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C. Packer; S. Altizer; M. Appel; E. Brown; J. Martenson; S. J. O'Brien; M. Roelke-Parker; R. Hofmann-Lehmann; H. Lutz

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Viruses of the Serengeti: patterns of infection and mortality in African lions

C. PACKER*, S. ALTIZER*, M. APPEL†, E. BROWN‡,
J. MARTENSON‡, S. J. O'BRIEN‡, M. ROELKE-PARKER‡,
R. HOFMANN-LEHMANN§ and H. LUTZ§

*Department of Ecology, Evolution and Behaviour, University of Minnesota, St. Paul, MN, USA; †James Baker Institute of Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, NY, USA; ‡Laboratory of Viral Carcinogenesis, National Cancer Institute, Frederick, MD, USA; and §Clinical Laboratory, Department of Internal Veterinary Medicine, University of Zurich, Zurich, Switzerland

Summary

1. We present data on the temporal dynamics of six viruses that infect lions (*Panthera leo*) in the Serengeti National Park and Ngorongoro Crater, Tanzania. These populations have been studied continuously for the past 30 years, and previous research has documented their seroprevalence for feline herpesvirus, feline immunodeficiency virus (FIV), feline calicivirus, feline parvovirus, feline coronavirus and canine distemper virus (CDV). A seventh virus, feline leukaemia virus (FeLV), was absent from these animals.
2. Comprehensive analysis reveals that feline herpesvirus and FIV were consistently prevalent at high levels, indicating that they were endemic in the host populations. Feline calici-, parvo- and coronavirus, and CDV repeatedly showed a pattern of seroprevalence that was indicative of discrete disease epidemics: a brief period of high exposure for each virus was followed by declining seroprevalence.
3. The timing of viral invasion suggests that different epidemic viruses are associated with different minimum threshold densities of susceptible hosts. Furthermore, the proportion of susceptibles that became infected during disease outbreaks was positively correlated with the number of susceptible hosts at the beginning of each outbreak.
4. Examination of the relationship between disease outbreaks and host fitness suggest that these viruses do not affect birth and death rates in lions, with the exception of the 1994 outbreak of canine distemper virus. Although the endemic viruses (FHV and FIV) were too prevalent to measure precise health effects, there was no evidence that FIV infection reduced host longevity.

Key-words: epidemic, population density, seroprevalence, susceptibles, virulence.

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Introduction

The temporal dynamics of viral pathogens depend on several factors, including transmission properties of the virus, and the survival, immune response and spatial distribution of the hosts (e.g. May 1983; Anderson & May 1991). In general, viruses that show low pathogenicity and prolonged infectious-

ness are likely to exhibit relatively high and constant prevalence (Anderson & May 1979a) and can therefore be termed 'endemic.' In contrast, viruses that spread rapidly, have a shorter duration of infectiousness and cause higher host mortality (or immunity) are more likely to generate discrete epidemics (Anderson & May 1979b). Epidemic diseases are characterized by rapid changes in the prevalence of infection and may disappear from the host population for extended periods. Such pathogens are likely to require high host densities for invasion and persistence, and the extent of outbreaks should increase with the size of the susceptible host population

Correspondence: Dr C. Packer, Department of Ecology, Evolution and Behavior, University of Minnesota, 1987 Upper Buford Circle, St Paul, MN 55108, USA.
Fax: 612-624-6777. E-mail: packer@biosci.umn.edu

(May 1983; Onstad & Carruthers 1990; Anderson & May 1982; Jaffee *et al.* 1992).

The population-level impact of viral infections will depend on their effects on host survival and reproduction (May 1983; Dobson & McCallum 1995). Recent empirical and theoretical studies have shown that virulence can be advantageous to the parasite and is not necessarily a side-effect of novel host-parasite combinations (e.g. Allison 1982; Ewald 1983; Anderson & May 1991; Herre 1993; Lenski & May 1994; Levin 1996). Although transient impacts of novel parasites can be immense, few studies have addressed the long-term effects of disease in wildlife populations (Grenfell & Gulland 1995). Most wildlife diseases are studied via incidental post mortems, and manipulative experiments in natural populations are often impossible (Dobson & McCallum 1995).

Viruses have been implicated as the cause of several major declines in carnivore populations (Young 1994). For example, canine distemper virus (CDV) killed over 70% of the last remaining colony of free-living black-footed ferrets (Thorne & Williams 1988) and phocine distemper killed over 18 000 harbour seals in northern Europe (Osterhaus & Vedder 1988). Rabies has been suggested to cause population decline in wolves, Ethiopian wolves and African wild dogs (e.g. MacDonald 1980; Kat *et al.* 1995; Weiler, Garner & Ritter 1995; Sillero, King & MacDonald 1996; Ballard & Krausman 1997; Laurenson *et al.* 1998). Perhaps the best-studied example is the canine distemper virus (CDV) outbreak that struck the Serengeti lions and several other species in late 1993–early 1994 (Roelke-Parker *et al.* 1996; also see Alexander & Appel 1994; Alexander *et al.* 1995). CDV originated from the large population of domestic dogs surrounding the Serengeti ecosystem and killed 35% of the Serengeti lions within 6 months. Over 85% of the lions were infected, and many victims showed neurological disorders, encephalitis, and pneumonia. While this outbreak followed a well-defined onset, many other viral epidemics have been inferred solely from cross-sectional serological surveys (e.g. Olmsted *et al.* 1992; Spencer & Morkel 1993; Creel *et al.* 1997) and detailed/long-term investigations of virus-carnivore interactions are rare (Grenfell & Gulland 1995; Dobson & McCallum 1995).

In the present study, we evaluate temporal changes in the exposure of African lions to six different viruses. These viruses show a variety of transmission modes, symptoms and durations of infectiousness in domestic carnivores (Table 1). For example, both feline immunodeficiency virus (FIV, a lentivirus closely associated with HIV) and feline herpesvirus permanently infect their hosts and do not elicit lasting immunity (Table 1). In contrast, canine distemper virus (CDV), feline calicivirus,

feline coronavirus and feline parvovirus generally cause only temporary infection, although a small proportion of infected hosts may persist as asymptomatic carriers. Using serological data from two different lion populations, we first classify these viruses as either endemic or epidemic. We estimate the timing of each epidemic by combining the temporal pattern of seroprevalence with information on the lions' ages at the time of sampling. We then examine the relationship between the extent of each epidemic, and the proportion and density of susceptible hosts in the population. Finally, we measure the impact of viral infection on lion mortality and birth rates.

Methods

Lions have been studied continuously in the Serengeti since March 1966 and in the Ngorongoro Crater since 1963 (Packer, Tatar & Collins 1998). All animals are individually recognized from natural markings (Packer & Pusey 1993) and most have been regularly observed since birth (Pusey & Packer 1994), and thus the precise age is known for each individual. Blood samples were collected in the Serengeti each year between 1984 and 1994, and the Crater lions were sampled in 1984, 1985, 1987 and 1991 (see Table 2 for annual sample sizes). These samples were originally collected for genetic assay (O'Brien *et al.* 1987; Packer *et al.* 1991a,b) and to investigate the CDV outbreak in 1994 (Roelke-Parker *et al.* 1996). Serological assays were later performed to assess the lions' exposure to FIV (Olmsted *et al.* 1992; Brown *et al.* 1994), CDV (Roelke-Parker *et al.* 1996), and feline leukaemia, herpes-, parvo-, corona- and calicivirus (Hofmann-Lehmann *et al.* 1996). Over 300 lions were also tested for FeLV, but none showed detectable levels of antigens (Hofmann-Lehmann *et al.* 1996). Table 3 summarizes the precise assays and criteria used to determine sero-status for the remaining six viruses. Many animals were tested repeatedly, and repeat samples are included in any descriptive analysis, but excluded from all statistical tests unless an animal seroconverted.

