FELINE INFECTIOUS DISEASES

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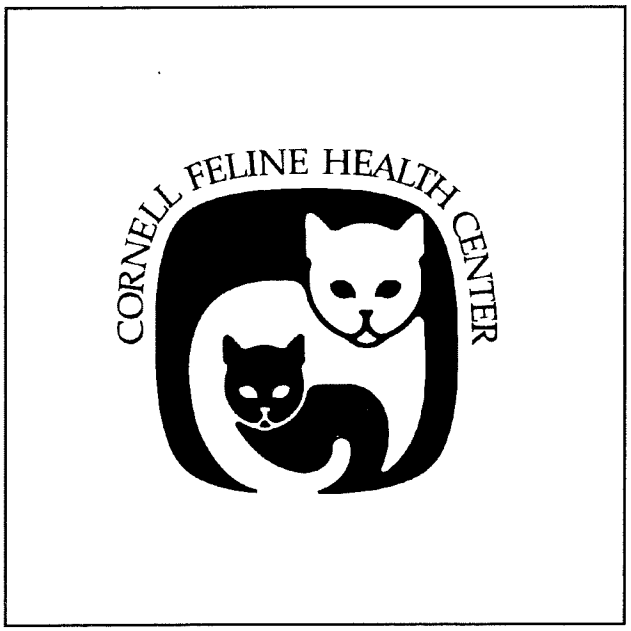

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OVERVIEW OF FELINE BIOLOGICS

I.VACCINES

A. **Panleukopenia vaccines**
   1. **Vaccination** - a must for all cats
      a. 8-10 weeks of age, repeat at 3-4 week intervals
      b. Last vaccination must be at least 12 weeks of age, 14 would be better.
      c. annual revaccinations - unnecessary
      d. optional program = similar to rabies 3-year program
         - vaccinate kittens
         - revaccinate (booster) one year later
         - then revaccinate every 3 years for life
      e. use MLV vaccine in contaminated area such as shelter = faster protection
   2. **Maternal immunity**
      a. provides solid protection and interferes with immunization
      b. most common cause of "vaccine failure" in the cat
      c. acquired via colostrum in first 24 hrs.
      d. antibody half-life = 8-10 days
      e. duration depends on dams VN antibody titer at queening
         - usually can overcome with vaccine by 12 weeks of age

B. **Respiratory Disease Vaccines**
   1. **Vaccines Available**
      a. **FHV-1** = feline viral rhinotracheitis, herpesvirus, "rhino"
         - MLV
         - Inactivated
         - Intranasal MLV
      b. **FCV** = feline calicivirus
         - MLV
         - Inactivated
         - Intranasal MLV
      c. **Chlamydia**
         - Modified live
         - Inactivated
   2. **Vaccination Protocols** - The vaccine protocol used for respiratory diseases depends upon the population being vaccinated, and the existing respiratory problems within that population.
      a. **Protocol #1** - routine vaccination, low risk populations
         - FHV-1/FCV/FPV (MLV or inactivated)
            - 8 & 12 weeks of age, repeat at one year, then every 3 years
      b. **Protocol #2** - high risk populations (catteries, shelters)
         - FHV-1/FCV/FPV (MLV)(+/- chlamydia)
            - 4, 8, 12 weeks of age, repeat at one year, then every 1-3 years
      c. **Protocol #3** - high risk breeding catteries with respiratory disease problems
         - FHV-1/FCV intranasal
            - 2 weeks of age
         - FHV-1/FCV/FPV MLV injectable vaccine (+/- chlamydia)

- 6, 10, 14 weeks

C. **Rabies Vaccines**
1. Vaccine recommendations must be consistent with state requirements
2. Use only inactivated vaccines approved for use in cats
3. Use only 3-year vaccines approved for use in cats
4. Vaccination schedule
   a. 1st rabies vaccine at 12+ weeks
   b. Repeat in 1 year, then every 3 years

