Vet Int Med 9:86-91, 1995.

Lutz TA, Rand JS, and Ryan E: Fructosamine concentrations in hyperglycemic cats. Can Vet J 36:155-159, 1995.

Medleau L, Jacobs GJ, and Marks MA: Itraconazole for the treatment of cryptococcosis in cats. J Vet Int Med 9:39-42, 1995.

Pu R, Okada ER, Little R, et .al.:Protection of neonatal kittens against feline immunodeficiency virus infection with passive maternal antiviral antibodies. AIDS 9:235-242, 1995.

Soderstrom MJ, Gilson SD, and Gulbas N: Fatal reexpansion pulmonary edema in a kitten following surgical correction of pectus excavatum. JAAHA 31:133-136, 1995.

Stalis IH, Bossbaly MJ, and Van Winkle TJ: Feline edomyocarditis and left ventricular ednocardial fibrosis. Vet Path 32:122-126, 1995.

VanSteenhouse JL, Taboada J, and Dorfman MI: Hemobartonella felis infection with atypical hematological abnormalities. JAAHA 31:165-169, 1995.

Copies of Articles

Photocopies of the above articles are available by making your request via mail to the Flower-Sprecher Library, College of Veterinary Medicine, Ithaca, NY 14853; or by telephone at 607-253-3510; or by fax at 607-253-3080. There is a charge for this service. The total charged is based on the number of pages copied, New York state sales tax of 8% if applicable, and delivery method (e.g., U.S. mail, Federal Express, or fax). ■

For You and Your Practice

The Cornell Book of Cats

The Cornell Feline Health Center offers a quantity discount for book orders placed by veterinary offices. The book retails for $27.50, but when you order 10 or more books the cost is only $21.50 per book plus shipping and handling ($6/10 books). Books are shipped by UPS. (Allow 4 to 6 weeks for delivery.)

Client Information Brochures

You'll find these brochures a welcome addition to the client resources you use. Topics include: *Feline Immunodeficiency Virus, Feline Infectious Peritonitis, Feline Leukemia, Toxoplasmosis, Feline Behavior Problems, Feeding Your Cat, Special Needs of the Older Cat, Urinary Obstruction, Choosing and Care of Your New Cat, Inflammatory Bowel Disease,* and *Parasites.* You can preview a sample of all 11 brochures by ordering our sampler for only $3. Or you can order quantities for your office by requesting order blanks on the form below.

Feline Memorial Program

The Cornell Feline Health Center's Memorial Program is a positive way to help your clients cope with the loss of their feline friends. Order a supply of memorial cards by completing the form below.

Dr. Louis J. Camuti Memorial Feline Consultation and Diagnostic Service

If you have a difficult feline case or want current information on feline diseases, call 1-800-KITTY DR and talk with our consulting veterinarian. The service is available from 9 a.m. to noon or 2 p.m. to 4 p.m. (Eastern time) on weekdays (excluding holidays). A $25.00 fee for the consultation helps the center defray the cost of this valuable service. *(Members receive a 20% discount.)*

Tee-shirts

These shirts are 100% preshrunk cotton and feature the Center's logo and two cats. Available colors: Stonewashed Blue, Teal Green, Fuchsia, Ash, Purple, and Turquoise. Adult sizes only: Large (42-44), X-Large (46-48), XX-Large (50-52).Cost per shirt is $14.99 (plus $2 shipping, and 8% sales tax for NY residents).

Order Form

ITEM	QUANTITY	UNIT PRICE	COST
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Client Information Brochure Sampler		**$3.00**	
Information Brochure Order Blank		**0**	**0**
Feline Memorial Program Cards		**0**	**0**
Tee-shirt		**$14.99 (plus $2 and 8% tax)**	
	Color		
		TOTAL	**$**

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Send this completed form and your remittance (checks made payable to "Cornell Feline Health Center") to: Orders, Cornell Feline Health Center, College of Veterinary Medicine,VRT 7018, Ithaca, NY 14853-6401.

Continuing Education Opportunities

Cornell Feline Practitioners Seminar

This year's seminar—sponsored by the College of Veterinary Medicine's Office of Continuing Education, Feline Health Center, and the American Association of Feline Practitioners—will introduce several new speakers and topics (e.g., hypertension, dermatology, nephrology, behavior problems). The seminar will be held July 28-31 at the Sheraton Inn in Ithaca, New York. The registration fee is $300. For more details or to register contact Linda Alfreds, Office of Continuing Education, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853; phone 607-253-3200; or fax 607-253-3198.

Infectious Disease Symposium

The American Association of Feline Practitioners will host its first Colloquiium of Infectious Disease of the Cat in Washington, D.C. on October 14 to 17. The program is a comprehensive informational seminar on all aspects of feline infectious diseases, including zoonoses, disease control, and vaccination. For registration details contact AAFP at (800)-204-3514.

AAFP Offers Many Benefits

If you are not currently a member of the American Association of Feline Practitioners (AAFP), you may be missing out on valuable practice-building opportunities. AAFP members receive discounted subscription fees for Feline Practice Journal and Veterinary Information Network (VIN); a membership directory; newsletters; the opportunity to take 36 hours of continuing education on feline-specific topics; and discounts on Cornell Feline Health Center client brochures; and the opportunity to network with veterinarians with similar interests through contacts at meetings, the newsletter, the directory, and the VIN Bulletin Board. If you would like more information on AAFP membership, contact Kristi Thomson at (800)-204-3514.

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