Guidelines on Feline Infectious Diseases

RABIES IN CATS
June 2008

The following recommendations have been formulated by the European Advisory Board on Cat Diseases.

The European Advisory Board on Cat Diseases is an independent panel of 17 veterinarians from ten European countries, with an expertise in immunology, vaccinology and/or feline medicine. The ABCD was set up to compile guidelines for the prevention and management of major feline infectious disease in Europe based on current scientific knowledge and available vaccines.

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6. Rabies in cats

6.1 Virus properties

Rabies is the cause of one of the oldest and most feared diseases of humans and animals - it was recognized in Egypt before 2300 BC and in ancient Greece, where it was well described by Aristotle. Perhaps the most lethal of all infectious diseases, rabies also has the distinction of having stimulated one of the great early discoveries in biomedical science. In 1885, before the nature of viruses was comprehended, Louis Pasteur developed, tested, and applied a rabies vaccine, thereby opening the modern era of infectious disease prevention by vaccination.

Rabies virus is one of the Rhabdoviridae, which encompass over 175 viruses of vertebrates, invertebrates and plants.

Based on virion properties and serologic relationships four genera containing animal viruses have been recognized in the family Rhabdoviridae.

The rabies virus belongs to the genus Lyssavirus, together with the Mokola virus, Lagos bat virus and Duvenhage virus from Africa and European bat viruses 1 and 2 and Australian bat lyssavirus. Each of these viruses is considered capable of causing rabies-like disease in animals and humans. All lyssaviruses use bats as reservoir hosts.

Rhabdovirus virions consist of an outer envelope with large peplomers and an inner, helically coiled cylindrical nucleocapsid. The precise cylindrical form of the nucleocapsid gives the viruses their distinctive bullet or conical shape. The genome is a single molecule of linear, negative-sense, single-stranded RNA, 11 to 15 kb in size. The genome encodes 5 genes in the order 3'-N-NS-M-G-L-5'. The viruses generally have 5 proteins. The glycoprotein that makes up the peplomers contains neutralizing epitopes which are targets of vaccine-induced immunity as well as epitopes involved in cell-mediated immunity. Virions also contain lipids, their composition reflecting the composition of host cell membranes, and carbohydrate side-chains on the glycoprotein. Rhabdoviruses may be stable in the environment especially at alkaline pH but are thermolabile and sensitive to the UV irradiation of sunlight. In clinical practice, rabies virus is easily inactivated by detergent-based disinfectants.

Viral entry into host cells occurs via fusion of the viral envelope with the cell membrane; all replication steps occur in the cytoplasm.

Virions are formed by the budding of nucleocapsids through cell membranes. Rabies virus budding takes place mostly upon intracytoplasmic membranes of infected neurons, but almost exclusively upon plasma membranes of salivary gland epithelial cells. The replication of rabies viruses is slow and usually non-cytopathic because it does not shut
down host cell protein and nucleic acid synthesis. Rabies virus produces prominent cytoplasmic inclusion bodies (Negri bodies) in infected cells.

Laboratory-adapted ("fixed") rabies virus replicates well in Vero (African green monkey kidney) cells and BHK-21 (baby hamster kidney) cells, which are the most common substrates for growing animal rabies viruses for vaccine production. Rabies virus also replicates to high titre in suckling mouse and suckling hamster brain.

6.2 Epidemiology

The disease occurs worldwide, with certain exceptions. Large regions in Europe became free of terrestrial rabies as a result of wildlife vaccination programmes.

The rabies situation and the regulations are continuously updated on the web sites of OIE and WHO (see reference section).

The number of human deaths caused each year by rabies is estimated to be approximately 40,000 to 100,000, worldwide, and an estimated 10 million people receive post-exposure treatments each year after being exposed to rabies suspect animals [WHO, 2006]. Dog rabies is still very important in many parts of the world and is the principal cause of human rabies cases. In many countries, wildlife rabies has become of increasing importance as a threat to domestic animals and humans, and transmission from vampire bats is an important issue. The red fox, raccoon, skunk and mink are the main reservoir species of terrestrial rabies in Europe and North and South America.

The control of rabies in various regions of the world poses very different problems, depending upon the reservoir host and prevalence of infection.