D. **FeLV Vaccines**
1. *Leukocell & Leukocell 2* ("Norden Laboratories", SmithKline Beecham) *(Pollock & Haffer, JAVMA 199:1406-1409, 1991)*
   a. First commercial vaccine
      - Leukocell licensed 11/13/84
      - Leukocell 2 licensed 8/2/88 - greater antigenic mass
   b. Inactivated "subunit" vaccine = "soluble tumor antigen vaccine"
   c. gp70 antigen is main component
   d. Contains dual adjuvants, aluminum hydroxide and a partially purified saponin
   e. From FL-74 cells infected with 3 subtypes A, B, and C
2. *VacSYN/FeLV; Panacine-5* (Synbiotics Corporation, mfg. by Bio-Trends *(York & York, JAVMA 199:1419-1422, 1991)*
   a. Licensed 8/30/89
   b. Whole-virus vaccine
      - from FL-74 cells infected with FeLV strain UCD-1
      - subtypes A, B, & C
   c. Inactivated with ethylenimine
   d. Purified
      - remove excess protein including BSA
      - remove free subunits of FeLV (gp70, p15E, p27)
      - concentrated 2X
      - removed salt by dialysis
   e. no adjuvant
3. *Fel-O-Vax Lv-K; Fel-O-Vax Lv-K III; Fel-O-Vax LV-K IV* (Fort Dodge) *(Sebring et al., JAVMA 199:1413-1419, 1991)*
   a. Licensed 11/16/89, 9/18/90, 12/18/90
   b. Molecularly cloned whole-virus vaccine
   c. Chemically inactivated vaccine
   d. Contains dual adjuvants
   e. Subtypes A, B, & C
4. *GenetiVac FeLV* (Pitman-Moore, Coopers Animal Health) *(Kensil et al., JAVMA 199:1423-1427, 1991)*
   a. Licensed 10/25/90
   b. Genetically engineered subunit vaccine
   c. Immunogen = purified recombinant protein containing entire amino acid sequence of FeLV subtype A gp70 envelope glycoprotein
   d. gp70 genome cloned a plasmid, then plasmid inserted into E. coli
   e. Purified to remove E. coli proteins
   f. Dual adjuvants
      - purified saponin, QS-21
      - aluminum hydroxide
5. *Fevaxyn FeLV; Eclipse 4 + FeLV; Eclipse 4 + FeLV/R* (Solvay)

(Hines et al., JAVMA 199:1428-1430, 1991)

a. Licensed 1991
b. Whole-virus vaccine
c. Subtypes A & B
d. Chemically inactivated
e. Selective concentration of viral components
f. Aqueous adjuvant

6. *RM Leucat; RM Feline 3 + Leucat; RM Feline 4 + Leucat* (Rhone Merieux) - (Similar to Fevaxyn-FeLV)
   a. Whole virus vaccine
   b. Subgroups A, B, and C
   c. Chemical inactivation
   d. No adjuvant

E. **Safety of FeLV vaccines**
   1. All FeLV vaccines are inactivated
      a. Safe from producing FeLV
      b. Safe from producing FeLV-related disease
      c. No indication of exacerbation of FeLV infection in an already FeLV-positive cat.
   2. No unusual adverse reactions from simultaneous vaccination with FeLV and vaccines
   3. No apparent interference with other antigens in multivalent vaccines
   4. Allergic-type reactions do occur to varying degrees
      - to FeLV antigen?
      - to bovine serum albumin (BSA) in vaccine?
      - to other proteins?
      - to adjuvant(s)

F. **Efficacy of FeLV Vaccines**
   1. Factors affecting efficacy of FeLV vaccines
      a. Antigenic mass of vaccine
      b. Adjuvant
      c. Challenge system used
         - immunosuppressed?
         - route of challenge?
         - challenge virus strain?
      d. Criteria for efficacy
         - prevent persistent viremia?
         - prevent viremia?
         - prevent latency?
         - stimulate VN antibody titer?
         - prevent tumor formation?
         - survival?
      e. Experimental design of study
      f. How results reported
         - % of vaccinates? = not accurate
         - preventable fraction = PF? - must use PF since controls not all come down with disease
      g. Age of cats
   2. Reported studies on efficacy (see table)

G. **FeLV Vaccine Guidelines - From FeLV/FIV Colloquium, 1991**
   JAVMA, 199(11), Nov. 15, 1991
   1. Vaccines should be referred to as feline leukemia virus vaccines, not feline leukemia vaccines. The vaccine protects against FeLV

infection, not against the neoplastic disease.

2. Only healthy, afebrile cats should be vaccinated.
3. All cats that are at risk of exposure to FeLV should be vaccinated.
4. Control of FeLV should involve proper husbandry, in addition to FeLV testing and vaccination. The FeLV-positive cats should not be housed in direct contact with FeLV-negative cats, even when such negative cats have been vaccinated against FeLV.
5. Vaccines should be administered according to manufacturers' recommendations.
6. All FeLV vaccines attempt to prevent virus infection, or at least persistent viremia if infection does occur. The gp70 virion glycoprotein is the immunogen; immunity against that viral protein prevents infection by the virus.
7. The preventive principle of all FeLV vaccines currently available is the same. Although it may be preferable to use the same vaccine for booster vaccinations as originally used (assuming equal efficacy of vaccines), a booster vaccination using a vaccine of a different brand should still stimulate an anamnestic immune response.
8. Testing for FeLV is encouraged prior to primary vaccination for FeLV of all cats whose background or exposure status to FeLV is either at risk or unknown.
9. Commercial companies should make only accurate and noninflated claims concerning the efficacy of vaccines.
10. The aim of FeLV vaccination should be to prevent virus infection entirely, including transient viremia.
11. The choice of which FeLV vaccine to use must be left to the practitioner.
12. The USDA should establish a Standard Requirement for FeLV vaccines.