Study animals and study sites

Lions are considered to be 'immatures' until 4 years of age. Most females do not start breeding until well after their third birthday, while males do not attain breeding status until they are about 5 years old (Packer *et al.* 1988, 1998). The Serengeti study area covers the south-eastern quarter of the Serengeti National Park. This 2000 km² area consists of two contrasting habitats: acacia woodland and open-grass plains (see Packer *et al.* 1988). Lions on the plains live at lower densities and endure lower levels of food availability than their woodlands counter-

Table 1. Natural history of the study viruses in domestic cats and dogs. Taken from Appel (1987), Gaskell & Bennett (1996) and Yamamoto *et al.* (1989)

Virus	Infective period outside host	Transmission	Symptoms	Course of infection	Mortality patterns in domestic carnivores
Feline immunodeficiency virus (FIV)	Brief	Biting	<i>Initial:</i> lymphadenopathy, depression, leucopenia. <i>Final:</i> lymphadenopathy, gingivitis, persistent calicivirus and/or herpes, wasting, anaemia, diarrhoea, neurological disease	After initial phase, animals may be healthy for years, but shed virus in the saliva. Antibody levels may become undetectable in final stages, but not all infected animals progress to AIDS	Mortality after 3–5 years of infection
Feline herpes virus	24 h at room temp.	Oral and aerosol	Sneezing, rhinitis, fever, tracheitis, glossitis, pharyngitis, anorexia and pneumonia	About 80% become active carriers after initial infection, shedding virus 1–2 weeks after stress and showing mild clinical signs	Mortality mostly restricted to 6–12 week kittens. Mortality rates higher if co-infected with FIV
Canine distemper virus (CDV)	1–3 h at 37°C	Aerosol, infects many carnivore spp.	Nasal and conjunctival discharges, myoclonous, encephalitis, lymphopenia, immunosuppression	Acute followed by complete recovery, although sometimes followed by subacute or persistent infection in CNS	In unvaccinated populations, most fatalities are immatures; most adults have survived earlier epidemics
Feline panleucopenia (parvovirus)	13 months at 25°C	Oral contact with infected animals or contaminated environment	Vomiting, anorexia, occasional diarrhoea, panleucopenia, unsteady gait and convulsions	Ataxic carriers can shed virus for up to a year; survivors have long-term immunity	6–14-week-old kittens are primary victims; mortality rates of 25–75%
Feline enteric coronavirus, which may mutate to Feline infectious peritonitis (FIP)	24–36 h (moist) at room temperature	Oral and aerosol, also infects domestic dogs	<i>FECV:</i> transient enteritis. <i>FIP:</i> fever, anorexia, lethargy, abdominal distention, peritonitis	Some strains allow viral elimination and rapid recovery; others cause sequestered infection where virus containment is due to cell-mediated immunity; humoral immunity may enhance infection	FIP mostly seen in kittens, occasionally seen in adults infected by carriers
Feline calicivirus	8–10 days at 37°C	Oral and aerosol	Rhinitis, conjunctivitis, oral ulcers, pneumonia, lameness	Acute often followed by carrier phase with constant viral shedding in saliva. About 50% are carriers > 75 days after initial infection; FIV+ animals more likely to become carriers and remain so longer. Non-carriers gain long-lived immunity	Most severe in kittens possibly in those receiving no maternal antibodies. Mortality much higher when co-infected with panleucopenia

Table 2. Number of lions sampled each year in the two study populations

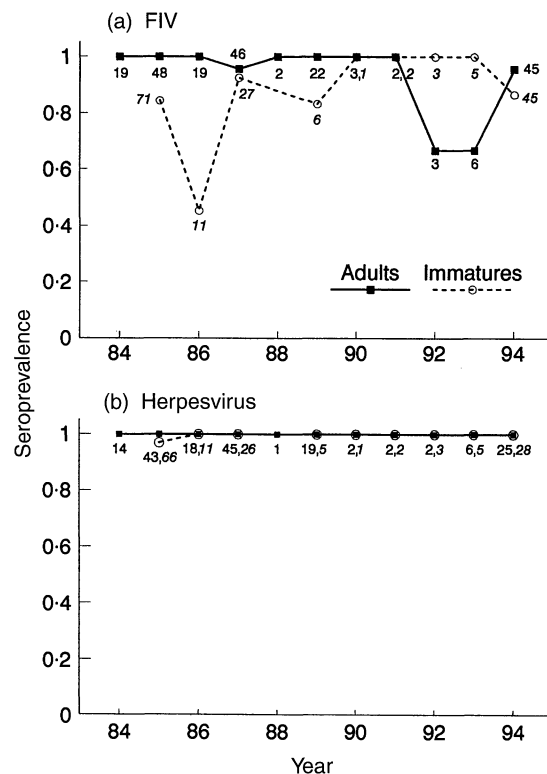
Year	Serengeti	Ngorongoro Crater
1984	19	8
1985	120	10
1986	30	0
1987	75	19
1988	2	0
1989	28	0
1990	4	0
1991	5	15
1992	6	0
1993	12	0
1994	93	0

parts. The Ngorongoro Crater is located about 90 km to the south-east of the Serengeti study area, and the Crater lions enjoy higher and more consistent levels of food availability than the Serengeti lions (Hanby, Bygott & Packer 1995). However, the Crater is a small, isolated population (80–100 animals) with an associated loss in genetic diversity compared to the much larger Serengeti population (O'Brien *et al.* 1987; Packer *et al.* 1991b), which includes an estimated 2000–3000 animals (Schaller 1972; Hanby & Bygott 1978).

Results and discussion

TEMPORAL PATTERNS OF INFECTION

Adult serostatus usually indicates prior exposure to the virus, rather than current infection, since an older animal may still be carrying antibodies from a childhood disease (see below). Therefore, seroprevalence in young animals provides stronger evidence of a recent exposure and, if all the younger cohorts are seronegative, the virus has probably been absent for several years. Under these assumptions, we first use the seroprevalence data to determine whether each virus was 'endemic' or 'epidemic' over a 10-year period. We then provide estimates for the tim-

**Fig. 1.** Annual seroprevalence rates in the Serengeti for (a) FIV, and (b) feline herpesvirus.

ing of specific outbreaks of the epidemic viruses based on sudden changes in the frequency of seropositive hosts.

Endemic viral infections

Consistent with a pattern of chronic infection, the lion populations showed constant and high levels of seroprevalence for FIV and feline herpes virus. Rates of FIV infection did not vary significantly across years for either adults or immatures (Fig. 1a) or by sex (cf. Courchamp *et al.* 1998). Combining data from all years, small cubs quickly seroconverted to FIV+, and this trend was similar in the

Table 3. Assay and criterion by which lions were considered to be seropositive for each virus

Virus	Assay	Criterion for seropositive	Reference
FIV	Western blot	Presence of antibodies	Brown <i>et al.</i> (1994), Hofmann-Lehmann <i>et al.</i> (1996)
Herpes	ELISA	$\delta OD > 0.080$	Hofmann-Lehmann <i>et al.</i> (1996)
CDV	Serum neutralization	Presence of antibodies	Roelke-Parker <i>et al.</i> (1996)
Parvovirus	Haemoagglutination inhibition assay	Titre > 30	Hofmann-Lehmann <i>et al.</i> (1996)
Coronavirus	IFA	Presence of antibodies	Hofmann-Lehmann <i>et al.</i> (1996)
Calicivirus	ELISA	$\delta OD > 0.095$	Hofmann-Lehmann <i>et al.</i> (1996)

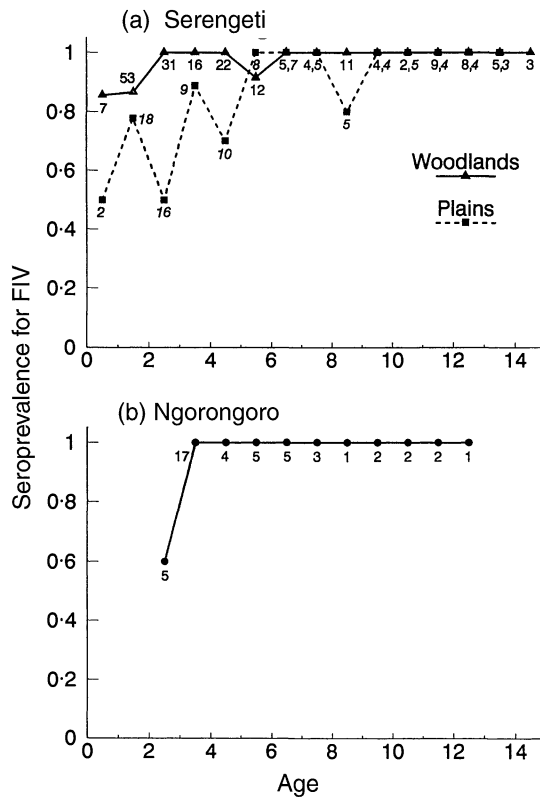


Fig. 2. Overall age-prevalence curves for FIV in (a) Serengeti woodlands and plains, and (b) Ngorongoro Crater. Virtually every animal has been infected with FIV by their 4th birthday, although lions in the Serengeti plains show a lower rate of infection than the other two habitats ($T = -3.54$, $P < 0.001$), even when controlling for age in a multivariate analysis (effect of age: $T = 5.94$, $P < 0.001$; effect of Serengeti plains: $T = -3.89$, $P < 0.001$).

Serengeti and Ngorongoro Crater (Fig. 2). All but two of 374 animals in the Serengeti and Ngorongoro were positive for herpes virus (Fig. 1b), including all eight cubs sampled before their first birthday.

Epidemic viral infections

Each of the remaining four viruses appeared to be absent from the Serengeti for 4–12 years followed by a sudden resurgence in the frequency of seropositive hosts (Fig. 3). The sporadic nature of these widespread infections is most conspicuous in the youngest age classes, and the precise timing of each outbreak differed between the Serengeti and Ngorongoro Crater.

CDV. Seroprevalence varied between years in the Serengeti in both adults and immatures (Fig. 3a). The sharp rise in 1993–94 in CDV seroprevalence of adults and immatures was due to the outbreak documented by Roelke-Parker *et al.* (1996), whereas the declining adult seroprevalence in the mid-1980s

reflected an earlier outbreak. The Ngorongoro Crater lions also appear to have been infected before 1984, with no further epidemics before the end of the sampling period in 1991 (see Fig. 4).

