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Keywords: *Acinonyx jubatus*/captive breeding/captive cheetahs/cheetah/CNS and non-CNS diseases/EEP/extrinsic factors/SSP

Abstract: Captive cheetahs (*Acinonyx jubatus*) worldwide suffer from a number of health problems rarely observed in free-ranging ones, and unusual in other species, especially felids. These include diseases of the central nervous system (CNS) as well as non-CNS diseases. Among the neurological diseases, the encephalomyelopathy represents a serious threat to the European Endangered Species Plan (EEP) cheetah population, whereas the leucoencephalopathy affects only the Species Survival Plan (SSP) North-American population. Both are degenerative disorders of the CNS white matter, affecting the spinal cord or the cerebellum, respectively. Furthermore, several cases of feline spongiforme encephalopathy (FSE), a disease caused by a prion and considered to be related to the bovine spongiforme encephalopathy (BSE), have been diagnosed in captive cheetahs. Most of the FSE-affected cheetahs were born in the United Kingdom (UK) and probably were fed with infected bovine carcasses. Among the non-CNS diseases, lymphoplasmacytic gastritis associated with *Helicobacter* spp. is prevalent in captive cheetahs worldwide (Europe, North-America, South-Africa, Japan). Mild gastritis has also been diagnosed in free-ranging cheetahs. Another important disease in the captive cheetah population is glomerulosclerosis. Systemic AA amyloidosis affecting the kidneys, liver and other organs is also frequently diagnosed in all captive populations. There is a high correlation between amyloidosis and chronic gastritis and glomerulosclerosis. Oxalate nephrosis and pyelonephritis are other frequently diagnosed renal diseases. Veno-occlusive disease of the liver resulting in progressive liver failure is a frequent disease in the North-American population but not in the European and South-African populations. Myelolipoma are common lesions seen in the spleen, sometimes also in the liver, but are however clinically not relevant. Among the infectious diseases, the clinical feline herpes virus (FHV) infection is widespread in captive cheetahs and frequently causes conjunctivitis, rhinitis and chronic facial dermatitis. Feline infectious peritonitis (FIP-caused by feline coronavirus [FCoV]) has been reported in cheetahs, but colitis caused by feline enteric corona virus (FECV) may deserve increased attention. Among parasites, in captive populations, massive infestation with *Ascarid* sp. is a common problem despite regular deworming. Pneumonia by lungworms (*Aelurostrongylus abstrusus*) has been reported. The primary cause of these unusual diseases is mostly unidentified and the reason for their high prevalence in captive cheetahs is unknown, but the low level of these disorders in free-ranging cheetahs suggests extrinsic causes as predisposing factors (Munson, 2005).

Notes: Incl. Spanish abstract

You can't do anything
about the length of
your life, but you can
do something about
its width and depth.

Henry Louis Mencken
(1880-1956)

Pathological disorders in captive cheetahs

Patologías de guepardos en cautividad

NADIA ROBERT AND CHRIS WALZER

RESUMEN

En todo el mundo, los guepardos (*Acinonyx jubatus*) en cautividad padecen varios problemas sanitarios que rara vez afectan a guepardos en libertad y son poco comunes en otras especies, sobre todo en los felinos. Entre estos problemas se incluyen las enfermedades del sistema nervioso central (SNC) y otras enfermedades que no afectan al SNC.

Entre las enfermedades neurológicas, la encefalomielopatía representa una seria amenaza para la población cautiva europea del European Endangered Species Plan (EEP), mientras que la leucoencefalopatía sólo afecta a la población cautiva norteamericana del Species Survival Plan (SSP). Ambas enfermedades son trastornos degenerativos de la sustancia blanca del sistema nervioso central (SNC) que afectan a la médula espinal o al cerebro, respectivamente. Además, en guepardos en cautividad han sido diagnosticados varios casos de encefalopatía espongiiforme felina (EEF), enfermedad causada por priones y que se considera relacionada con la encefalopatía espongiiforme bovina (EEB). La mayoría de los guepardos afectados por la EEF nacieron en el Reino Unido y probablemente fueron alimentados con carne bovina infectada.