6.2.1 Rabies-free Countries

Strictly enforced quarantine of dogs and cats for various periods before entry has been used effectively to eliminate rabies virus from Japan, the United Kingdom (UK), Australia, New Zealand and several other islands. Rabies was never endemic in wildlife in the UK and was eradicated from dogs in the UK in 1902, and again in 1922 after it became established in the dog population in 1918. Since then, there had been no rabies in the UK until recently when there were isolated reports of bats infected with European bat virus 1. However, such isolated incidents did not alter the (terrestrial) rabies-free status of the UK. In contrast, rabies was not recognized in Australia until recently when Australian bat lyssavirus was discovered, and found subsequently to be endemic in Southeast Australia.

6.2.2 Developing Countries

In most countries of Asia, Latin America and Africa, endemic dog rabies is a serious problem, causing significant domestic animal and human mortality. In these countries, large numbers of doses of human vaccines are used and there is a continuing need for
comprehensive, professionally organized and publicly supported rabies control agencies. That such agencies are not in place in many developing countries is a reflection of their high cost; nevertheless, progress is being made. For example, a substantial decrease in rabies incidence has been reported in recent years in China, Thailand and Sri Lanka, following implementation of dog vaccination programmes and improved post-exposure prophylaxis of humans. Similarly, the number of rabies cases in Latin America is declining significantly; the Pan American Health Organization has implemented a vaccination program to eliminate urban dog rabies from the Southern hemisphere.

6.2.3 Industrial Countries

In most industrial countries, even those with modest disease burden, publicly supported rabies control agencies operate in the following areas: (1) programmes of oral vaccination of wildlife, in Europe of the red fox; (2) stray dog and cat removal and control of the movement of pets (quarantine is used in epidemic circumstances, but rarely); (3) immunization of dogs and cats, so as to break the chain of virus transmission; (4) laboratory diagnosis, to confirm clinical observations and obtain accurate incidence data; (5) surveillance, to measure the effectiveness of all control measures; and (6) public education programs to assure cooperation.

The cat is considered in some European countries to be high-risk species for transmission to human beings. For example, of more than 20,000 inhabitants in Switzerland that had to be vaccinated after exposure to rabies in the years from the late 1960s until the early 1990s, around 70% had been either bitten or in close contact with cats [Hohl et al, 1978].

Even if feline rabies is considered to be a by-product of canine or wild rabies [Blancou & Pastoret 1990], behavioural characteristics of cats and clinical aspects of the disease in this species render it important for public health reasons. In fact, despite a lower number of post-exposure prophylaxis treatment for people following cat bites compared to dog bites, treatment is justified more often [Blancou & Pastoret 1990].

6.3 Pathogenesis

Rabid animals are the only source of virus. Virus is shed in the saliva some days before the onset of clinical signs and virus is transmitted through a bite or a scratch of the skin or mucous membranes (eyes, nose, mouth). The blood of rabid animals is not considered infectious. The average incubation period in cats is two months but may vary from 2 weeks to several months or even years depending on the dose of virus transmitted and the severity and site of the wound [Jackson 2002, Charlton et al, 1997].

The incubation period is variable because the virus moves along peripheral nerves with the normal axoplasmic flow from the inoculation site to the central nervous system.
(CNS): hence the greater the distance from the CNS, the longer the incubation period; and the greater the density of innervation of the inoculated tissue the shorter this duration [Greene and Rupprecht, 2006]. Very long incubation periods have been described in some experimental cases [Murphy et al, 1980], and this must be taken into account when evaluating wound history, especially in free-roaming cats exhibiting sudden behavioural change and/or signs of motor neuron dysfunction that may initiate the clinical phase.

The virus replicates in striated muscle and in connective tissue at the site of inoculation and then enters the peripheral nerves through the neuromuscular junction [Murphy et al, 1973]. Alternatively, it can infect directly the peripheral nerves, spreading to the central nervous system via the axonal route. The virus can then travel to the salivary glands by the retrograde axonal route. At this time, the animal becomes infectious, i.e. about 3 days before the first clinical signs appear. By the time clinical signs appear, the virus is widely disseminated throughout the organs. In most cases, death occurs within 5 days so that a cat or a dog will be shedding the virus in saliva for about 8 days in total.

