Feline herpesvirus infection in a group of semi-captive cheetahs

M van Vuuren\textsuperscript{a}, T Goosen\textsuperscript{a} and P Rogers\textsuperscript{b}

ABSTRACT
Clinical disease caused by feline herpesvirus type-1 in wild felid species is similar to that in domestic cats. Herpesviruses are endemic in free-ranging lions in South Africa but actual clinical disease due to them has not been reported in free-ranging felids. The first reports of feline herpesvirus infection associated with clinical disease in wild felids came from Australia and the USA in 1970. Subsequent reports of clinical disease in cheetahs and other wild felid species were limited to captive animals. This report deals with clinical disease in a group of semi-captive cheetahs in which 18 animals were affected, and included 12 adult males, 4 adult females and 2 subadults. No mortalities occurred in this group, the most common clinical signs being sneezing, nasal discharge and loss of appetite.

Key words: cheetahs, feline herpesvirus, serology, vaccination.

INTRODUCTION
The documented history of feline herpesvirus (FHV) is recent, and disease associated with this virus was first described in domestic cats in 1958\textsuperscript{1}. The first published reports of infection with FHV and clinical disease in wild felids appeared in the same year, i.e. 1970. One report documents cases in cheetahs in New South Wales\textsuperscript{2} from which the virus was isolated, and the other cases in different felid species in the Cincinnati Zoo, Ohio\textsuperscript{3}, although the virus was not isolated in the latter instance.

The 2nd documented isolation of FHV from a wild felid species was from clouded leopards in a colony in the St Louis Zoo, Missouri in 1977\textsuperscript{4}. Further isolations in the same collection followed. One of these was from the ocular secretion of a 1-year-old female cheetah in 1984, and the other from a biopsy specimen of a cutaneous ulcer of one of her 7.5-month-old cubs in 1987\textsuperscript{5}. Scherba and co-workers compared the latter isolate (ChHV) with feline herpesvirus type 1 (FHV-1)\textsuperscript{6}. Antigenic comparison by serum neutralisation test with goat anti-FHV-1 serum revealed no significant differences between the 2 viruses. Similarly, there were no morphological differences observed in transmission electron micrographs and in the cytopathic effects in cell cultures. Based on the electrophoretic profiles of restriction endonuclease-digested DNA of FHV-1 and ChHV, an extensive degree of homology was found, although there was some restriction fragment length polymorphism. These results suggested that ChHV is a strain of FHV-1.

Truyen et al.\textsuperscript{7} isolated FHV from the tonsil of a lion that was one of several lions and tigers that had died in a German safari park in 1990 after showing nervous signs. Histopathological examination and other laboratory tests did not incriminate FHV as the cause of the illness and mortality, and an aetiological diagnosis was not made.

Clinical disease in wild felids following infection with FHV has so far been described only in captive populations, although serological surveillance among free-living lions in South Africa has revealed high levels of exposure to the virus\textsuperscript{8}.

CASE HISTORY
During April/May 1997, upper respiratory tract infection was diagnosed in 18 cheetahs in a breeding facility. The affected animals were kept in groups of 2–6 in fenced camps approximately 320 m\textsuperscript{2} in extent in unspoilt savanna. All the cheetahs were vaccinated annually with attenuated vaccine against FHV-1, feline calicivirus (FCV) and feline panleukopenia virus, some as recently as 8 months before the appearance of clinical signs.

A variety of clinical signs were seen that included listlessness, sneezing, nasal discharge, ocular discharge, salivation, anorexia, ulcerative rhinitis and ulcerative conjunctivitis. Pneumonia was diagnosed in 2 cheetahs. The clinical signs in the remaining 16 animals were of a milder nature and were essentially sneezing and isolated instances of inappetence. One animal exhibited severe ulcerations of the tongue, salivation and inappetence but did not sneeze or show evidence of nasal discharge. Another suffered from a unilateral ulcerative conjunctivitis and bouts of sneezing.

Most of the cheetahs were caught in a cage and blood collected from the saphenous vein without immobilisation. The remainder were immobilised by administration by dart of Domitor (medetomidine HCl) at a dosage rate of 50 µg/kg (Novartis Animal Health) and ketamine at 3 mg/kg (Kyron Laboratories). After bleeding, those darted were given Antisedan (atipamizole HCl) at 200 µg/kg intramuscularly (Novartis Animal Health) to reverse the effect of the medetomidine.

Sterile cotton-tipped swabs were used to collect mucus and cells by deep insertion into the nasal cavities of 10 cheetahs. The swabs were thereafter immediately placed in minimum essential medium containing 5% foetal bovine serum plus antibiotics, and stored in liquid nitrogen. Following transport to the laboratory, the swabs were stored at –80 °C.