Entre las enfermedades que no afectan al SNC, la gastritis linfoplasmocítica asociada a *Helicobacter* spp. es prevalente en guepardos cautivos en todo el mundo (Europa, Norteamérica, Sudamérica y Japón); la gastritis leve también ha sido diagnosticada en guepardos de vida libre. Otra enfermedad importante en la población cautiva de guepardos es la glomeruloesclerosis. La amiloidosis sistémica de proteína amiloide AA con afección al riñón, al hígado y a otros órganos también aparece con frecuencia en todas las poblaciones cautivas, y existe una alta correlación entre esta enfermedad, la gastritis crónica y la glomeruloesclerosis. Otras enfermedades renales diagnosticadas con frecuencia son la nefropatía por oxalatos y la pielonefritis. La enfermedad venooclusiva hepática (VOD), que causa una insuficiencia hepática, es frecuente en la población del SSP, pero no así en las poblaciones del EEP o en África austral. Sin embargo, el mielolipoma, siendo una de las lesiones más comunes que se observan en el bazo y, en ocasiones, también en el hígado, no es clínicamente relevante.

Entre las enfermedades infecciosas, el herpesvirus felino (FHV) está ampliamente extendido en la población cautiva y, a menudo, causa conjuntivitis,

rinitis y dermatitis facial crónica. Aunque se han descrito casos de peritonitis infecciosa felina (FIP, causada por FCoV), también hay cuadros de colitis causada por coronavirus entéricos felinos (FECV), que necesitan una mejor y mayor atención epidemiológica. Entre los parásitos, la infestación masiva de *Ascaris* sp. es un problema común en la población cautiva, a pesar de llevar a cabo una desparasitación regular, y también han sido descritas neumonías por *Aelurostrongylus abstrusus*.

En la mayoría de los casos, la causa primaria de estas enfermedades atípicas, pero con una alta prevalencia en la población cautiva, no ha sido identificada. No obstante, la baja incidencia de estas enfermedades en los guepardos de vida libre sugiere que existen causas extrínsecas que actúan como factores que predisponen a ellas. (Munson, 2005).

PALABRAS CLAVE

Guepardos en cautividad, enfermedades del SNC, enfermedades que no afectan al SNC, EEP, SPP

ABSTRACT

Captive cheetahs (*Acinonyx jubatus*) worldwide suffer from a number of health problems rarely observed in free-ranging ones, and unusual in other species, especially felids. These include diseases of the central nervous system (CNS) as well as non-CNS diseases. Among the neurological diseases, the encephalomyelopathy represents a serious threat to the European Endangered Species Plan (EEP) cheetah population, whereas the leucoencephalopathy affects only the Species Survival Plan (SSP) North-American population. Both are degenerative disorders of the CNS white matter, affecting the spinal cord or the cerebellum, respectively. Furthermore, several cases of feline spongiform encephalopathy (FSE), a disease caused by a prion and considered to be related to the bovine spongiform encephalopathy (BSE), have been diagnosed in captive cheetahs. Most of the FSE-affected cheetahs were born in the United Kingdom (UK) and probably were fed with infected bovine carcasses.

Among the non-CNS diseases, lymphoplasmacytic gastritis associated with *Helicobacter* spp. is prevalent in captive cheetahs worldwide (Europe, North-America, South-Africa, Japan). Mild gastritis has also been diagnosed in free-ranging cheetahs. Another important disease in the captive cheetah population is glomerulosclerosis. Systemic AA amyloidosis affecting the kidneys, liver and other organs is also frequently diagnosed in all captive populations. There is a high correlation between amyloidosis and chronic gastritis and glomerulosclerosis. Oxalate nephrosis and pyelonephritis are other frequently diagnosed renal diseases. Venous-occlusive disease of the liver resulting in progressive liver failure is a frequent disease in the North-American population but not in the European and South-African populations. Myelolipoma are common lesions seen in the spleen, sometimes also in the liver, but are however clinically not relevant. Among the infectious diseases, the clinical feline herpes virus (FHV) infection is widespread in captive cheetahs and frequently causes conjunctivitis, rhinitis and chronic facial dermatitis. Feline infectious peritonitis (FIP)-caused by feline coronavirus [FCoV] has been reported in cheetahs, but colitis caused by feline enteric corona virus (FECV) may deserve increased attention. Among parasites, in captive populations, massive infestation with *Ascarid* sp. is a common problem despite regular deworming. Pneumonia by lungworms (*Aelurostrongylus abstrusus*) has been reported.