Table 1: Reported Efficacy of FeLV Vaccines
(Colloquium on FeLV/FIV, JAVMA 199(10), 1991)

Vaccine Name	# Studies	# Cats Vac/Ctrl	# Cats PV Vac/Ctrl	% Cats PV Vac/Ctrl	PF
Leukocell	5	88/88	31/60	35/75	53
Leukocell 2	13	213/129	42/82	20/64	69
Covenant	4	143/121	19/80	13/66	80
VacSyn/FeLV	4	77/49	21/34	27/69	61
Fel-O-Vax Lv	4	102/69	8/60	8/87	91
GenetiVac	1	20/20	3/14	15/70	79
Fevaxyn-FeLV	1	144/45	12/39	8/87	91

PV = persistent viremia after FeLV challenge (= >12 weeks)
PF = preventable fraction, as a measure of percent efficacy
Vac/Ctrl = number of vaccinated cats/number of unvaccinated control cats

II. DURATION OF IMMUNITY

A. Historical Perspective of Feline Vaccines

1. First feline vaccine developed in 1930s for FP. Was a tissue origin vaccine prepared from infected cat tissues which were inactivated with formalin.
2. Pneumonitis vaccines appeared in 1950s.
3. First cell culture origin inactivated and MLV FP vaccines developed in late 1960s.
4. FHV and FCV vaccines first licensed in 1970s.
5. First FeLV vaccine appeared in 1985.
6. Intranasal FIP vaccine licensed in 1991.
7. Rabies vaccines developed more than 100 years ago.

B. Current situation:

1. Multivalent vaccines used routinely
   a. FP/FHV/FCV used for all cats.
   b. Some cats also receive chlamydia or FP/FHV/FCV/Chlamydia multivalent vaccine
   c. Most cats routinely vaccinated for FeLV.
   d. Rabies vaccination mandatory in many states or rabies endemic areas.
   e. FIP vaccine is used sparingly in high-risk situations.

C. Licensure of Feline Vaccines

1. All veterinary biologics are licensed by the "Veterinary Biologics" (VB) division of the "Biotechnology, Biologics, and Environmental Protection Agency" of the "Animal and Plant Health Inspection Service" of the "United States Dept. of Agriculture"
2. Licensure is covered by the Virus-Serum-Toxin Act, as amended.
   a. Title 9 (Animals and Animal Products), Code of Federal Regulations (CFR), parts 101 to 117.
   b. Veterinary Services Memorandum No. 800.50, Basic License Requirements for Applicants (12/6/84)
   c. Standard Requirements established for licensure of each veterinary biologic after an appropriate time.

D. Duration of Immunity - Regulations

1. Until recently, there was no requirement by VB for a manufacturer of veterinary biologics to show any "duration of immunity" unless they label specifically stated that the vaccine would protect for a specified time such as "one", "two", or "three" years.
2. Rabies vaccines have generally been the only feline biologics that have carried a specific label claim for duration of protection.
3. Recent changes in licensure requirements now include "duration of immunity" as well as potency and safety.

E. Cornell Studies on duration of immunity in a closed colony

1. SPF cat breeding colony established in December, 1990
   a. Purchased 15 5-month-old kittens
      - 13 females
      - 2 males

b. Kittens had been vaccinated twice in October 1990 at approximately 9 and 12 weeks of age
c. Vaccine = commercial inactivated FP/FHV/FCV vaccine with an adjuvant
d. No vaccines given to cats after arrival at Cornell
e. As kittens from this colony became available, about 15 additional queens were added to the breeding colony
f. Replacements were never vaccinated
g. Breeding cats were gang-housed with free contact between vaccinated and non-vaccinated cats.

2. Serological studies
   a. All cats in colony bled for serum
      - January 1991 (6 months of age)
      - October of 1993 (3 years after vaccination)
      - October 1994 (4 years after vaccination)
      - March 1995 (4 1/2 years after vaccination)
      - October 1995 (5 years after vaccination)
   b. In March 1995, all cats were negative for FeLV antigen, FIV antibodies, feline coronavirus antibodies, and toxoplasma antibodies, and negative on isolation for chlamydia and pathogenic bacteria. All non-vaccinates were negative for FP, FHV, and FCV antibodies.
3. Results: Table 1 lists the virus neutralizing antibody titers of vaccinates and non-vaccinated control cats in January 1991, October 1993 (3 years), and October 1994 (4 years). The October 1995 samples have not been assayed to date.