Antibodies against FHV and FCV were detected by indirect fluorescent antibody (IFA) tests. The target antigens used in the preparation of antigen slides were field strains of herpes- and calicivirus isolated from domestic cats that had shown clinical signs of respiratory tract infection. They were identified by means of specific conjugated antisera (VMDR Inc., USA), and obtained from the Department of Veterinary Tropical Diseases, Faculty of Veterinary Science, University of Pretoria.

The transport media containing the swabs were thawed and vortexed and the swabs discarded. Aliquots of the transport fluid were inoculated into plastic tissue culture flasks containing monolayers of Crandell feline kidney cells (CrFK) and incubated at 37 °C.
Results of the IFA tests for antibodies against FHV-1 and FCV in 7 of the 18 sick animals are shown in Table 1.

Results of the IFA test for antibodies against FHV-1 and FCV in a group of vaccinated, healthy subadult cheetahs bled during the outbreak of respiratory disease are shown in Table 2.

Cytopathic effects compatible with herpesviruses were noticed in all cell cultures within 24 hours of inoculation. Viruses were identified by (1) the nature of the cytopathic effect on host cells, (2) electron microscopic examination of cell culture fluid, and (3) the direct fluorescent antibody test using fluorescein-conjugated FHV-1-specific antibodies (VMRD Inc., USA).

**DISCUSSION**

Most of the cheetahs affected by the disease stopped eating for 3–5 days, and the condition of the 2 animals that suffered from pneumonia gave reason for concern. Nevertheless, none of the cheetahs were hospitalised or required administration of parenteral fluids or force-feeding. All the affected animals received supportive treatment in the form of antibiotics for 2 weeks, and it took at least 14 days before all clinical signs had disappeared.

The results of the IFA tests of 5 of the 7 cheetahs that showed clinical evidence of upper respiratory tract infection and of 1 of the 12 apparently healthy animals are consistent with those that develop after natural exposure to FHV-1. The anti-FCV antibody titres of both the sick and healthy groups are similar to vaccination titres that are consistently monitored in cheetahs at this facility.

The current perception is that FHV infection in free-ranging felids is benign. This outbreak in semi-captive cheetahs occurred in a population that was apparently not subjected to environmental stress or population pressure. It suggests, however, that even though living conditions may seem comfortable, cheetahs living in an environment where exercise is restricted, prey is limited or absent, and contact with other predators cannot be avoided altogether, may be maladapted to captivity, which in turn may contribute to susceptibility to a viral infection despite annual vaccination. The role of confinement stress in the pathogenesis of disease conditions in cheetahs is the focus of current research.

In domestic cats the major method of spread of FHV is by direct animal-to-animal contact. Although several camps housing the cheetahs were separated from each other by wire fences, the virus could only have successfully spread from the animals affected first, by crossing 2 roads 4 m and 6 m in width, respectively. Owing to the high susceptibility of FHV to high temperatures and dry environments, mechanical transmission by flies might have played a role, although transmission by means of animal handlers or feed containers cannot be discounted.

Immunity to herpesviruses in all species, whether induced by wild strains or vaccine strains, is characteristically short-lived, and this, together with viral latency, determines its variable clinical expression and makes treatment and prevention of herpesvirus infections difficult. Captive and semi-captive cheetahs have been vaccinated with attenuated vaccines in South Africa for several years without adverse effects having been reported. Until the time of the outbreak reported here, annual vaccination has been regarded as adequate to provide protection from clinical disease. It seems, however, that severe virus challenge, which apparently occurred in this outbreak, can overcome vaccinal immunity against feline herpesvirus-induced clinical disease in cheetahs.

**ACKNOWLEDGEMENT**

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**REFERENCES**


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**Table 1: Indirect fluorescent antibody titres against feline herpesvirus and feline calicivirus in the sera of cheetahs with clinical signs of upper respiratory tract infection.**

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Clinical signs</th>
<th>Herpesvirus</th>
<th>Calicivirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe ulceration of the nares Sneezing, anorexia</td>
<td>1:2560</td>
<td>1:160</td>
</tr>
<tr>
<td>2</td>
<td>The same as No. 1 plus pneumonia</td>
<td>1:5120</td>
<td>1:160</td>
</tr>
<tr>
<td>3</td>
<td>Sneezing</td>
<td>1:2560</td>
<td>1:20</td>
</tr>
<tr>
<td>4</td>
<td>Sneezing</td>
<td>1:1280</td>
<td>1:640</td>
</tr>
<tr>
<td>5</td>
<td>Sneezing</td>
<td>1:160</td>
<td>1:160</td>
</tr>
<tr>
<td>6</td>
<td>Sneezing</td>
<td>1:80</td>
<td>1:20</td>
</tr>
<tr>
<td>7</td>
<td>Sneezing</td>
<td>1:2560</td>
<td>1:80</td>
</tr>
</tbody>
</table>