The primary cause of these unusual diseases is mostly unidentified and the reason for their high prevalence in captive cheetahs is unknown, but the low level of these disorders in free-ranging cheetahs suggests extrinsic causes as predisposing factors (Munson, 2005).

KEYWORDS

Captive cheetahs, CNS and non-CNS diseases, extrinsic factors, EEP, SSP

Pathological disorders in captive cheetahs

NADIA ROBERT AND CHRIS WALZER

INTRODUCTION

In 2004 the cheetah EEP population included 345 cheetahs within 75 institutions. Two hundred and seventy cheetahs in Europe originated from Southern Africa (Republic of South Africa [RSA] and Namibia). Seventy five captive cheetahs held in the United Arab Emirates, were originally from Northern Africa (Chad, Sudan, Ethiopia and Somalia). The European Cheetah Disease Working Group was established in 2002. The main goals of the group were: a) to centralize data management; b) to standardize disease description; c) to carry out comparative disease description and prevalence – USA/RSA; d) to conduct research on cheetah ataxia and encephalomyelopathy, and e) to comply with the Global Cheetah Conservation Plan. As of December 2004 the necroscopy database included 136 cheetahs from which we have samples. The material comes from 26 different institutions in 10 countries. An EEP Cheetah Necropsy Protocol has been established and sent to all EEP cheetah institutions. In this chapter we present information regarding diseases affecting the captive cheetah population. We will first discuss diseases affecting the Central Nervous System (CNS), followed by information regarding the incidence of non-CNS diseases. For general information regarding diseases in captive and free-ranging felids, see also Terio, this book.

CENTRAL NERVOUS SYSTEM (CNS) DISORDERS IN CHEETAHS

CHEETAH ENCEPHALOMYELOPATHY

The cheetah encephalomyelopathy, a neurological disease characterized by degenerative lesions of the spinal cord and cerebellum that cause ataxia and paresis, has emerged in the past 20 years in the EEP cheetah population. The disease accounts for 25% of all deaths 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. The course of the disease is variable, from rapid onset of ataxia to a slower progressive development with stabilization and acute relapsing episodes (Figure 1). Pathologically, the disease is characterized by bilateral symmetrical degeneration of the white matter of the spinal cord (Figure 2), with loss of myelin exceeding axonal

Photo: N. Robert



FIGURE 1. ENCEPHALOMYELOPATHY: TYPICAL STANDING POSITION OF AN ATAXIC CHEETAH WITH ABDUCTED HIND LEGS AND REDUCED SUPPORT OF THE TAIL.

FIGURA 1. ENCEFALOMIELOPATÍA: POSTURA TÍPICA DE UN GUEPARDO CON ATAXIA, CON LAS PATAS TRASERAS SEPARADAS Y EL RABO MÁS DÉBIL.

Photo: N. Robert



FIGURE 2. CUT SECTION THROUGH THE SPINAL CORD IN A CHEETAH WITH ENCEPHALOPATHY SHOWING BILATERAL SYMMETRIC, PERIPHERAL, WHITISH DISCOLORATION CORRESPONDING TO THE FOCI OF WHITE MATTER DEGENERATION.

FIGURA 2. CORTE TRANSVERSAL DE LA ESPINA DORSAL DE UN GUEPARDO MOSTRANDO UNA DECOLORACIÓN BILATERAL SIMÉTRICA Y PERIFÉRICA, QUE CORRESPONDE A LOS FOCI DE LA DEGENERACIÓN DE LA SUSTANCIA BLANCA.

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 causes of this cheetah disorder have been based on known causes of encephalomyelopathy in human and domestic animals that are characterized by white matter demyelination. Several causes have been considered, including genetic, environmental, toxic, nutritional (especially copper [Cu]) and viral factors. The pattern of incidence does not indicate a major genetic basis for this disease, however, a genetic component leading to general disease predisposition and response cannot be ruled out, and multifactorial inheritance might also 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/or vaccination regimen has been identified to date (Walzer 1995, 2003; Palmer 2001; Robert, 2008).