Parvovirus. Annual seroprevalence of adult lions varied somewhat in the Serengeti, and the seroprevalence of immatures varied significantly among years (Fig. 3b). Immatures showed the highest frequency of exposure in 1985 (see Hofmann-Lehmann *et al.* 1996) and in 1992. None of the immatures in Ngorongoro Crater tested positive for parvovirus (see below).

Coronavirus. Annual seroprevalence in the Serengeti only varied significantly in immatures (Fig. 3c). In Ngorongoro Crater, there was evidence of new infections between 1984 and 1991, but our sample size was inadequate to confirm significant variation between years.

Calicivirus. Seroprevalence varied across years in the Serengeti, but varied most dramatically in immatures (Fig. 3d). Immatures showed the highest seroprevalence in 1985 and 1990/91. Calicivirus was absent from Ngorongoro Crater (Hofmann-Lehmann *et al.* 1996).

ESTIMATING THE TIMING OF EPIDEMICS

The four 'epidemic' viruses showed fluctuating prevalence in each study population, often increasing in discrete outbreaks. The timing of these outbreaks can be estimated from the seroprevalence data in conjunction with the age of each study animal. For example, out of all the Serengeti lions sampled between 1984 and October 1993, only those animals that had been born before July 1981 were seropositive for CDV (Fig. 4a). Every lion born after 1981 was seronegative for CDV until 1993/94, when a new epidemic swept through the population, infecting lions of all ages (Fig. 4b). This pattern strongly suggests that the virus had been absent from the Serengeti from 1981 until the end of 1993. Data from Ngorongoro suggest that CDV infected the Crater lions sometime in 1980, but then disappeared from the population for the following 11 years: the youngest seropositive animal had been born in June 1980, but no animal born later than this date had been infected by the end of our last sampling effort in 1991 (Fig. 4c).

Similar heterogeneities in the age-prevalence data could be discerned for the other three viruses and one example from each virus is plotted in Fig. 5. We interpret the marked discontinuities in seroprevalence for these viruses to indicate a high rate of infection, similar to the CDV outbreak of 1994 (Fig. 4b). In support of this assumption, almost all of the putative outbreaks simultaneously infected multiple prides and included cubs as well as adults. The only exception was an outbreak of calicivirus in

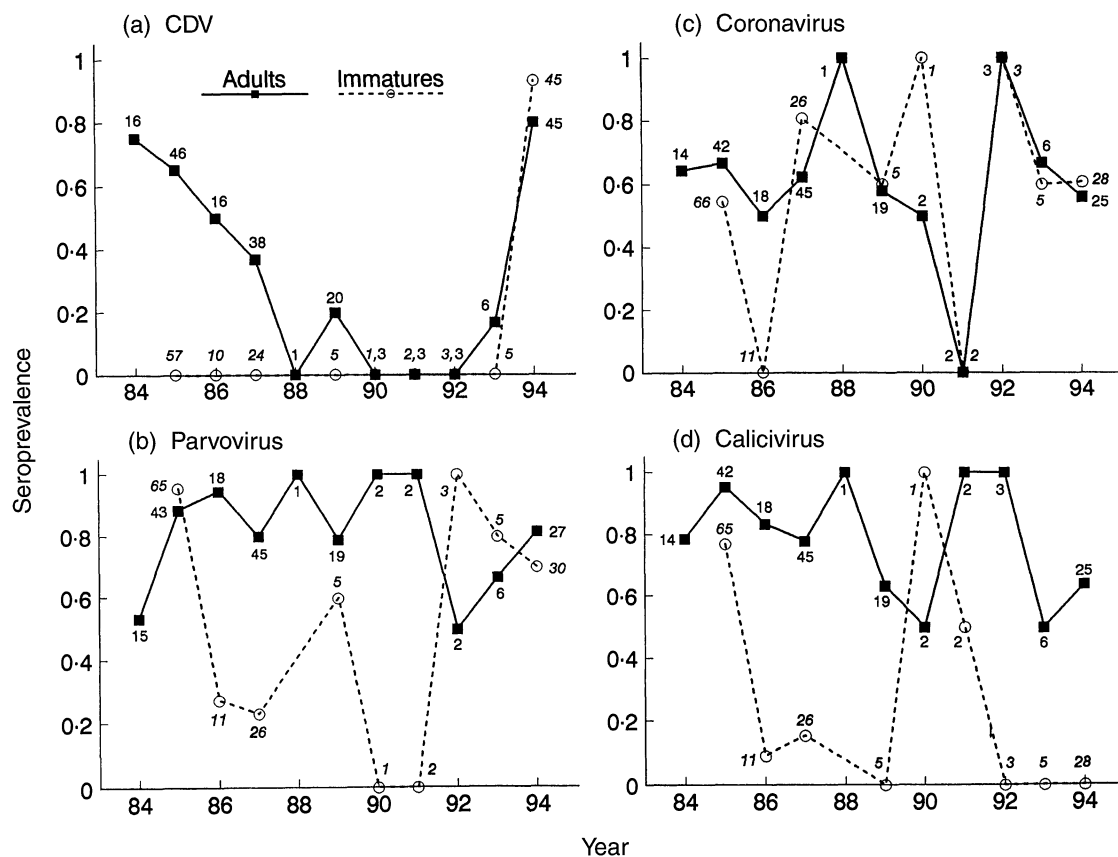


Fig. 3. Annual seroprevalence in the Serengeti for CDV, parvovirus, coronavirus and calicivirus. Note: the statistical analyses only include those years with sufficient sample size ($n \geq 5$) to perform chi-square tests. (a) CDV: seroprevalence of adults varied significantly across years ($\chi^2 = 34.65$, d.f. = 6, $P = 0.0000$), but varied even more in younger lions ($\chi^2 = 132.3$, d.f. = 5, $P = 0.0000$). (b) Parvovirus: seroprevalence of adults varied non-significantly across years ($\chi^2 = 11.94$, d.f. = 6, $P = 0.0633$), but varied significantly in younger animals ($\chi^2 = 56.94$, d.f. = 5, $P < 0.0000$). (c) Coronavirus: seroprevalence of adults did not vary across years ($\chi^2 = 1.99$, d.f. = 6, $P = 0.9203$), but varied significantly in younger lions ($\chi^2 = 20.90$, d.f. = 5, $P = 0.0008$). (d) Calicivirus: seroprevalence of adults varied across years ($\chi^2 = 15.66$, d.f. = 6, $P = 0.0157$), but varied more in younger animals ($\chi^2 = 73.62$, d.f. = 5, $P = 0.0000$).

1987 that infected only a few members of a single pride located along the northern boundary of our Serengeti study area. The approximate end-dates of outbreaks of each virus are summarized in Table 4. Except for the 1994 CDV epidemic (where comparable data are not yet available), these dates are presumed to have been the beginning of prolonged intervals where no new seroconversions occurred.

Besides these extreme discontinuities in exposure, the seroprevalence data also suggest several earlier outbreaks through a 'stair-step' pattern. For example, Fig. 4a shows that virtually all animals born between 1970 and 1977 were seropositive for CDV during the 1984–93 sampling period, whereas animals born in 1978–81 showed a consistently lower prevalence. This pattern may be most easily explained by two epidemics that ended in 1977 and 1981. A similar pattern is evident for calicivirus, where separate epidemics resulted in a higher sero-

prevalence for animals born in 1979–86 than for those born in 1987–90 (Fig. 5c).

If these viruses do occur in discrete epidemics, antibody titres and seroprevalence should both decline in the years following an outbreak because the strength of each individual's immune response weakens through time. However, we only resampled enough individuals to test this prediction directly for two viruses. Fifteen parvo+ animals were resampled between the 1985 and 1992 parvovirus outbreaks. Their titre levels declined significantly ($n = 13$ animals whose titre levels changed, $T = 15$, $P < 0.05$ signed-ranks test), and two seropositive animals became seronegative after 1.25 and 4.25 years, respectively. Only two CDV+ animals were resampled in the 1980s, and both showed a decline in antibody titres between 1985 and 1987.

