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This article describes the infectious and non-infectious diseases in cheetahs (*Acinonyx jubatus*), snow leopards (*Panthera uncia*), black-footed cats (*Felis nigripes*), lions (*Panthera leo*) and other captive and wild felids.

Felid diseases – review and update on actual literature

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Extended abstract

A. Cheetah diseases

a. CNS diseases

i. Cheetah ataxia - Encephalomyelopathy

The cheetah encephalomyelopathy, a neurological disease characterized by degenerative lesions of the spinal cord and cerebellum causing ataxia and paresis, has emerged in the past twenty years in the European Endangered Species Program (EEP) cheetah population, and represents a serious threat to a sustainable captive European cheetah population. This disease accounts for 25% of all deaths in the European cheetah population and represents a limiting factor in the growth of the European captive population. Cheetahs of every age group are affected and often several or all cheetahs of the same litter will eventually develop the disease, either simultaneously or successively over a period of several months or years interval. The course of the disease is variable, from rapid onset ataxia to a slower progressive development with stabilization and acute relapsing episodes. Pathologically, the disease is characterized by bilateral symmetrical degeneration of the white matter of the spinal cord, with loss of myelin exceeding axonal loss, suggesting a primary myelin disorder. Changes in the cerebellar white substance characterized by myelin and axonal loss associated with astrogliosis and microgliosis, as well as with degeneration of Purkinje and granular cells, are also frequently observed. The etiology of the disease is still unknown and investigations to determine the cause of the cheetah disorder have been based on known causes of encephalomyelopathy in human and domestic animals that features white matter demyelination. Several causes has been considered, including genetic, environmental / toxic, nutritional (especially Copper) and viral factors. The pattern of incidence does not indicate a major genetic basis for this disease, however, a genetic component to general disease predisposition and response cannot be ruled out, and multifactorial inheritance might play a role. Extrinsic factors, either related to the management or the environment have to be considered, however, no “common denominator” in nutrition, holding and environmental conditions, husbandry, deworming and vaccination regimen has been identified to date (WALZER et al., 1995, 2003; PALMER et al., 2001; SHIBLY, 2006; ROBERT, 2008).

ii. Lenkoencephalopathy

The leucoencephalopathy is a serious degenerative disease affecting North American cheetahs and has never been observed in the European and South-African populations despite thorough investigations. The most distinctive clinical signs are blindness or visual abnormalities, lack of responsiveness to the environment, behavioral change, incoordination or convulsions. The disease emerged in 1996, peaked between 1998-2001, and is now declining. About seventy animals have been affected to date at about 30 different facilities. Most affected animals are at least 10-yr old. The pathological lesions are restricted to the cerebral cortex and characterized by loss of white matter with associated bizarre astrocytosis. The cause is unknown, but epidemiological features suggest exposure to an exogenous agent through diet or medical management (MUNSON, 2005).

b. Non-CNS diseases

i. Gastritis

Lymphoplasmacytic gastritis associated with *Helicobacter* spp. causes significant morbidity and mortality in captive cheetahs worldwide (Europe, North-America, South-Africa, Japan). Spiral bacteria consistent with *Helicobacter* spp. are detected in most cases, but there is no correlation between the severity of the gastritis and the amount of bacteria in stomach glands. An altered immune response to a commensal bacteria related to chronic stress is postulated. Previous studies identified a novel bacteria, *Helicobacter acinonychis*, as well as *H. heilmannii,* and *H. felis* within the stomachs of captive cheetahs with gastritis. The disease causes vomiting, weight loss and failure to thrive and many cheetahs will develop secondary systemic amyloidosis (Type AA) resulting in renal failure. Furthermore, gastritis doesn't resolve with antibiotic treatment. In the EEP population, gastritis was observed in 81% of the samples, ranging from mild to severe, characterized mainly by lymphoplasmacytic inflammation of the mucosa, at times associated with neutrophilic infiltration. Interestingly, despite abundant spiral bacteria colonization, wild cheetahs have been shown to develop only mild gastritis in few cases, suggesting that a direct cause-effect is unlikely.
More and more acquired hiatal hernias, probably secondary to chronic gastritis, have been observed in a N-Am. Zoo. These are generally diagnosed on routine endoscopy and have a wide range of severity – mild bulging at the lower esophageal sphincter, improper sphincter motility, prolapse of the stomach into the esophagus, various degrees of gastroesophageal reflux disease (GERD), and herniation of the stomach into the thorax (CITINO, 2005; TERIO et al., 2005; WALZER et al., 2005).