CHEETAH LEUCOENCEPHALOPATHY

Leucoencephalopathy is a serious degenerative disease affecting SSP cheetahs and has never been observed in the EEP 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 70 animals have been affected to date in about 30 different facilities. Most affected animals are at least 10-year old. The pathological lesions are restricted to the cerebral cortex and characterized by loss of white matter with associated bizarre astrogliosis. The cause is unknown, but epidemiological features suggest exposure to an exogenous agent through diet or medical management (Munson 1999b).

FELINE SPONGIFORM ENCEPHALOPATHY

Feline spongiform encephalopathy (FSE), affecting domestic cats and captive non-domestic felids, is a prion disease considered to be related to bovine spongiform encephalopathy (BSE). FSE has been reported in cheetahs, pumas, ocelots, tigers, lions and cougars, but the relatively high incidence in captive cheetahs suggests that they may be more susceptible than other captive felids. To date nine cases of FSE have been diagnosed in cheetahs. All affected cheetahs were older than five years of age, and with the exception of two cheetahs born in France, all were born in the UK. Clinically, chronic progressive ataxia initially involving the hind limbs but later the forelimbs as well was consistently seen. Further clinical signs appear with variable

Photo: N. Robert

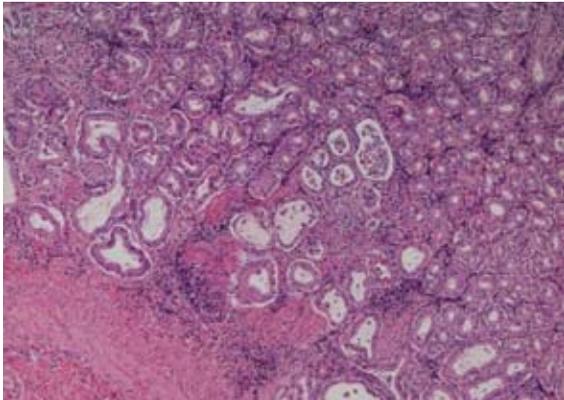


FIGURE 4. HISTOLOGICAL SECTION OF A STOMACH WITH GASTRITIS CHARACTERIZED BY MARKED LYMPHOPLASMACYTIC INFILTRATION (H&E STAIN).

FIGURA 4. CORTE HISTOLÓGICO DE UN ESTÓMAGO CON GASTRITIS CARACTERIZADA POR UNA MARCADA INFILTRACIÓN LINFOPLASMÁTICA (TINTURA H-E).

Photo: N. Robert

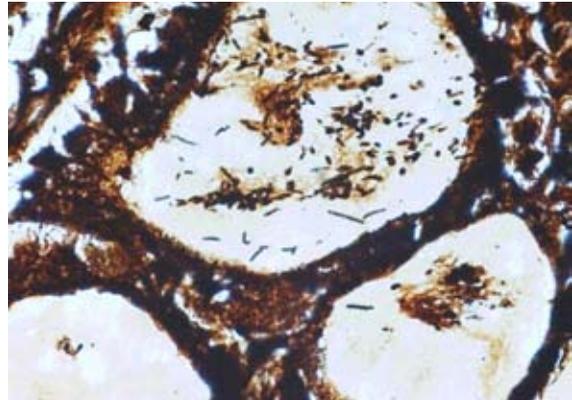


FIGURE 5. HISTOLOGICAL SECTION OF A STOMACH WITH GASTRITIS SHOWING DILATED GASTRIC GLANDS CONTAINING ARGYROPHILIC SPIRAL-SHAPED BACTERIA (SILVER STAIN).

FIGURA 5. CORTE HISTOLÓGICO DE UN ESTÓMAGO CON GASTRITIS. SE OBSERVAN DILATADAS LAS GLÁNDULAS GÁSTRICAS QUE CONTIENEN BACTERIAS ARGIRÓFILAS DE FORMA ESPIRAL (TINTURA DE PLATA).