Including all animals that were old enough to have been exposed to each virus, seroprevalence consistently declined after the presumed end of each

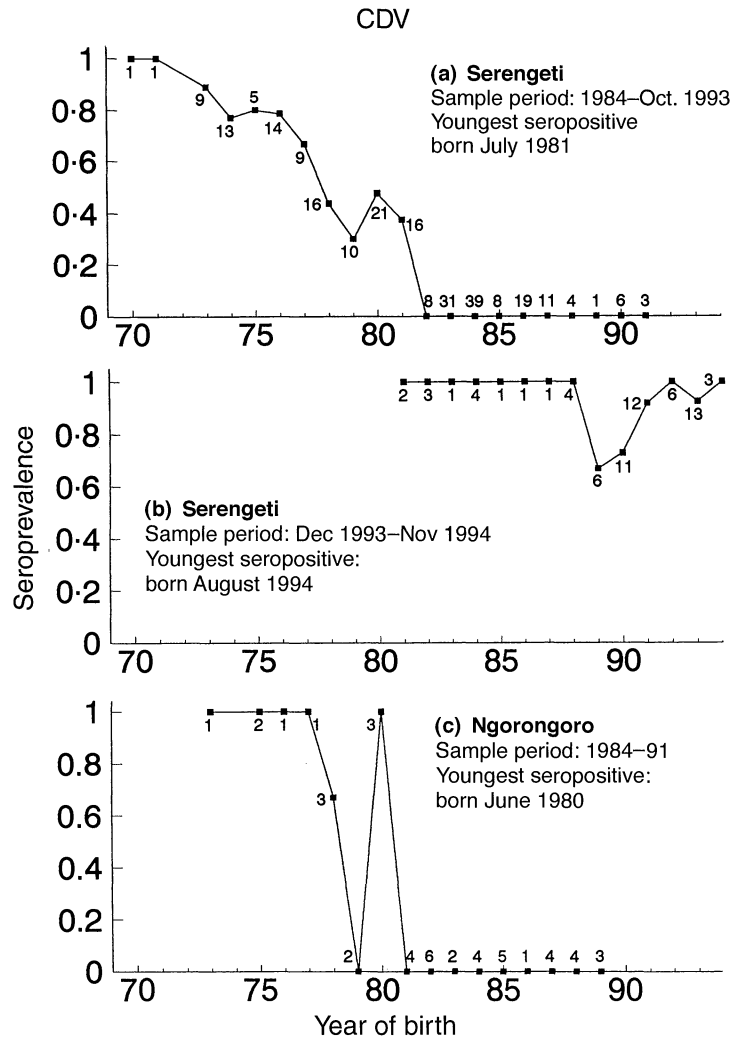


Fig. 4. Seroprevalence curves for CDV. (a) Serostatus of animals sampled between 1984 and October 1993 plotted according to their year of birth. Numbers above each point give sample sizes. Prevalence varies significantly with birth-year for animals born within ± 4 years of 1981 ($\chi^2 = 40.18$, d.f. = 1, $P = 0.0000$). (b) Serostatus of lions sampled during the 1994 CDV outbreak. Note that many of these animals had been sampled in earlier years and were known to have seroconverted during the outbreak. (c) Serostatus of crater lions sampled between 1984 and 91; prevalence varies significantly with birth-year for animals born within ± 4 years of 1980 ($P = 0.0005$, two-tailed Fisher Test).

epidemic (Fig. 6). Responses to three viruses (CDV, calici- and parvovirus) declined at a remarkably similar rate, but coronavirus response declined more rapidly. As predicted, individual titre levels also declined through time for CDV ($T = -8.08$, $n = 139$ seropositive animals, $P < 0.0001$, $r^2 = 0.3209$) and parvovirus ($T = -5.96$, $n = 233$ seropositives, $P < 0.0001$, $r^2 = 0.1333$), although not for coronavirus ($T = -0.35$, $n = 179$, $P = 0.7266$). Because of batch effects in the calicivirus assays, ELISA values could not be tested. Note that titre levels also declined with the animal's age at the end of each epidemic for both CDV ($P = 0.0162$) and parvovirus ($P < 0.0001$), but the drop through time after each epidemic remained highly significant in a multiple regression model that controlled for age

($P < 0.0001$, with the effect of age also significant at $P < 0.0001$).

EFFECTS OF HOST POPULATION DENSITY

Epidemics should be more frequent and more extensive in large host populations, and there is some indication that viral outbreaks varied according to the overall host population size. Figure 7 shows the size of the study populations in the Serengeti and Ngorongoro Crater over the past 20+ years, as well as the approximate timing of the outbreaks listed in Table 4. In the Serengeti, both corona- and parvovirus typically occurred in years of high population density.

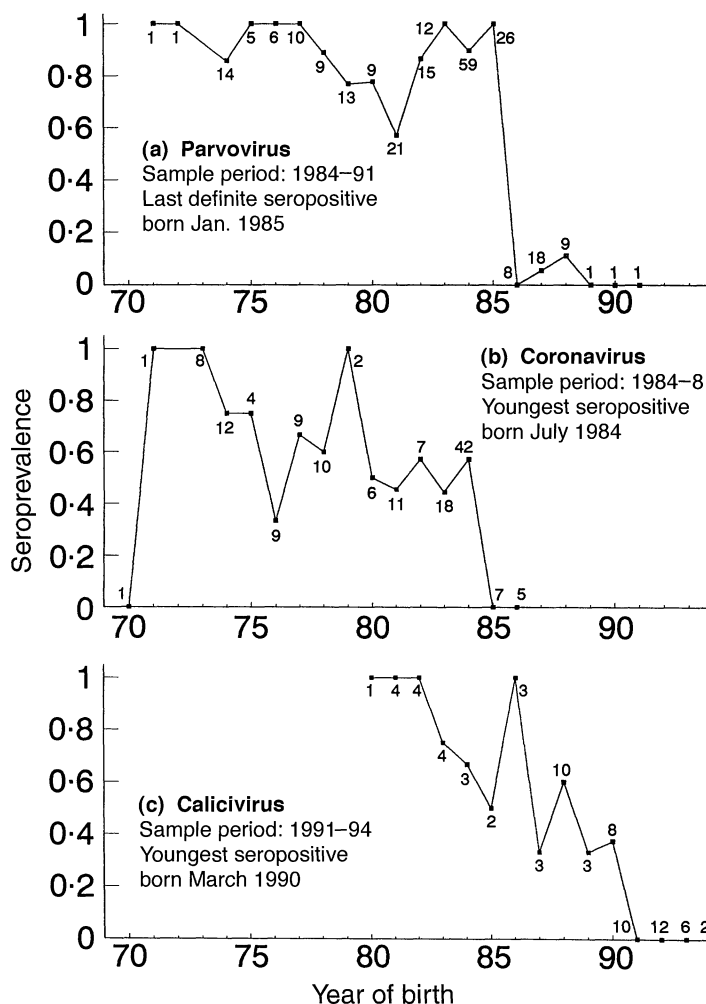


Fig. 5. Representative seroprevalence curves for three ‘epidemic’ viruses. (a) Seroprevalence for parvovirus in lions sampled between 1984 and 1991 with data plotted according to the year of birth. Prevalence varies significantly with birth-year for animals born within ± 4 years of 1985 ($\chi^2 = 99.95$, d.f. = 1, $P = 0.0000$). Note that the two seropositives born in 1986–87 both had marginal titres and are probably false positives: titres above 30 are considered ‘positive’, some animals carried titres above 5000, and titres for these two were only 40. (b) Seroprevalence for coronavirus between 1984 and 1987 plotted by year of birth. Prevalence varies significantly with birth-year for animals born within ± 4 years of 1984 ($\chi^2 = 9.56$, d.f. = 1, $P = 0.0020$). (c) Seroprevalence for calicivirus between 1991 and 1994 plotted by year of birth. Prevalence varies significantly with birth-year for animals born within ± 4 years of 1990 ($\chi^2 = 14.56$, d.f. = 1, $P = 0.0001$).

Our study areas include three contrasting habitats with associated differences in lion density. Calicivirus was absent from the small, isolated Crater population. Prevalence after each coronavirus outbreak was lower ($\chi^2 = 12.63$, $P < 0.001$, $n = 221$) in the low-density Serengeti plains (where prides are small and pride ranges are 150–500 km²) than in the adjacent woodlands (where prides are large and pride ranges are 40–75 km²). Age-prevalence of FIV was also lowest in the plains (Fig. 2); a pattern similar to domestic cats where FIV prevalence is lower in low-density areas (Malik *et al.* 1997).

Although total host density was associated with changes in disease prevalence in the above cases, epidemiological theory specifies that only the suscep-

tible subset of hosts will regulate the invasion and rate of spread of viral infection. In the following sections, we therefore estimated the size of the susceptible population for each virus through time, and we use these estimates to evaluate the association between susceptible host density and viral outbreaks.