ii. Nephrosclerosis

Glomerulosclerosis and associated nephrosclerosis are the leading cause of death in captive cheetahs. The prevalence in European, >1y-old cheetahs is 80% (nearly 70% in N-Am. and S-Afr.).
Glomerulosclerosis is characterized by progressive thickening of the glomerular basement membrane that leads to glomerular ischemia and sclerosis. The lesion resembles that of diabetic nephropathy which results from glucose and subsequent glycosolation of basement membrane proteins. The lesion also is similar to rat nephropathy which has both genetic and dietary predisposing factors. The reason for the high prevalence in captive cheetahs is not known, but the relative absence of this lesion in all be a few wild cheetahs with very mild disease, suggests an extrinsic cause. Either diet or metabolic changes due to chronic stress are proposed (BOLTON and MUNSON, 1999).
Other renal pathological findings reported in the EEP population were pyelonephritis and/or papillary necrosis, presence of crystals in the tubular lumen (oxalate crystals), and amyloidosis (MUNSON, 2005; WALZER et al., 2005)

iii. Amyloidosis

Systemic AA amyloidosis affecting the kidney, liver, and other organs is highly prevalent in all captive populations (38% NA; 82% SA; 48% Europe) and is the cause of death in many cheetahs. The amyloid is deposited in the renal medullary interstitium, along sinusoids in the liver, in the lamina propria of the GI tract, and in the interstitium of endocrine organs. Amyloidosis in the kidney may be associated with renal papillary necrosis. The occurrence of amyloidosis is highly correlated with inflammatory diseases, especially with chronic gastritis (PAPENDICK et al. 1997; MUNSON, 2005).
Based on recent demonstration of transmissibility of AA amyloidosis in mice via "infection" with AA-amyloid-laden tissues, it has been postulated that fecal transmission of AA amyloidosis in the cheetah contributes to high incidence of disease. Recent experimental analyses in mice suggest that AA amylodosis could be transmitted horizontally by a prion-like process through a seeding-nucleation mechanism, as observed in sheep with scrapie and cervids with CWD. Distinct AA amyloid fibrils were detected in the feces of cheetah with amyloidosis, and transmissibility of the disease was demonstrated in mice experimentally infected with these isolated fibril fractions. Therefore, the holding

and breeding conditions in cheetahs might favor the horizontal propagation of AA amyloidosis via the "AA amyloid seeds" excreted in the feces. (ZHANG et al., 2008).

iv. Splenic myelolipoma

Multiple splenic myelolipomas, nodules composed of fat tissue admixed with hematopoietic cells, are frequently found (>50%) as incidental finding in cheetahs. Nodules might also appear in the liver. The youngest cheetah affected was 1y old. These lesions are not clinically important, but should be recognized because they have been misdiagnosed as metastatic cancer. The cause is not known, but dietary or stress-induced metabolic changes are suspected (WALZER et al., 1996).

v. Liver VOD

Veno-occlusive disease is caused by fibrous occlusion of the efferent blood vessels of the liver (central and sublobular veins), resulting in progressive liver failure and ascites, especially in animals older than 6y. The cause of this condition is not known. There is no indication of known causes of VOD such as hypervitaminosis A or intoxication with pyrrolozidine alkaloid or aflatoxin. The prevalence is high in the North-Am. captive cheetah population (63%), low in the S-Afr. captive population (10%), whereas only single historical cases were recorded within the European population. In the recent EEP liver samples, only mild increases of collagen and reticulin fibers were observed around the central veins and in the sinusoids, corresponding to the earliest lesions described in the American cases (GOSSELIN et al., 1988; MUNSON, 2005, WALZER and al., 2005).

vi. Genetic diseases

This "Peaugres syndrome" might be one of the few "true" genetic diseases in cheetahs. 27 cubs were born in 5 litters from 2 normal dams which were sisters (Fanny and Rina) and 1 unrelated normal male (Fota). From these 27 cubs, 26 died between 1 and 134d of age. The cubs were more or less affected and presented with various pathological lesions including poor hair coat, heart malformation (aortic aneurysma and heart hypertrophy), liver fibrosis, stunted growth, osteoporosis and CNS diseases (encephalitis). The etiology of the disease remains unclear, however a genetic cause is probable. Similar lesions are described in a human multisystemic genetic disease known as "Menkes disease", related to a defect in copper transport proteins (WALZER et al., 2005).
Sporadic cases of gastroschisis and cleft palates have been observed in related cheetah cubs (T.PETIT, pers. comm.)

vii. Mastocytosis

Mast cell "tumors" and generalized mastocytosis are being seen with some frequency in captive cheetahs. Cheetahs may present with single or multiple firm raised skin masses. Caution must be given, not to classify these tumors as highly malignant mast cell tumors with a poor prognosis as they generally disappear on their own. They may be associated with insect bites. A few cheetahs have been seen with generalized or regionalized severe exudative dermatitis with mast cell infiltration. These cheetahs are often uncomfortable and lose weight. This lesion has been very responsive to short term corticosteroid therapy (allergic reaction?) (CITINO, 2005)

viii. Infectious / parasitic diseases

Within the EEP captive cheetah population, following death related, infectious and parasitic diseases have been reported (WALZER et al., 2005):