Most clinical signs are related to the virus-induced central and peripheral nervous system dysfunction rather than neuronal death and abnormalities in neurotransmission have been described [Jackson 2002]. Rabies glycoprotein probably plays an important role in the trans-synaptic spread of the virus between neurons and in the topographic distribution of virus infections through the nervous system [Etessami et al, 2000].

### 6.4 Immunity

#### 6.4.1 Passive immunity acquired via colostrum

Kittens from vaccinated queens obtain maternal antibodies (MDA) via colostrum. The MDA titre in kittens depends on both the antibody titre of the queen as well as the amount of colostrum ingested during the first day of life. In most kittens, MDA will not persist for longer than 12 weeks.

MDA have been demonstrated even in sera of fox cubs whelped by orally immunized vixens [Vos et al, 2003].

Passive immunity may neutralize vaccine antigens, thereby inhibiting the immunoglobulin production, interfering in the immunization process during the first weeks of life. Therefore, it is generally recommended to perform the primary vaccination against rabies in kittens not earlier than at 12 weeks of age.
6.4.2 Active immune response

Although rabies antigens are highly immunogenic and capable of eliciting the full spectrum of protective immune responses, the virus is not highly cytopathic, since no cell lysis occurs during replication or maturation. Therefore, little antigen is presented to the immune system. Neither humoral nor cell-mediated specific responses can be detected during the early stages of movement of virus from the site of the bite to the central nervous system [Green 1997]. Hence, infection of naive animals with rabies virus most often results in disease and death. Such sequelae may be averted by prompt immunization following exposure, demonstrating that the development of anti-rabies viral immunity prior to extensive infection of neurons is protective. It is well documented that virus neutralizing antibody is a crucial factor in this immunity. Rabies is an example of a "Th-2 healing disease" in which activation of B lymphocytes, with the help of CD4 T cells, is important for protection [Garenne and Lafon 1998]. When activated, primarily by the N protein of the rabies virus, CD4 T cells produce cytokines (i.e. IL-4) that stimulate B cells to produce antibodies. In contrast, rabies-specific CD8 T cells cause neuronal damage when a Th-1 response (IFN-γ and TNF-α) predominates [Lafon 2002, Hooper 2005]. However, published reports exist that describe vaccinated animals that had no detectable virus neutralizing antibody and yet survived rabies challenge, indicating that other mechanisms may also protect against this disease [Aubert 1992, Hooper et al, 1998].

After intramuscular infection, the virus replicates locally for several weeks in the myocytes or nervous tissue. In vaccinated cats with adequate serum antibody titres, the virus is often neutralized during this early incubation period. In contrast, unvaccinated cats exposed to rabies virus can produce an antiviral immune response, usually late in the clinical course, that fails to prevent disease [Johnson et al, 2006]. However, protection against the early stages of infection is provided by non-specific immunity, in which interferon seem to play a critical role. High levels of interferon are detectable in sera of mice inoculated with rabies virus by peripheral or intracerebral routes [Marcovistz et al, 1984, 1994; Johnson et al, 2006]. It is not clear how effective these mechanisms are in naturally exposed naive cats. It is believed that factors, determining morbidity include the amount and strain of the virus, the age and immunocompetence of the cat and the bite, such that in unvaccinated cats the risk of developing rabies is higher (and the incubation period shorter) in a young animal that has been bitten severely in the head, with a high saliva deposit in the wound, compared to the risk for an adult cat, bitten in a limb, especially after extensive bleeding [Pastoret et al, 2004].

In natural infections of unvaccinated animals, neutralizing antibody appears usually after the virus has entered the central nervous system. Hence, once symptoms are evident, recovery from rabies is exceedingly rare, although there have been reports of humans
and animals that have recovered following confirmed clinical rabies [Bernard 1985, Fekadu 1991]. Furthermore, antibodies to lyssaviruses have been detected occasionally in domestic or wild cats with no history of vaccination, consistent with a non-fatal disease or subclinical infection [Tjørnehøj et al, 2004; Deem et al, 2004].