Timing of outbreaks

Because our serological survey included a small subset of the study populations and our sample size varied from year to year (Table 2), we can only provide rough estimates of the overall number of susceptibles. We base these estimates on the following simplifying assumptions: (i) every animal in the

Table 4. Dates when viral epidemics are presumed to have ended. ‘Pattern’ distinguishes between two situations; ‘presence/absence’ indicates that consecutive cohorts were seronegative whereas older cohorts were largely seropositive; and ‘stair-step’ designates when consecutive cohorts were moderately seropositive, while older cohorts showed even higher seroprevalence. ‘Significance’ refers to the difference in seroprevalence between cohorts born within the 4 years prior to the endpoint vs. those born in the first 4 years thereafter (as tested by χ^2 with 1 d.f.). The 1976 parvovirus, and 1988 and 1993 coronavirus epidemics all showed the same qualitative pattern as the statistically robust outbreaks, and are therefore included in subsequent analyses. However, the 1987 calicivirus outbreak is omitted from further consideration, because only a small proportion of at-risk individuals became seropositive, and all three of these animals lived in the same pride at the edge of the study area

Virus	Population	Date	Pattern	Significance
CDV	Serengeti	1977	Stair-step	$P < 0.01, n = 104$
		1981	Presence/absence	$P < 0.001, n = 149$
		1994	Presence/absence	$P < 0.001, n = 93$
Parvovirus	Ngorongoro	1980	Presence/absence	$P < 0.001, n = 25$
	Serengeti	1976	Presence/absence	NS, $n = 14$
		1985	Presence/absence	$P < 0.001, n = 148$
		1992	Presence/absence	$P < 0.001, n = 43$
Coronavirus	Ngorongoro	1979	Presence/absence	$P < 0.05, n = 21$
	Serengeti	1984	Presence/absence	$P < 0.01, n = 90$
		1988	Presence/absence	NS, $n = 8$
Calicivirus	Serengeti	1993	Presence/absence	NS, $n = 40$
		1980	Stair-step	$P < 0.05, n = 145$
		1985	Presence/absence	$P < 0.001, n = 118$
		(1987)	Presence/absence	NS, $n = 33$
		1990	Presence/absence	$P < 0.001, n = 54$

population was exposed to the virus during each outbreak; (ii) survivors of each outbreak gained immunity that persisted over their remaining life-

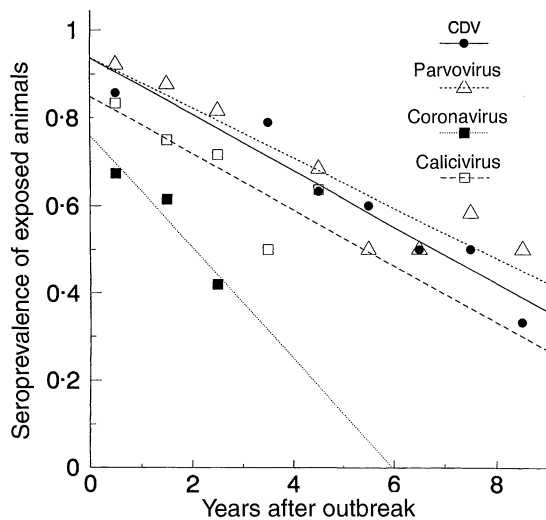


Fig. 6. Seroprevalence plotted as a function of the number of years that had elapsed after the presumed end of each epidemic. Data are restricted to animals who were alive during the putative outbreak and thus who could have been exposed to the virus. The decline in seroprevalence through time was statistically significant for all four viruses (CDV: $T = -4.88, P < 0.001, n = 223$, logistic regression; parvovirus: $T = -4.81, P < 0.001, n = 277$; coronavirus: $T = -2.46, P = 0.014, n = 293$; calicivirus: $T = -4.31, P = 0.001, n = 240$). These all remain significant when other age effects are included in a multivariate logistic-regression analysis.

spans; thus (iii) only animals born after the most recent outbreak were ‘susceptible’ to viral infection. These assumptions clearly underestimate the size of the susceptible population because, first, it is unlikely that 100% of the population is exposed to the virus during an outbreak, and, secondly, a proportion of seropositive animals may lose their immunity over time (as implied by Fig. 6). However, in the absence of complete information, this procedure at least provides a standardized estimate of the minimum number of susceptibles in the population.

The total number of ‘new susceptibles’ (i.e. individuals born after an epidemic who had not yet been exposed to the virus) is presented in Fig. 8. Note that this analysis is restricted to the Serengeti, since estimates require at least two outbreaks of the same virus. For parvovirus and calicivirus, successive outbreaks occurred shortly after the population crossed an apparent threshold number of new susceptibles: parvovirus outbreaks occurred after the number of new susceptibles reached 150 animals, whereas calicivirus outbreaks required at least 90 new susceptibles. In contrast, there were no consistent patterns for CDV (with the 1981 outbreak coinciding with only 70 new susceptibles vs. 250 susceptibles in late 1993) or coronavirus (approximately 80 susceptibles in 1988 vs. approximately 160 in 1992). In the case of CDV, it is important to note that the lions should not be measured in isolation: CDV infected large numbers of Serengeti canids in the late 1970s and early 1980s, so the true number of susceptibles in the ecosystem should also include these other host species.

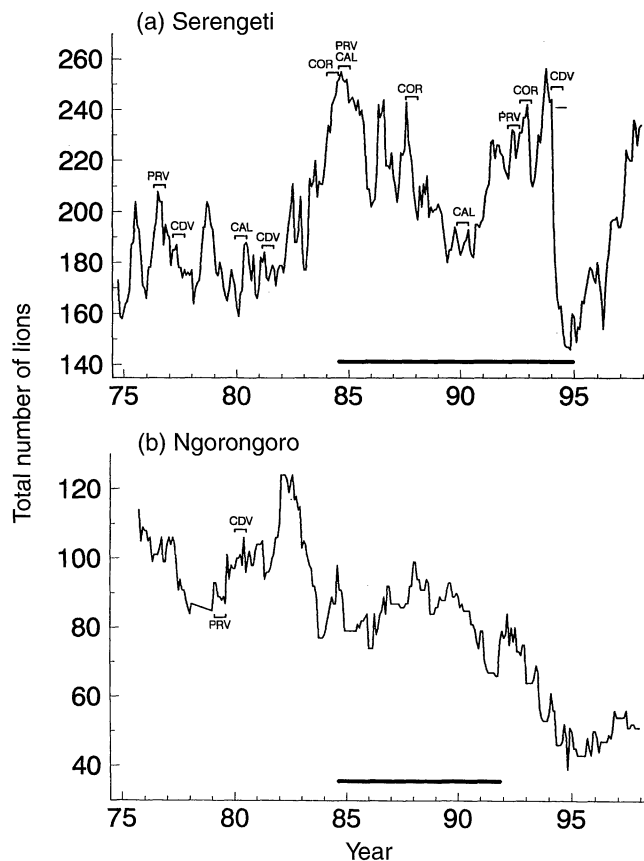


Fig. 7. Monthly population totals of (a) the Serengeti study area, and (b) Ngorongoro Crater. Labels show the estimated onset/ending of each viral epidemic (as given in Table 4) and horizontal lines show the span over which samples were collected.

Extent of outbreaks

To estimate the proportion of susceptibles that became infected during each outbreak, we recalculated the annual seroprevalence of the Serengeti lions. In this analysis, we assumed that seronegative animals had never been infected between birth and the time they were sampled. We assumed that seropositive animals had been seropositive each year following the most recent outbreak for that particular virus, but we made no assumptions about their serostatus prior to the most recent outbreak. In this way, the age and serostatus of sampled lions was used not only to estimate seroprevalence in the year sampled, but also in previous years (thus reducing the random variance produced by small sample sizes).

These estimates are presented in Fig. 9, and they are broadly similar to the raw data presented in Fig. 3. However, these estimates interpolate data for the years 1988–92 (when few samples were collected) and extrapolate backwards to years before our serological samples were collected. Most important, Fig. 9 provides an approximation of the magnitude of each outbreak. For example, the 1993–94 CDV

outbreak struck when the population was entirely seronegative and over 85% of the population seroconverted in the course of the epidemic. In contrast, the 1990 calicivirus epidemic struck when nearly 30% of the population was seropositive for calicivirus, and seroprevalence only increased to about 50%.

We used these data to estimate the extent of each outbreak. We define 'incidence' as the proportion of susceptibles that became seropositive during the time course of a single outbreak. Thus, an increase in seroprevalence from 20 to 90% indicates a reduction in susceptibles from 80 to 10%, and an 'incidence' of $0.70/0.80 = 0.875$; an increase in seroprevalence from 55 to 60% would give an 'incidence' of $0.05/0.45 = 0.111$. Using data from all four viruses, Fig. 10 shows that epidemics with the highest 'incidence' were associated with the highest initial proportion of susceptibles. This trend verges on statistical significance if restricted to the well-defined epidemics listed in Table 4 (arcsine-transformed linear regression: $T = -2.49$, $r^2 = 0.5535$, $n = 7$, $P = 0.0552$), and the relationship becomes highly significant if we include the 1987 calicivirus