- FCoV (FIP), FPV, FHV
- *Clostridium perfringens* A (enterotoxicosis), *Salmonella* sp., *Campylobacter* sp. (enteritis)
- *Pasteurella* sp. (bronchopneumonia)
- *Hemobartonella felis* (=*Mycoplasma felis;* Feline Infectious Anemia)
- *Toxocara* sp., *Toxascaris leonine* (intestinal parasites)

- *Aelurostrongylus abstrusus* (parasitic pneumonia)

Furthermore, suspected clinical ehrlichiosis, with *Ehrlichia*-like inclusion bodies in circulating lymphocytes was reported in a group of recently imported cheetahs in Dubai (from Tanzania). Clinical signs were inappetence, lethargy, fever, diarrhea, dehydration. Five cheetahs died whereas 7 others were successfully treated with enrofloxacin and imidocarb (TARELLO and RICCIERI 2008).

ix. Stress and immunity

Given the disparity in disease prevalences between captive and free-ranging cheetahs, factors associated with captive management must be considered to have a significant role in disease pathogenesis. Poor genetic variability may predispose cheetahs to develop certain diseases, but it certainly does not explain the high prevalence of these diseases only in the captive population as homogeneity is present in both captive and free-ranging populations. Therefore, other aspects of captive management and chronic stress may play a role in the unusual degenerative diseases and the florid inflammatory responses to infectious diseases in captive, but not free-ranging cheetahs. Captive cheetahs have been shown to have larger adrenal cortices (adrenal hyperplasia) and higher levels of fecal corticoids than captive cheetahs, suggestive of chronic stress.
Because of striking differences in prevalence of moderate to severe gastritis between captive (64%) and free-ranging (3%) cheetah populations, gastritis is an optimal disease to study the effects of corticoids on disease development and the immune response The results suggest that higher levels of corticoids in captive cheetahs have inappropriately altered local gastric cytokine expression and therefore may have inappropriately altered the immune response against *Helicobacter*. Further research is needed to determine whether immune responses to other infectious agents are similarly modulated in captive cheetahs (TERIO et al., 2004).

B. Snow leopards (*Uncia uncia*)

Similarly to the cheetah, the snow leopard deserves some attention regarding general disease susceptibility, as several “usual” reports have been published, pointing possibly to an immune system dysfunction. It has also been suggested, that snow leopards, because of a relative lack of exposure to infectious organisms in their natural habitat, may be more susceptible to infectious agents present in more temperate climates (WORLEY, 1982).
Cerebral or extramedullary spinal fungal abcesses were diagnosed in four snow leopard cubs. In two subadult littermates from a North-American zoo, *Scopulariopsis* sp, a common saprophytic fungi, was isolated from a spinal abcess. A further myelitis case caused by a phaehyphomycete (*Cladiophalophora bantiana*) has been observed in a cub in a Swiss zoo and a cerebral chromomycosis was diagnosed in juvenile individual in another North-American zoo. Invasive Infections with both fungi have been reported in immunocompromised people (CALLE et al. 1989; JOYNER et al., 2003; JANOVSKY et al., 2005). Further opportunistic infections include a mycotic pneumonia and meningencephalitis due to *Aspergillus terreus* in a neonatal cub (PEDEN and RICHARD, 1984), demodicosis is group of juvenile snow leopards (FLETCHER, 1980), Tyzzer’s disease in five kittens (SCHMIDT et al., 1984) and multifocal osteomyelitis caused by *Klebsiella oxytoca* in a juvenile animal (WACK and KRAMER, 1995). Furthermore co-infection with feline panleukopenia virus and canine distemper virus (FIX et al,. 1989), and with toxoplasma an CDV (SILINSKI et al., 2003) were documented. A unusual number of oral and cutaneous number of papillomavirus infection sometimes associated with malignant transformation (squamous cell carcinoma), have been documented in snow leopard (OTT JOSLIN et al., 2000).
Two distinct neurodegenerative disorders of unknown etiology were reported in juvenile snow leopards. One disease was found in three young cubs from the same litter from a French zoo and characterized by neuronal degeneration in the spinal cord. Symptoms were head and body tremor and swaying gait followed by paresis of the hind limbs. The second disorders was diagnosed in several litters in Finland, France, Switzerland and UK and characterized by bilateral symmetric Wallerian-type

degeneration in the spinal cord associated with depletion of Purkinje cells and gliosis in the cerebellum. The cause of this disorder is unknown, but feeding a diet with unsupplemented poultry has been implicated (HALTIA and WAHLBERG, 1984, ROBERT, 2008; STIDWORTHY et al., 2008).
Also noteworthy is the frequent development of veno-occlusive disease (VOD) in the liver in snow leopards in the European and North-American captive populations (VAN DEN INGH et al., 1981, MUNSON and WORLEY, 1991).
Among the disease with possible genetic background, several cases of coxofemoral dysplasia have been documented in captive born snow leopards (KÄRKKAÏNEN and WAHLBERG, 1984), as well as cases of multiple ocular colobomas, which are congenital malformations in which a portion of the structure of the eye is lacking (reviewed by BARNETT and LEWIS, 2002).