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, probably from the ingestion of infected bovine carcasses, and the incubation period appears to be 4.5-8 years in cheetahs (Robert, 2008).

NON-CNS DISEASES IN CHEETAHS

GASTRITIS

Lymphoplasmacytic gastritis associated with *Helicobacter* spp. causes significant morbidity and mortality in captive cheetahs worldwide (Europe, North-America, South-Africa, Japan). Despite abundant spiral bacteria colonization, free-ranging cheetahs have been shown to develop only mild gastritis in few cases, suggesting that a direct cause-effect is unlikely. 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. Spiral bacteria consistent with *Helicobacter* spp. were detected in most cases (Figure 3), but there was 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 (Munson, 1993, 1999a; Terio et al., 2005; Walzer, 2006).

AMYLOIDOSIS

Systemic protein AA amyloid deposition in liver, kidney and other organs (adrenals, thyroid, gastrointestinal tract) is a common finding in all captive populations worldwide. Mild to marked amyloid deposition was recorded in 17 cases (48% of EEP cheetahs older than 1 year of age) mostly in kidneys and liver (Figure 4). In three cases amyloid was also seen in the adrenals, thyroid and/or spleen. In 16 cases amyloidosis was associated with glomerulosclerosis/nephrosclerosis and in 13 cases with gastritis (Munson, 1993, 1999a; Walzer, 2006).

GLOMERULOSCLEROSIS AND OTHER RENAL DISEASES

The most prevalent renal disease was glomerulosclerosis, affecting 80% of the cheetahs older than one year of age. The disease was severe in about 40% of the animals older than six years, making it one of the main cause of mortality in adult cheetahs. Glomerulosclerosis is characterized by progressive thickening of the glomerular basement membrane that leads to glomerular ischemia and sclerosis (Figure 5). The lesion resembles that



FIGURE 6. SPLEEN WITH MULTIPLE MYELOLIPOMAS.

FIGURA 6. BAZO CON MIELOLIPOMAS MÚLTIPLES.

Photo: C. Walzer

of diabetic nephropathy and is often accompanied by some degree of interstitial fibrosis and nephritis, glomerulonephritis and calcifications. Other renal pathological findings were pyelonephritis and/or papillary necrosis, presence of crystals in the tubular lumen (oxalate crystals), and amyloidosis (Munson, 1993, 1999a; Walzer, 2006).

LESIONS OF THE SPLEEN

Multiple splenic myelolipomas were present in 39 cheetahs (54% of the examined spleens) (Figure 6). The youngest cheetah affected was one year 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. More than 50% of the cheetahs had lymphoid depletion (Walzer, 1996).

LESIONS IN THE LIVER

Veno-occlusive disease (VOD) is caused by fibrous occlusion of the efferent blood supply of the liver (central and sublobular veins), resulting in progressive liver failure and ascites. The cause is not known. Whereas the prevalence in the SSP population is high (63%), no VOD could be observed in the 76 liver samples examined (animals older than one year) in the EEP. Only mild increase of collagen fibers and reticulin fibers were observed around the central veins and in the sinusoids (Munson, 1993, 1999a; Walzer, 2006).

INFECTIOUS DISEASES

VIRAL DISEASES

- Feline coronavirus (FCoV): As reported in the cheetah SSP population, feline infectious peritonitis (FIP) seems to be a rare problem in captive populations despite frequent exposure to FCoV. In the EEP population, only two cheetahs with granulomatous lesions consistent with FIP were recorded. The viral etiology of these cases still need to be confirmed by molecular techniques. However, feline enteric corona virus FECV induced colitis may be an emerging disease of concern and therefore enhanced attention should be given to possible FeCoV infection in case of diarrhea problems (see also Terio, this book).
- Feline herpesvirus: Infection with feline herpes virus (FHV) is widespread in all captive populations. Occasionally neonatal cubs may die from acute infection (i.e., pneumonia) or may develop severe and persistent lesions such as corneal scars, prolapsed third eyelids, chronic epiphora or 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 third eyelids or corneal scarring. In the EEP population, two adult cheetahs (six and seven years of age) were reported to have chronic conjunctivitis with typical histological lesions associated with intranuclear inclusion bodies. The herpesvirus genom has been sequenced from one conjunctival swab; the gene sequence has >99% overlapping with FHV-1 (Genebank entry).