6.5 Clinical signs

Aggressive behaviour towards humans is unusual in healthy cats, so any unjustified aggressive behaviour in cats must be considered highly suspicious.

Rabies should be suspected not only when there has been a recent history of a bite by or exposure to a rabid animal but also where an unvaccinated cat may have been in contact with potentially infected wildlife, such as bats. Indeed, only recently (November 2007), a cat in France died of rabies as a result of infection with bat lyssavirus. However, although rabid bats having been reported in the UK [Johnson et al, 2003; Fooks 2003; Harris et al, 2007] and the Mammal Society estimates that British cats could be killing 230,000 bats a year [Fooks, personal communication], no cases of cat rabies have been documented in the UK. These findings indicate that the risk of cats becoming infected with rabies from bats may be low.

Two disease forms can be identified in cats: the furious and the paralytic one. The furious form of rabies has three clinical phases (prodromal, furious or psychotic and paralytic or dumb) but they are not always clearly distinct in cats. The other has only two phases: prodromal and paralytic. During the very short prodromal phase (12-48 hours) of both forms, a wide range of quite non-specific clinical signs (fever, anorexia, vomiting, diarrhoea) may occur, sometimes accompanied by neurological signs. Marked behavioural changes may be noticed at first, such as unusually friendly or shy or irritated behaviour or increased vocalization. Altered behaviour depends on forebrain involvement and may be associated with other neurological signs reflecting the inoculation site. If the bite occurs in the face, clinical signs reflect cranial nerve and forebrain involvement: the former may produce depressed or absent reflexes (palpebral, corneal, pupillary, etc.), strabismus, dropped jaw, inability to move whiskers forward, dysphagia, laryngeal paralysis, voice change, tongue paralysis. Forebrain involvement is responsible for seizures, muscular twitching or tremors, aimless pacing, exaggerated emotional responses (irritability, rage, fearfulness, photophobia, attacking inanimate objects, etc). The tendency to bite may be the consequence of the loss of inhibitory control by cortical
neurons over the subcortical bite reflex whereby dogs and cats turn and snap at anything that touches them around the mouth [O’Brien and Axlund, 2005]. If this is the case, the animal snaps without warning or showing any emotion when doing it. Pruritus at the bite site can be observed. If the infecting bite was on the limbs, neurological signs start from the spinal cord and an ascending lower motor neuron (LMN) paralysis occurs before the brain signs. The encephalitis rapidly spreads throughout the CNS producing severe ataxia, disorientation, paralysis, seizures, *status epilepticus* eventually followed by coma and death from respiratory arrest.

The furious phase is more consistently developed in cats showing behaviour abnormalities (described above) [Fogelman et al, 1993]. The paralytic phase (paraparesis, incoordination, generalized paralysis, coma and death) usually begins after five days of starting first clinical signs.

Isolated reports of survival after a confirmed clinical disease are available in cats, dogs and humans [Bernard 1985, Fekadu 1991], but death usually occurs after a clinical course of 1-10 days. Cats often die in 3-4 days [Rupprecht and Childs, 1996] and according to a more recent report, 25% of deaths occur in cats within 4 days of clinical course, while in dogs within 2 days only [Tepsumethanon et al, 2004].

Atypical forms with chronic course have been described after experimental infection in cats [Murphy et al, 1980].

The severe public health risk (veterinarians included!) requires that differential diagnosis of CNS diseases characterized by sudden onset and rapidly evolving clinical signs, always includes rabies for free roaming, unvaccinated cats living in endemic areas or travelling there. In this case, the clinical approach must make safety the priority because the manipulation and restraint of the cat easily may provoke biting at the time when salivary

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**Box 1. Clinical signs of rabid cats infected by classical rabies virus (Genotype I)**

**History and clinical signs by the owner:**
1. Dramatic changes from normal behaviour.
2. Very aggressive, biting human and/or animal with no apparent reason.

http://www.oie.int/eng/normes/mmanual/A_summary.htm

**General appearance and clinical signs at observation:**
1. 90% of rabid cats show clinical signs of the furious form.
2. Thin (the cat cannot eat)
3. Ruffled and dirty coat. (the cat cannot clean itself)
4. Mucous membranes, tongue, nose and footpads are reddish pink, high fever.
5. The chin and front legs are wet from saliva (salivation).
6. Permanent movement and excitement (restlessness).
7. Imbalanced gait due to paresis of the hind legs.
8. Pupil dilatation unresponsive to light.
9. Abnormal water uptake (water runs back out of mouth).