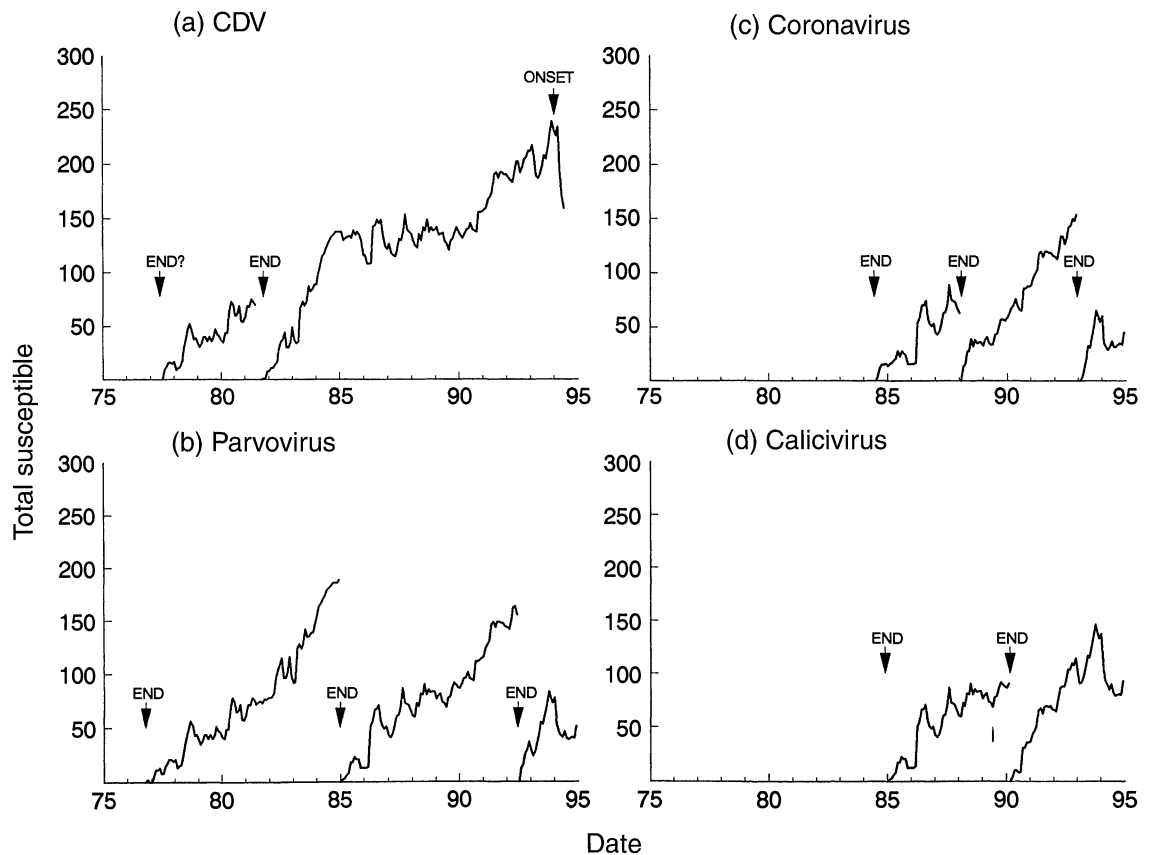


Fig. 8. Estimated number of 'new' susceptibles for each virus each year in the Serengeti. 'New susceptibles' only include animals that were born subsequent to an outbreak and they only remain susceptible until the next successive outbreak, whereupon further cubs contribute to the next set of new susceptibles.

'outbreak' that did not spread beyond a single pride ($T = -4.21$, $r^2 = 0.7434$, $n = 8$, $P = 0.0056$).

Although the overall trend in Fig. 10 is quite striking, the data are based on very rough approximations and on only 1–3 outbreaks per virus. Within each virus, only calicivirus shows a trend in the same direction as the overall pattern. The paired outbreaks of parvovirus and coronavirus show slight trends in the opposite direction to the overall pattern, but it is perhaps more noteworthy that the two points in each pair are so similar. This suggests that epidemics of parvovirus and coronavirus each spread with a typical magnitude and each strike at a typical level of seroprevalence. Noteworthy, too, is the possibility that parvovirus may consistently infect a higher proportion of susceptibles than does coronavirus, perhaps due to a longer persistence outside the host (weeks for parvovirus vs. hours for coronavirus).

EFFECTS ON HOST FITNESS

We can only provide limited data on the precise cause of mortality in these animals. Most lions sim-

ply disappear from the study area, and most observed fatalities result from direct combat with other lions or from injuries sustained during prey capture (Packer *et al.* 1988). The only clear-cut examples of death due to disease occurred during the CDV outbreak in 1994 (Roelke-Parker *et al.* 1996). In the following section, we rely on a demographic analysis to determine whether any of these viruses is associated with widespread mortality or infertility. These assessments depend on whether the virus is endemic or epidemic.

ENDEMIC

Because only two lions tested negative for herpesvirus, we lack a control group with which to compare infected animals. We are therefore unable to measure effects of herpes infection on host fitness.

Although virtually every lion was FIV+ by the age of 4 years (Fig. 2), about 20% of 1–2-year-olds were FIV–; thus, we restrict our analysis to the long-term survival of young animals. In domestic cats, FIV infection is permanent and inflicts most mortality 3–5 years after the initial infection (see

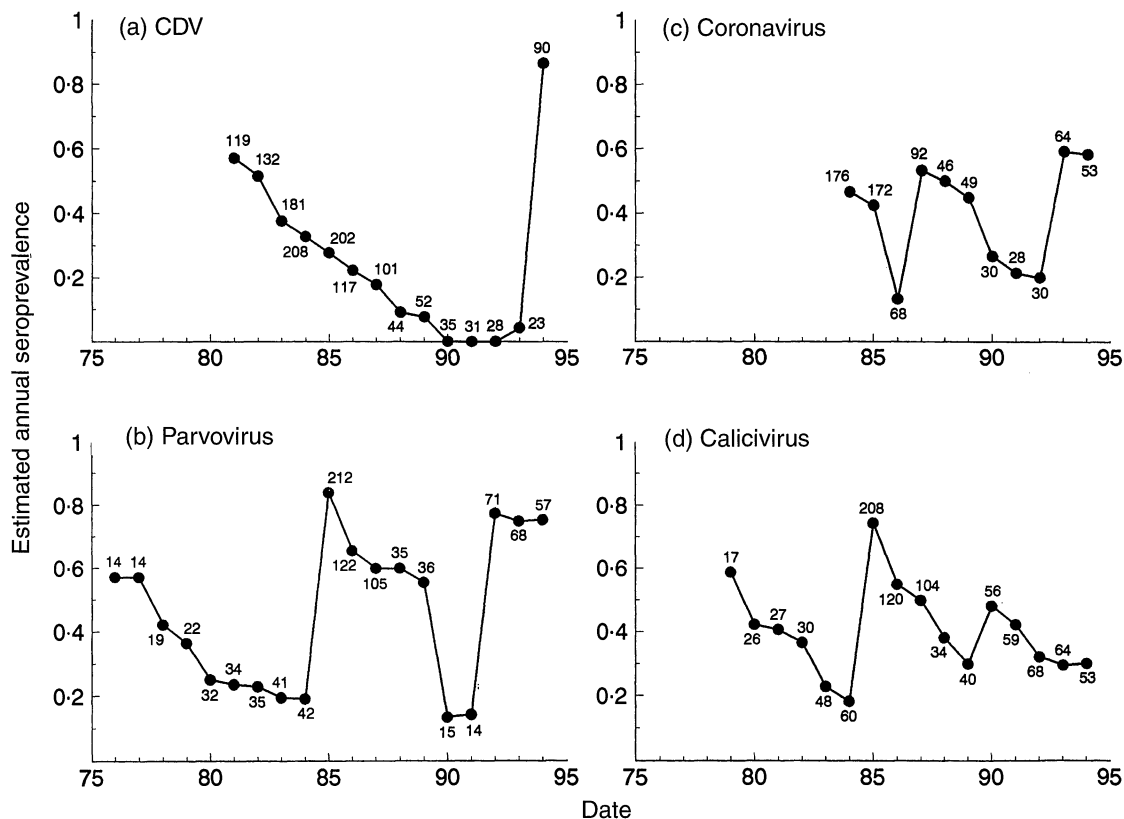


Fig. 9. Estimated annual seroprevalence for each virus in the Serengeti. All seronegatives are assumed to have been seronegative for their entire lives. Seropositives are assumed to have been exposed to the virus at the most recent outbreak, but no assumptions are made about their earlier serostatus.

Table 1). If FIV is similarly harmful to lions, we would expect FIV+ lions to suffer a shorter life expectancy than FIV- lions of a comparable age. Note, though, that all the FIV- animals presumably contracted the virus by their fourth birthday, and

our analysis therefore contrasts the survival of animals infected early in life vs. those that would have been infected at a later age.

Figure 11 shows the annual age-specific mortality of lions according to their FIV status as yearlings (top) or as 2-year-olds (bottom). Data are plotted separately for males and females because of their contrasting life histories as subadults (Packer *et al.* 1988). FIV did not measurably increase mortality either in the short term (when FIV- animals were presumably still uninfected) or in the long term (overall, seven FIV+ animals survived > 10 years). Although these data are too limited to detect subtle effects on mortality, we have seen no clinical signs of immune deficiency except during the CDV outbreak in 1994. CDV is immunosuppressive, but there was no association between clinical pathology and FIV status of CDV victims (Roelke-Parker *et al.* 1996). Further, we found no evidence that co-infection with any of the other viruses influenced longevity of FIV+ individuals (all statistical tests non-significant).

The entire adult population was FIV+, so we cannot assess the effects of viral infection on fecundity.