- Parvovirus: Chronic diarrhea and mild necrotizing enteritis have been associated with canine parvovirus (CPV) and feline parvovirus (FPV, that caused feline panleukopenia) virus in cheetahs. In the EEP population two cases of feline panleukopenia were observed in a seven week-old cub and in a one year-old animal (Walzer, 2006).

BACTERIAL DISEASES

Only occasional bacterial infections have been reported as major cause of disease or as cause of death in the EEP population:

- One bronchopneumonia by *Pasteurella* sp. infection in a one year-old animal.
- *Clostridium perfringens* was isolated from colon content in animals. In one case a perforating enterocolitis was caused by *C. perfringens* type A.
- *Campylobacter* spp. and *Salmonella* spp. are regularly isolated in cases of diarrhoea in cubs and also in adult cheetahs. Some of the cases are food associated.
- Two institutions had reported deaths related to *Hemobartonella felis* infection (now *Mycoplasma haemofelis*) (Walzer, 2006).

Photo: N. Robert



FIGURE 7. STUNTED AND CACHECTIC CUB WITH “PEAUGRES-SYNDROME”, PRESENTING DIFFUSE ALOPECIA AND SEBORRHEA.

FIGURA 7. CACHORRO POCO DESARROLLADO Y CAQUÉCTICO CON “SÍNDROME DE PEAUGRES”, QUE PRESENTA ALOPECIA DIFUSA Y SEBORREA.

PARASITIC INFECTIONS

- Massive infestation with *Ascarid* worms (*Toxascaris leonina*, *Toxocara* sp.) is a frequent problem in young and adult captive cheetahs despite regular deworming (up to six times a year in some institutions).
- Lungworms (*Aelurostrongylus abstrusus*) are frequently detected in feces. Two adult cheetahs showed severe parasitic pneumonia at post-mortem (Walzer, 2006).

GENETIC DISEASES. THE “PEAUGRES-SYNDROME”

This “syndrome” might be one of the first “true” genetic diseases in cheetahs. Twenty seven cubs born in five litters from two normal dams which were sisters (*Fanny* and *Rina*) and one unrelated normal male (*Fota*). Twenty six cubs died between one and 134 days-old. The cubs were more or less affected and presented with various pathological lesions including poor hair coat, heart malformations (aortic aneurysma and heart hypertrophy), liver fibrosis, stunted growth, osteoporosis and encephalitis (Figure 7). 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 the copper transport proteins (Walzer, 2006).

CONCLUSION

- Myelopathy accounts for 25% of all deaths, including young and adult animals, and represents a limiting factor in the cheetah population growth within the EEP.
- Gastritis, glomerulosclerosis and amyloidosis are the most important non-CNS diseases.
- Most adult cheetahs in captivity are dying from a combination of gastritis and kidney disease, often with additional amyloidosis. It is therefore difficult to estimate the true prevalence of gastritis, renal failure or amyloidosis as main cause of death.
- VOD has not been observed in the EEP population, but is present in the SSP and the South African captive populations. Only mild centrilobular liver fibrosis is often recorded in the EEP cheetahs, but this is considered to be an incidental finding.
- Myelolipomas are common lesions seen in the spleen, sometimes also in the liver, but are not clinically relevant.

- While infectious diseases mostly cause mild clinical signs, they do not appear to be “major” causes of disease or death in the cheetah captive populations. FHV frequently causes transient sneezing and conjunctivitis in cubs. Rarely, chronic FHV-carriers may develop severe ulcerative dermatitis or conjunctivitis. FIP has rarely been reported in captive animals; however, attention should be given to FECV as a potentially emerging disease. Despite regular and frequent deworming, captive cheetahs tend to have significant *Ascarid* sp. infestation.
- Cheetahs in captivity frequently suffer of a number of diseases which are unusual in other animal species, especially in felids, and the reason for this high prevalence is still unknown, but the low level of these disorders in wild cheetahs suggest extrinsic causes, associated with the captive environment, as potential predisposing factors.

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