C. Black footed cats (*Felis nigripes*)

Black footed cats (*felis nigripes*), small, nocturnal, South-African cats, have a shorter life span in captivity then in the wild (2 to 5y versus 5-6y). A review of necropsy reports indicates that amyloidosis with resultant renal failure represents a main cause of mortality in the decreased of survival on captive black-footed cats. AA-type amyloid is mostly deposited in renal medullary interstitium, glomeruli, splenic follicular germinal centers, gastric and intestinal lamina propria. The amyloid deposition is not associated with concurrent inflammatory diseases and heritability analyses suggest a familial predisposition. Mild amyloidosis was also detected in a wild free-ranging cat. Elevated SAA or other precursors of amyloid were not measured in serum, whereas deposits of amyloid could be detected in biopsies of subcutaneous fat and submucosa of the colon, suggesting these techniques as helpful diagnostic tools (TERIO et al.,, 2008; ZIMMERMANN et al., 2008)

D. Lion: the “star gazing syndrome”

In the past numerous cases of ataxia associated with vitamin A deficiency have been reported in growing lions (also known as Chiari I-like malformation). A resurgence of the disease has been observed lately, as several cases were observed and reported in European, North-American and Middle- East zoos. The nervous clinical symptoms, including swaying, loss of balance, ataxia, tremor, head tilt, “star-gazing”, are caused by a thickening of the cranial bone, especially visible at the occiput and cerebellar tentorium, leading to crowding of the caudal cranial fossa and consecutive herniation of caudal cerebellar folia and cervical synringohydromelia. Generally low vitamin A was measured in serum and liver. The disease is presumed to be due to vitamin A deficiency causing metabolic bone lesions. The underlying skeletal abnormality involves defective remodeling of bone, presumably due to the stimulatory effect of vitamin A on osteoclastic activity (deficiency in vit A leads to inadequate resorption of endosteal bone and therefore increased bone mass). Consistent lesions can also be observed in the long bones. Improvement and resolution of the symptoms were achieved in young cubs through parenteral vitamin A supplementation. This therapy is probably only limited to young animal which are in a phase of rapid bone metabolism. Recently, successful surgical therapy in subadult lions using sub-occipital craniectomy was reported in the literature. Beside a single “unconvincing” report in a cheetah, this syndrome has never been reported in other felid species, and experimental hypovitaminosis A in domestic cats failed to reproduce the lesions, indicating a species predisposition for this disorder (reviewed by WENKER et al., 2008).

E. Mycobacterial diseases in felids

Although carnivores are not considered very susceptible to mycobacterial diseases, infections with the three main major groups of pathogenic mycobacteria have been documented (*M. tuberculosis* complex, *M. avium* complex and *Mycobacterium* spp. (atypical)). Cases of *M. tb*-complex have been documented in captive and free-ranging felids, mostly caused by *M. bovis*. The source of infection is

likely due to ingestion of infected prey species or contaminated carcasses. Pulmonary involvement in *M. bovis* infection has been the most consistently reported finding in captive (lion, tigers, leopard, snow leopards) and free-ranging felids (lions, cheetahs), causing multilobular, cavitating, pulmonary lesions. Hypertrophic pulmonary osteoarthropathy of bones of forelimbs was also noted in a Siberian tiger. Tuberculosis caused by *M. bovis* has been reported in many free-ranging wildlife populations in geographically and climatologically diverse parts of the world. Historically, Bovine TB appears to have been a domestic cattle disease and the native livestock is considered as the source of infection for free-ranging ruminants sharing pasture and habitats and in which infection persistently cycles. Free-ranging felids, and carnivores in general, infected with *M. bovis* appear to be spill-over hosts that have become incidentally infected by ingesting contaminated carcasses, but they cannot maintain the disease in their population without external source of infection (reviewed by BACKUS, 2008).
M. bovis infection has been diagnosed as cause of lung lesions in free-ranging Iberian lynx (*Lynx pardinus*) in south of Spain. This disease is of big concern for the Iberian lynx, which is a critically endangered species, as *M. bovis* is widespread in free-ranging deer in the south of Spain and lynx potentially scavenge on tuberculous carcasses (PEREZ et al., 2001; ARANAZ et al., 2004).
M. pinnipedii, another member of the *M. tb*-complex previously classified as *M. bovis*, was reported to have caused cavitating pulmonary lesions in several large cat species (snow leopards, Amur leopards, Amur leopards cats and Amur tigers) during an outbreak in a French Zoo which also affected southern sea lions. It has been suspected that the felids have been infected through indirect contamination from the sea lions by the production of infectious aerosols using the high pressure steam cleaning procedure routinely used for the sea lions' pool (GOMIS et al., 2008).
Antemortem diagnosis of tuberculosis might be difficult due to the lack of value of intradermal tuberculin skin test but newly developed ELISA, MAPIA and Rapid test (based on lateral flow technology) are promising.
Domestic cats are also susceptible to *M. microti*, another member of the *M. tb*-complex (GUNN-MORE, 1996). To date no case concerning large felids have been documented.
The *M. avium* complex (MAC) and atypical *Mycobacterium* spp. are saprophytic bacteria that are ubiquitous in the environment. Reports of MAC are limited to domestic cats and to date no reports on large felids have been published. MAC in cats causes generally cutaneous and subcutaneous masses, but an increasing number of disseminated mycobacteriosis are reported in the literature (BARAL et al., 2005). To note is the potential role of carnivores in the epidemiology of *M. avium* subsp. *paratuberculosis* (Map), the causative agent of paratuberculosis (Johne's disease) in cattle. A study done in an endemic paratuberculosis region in North-America, Map was isolated from the mesenteric lymph nodes and ileum of 28% of feral cats, although neither macroscopic nor microscopic lesions consistent with paratuberculosis were observed. While the role of the cat (and other non-ruminants carrier animals) in the epidemiology of the disease is still debated, one should be aware of the susceptibility of the felids for Map (PALMER et al., 2005).