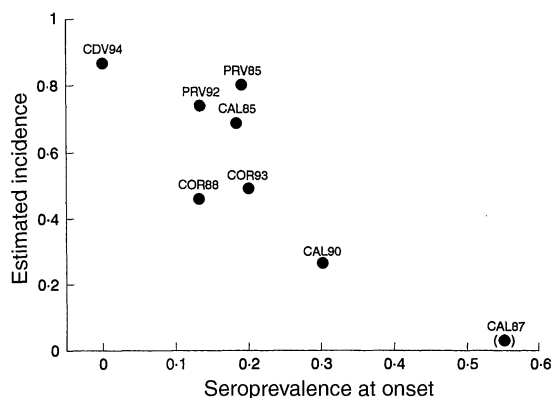


Fig. 10. The 'incidence' of each Serengeti outbreak plotted as a function of the estimated seroprevalence at the onset of the epidemic. Incidence is defined in the text. The 1987 calicivirus 'outbreak' is plotted in parentheses, since it did not spread beyond a single pride.

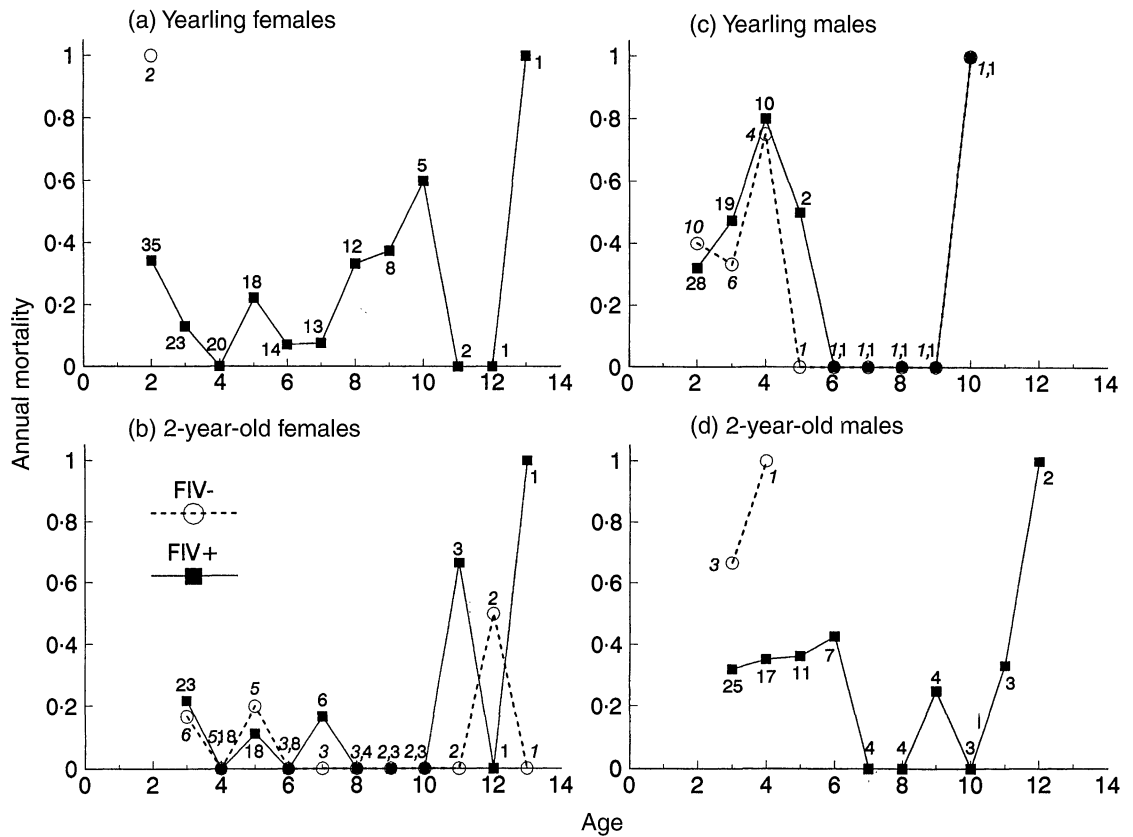


Fig. 11. Age-specific mortality rates of (a) females and (b) males according to their FIV status when sampled between the ages of 1–2 years (top) and 2–3 years (bottom). Sample sizes of FIV+ animals are given in normal type, of FIV- animals in italics. There was no significant effect of FIV status on the mortality rates of either sex or either age-class or in the combined data set.

EPIDEMICS

The sporadic appearance of each epidemic virus enabled us to test whether epidemics coincided with overall reductions in lion mortality or fecundity. For this analysis, we only examine the survival and reproduction of individuals that could have been susceptible to the virus at the onset of each epidemic.

Mortality

Outbreaks of each virus occurred at 4–12-year intervals (Table 4). We therefore restricted our analysis to the annual mortality of lions < 4 years old, since these cohorts consisted entirely of 'susceptibles' at the onset of each outbreak. Cub mortality is of particular interest here, since most disease-induced mortality is restricted to kittens in domestic cats (Table 1). Survival rates in young lions depended on age and fluctuated from year to year (Fig. 12), but there was no consistent pattern associated with any particular virus. For example, cub survival was significantly reduced during the calicivirus outbreak of 1980 ($\chi^2 = 19.35$, d.f. = 1, $P = 0.0000$). Although

cub survival was also below-average in the calicivirus outbreak of 1985, cubs enjoyed higher survival than average during the 1990 calicivirus epidemic. Only the 1994 CDV outbreak inflicted lower survival on every age-group (with significant declines for yearlings ($\chi^2 = 24.09$, d.f. = 1, $P = 0.0000$) and 3-year-olds ($\chi^2 = 10.61$, d.f. = 1, $P = 0.0011$). However, neither the 1981 CDV outbreak in the Serengeti nor the 1980 outbreak in Ngorongoro had any appreciable impact on lion survival, although two Serengeti lions developed myoclonus in 1981.

Without clear signs of illness, we cannot rule out the possibility of a spurious association between a single disease outbreak and a year of low survival. However, the CDV outbreak of 1994 was well-documented and included clearly observed cases of seizures and myoclonus (Roelke-Parker *et al.* 1996). This suggests that the high survival rates during earlier outbreaks of CDV may have been due to non-pathogenic strains of the virus. It was not possible to estimate the extent of the earlier CDV epidemics, but it is at least noteworthy that CDV in 1994 was the most extensive of any documented outbreak and struck the largest population of susceptibles.

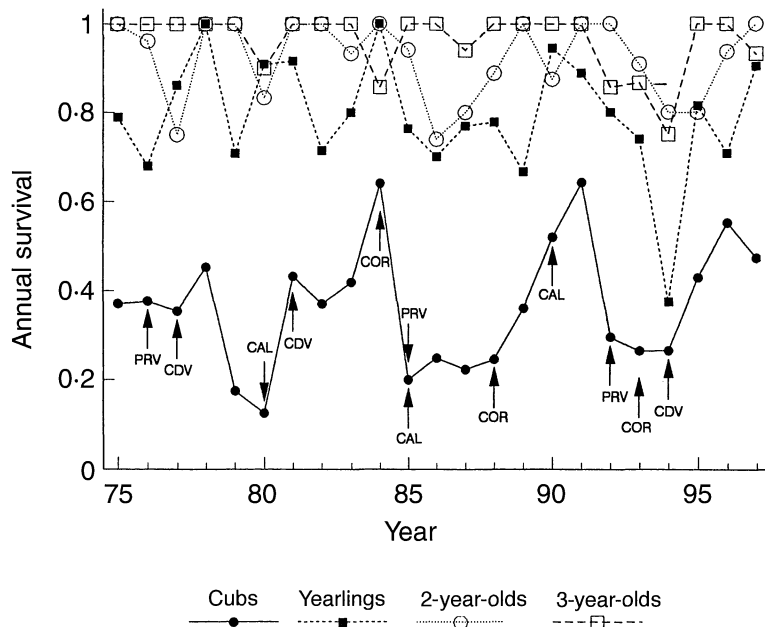


Fig. 12. Annual survival rates for cubs (< 1 years), yearlings (1–2 years), and 2- and 3-year-olds from 1975 to 1997 in the Serengeti. ‘Annual survival’ is defined as the proportion of each cohort that survived to their 1st, 2nd, 3rd or 4th birthday. Approximate end-points of viral outbreaks are indicated by vertical arrows. The only significant declines in survival that coincided with epidemics were for cubs in 1980 (calicivirus), and for yearlings and 3-year-olds in 1994 (CDV, see text).

Unfortunately, we have been unable to collect any blood samples from Ngorongoro Crater since 1991, so we cannot test whether the recent decline in this population (see Fig. 7) was associated with a viral outbreak. A domestic dog with CDV was found on the Crater rim in October of 1994 (Cleaveland 1996), and several of the Ngorongoro Crater lions were conspicuously ill at about the same time, but none showed neurological symptoms of CDV.