(Courtesy Dr Veera Tepsumethanon)
glands are usually already infected and rabies virus is shed in saliva. Guidelines indicating that a clinical diagnosis of rabies should be included in the differential diagnosis in live cats with suspected encephalitis based on history and observation of the cat inside the carrier would help to reduce the risk of exposure for the veterinary team (see the flow chart below that was adapted for cats from Tepsumethanon et al, 2003).

Vaccine-induced rabies in cats was observed in the past when modified-live vaccines were available. Neurological signs occurred several weeks after vaccination and were characterized mostly by progressive upper motor neuron (UMN) limb paralysis and cranial nerve deficits.
Is the cat from or near to an endemic area, or traveling from there?

- **YES or unknown**

Does the cat have outdoor access?

- **YES or unknown**

Has the cat been vaccinated against rabies?

- **YES or unknown**

Is the cat less than 1 month of age?

- **YES or unknown**

Is the cat sick?

- **YES or unknown**

Has the onset been sudden (<1 day)?

- **YES or unknown**

The clinical signs have progressed (worsened) in the last 3-5 days?

- **YES or unknown**

Does the cat show at least 1 of the following clinical signs?
- Behavioural changes
- Cranial nerve deficits
- Seizures
- Muscular twitching or tremors
- Aimless pacing
- Tendency to bite
- LMN paralysis
- Severe sensorial ataxia
- Depressed sensorium

- **RABIES POSSIBLE**

- **RABIES UNLIKELY**
6.6 Diagnosis

Because clinical diagnosis of rabies is not reliable, a definitive diagnosis can only be obtained by laboratory investigations post-mortem.

However, serological tests are used for surveys and post-vaccinal control in order to test immunity level in vaccinated animals, especially in the context of international movements.

6.6.1 OIE recommendations

The recommendations from the experts of the OIE First International Conference “Rabies in Europe” Kiev, Ukraine, 15-18 June 2005 are the following:

i) Routine laboratory diagnosis should be undertaken using only the techniques specified by the OIE (Terrestrial Manual) and the WHO (Laboratory Techniques in Rabies).

ii) The FAT (Fluorescent antibody test) is the primary method recommended.

iii) The confirmation test should use rabbit tissue culture inoculation test (RTCIT). The mouse inoculation test can be used only if rabbit tissue culture is not available.

iv) PCR is presently not recommended for routine diagnosis but may be useful for epidemiological studies or for confirmatory diagnosis only in reference laboratories.

Reference laboratories: The list of reference experts and laboratories can be found on the OIE web site (http://www.oie.int/eng/OIE/organisation/en_listeLR.htm).

6.6.2 Direct viral detection methods

Only direct detection methods are recommended to confirm rabies in human beings and animals.

Samples (animal heads, brain tissues or other organs) should be sent according to the national and international shipping regulations and care should be taken in order to avoid potential human contamination. Because rabies virus is rapidly inactivated, the specimen should be shipped (preferably) refrigerated or at room temperature in 50% glycerine in phosphate buffered saline solution.

Brain tissue (especially thalamus, pons and medulla) is the preferred sample for post-mortem diagnosis but other organs such as salivary glands can also be used.

6.6.2.1 Fluorescent antibody test

Fluorescent antibody test (FAT) is the method recommended by WHO and OIE for fresh or glycerol samples [Bourhy et al, 1989, Birgham & van der Merwe 2002], but is less sensitive in formalin-fixed tissues. FAT provides a reliable diagnosis in 95% to 99% of
cases for all genotypes and in fresh samples. It can also be used for rabies detection in cell cultures and in brain tissue of mice that have been inoculated for diagnosis.

6.6.2.2 Immunochemical methods
Other methods available include immunochemical tests (e.g. avidin-biotin peroxidase system, ELISA, direct blot enzyme immunoassay). The rapid rabies enzyme immunodiagnosis (RREID) is an alternative to FAT but detects only one genotype. Correlation between FAT and RREID is between 96 and 99% [Barrat 1993].