F. Viral diseases / Prion in felids

a. Feline Parvoviruses (FPV)

The family *Parvoviridae* includes several antigenetically and genetically closely related viruses, such as feline panleukopenia virus (FPLV), canine parvovirus (CPV-2), mink enteritis virus (MEV), blue fox parvovirus (BFPV), raccoon parvovirus (RPV), raccoon dog parvovirus (RDPV), all grouped in the feline parvoviruses. Other strains include the Aleutian mink disease virus (ADV) and canine minute virus (MCV = CPV-1). The genus Parvovirus does not include a DNA polymerase, therefore the viruses can only replicate in the nucleus of dividing cells. In fetal and newborns, the virus can replicate in numerous organs, whereas in adults the lymphatic system and particularly the epithelium of the gut are main targets for parvovirus infection. Parvoviruses are very stable in the environment, therefore disinfection of contaminated premises or fomites is required in case of contamination (STEINEL et al., 2001).

Based on the numerous cases described, it is generally assumed that all members of the family *Felidae* are susceptible to feline panleukopenia virus (FPLV) infection. Domestic and large cats seem to be resistant to CPV-2, but they are also susceptible (especially the large cats) to the new antigenetic types CPV-2a and CPV-2b, as shown in cheetahs and a tiger with clinical parvovirosis (diarrhea, enteritis) (STEINEL et al., 2000).

b. Feline Herpes virus (FHV)

Infection with feline herpes virus (FHV) is widespread in all captive cheetah populations, but doesn't seem to cause serious problems in other large felids. Herpesvirus in cheetah is frequently associated with mild clinical signs including sneezing, watery eyes and conjunctitis especially in cubs. Mild signs are generally self-limiting. Occasionally neonatal cubs may die from acute infection (ie, pneumonia) or may develop severe and persistent lesions such as corneal scars, prolapsed 3rd eyelids, chronic epiphora, or eosinophilic, ulcerative dermatitis. All infected animals become chronic FHV carriers. Rarely, chronic carriers develop severe ulcerative dermatitis at sites of exposure to lacrimal and salivary secretions or persistent, non-resolvable ocular signs such as prolapsed 3rd eyelids or corneal scarring (MUNSON et al., 2004). Herpesvirus genom has been sequenced from one conjunctival swab; the gene sequence has >99% overlapping with Feline Herpesvirus-1 (Genebank entry).
Pallas'cats (*Otocolobus manul*) are also susceptible to FHV infection. Interestingly Pallas'cats are also very sensitive to infection with *Toxoplasma gondii* which causes disseminated necrotizing lesions in neonates and adult animals (KETZ-RILEY et al., 2003).