**Table 2: Indirect fluorescent antibody titres against feline herpes- and calicivirus in the sera of a group of subadult cheetahs without clinical signs.**

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Herpesvirus</th>
<th>Calicivirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>2</td>
<td>1:20</td>
<td>1:640</td>
</tr>
<tr>
<td>3</td>
<td>1:20</td>
<td>1:640</td>
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<tr>
<td>4</td>
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<td>5</td>
<td>1:10</td>
<td>1:640</td>
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<tr>
<td>6</td>
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<td>1:640</td>
</tr>
<tr>
<td>7</td>
<td>Negative</td>
<td>1:10</td>
</tr>
<tr>
<td>8</td>
<td>Negative</td>
<td>1:10</td>
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<td>9</td>
<td>1:80</td>
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<tr>
<td>12</td>
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</table>
Book review — Boekresensie

The use of drugs in food animals: benefits and risks

Compiled by the Committee on Drug Use in Food Animals, National Research Council and Institute of Medicine, USA

This publication addresses an extremely important and very topical subject for veterinarians involved with food-producing animals. The report was researched and compiled by the Committee on Drug Use in Food Animals, convened by the Panel on Animal Health, Food Safety and Public Health (a joint panel of the Board on Agriculture and the Institute of Medicine) in the United States of America. A committee consisting of members of the National Academy of Sciences, the National Academy of Engineering and the Institute of Medicine reviewed the report. In my opinion this is an indication of a well-balanced scientific approach to the information recorded, the conclusions that are drawn and recommendations made. However, one should remember that the work was performed with reference to specific practices in farming, food harvesting, food processing, control over drug use etc applicable in the USA.

Veterinary drugs are critical components in the production of sufficient food from animals to satisfy an ever-increasing demand by a growing consumer population. These chemicals provide many benefits related to animal health, animal welfare and economical return. On the other hand, drugs used in food animal production could be present in food destined for humans and increase the risk of ill health in persons consuming such products.

The committee reviewed the major classes of drugs used in food production in the USA. The members concluded that most drugs pose a relatively low risk to the public as long as the drugs are used responsibly and in accordance with registration instructions. The greatest concern of the committee revolved around the use of antibiotics, for example microbial resistance to antibiotics.

The book comprises 8 chapters. At the end of each, a summary of findings is given and some recommendations are formulated.

An 11-page executive summary is useful for orientation in the subject matter. An overview is given of the use of drugs in food animals over the past 30 years. It refers also to public concerns and perceptions. The current production practices and use of drugs in the USA for each of the major food animal species are described. Reference is also made to the industry-initiated quality-assurance programmes that are in place, as demanded by the consumer. Chapter 3 discusses the primary benefits and hazards to human health of the use of drugs in food animals.

Chapter 4 presents issues related to development of new drugs, the current government approval system and the regulatory process in the USA. Recommendations are offered to improve drug availability and focus resources on public health risks, and reference is made to worldwide harmonisation of drug approvals. Chapter 5 summarises the pertinent features of the drug residue monitoring programme in the USA, explaining that an effective control system is the critical assumption upon which all other strategies rest. Information on microbial contamination in food and results of surveys of pork, beef, lamb and poultry are given.

A entire chapter is devoted to issues related specifically to antibiotics and the concern for their implications for human health. The effects of therapeutic and sub-therapeutic use of antibiotics on bacterial resistance in animals are discussed, as are the mechanisms through which resistance can develop. The committee strongly recommends that the further development and use of antibiotics in human medicine and food animal practices should be supervised by a multidisciplinary panel of experts. Increased education about practices and uses of antibiotics is seen as very important to prevent the misuse of these substances.

Chapter 7 attempts to compute the economic implications of eliminating sub-therapeutic drug use in food animals. A total versus partial ban of sub-therapeutic use is compared. Chapter 8 discusses alternative strategies to reduce the need for drug use and highlights promising areas for further research on the effect of nutrition and management practices on immune function and disease resistance. Controlled environmental factors can promote host resistance to disease, e.g. keeping milk cows cool to prevent mastitis. Reference is made to developing comprehensive biosecurity programmes to protect animals from pathogen transmission. Selection programmes for specific traits in livestock that have disease resistance and immune-responsive properties are advocated.

This book has a user-friendly index, clear figures and tables and a detailed list of references. It should be useful to the pharmaceutical industry, researchers, drug registration authorities and veterinarians involved with food-producing animals.

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134