Fecundity

We measured ‘fecundity’ as the proportion of females that gave birth during a particular year. Because of high adult seroprevalence for all viruses, adult females could only have been ‘susceptible’ to a virus if the interval between outbreaks was sufficiently long. This analysis is therefore restricted to seven widely-spaced outbreaks in the Serengeti and only includes young (and hence susceptible) females. Because of age-related changes in fecundity (Packer *et al.* 1998), as well as medium-term ecological variations (Hanby *et al.* 1995), we compare the reproductive performance of 4–13-year-old females over the first 2 years before and/or after each outbreak. As in the mortality analysis, none of the four viruses consistently inflicted a significant loss in fecundity, although there seems to be a recurring effect of CDV (Fig. 13). Again, it is possible that there were strain differences, as fecundity was slightly lowered during the 1985 parvovirus and calicivirus out-

breaks. The high annual variation around the 1990 calicivirus and 1993 coronavirus epidemics is difficult to interpret and presumably reflects other ecological factors (such as annual variations in prey availability, population density, and social disruption; see Packer *et al.* 1988)

Conclusions

Temporal variation in seroprevalence indicates that both FIV and herpesvirus are endemic in these lion populations. Both show consistently high prevalence (Figs 1 and 2) and both appear to be relatively harmless, although it is difficult to compare the fitness of infected and uninfected hosts. In domestic cats, FIV follows a similar aetiology as HIV in humans (Pedersen *et al.* 1987; Yamamoto *et al.* 1988; Torten *et al.* 1991) and, like HIV in humans, FIV appears to have infected domestic cats only recently (Rigby *et al.* 1993; Carpenter & O’Brien 1995). We could find no evidence that FIV status influenced lion mortality (Fig. 11), nor did we observe any obvious signs of immunodeficiency or clinical pathology in FIV+ individuals (but see Poli *et al.* 1995). Phylogenetic analysis of FIV sequences in our study animals suggests that lions have been hosts to the virus for long periods of time (Brown *et al.* 1994), and an attenuated effect from FIV infection may have arisen through a variety of co-evolutionary mechanisms (reviewed by Carpenter & O’Brien 1995). Alternatively, studies of domestic cats suggest

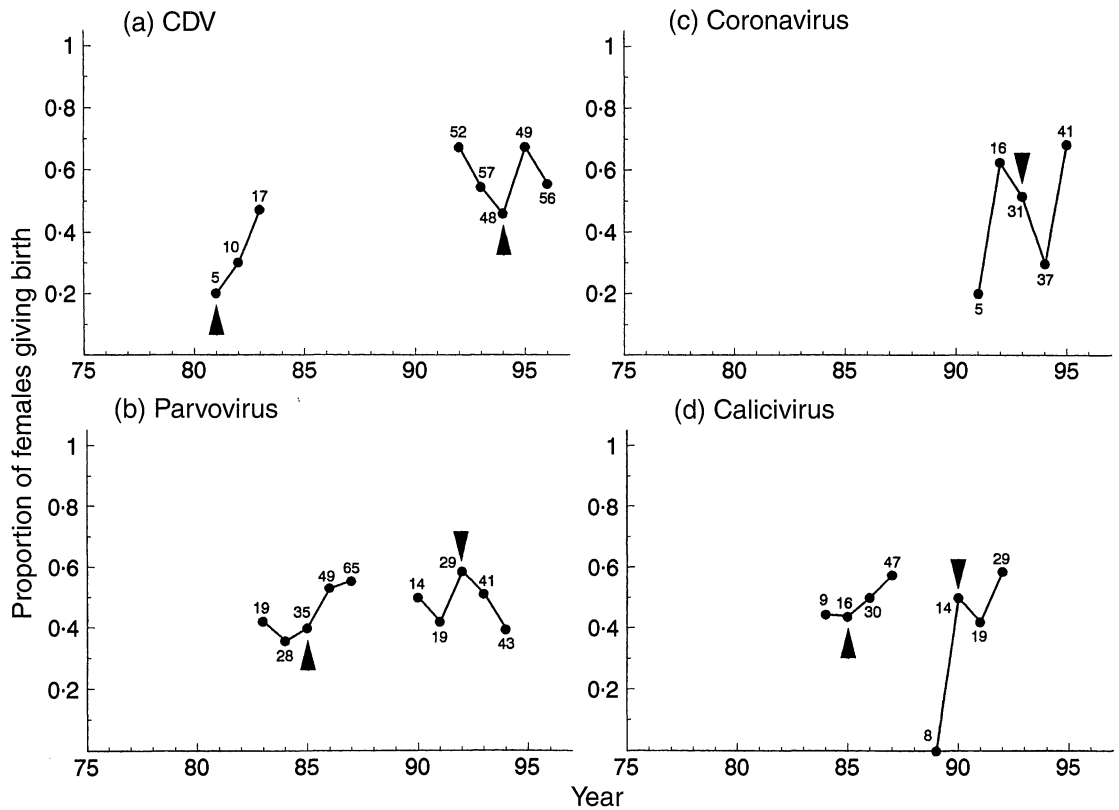


Fig. 13. Annual female fecundity before, during and after associated epidemics. Numbers indicate sample sizes and arrows indicate the years in which the epidemics occurred. For years prior to each outbreak, data only include adult females that had not yet been exposed to the virus. In the year of an outbreak, the data only include adult females who were exposed to the virus for the first time that year. For the following years, data include all adult females who had been exposed for the first time during that outbreak (including females who had been exposed as subadults). Analysis only includes data-points based on at least five females. Annual fecundity varied significantly in the years around the 1993 coronavirus outbreak ($\chi^2 = 14.37$, d.f. = 3, $P = 0.0062$) and the 1990 calicivirus outbreak ($\chi^2 = 8.89$, d.f. = 3, $P = 0.0308$).

that FIV may be more pathogenic in individuals that are co-infected with FeLV (Courchamp *et al.* 1997). Thus, the low impact of FIV in these lions may be because they are not co-infected with FeLV.

The remaining four viruses showed high temporal variation in seroprevalence, indicative of epidemic outbreaks of disease (Figs 3 and 4). These outbreaks typically occurred after a large number of susceptibles were recruited into the population (Fig. 8), and the extent of each outbreak apparently depended on the size of the susceptible host population (Figs 9 and 10). Previous studies have documented the existence of threshold host densities for the establishment of pathogens in natural populations (Jaffee *et al.* 1992; Dobson & Hudson 1995; Dobson & Meagher 1996). In the lions, calicivirus, parvovirus, and to some extent coronavirus showed evidence that viral invasion required a threshold density of susceptible hosts (Fig. 8). Minimum estimates of susceptible host density varied among the viruses, and ranged from 75 to 200 animals in the Serengeti study area (which includes about 10% of the overall Serengeti lion population).

Viruses that were associated with higher initial rates of spread (as estimated by our measure of 'incidence') also required the highest threshold densities of seronegative hosts. For example, calicivirus and coronavirus outbreaks occurred when susceptible host densities were relatively low and were associated with smaller increases in seroprevalence. In contrast, parvovirus required a larger number of susceptibles and infected a larger proportion of susceptibles during outbreaks. CDV is both the exception and the rule for this pattern. CDV infected numerous carnivore species in the late 1970s, as well as in 1994 (reviewed in Roelke-Parker *et al.* 1996; Cleaveland 1996), so the 'susceptible population' of only 75 lions in 1981 and over 200 lions in 1994 actually included uncounted numbers of susceptible canids, hyenas and other large felids. However, the lion population was not only large, but also 100% susceptible during the 1994 CDV epidemic, and over 85% of the lions were infected within a few months.

None of the epidemic viruses consistently lowered host fitness. The 1994 CDV outbreak was conspicuously harmful (as emphasized by the sharp decline

in the Serengeti population, see Fig. 7), and the 1980 calicivirus epidemic may have inflicted considerable cub mortality, but other outbreaks of these same viruses appeared to be essentially harmless. Indeed, none of these viruses regularly inflicted the same degree of mortality observed in domestic cats (Table 1). Sequence data are only available for the 1994 CDV strain (Roelke-Parker *et al.* 1996), so we cannot make similar assessments of co-evolutionary history as for FIV, nor can we comment on genetic differences between strains of the same virus. However, strain differences in pathogenicity have been well documented in other morbilliviruses besides CDV (e.g. rinderpest, Plowright 1982). It is also possible that all of these viruses were harmful to some extent, but our demographic analysis was too coarse-grained to detect their effects. The timing of each outbreak was estimated retrospectively, we could not control for confounding interactions with other ecological variables, and the lions were no doubt co-infected with additional pathogens and parasites. No field analysis could ever provide the sort of comparisons that would be available from controlled experiments (Dobson & McCallum 1995).

Dobson & McCallum (1995) and Jaenike (1998) have shown that host populations can be limited by pathogens that inflict moderate effects on host mortality and moderate to large effects on fertility. Out of all the viruses included in this study, only CDV appears to be sufficiently virulent to cause measurable declines in the Serengeti/Ngorongoro lion populations. CDV caused considerable mortality in 1994 and may have lowered host fertility during the 1981 and 1994 outbreaks. However, CDV entered the lion population in discrete, widely-spaced epidemics, and these epidemics have been sufficiently infrequent to inflict lasting consequences. The Serengeti population recovered rapidly from the 1994 epidemic, regaining its former size by the middle of 1997 (Fig. 7). Domestic dogs are the primary reservoir for CDV in the Serengeti/Ngorongoro region (Cleaveland 1996), and the dog population has grown dramatically with the growing human population over the past 30 years, raising the prospects of more frequent, extensive, and virulent CDV epidemics in the lions and other wild carnivores. Attempts to inoculate this reservoir against CDV are currently underway (Kaare & Cleaveland 1997).

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