c. Coronavirus

Coronaviruses are enveloped RNA viruses owning a high mutation rate during replication. Serotypes of feline coronaviruses (FCoV) are defined by antigenicity, with most field strains classified as type I FCoV, and biotypes are defined by virulence. Enteric strains primarily target mature epithelia at intestinal villus tips, leading to diarrhea. More virulent strains infect monocytes and macrophages efficiently, and lead to a mostly fatal, immune-mediated disease producing vasculitis (feline infectious peritonitis FIP). No current assay can distinguish infection with virulent vs avirulent FCoV as the precise genetic basis for variation in virulence is still unknown. Moreover host factors such as defects in cell-mediated immunity, MHC expression, alteration in cytokine levels, and stressors have been postulated to play a role in the pathogenesis of FIP. The virus has a worldwide distribution, is relatively resistant in the environment and transmission is generally fecal-oral. Detection of infection involves serology for FCoV-specific antibodies (although seropositive animals may not be actively infected and shedding) and genetic detection of the virus in feces using PCR. Because virus shedding may be intermittent, several fecal samples over time are usually recommended for testing by PCR or (better) rtPCR. Chronic shedders (from persistently infected animals) are an important source of the virus for contact animals and may be a source for mutant viruses. Control should be aimed at removal of chronic shedders, quarantine and testing of new arrivals, and adequate disinfection of enclosures and fomites.
Enteritis associated with FCoV infection has resulted in mild to chronic diarrhea, weight loss, lethargy, and inappetence in several felid species, and should stay of concern due to risk of FIP development and the emerging threat of corona viral colitis.
Corona viral-induced colitis in cheetah may be an disease of concern and therefore enhanced attention should be given to possible FeCoV infection in case of diarrhea problems, beside infection with *Clostridium perfringens*, *Plesiomonas shigelloides*, and *Salmonella* sp. A survey in the cheetah SSP population indicates that FeCoV is widespread, even at sites with strict quarantine measures and best practices, and the virus has also been detected in free-ranging animals, therefore a pathogen-free population is probably not feasible (Kennedy 2005, 2006). Although rare, outbreaks of FIP have been reported in several nondomestic species, most cases involving cheetahs and European wild cats, and a single report in servals (KENNEDY, 2005; KENNEDY et al., 2006)
A further coronavirus affecting felids is the strain causing the severe acute respiratory syndrome (SARS), which has emerged in the human population in 2002, causing numerous clinical diseases and

death (mainly in Asia). Numerous studies have shown that cats, ferrets and palm civets are susceptible to SARS-CoV infection and that they were able to transmit the virus (VAN DER BRAND et al., 2008; XIAO et al., 2008). Pathological lesions in cats are trachea-bronchoadenitis and diffuse alveolar damage, similar to those described in humans.

d. Feline Calicivirus (FCV)

Feline Calicivirus (FCV) is a RNA virus with a genom plasticity allowing to respond rapidly to environmental pressures. FCV in domestic cats is associated with a range of clinical syndromes from inapparent infections to relatively mild oral and upper respiratory tract disease with or without acute synovitis. Recently, highly virulent forms of the virus have emerged, associated with a systemic infection that is frequently fatal (subcutaneous edema, ulcerations of the mouth, and of the skin (ear pinneae, pawpads), broncho-interstitial pneumonia, necrosis in the liver or pancreas) (RADFORD et al., 2007).
Transient mild calicivirus infections with a new calicivirus strain have been observed in large felids but are rarely reported in the literature. In 1992 a group of African lions and Siberian tigers in a zoo in Japan developed characteristic clinical symptoms of acute vesicular formations in tongue and snout (KADOI et al., 1997).
A novel calicivirus, related to human noroviruses (NoVs) of genogroup IV, was isolated in a lion cub that died of severe hemorrhagic enteritis. Bacterial co-infections were also detected and likely enhanced the severity of the enteritis. NoVs are now regarded as the major cause of epidemic, non-bacterial gastroenteritis in humans (MARTELLA et al., 2007). Caliciviruses have also been isolated in from faeces of dogs with diarrhea.

e. Canine Distemper Virus (CDV)

Large cats have been kept in captivity for centuries in fairly close contacts to canids or other susceptible species, yet canine distemper (CD) in felids have been reported only sporadically and only rarely as large-scale epidemics. Felids are thought to be fairly resistant to CDV, as demonstrated by experimental infection of domestic cats which produced only subclinical diseases. It is assumed that predisposing factors such as concurrent illness, stress or immune suppression are important co-factors. CD related death have been reported in lions, tigers, leopards, jaguars and snow leopards. Disease included gastrointestinal, respiratory and/or CNS symptoms. Co-factors have been demonstrated in several cases (panleukopenia, stress with concurrent infection with *Toxoplasma*, FIV). During a 1992 CD epidemic in North-America, among 74 large felids, fatal infection was confirmed only in members if the genus *Panthera*, whereas mountain lions (*Felis concolor*) demonstrated only mild gastrointestinal or respiratory signs, suggesting variable species susceptiblity among nondomesticated felids. To the author´s knowledge, CD has never been reported in cheetahs, although serologic analyses have shown wide spread exposure in captive and free-ranging cheetahs. Immunohistochemical investigations in a retrospective study in Switzerland showed however that CDV in large cats might be more widespread than generally assumed (APPEL et al., 1994; MYERS et al., 1997; DEEM et al., 2000; SILINSKI et al., 2003).
In 1994 a CDV epidemic in Serengeti lions (*Panthera leo*) was reported to have caused the death of 30% of the population. The source of epidemic was thought to be the domestic dogs of the local villages adjacent to the park. A serological survey failed to determine another virus (FIV, FeCoV, FePV, FeHV, FeCV) as cofactor for the epidemic (ROELKE-PARKER et al., 1996). A second high-mortality CDV epidemic struck the nearby Ngorongoro Crater lion population in 2001. Serological analyses indicated that at least five “silent” CDV epidemics swept through the same two lion populations between 1976 and 2006 without clinical signs or measurable mortality, indicating that CDV was not necessarily fatal. Subsequent clinical and pathology investigations suggested that hemoparasitism was a major contributing factor during fatal epidemics. A significantly higher levels of *Babesia* during the 1994 and 2001 epidemics was demonstrated using quantitative real-time PCR. Extreme drought conditions with wide-spread herbivore die-offs were preceding the lion CDV

epidemics. After the resumption of rains, the starving buffaloes were heavily infested with ticks, exposing the lions to unusually high numbers of *Babesia*. These mortalities exemplifies the immunosuppressive effects of CDV coupled with a co-factor (here the hemoparasites) associated with environmental and climatic changes (MUNSON et al., 2008).