F. Cornell studies on antibody titers on cats presented to a multiperson feline practice (Cats Only Veterinary Clinic, Columbus, Ohio)
1. Veterinarians in Clinic were concerned that they were over vaccinating. They were seeing what they believed to be excess adverse vaccination reactions following routine annual vaccination.
2. A collaborative study was established between "Cats Only" and the "Cornell Feline Health Center"
3. Cats presented for annual physical exams are routinely sampled, with serum and detailed vaccination history sent to Cornell.
4. Unless there is an unknown vaccination history, or the cats are from a "high risk" situation, cats are not routinely vaccinated for FPV/FHV/FCV.
4. VN titers for FPV, FHV, and FCV are determined on serum samples.
5. Results are periodically reported back to Cats Only, but any negative results are immediately reported so that these cats can be revaccinated.
6. Results: VN titers are summarized in Table 2.

Table 1: Virus neutralizing antibody titers against feline parvovirus (FPV), feline herpesvirus (FHV), and feline calicivirus (FCV) in serum samples from SPF cats vaccinated with 2 doses of inactivated triple vaccine at 8 and 12 weeks of age and then housed in a barrier breeding colony.

CAT No.	FPV 1/91 1/6 YPV	FPV 10/93 3 YPV	FPV 10/94 4 YPV	FPV 10/95 5 YPV	FHV 1/91 1/6 YPV	FHV 10/93 3 YPV	FHV 10/94 4 YPV	FHV 10/95 5 YPV	FCV 1/91 1/6 YPV	FCV 10/93 3 YPV	FCV 10/94 4 YPV	FCV 10/95 5 YPV
Vaccinates												
0513	5,000	5,000	--	--	12	12	--	--	192	64	--	--
0515	5,000	5,000	5,000	5,000	96	4	3	<2	>256	24	32	8
0517	>10,000	5,000	10,000	5,000	12	6	16	<2	256	32	24	24
0519	--	5,000	5,000	1,000	--	3	6	3	--	8	6	3
0521	5,000	500	500	500	8	32	6	6	>256	128	64	48
0523	5,000	1,000	5,000	500	8	3	8	<2	128	192	192	32
0527	10,000	10,000	5,000	>10,000	12	2	<2	<2	24	32	24	16
0531	--	5,000	5,000	5,000	--	4	<2	2	--	6	6	<2
0533	>10,000	5,000	500	5,000	6	2	<2	2	32	6	3	3
0535	10,000	>10,000	10,000	10,000	6	4	8	3	128	48	64	48
0539	5,000	10,000	5,000	5,000	2	<2	4	<2	64	24	48	16
0541	>10,000	>10,000	>10,000	5,000	6	48	48	<2	128	>256	256	8
0543	5,000	10,000	5,000	5,000	8	2	<2	6	64	6	8	128
0568	5,000	5,000	1,000	--	8	12	6	--	96	128	96	--
0572	5,000	>10,000	10,000	5,000	48	48	24	24	256	>256	256	>256
Mean	**6,923**	**6,433**	**5,500**	**4,769**	**18**	**12**	**9**	**4**	**145**	**81**	**77**	**45**

CAT No.	FPV 1/91 1/6 YPV	FPV 10/93 3 YPV	FPV 10/94 4 YPV	FPV 10/95 5 YPV	FHV 1/91 1/6 YPV	FHV 10/93 3 YPV	FHV 10/94 4 YPV	FHV 10/95 5 YPV	FCV 1/91 1/6 YPV	FCV 10/93 3 YPV	FCV 10/94 4 YPV	FCV 10/95 5 YPV
Controls												
A002	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	3
A012	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A013	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A014	--	<10	<10	<10	--	<2	<2	<2	--	2	<2	<2
A021	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A022	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A031	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	2
A032	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A061	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A082	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A101	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A102	--	<10	<10	--	--	<2	<2	--	--	<2	<2	--
A171	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A242	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A401	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A402	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
A481	--	<10	<10	<10	--	<2	<2	<2	--	<2	<2	<2
Mean	**--**	**<10**	**<10**	**<10**	**--**	**<2**	**<2**	**<2**	**--**	**<2**	**<2**	**<2**

-- = Not Tested; YPV = Years post vaccination

TABLE 2: Virus neutralizing antibody titers against feline parvovirus, feline herpesvirus-1, and feline calicivirus in cats presented to a private feline practice for routine annual vaccination.

Sample #	# Cats Tested	Virus Neutralizing Antibody Titer				
Feline Parvovirus		**<10**	**10-100**	**101-1,000**	**1,001-10,000**	**>10,000**
1	347	7	8	36	93	201
2	36	0	3	3	10	20
3	11	0	0	1	3	7
Feline Herpesvirus-1		**<2**	**2-10**	**11-50**	**51-100**	**>100**
1	347	63	103	116	32	28
2	36	5	5	18	4	4
3	11	0	3	3	1	4
Feline Calicivirus		**<2**	**2-10**	**11-100**	**101-1,000**	**>1,000**
1	347	4	22	82	133	105
2	36	1	3	15	13	4
3	11	0	1	2	7	1