6.6.2.3 Inoculation to laboratory animals and cell cultures
These tests are used to confirm inconclusive results with FAT in organs or when FAT is negative if human exposure has been reported.
Intracerebral inoculation of mice is performed in newborn or 3 to 4 week-old mice. FAT is used to detect virus 5 days to 11 days post-inoculation. Ideally, these inoculation tests should be replaced by cell culture tests, which are as sensitive, less time-consuming and more ethical. Neuroblastoma cell lines may be used and presence of the rabies virus is revealed by FAT, with results being available within 2 to 4 days.

6.6.2.4 Histology – Immunochemistry
Since histology and immunohistochemistry to detect Negri bodies are less sensitive methods than FAT, especially in autolysed tissues, these methods are not recommended for routine diagnosis.

6.6.2.5 Other direct methods
Reference laboratories may identify rabies virus, and especially some variants, using monoclonal antibodies, nucleic probes or PCR and sequencing. These techniques can distinguish vaccine and field strains and may identify the geographic origin of the strain.

6.6.3 Indirect detection methods
6.6.3.1 Seroneutralisation
Seroneutralisation tests in cell cultures, such as fluorescent antibody virus neutralisation (FAVN) or rapid fluorescent focus inhibition test (RFFIT) are widely used.
The principle of FAVN is neutralisation in vitro of a rabies CVS strain before inoculating BHK-21 C13 cells. The titre is expressed in IU/ml and is the reciprocal value of the dilution at which 100% of the virus is neutralised in 50% of the wells. RFFIT and FAVN give equivalent results. A titre of 0.5 IU/ml of serum antibodies is considered to be the minimum titre to correlate with immune protection.
6.6.3.2 **ELISA**

ELISA has recently been developed and is used for testing vaccinated animals. Commercial kits are now available for the detection of antibodies in sera from vaccinated cats and dogs. ELISA tests do not require the culture of live virus and the result can be obtained within 4 hours. The sensitivity and specificity of ELISA tests still need to be confirmed before it can be accepted as an official method [Servat et al, 2006].

For further details, refer to Barrat et al, [2006] and the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals [OIE 2007].

### 6.7 Rabies control in cats

#### 6.7.1 Treatment (post-exposure vaccination)

The post-exposure management of cats depend on the national public health regulations, but is forbidden in many countries. Usually, it is not authorised in case of clinical suspicion. No supportive or specific treatment has proved to be effective in rabid cats, so treatment is not recommended [Greene & Rupprecht, 2006].

#### 6.7.2 Prophylaxis (preventive vaccination)

Rabies in cats is usually controlled by traditional inactivated vaccines [OIE 2007] and at present, several inactivated rabies vaccines are available commercially. These products have been shown to induce protective immune responses following a single vaccination [Fu 1997, Perez and Paolazzi 1997]. In cats and dogs, the peak of rabies neutralizing antibodies is generally reached between 4 to 6 weeks after the first immunization [Cliquet 2006]. Currently available inactivated vaccines are very efficient. Cats and dogs with a neutralization titre above 0.5 IU/ml, regardless of the period of time elapsed since vaccination have a very high probability of survival after a rabies infection [Cliquet, 2006]. Cats respond better to rabies vaccination than dogs and as much as 97.4% of them develop a titre of 0.5 IU/ml or higher after the first vaccination, many even above 5 IU/ml [Cliquet, 2006]. A very small proportion of cats identified with rabies have had at least one rabies vaccination during their lifetime [Greene et al, 2006]. Since the new EU regulations in pet movement were put in place in 1993, no single case of vaccine failure has been documented [Cliquet 2006]. Rabies vaccines are generally considered to be safe, even in neonatal kittens.