f. Retroviridae

Feline leukemia virus (FeLV) in subfamily *Oncovirinae* and feline immunodeficiency virus (FIV) in subfamily *Lentivirinae* causes significant diseases in domestic cats. Only rare clinical cases have been reported large felids, but these viruses are of concerns in captive felid collection, primarily because seropositivity limits the movements of animals between breeding facilities. Like FeLV, FIV does not remain infectious for long outside its host and is readily inactivated with common desinfectants.
In the majority of cats, FeLV causes a self limiting infection but persistent infection remains in some 30% of infected cats. Some of them will not shed viruses whereas others may develop clinical disease and become infectious (through saliva, excretions…). FeLV causes cytoproliferative (leukemia, lymphoma) but also cytosupressive diseases (anemia, leucopenia) (PATEL and HELDENS, 2009). Reports on clinical FeLV infection in nondomestic felids are scattered and FeLV does not appear to be endemic in both captive and free ranging felids, except in European wildcats. Introduction of FeLV in free ranging felid populations could have devastating effects (KENNEDY-STOSKOPF, 1999), as suggested in the critically endangered Iberian lynx population, in which the strain presumably introduced by domestic cats invading the lynx's habitats, showed to be highly virulent for the lynx (MELI et al., 2009). One Namibian cheetah infected with FeLV developed viral-associated lymphoma. This animal presumably acquired the virus from an infected cheetah in the adjacent enclosure (MUNSON, 2005). FeLV was diagnosed in a captive bobcat (*Felis rufus*) presented with lethargy, leucopenia, neutropenia, lymphopenia and non-regenerative anemia and which died of encephalitis, interstitial pneumonia, hepatitis and peritonitis (SLEEMAN et al., 2001). The domestic cat is the reservoir for FeLV, and large cats, particularly in zoological settings, do not appear to be at high risk for becoming infected because intimate contact with domestic cats is rare. Both ELISA and IFA should be used for detection of FeLV antigen in peripheral circulation (however keeping in the mind the risk of false-positive in ELISA and false-negative in IFA). Detection of antibodies to FeLV is additional evidence of virus exposure, which is helpful for interpretation of conflicting or inconsistent FeLV antigen tests. The issue for AG-negative and AB-positive cats being latently infected and subject to periodic reactivation with virus shedding is problematic (KENNEDY-STOSKOPF, 1999).

FIV is found worldwide in domestic cats and has been confirmed to be endemic in free-ranging populations of nine felid species (Africa: lion, leopard, cheetah. Asia: Pallas' cat, leopard cat. South-Africa: puma, jaguar, ocelot, margay, Geoffroy's cat, tigrina). Seroprevalence is very high in certain free-ranging lions and mountain lions without overt clinical diseases, raising the question about pathogeneticity of the virus and host adaptation. Seroprevalence appears to be low in cheetahs and leopards, except in certain areas, maybe related to the solitary nature of these species. Species-specific strains of FIV have been described for domestic cats (*Felis catus*), puma (*Puma concolor*), lion (*Panthera leo*), leopard (*Panthera pardus*) and Pallas' cats (*Otocolobus manul*). There is strong evidence that that FIV evolves in different ways within each species, therefore clinical effects of species specific FIV infection other than domestic cats are controversial.
Presence of FIV antibodies correlates with persistent infection and the ability to transmit the virus. For diagnostic screening in nondomestic species, ELISA and IFA test should be confirmed by an immunoblot (Western blot) assay. For nondomestic felid species, the test should however not only contain domestic cat antigen, as the *env* protein are very variable and wild felids might not have cross-reacting antibodies. FIV infection in cats results in AIDS-like pathology typified by a period of latency, followed by CD4 depletion, immune suppression, subsequent secondary infection. Clinical signs of FIV infection in domestic cats are vague and nonspecific and the situation in nondomestic felids is similar.

Periodic behavior changes and neurologic deterioration, retinopathies, leukemia, tumor have been reported in captive FIV positive lions (KENNEDY-STOSKOPF, 1999; TROYER et al., 2005, 2008).

g. Avian Influenza

Highly pathogenic avian influenza H5N1 virus has jumped to domestic cats and wild felids and natural H5N1 infection was the cause of fatal disease in domestic cats and other large felids such as tigers and leopards in Thailand (KEAWCHAROEN et al., 2004; KUIKEN et al., 2006).

h. Astrovirus

Astroviruses are small, non-enveloped RNA viruses which have been recently discovered (1975) as cause of gastroenteritis (diarrhea) in human, mainly in children. The *Astroviridae* are divided in *Avastrovirus*, found in avian hosts, and *Mamastrovirus*, found in mammals. In carnivores, astrovirus associated enteritis has been described in mink (*Mustela lutreola*) and domestic cats. Recently, a *mamastrovirus* has been identified in an outbreak in a North-American cheetah group. The virus has been identified by electron microscopic investigation and PCR in fecal samples of young and adult cheetahs with lethargy, anorexia, watery diarrhea, and regurgitation. All affected cheetahs were treated with bismuth subsalicylate tablets (524mg PO BID for 5 days) and recovered without additional intervention (ATKINS et al., 2009).

i. Feline Papillomavirus (PV)

Viral papillomas has been documented in several felid species. Oral, PV-induced, proliferative lesions have been seen in domestic cats, Asiatic lions, snow leopards, Florida panthers, bobcats, and clouded leopards. Both oral and cutaneous lesions with malignant transformation have been reported only on domestic cats and snow leopards (OTT JOSLIN et al., 2000; SUNDBERG et al., 2000).

j. Poxvirus

Numerous cases of Orthopoxvirus infection have been reported in domestic cats throughout Europe (mostly UK). Outbreaks of the disease considered to be due to cowpox has been reported in a number of species of zoo animals in Moskow zoo in the seventies, affecting several species of *felidae* (MARENNIKOVA et al., 1977). Interestingly the bears and the hyena which were kept in the same building didn't develop the disease. In 1977 a serious outbreak occurred among cheetahs in an UK zoo, causing ulcerating and crusted skin lesions in two cheetahs and a fatal hemorrhagic pneumonia in a third case, and another outbreak killed two out of three cheetahs in another zoo in 1978 (BAXBY et al., 1982). Cowpox virus is believed to circulate in small wild mammals (rodents).
Recently a cowpox outbreak was reported in a German zoo causing the death or euthanasia of 13 banded mongooses (*Mungos mungo*). Most animals showed disseminated nodular skin lesions, especially on the head. Subsequently, a female and a male jaguarundis (*Herpailurus yaguaroundi*) also showed disseminated circular, ulcerated skin and oral lesions and lethargy. The male died within 10 days despite antibiotic treatment. Subsequently all carnivores of the zoo were vaccinated with a human Orthopoxvirus vaccine. A retrospective serological survey showed positive titers years before the outbreak, suggesting the virus had been circulating in the zoo without causing clinical problems (STRAUBE et al., 2008).

k. Blue tongue virus (BTV)

The bluetongue virus (*Orbiviridae*) is an insect transmitted virus (by *Culicoides* sp.) which infects wild and domestic ruminants, mainly sheep, mostly in tropical and subtropical countries. BTV-8 was first

introduced to northern Europe in 2006 and has since then spread rapidly throughout the continent. In 2007, two lynx from a Belgian zoo were reported to have died of Bluetongue infection after having been fed ruminant fetuses and stillborns. Reported clinical signs were limited to lethargy. Necropsy revealed anemia, petechial hemorrhages, pulmonary congestion and edema, and pneumonia in 1 case. Microscopic examination showed edematous vascular walls, enlarged endothelial cells and evidence of vasculitis in various tissues. BTV-8 Infection was confirmed by rtPCR, virus isolation (case 1) and presence of anti-BTV antibodies in lung tissue fluid (case 2). Oral infection is strongly suspected in these cases (JAUNIAUX et al., 2008). The natural hosts of BTV are ruminants although death has been documented in dogs accidentally infected with a BTV-contaminated vaccine. Futhermore seroconversion without causing clinical diseases has been documented in African carnivores presumably infected by ingestion of meat or organs from BTV-infected prey species (ALEXANDER, 1994).

I. FSE

Feline spongiform encephalopathy (FSE) affecting domestic and captive feline species is a prion disease considered to be related to bovine spongiform encephalopathy (BSE). FSE has been reported in several non-domestic cat species, including cheetah, puma, ocelot, tiger, lion and cougar, but the relatively high incidence in cheetahs suggests that they may be more susceptible than other zoo felids. To date 9 cases of FSE have been diagnosed in cheetahs. All affected cheetahs were older than 5 yr, and with the exception of 2 cheetahs born in France, all were born in the U.K. Clinically, chronic progressive ataxia initially involving the hind limbs but later the forelimbs was consistently seen. Further clinical signs appear with variable frequency and include postural difficulties, hypermetria, muscle tremors (particularly affecting the head), changes in behavior (aggressiveness / anxiety), hyperesthesia, ptyalism and blindness. The diagnosis of FSE requires histopathological examination of the brain and the finding of characteristic vacuolation in the neuropil and neurons. It is broadly accepted that FSE is the result of BSE infection in felids and the incubation period appears to be 4 to 8 years in cheetah (ROBERT, 2008).

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