Inactivated vaccines may carry a risk due to the remote possibility of incomplete inactivation of the virus and the inadvertent spread of residual pathogenic particles of rabies virus [Schneider, 1995]. Furthermore, inactivated rabies vaccines may be associated with the development of injection site sarcomas in cats [Dubielzig et al, 1993].
Such problems led to continued efforts to develop safer rabies vaccines. New vaccines include recombinant subunit proteins [Wunner et al, 1983], recombinant viral vectors [Paoletti 1996, Xiang et al, 1996] and deoxyribonucleic acid (DNA) based vaccines [Osorio et al, 1999, Cupillard et al, 2005]. Recombinant live vector vaccines have some advantages over traditional vaccines: they are innocuous, they induce suitable humoral immune responses and they do not require rabies virus to be handled [Paoletti 1996]. They also induce less inflammation at the site of injection [Day et al, 2007].

Fortunately, current vaccines are also cross-protective against a number of other Lyssavirus genotypes. All cat and dog sera with a titre above 5 IU/ml neutralize EBL-1 and EBL-2 regardless of vaccine/virus strain and among sera with a titre between 0, 5 and 5 IU/ml 87% neutralize EBL-1 and 53% EBL-2 [Fooks, personal communication]. However, against some novel lyssaviruses isolated from bats in Eurasia the protection may be reduced or negligible depending on the genetic distance between the new isolate and traditional rabies viruses [Hanlon et al, 2005].

Because of the public health risk associated with susceptible domestic cats becoming infected following exposure to rabid wild or domestic animals, rabies virus vaccines should be considered as core vaccines in countries where rabies is endemic and should be administered in accordance with local or state regulations.

In countries where rabies is not present, rabies vaccination may be considered optional, to be recommended by the veterinarian if the cat should move to an endemic rabies area.

6.7.2.1 Primary vaccination course
In contrast to all other inactivated vaccines, a single rabies vaccination induces a long-lasting immunity due to the immunogenic properties of the vaccinal antigen.

Kittens should be vaccinated at 12 to 16 weeks of age to avoid interference from maternal antibodies, with revaccination one year later (depending on data sheet recommendations for each brand of vaccine). With this schedule, a single vaccination is sufficient. However, national or regional legislation regarding vaccination type and interval should be adhered to.

6.7.2.2 Booster vaccinations
Although some commercial vaccines provide protection against virulent rabies challenge for 3 years or longer [Lakshmanan et al, 2006], national or local legislation may require annual boosters.
6.8 Disease control in specific situations

6.8.1 Shelters
In endemic areas, stray cats should be always considered at exposure risk and handling and nursing of rescued animals should be considered dangerous even if they are asymptomatic.

6.8.2 Breeding catteries
Risk exposure is generally almost nil in breeding catteries because usually pedigree cats are kept strictly indoors, but their vaccination is under local or state regulation.

6.8.3 Vaccination of immunocompromised cats

6.8.3.1 FIV-positive cats
FIV-positive cats should be kept confined indoors to avoid transmission to other cats, to protect them from other infections and to slower the progression of FIV infection itself. This is an efficient preventive measure for rabies in areas at risk, but national or regional legislation should be adhered to. In outdoor cats with risk of exposure to rabies, vaccination is strongly advised.

6.8.3.2 FeLV-positive cats
In vaccination studies it was demonstrated that FeLV-infected cats may not be able to mount adequate immune response to some rabies vaccines [Franchini 1990]. FeLV-infected cats should be confined strictly indoors to prevent spread to other cats in the neighbourhood: if cats are allowed to go outside in area at risk for rabies, more frequent vaccination may need to be considered (e.g. every 6 months).

6.8.3.3 Chronic disease
There is general agreement that cats with acute illness should not be vaccinated but cats with chronic illness such as renal disease, diabetes mellitus or hyperthyroidism should be vaccinated regularly if they are at risk of exposure.

6.8.3.4 Cats receiving corticosteroids or other immunosuppressive drugs
In cats receiving corticosteroids, every vaccination should be considered carefully. Depending on dosage and duration of treatment, corticosteroids may cause functional suppression of immune responses, particularly cell-mediated immune responses, but studies exploring rabies vaccine efficacy in cats receiving corticosteroids are lacking. In dogs, corticosteroids do not appear to result in ineffective immunizations if given for
short periods of time at low to moderate doses [Nara et al, 1979]. However, concurrent use of corticosteroids at the time of vaccination should be avoided if practical.
6.9 References


