

Disease Risk and Inter-institutional Transfer of Specimens in Cooperative Breeding Programs: Herpes and the Elephant Species Survival Plans

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Managers of cooperative breeding programs and re-introduction projects are increasingly concerned with the risk of disease transmission when specimens are transferred among facilities or between facilities and the natural environment. We used data maintained in North American studbooks to estimate the potential risks of disease transmission by direct and indirect contact of specimens in the American Zoo and Aquarium Association's Elephant Species Survival Plan. Histological evidence for a novel herpesvirus disease transmitted between and within elephant species housed in North American facilities prompted an examination of the scope of possible transmission routes within the captive population. We found that, compared with other species managed through Species Survival Plans, elephants experience relatively few transfers between zoos. Nevertheless, the number of direct contacts with other elephants born during the study period of 1983–1996 (excluding stillbirths) was much higher than we had anticipated ($\mu = 25 \pm 27$; $N = 59$) and the number of potential indirect contacts was surprisingly large ($\mu = 143 \pm 92$; $N = 59$). Although these high rates of potential contacts complicate exact identification of infection pathways for herpesvirus, we were able to propose potential routes of transmission for the histologically identified cases. Furthermore, the extraction of data from studbooks allowed us to readily identify other specimens that did not succumb to the disease despite similar exposure. Moreover, we were able to identify other possible cases to recommend for histological examination. Herein we reveal the possibilities of multiple disease transmission pathways and demonstrate how complex the patterns of transmission can be, confounded by the unknown latency of this novel herpesvirus. This emphasizes the need for zoo veterinarians and cooperative breeding programs to consider the full potential for disease transmission associated with each and every inter-zoo transfer of specimens. Zoo Biol 20:89–101, 2001. © 2001 Wiley-Liss, Inc.

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INTRODUCTION

Cooperative management programs, such as the American Zoo and Aquarium Association's (AZA) Species Survival Plans (SSPs) treat all specimens in a region as a single population. SSPs make breeding recommendations that require transfer of specimens among participating institutions and coordinate transfers of specimens for display and re-introduction into the wild. Managers and veterinary advisors to these programs are becoming more concerned about the risks of disease transmission associated with movement of specimens among institutions and/or between those institutions and natural habitats. Baseline risk of disease transmission between animals in managed populations depends on the frequency of movement between the sub-populations maintained at individual institutions. Extraction of this information from paper records has proven complicated, hampering complete assessment of potential routes and rates of direct and indirect disease transmission. Therefore, we designed software to extract the relevant data from North American regional studbook databases maintained in the Single Population Analysis and Records Keeping System (SPARKS) 1.42 software [International Species Information System, 1996]. In this paper, we use the North American captive African and Asian elephant populations as a means to examine the magnitude of disease risk in a captive population. Furthermore, we examine the utility of studbook data in evaluating routes of transmission for a newly described herpesvirus determined to cause significant mortality in elephants [Richman et al., 1999].

North American regional studbooks are maintained as electronic databases by studbook keepers who collect and verify all records for a single species at all institutions throughout the region. Each studbook contains the entire life history of a captive population: the date and location for all imports from the wild, transfers among institutions, births, sire identity, dam identity, and deaths are maintained within the database. The data amassed on a single species in a studbook may stretch back to the past century, providing a rich resource for population management, genetic analyses, and epidemiological research. Thus, with careful consideration of missing data and other data quality issues [Earnhardt et al., 1995], the locational and genetic history for each individual can be extracted from many of the more than 350 studbooks for species in North American zoos and aquariums.

One would expect that the difficulty and expense of transferring elephants among institutions would result in relatively low levels of disease transmission. The Asian Elephant SSP was officially initiated in 1985 and was combined with the African Elephant SSP in 1990. Although most SSPs have made many recommendations for inter-zoo transfers, elephants are large and require much preparation and financial support to move. These logistical factors, added to rising concerns about disease risk in general and tuberculosis in particular, should act to minimize inter-zoo transfers of elephants. Nevertheless, recent reports suggest that virulent diseases such as a novel herpesvirus [Richman et al., 1999] and tuberculosis [Mann et al., 1981; Saunders, 1983; Hancox, 1991; Michalak et al., 1998] have moved through the Asian and African Elephant SSP populations.

Historically, African (*Loxodonta africana*) and Asian (*Elephas maximus*) elephants have either shared enclosures or have been housed such that direct contact is

possible. Only in recent years have institutions begun to separate the species as a result of moving conspecifics together for managed breeding purposes [M. Keele, personal communication]. Although African and Asian elephants may share enclosure requirements, be behaviorally compatible, and appear to successfully share their captive homes, their disparate geographic origins may make either species susceptible to endemic, non-clinical diseases originating in the other species.

Richman et al. [1999] reported that the high mortality rate of elephants born in North American zoos is attributable partly to the presence of two new herpesvirus strains, one originating in the wild African elephant population and the other from the wild Asian elephant population. They interpret necropsy data for 10 Asian and two African elephants to indicate that under unspecified environmental conditions such as stress, cross-infection of young specimens of either species may prove fatal. However, they were unable to test all routes of transmission and, more important, were unable to examine potential risks of transmission to those specimens that did not succumb to this disease.

We used data from Richman et al. [1999] to prepare a template for further studies of intra- and inter-specific disease transmission contacts within studbook populations. This disease calls attention to the circumstances by which it is possible for transmission to occur in captive populations of endangered species. Herpesviruses, once outside the host, are not long-lived or hardy and therefore cannot simply be transmitted in an aerosol or indirect manner through keepers' boots or food handling. Herpesvirus transmission entails intimate contact; in the case of these elephants, trunk examination of lesions or pseudo-sexual contact across species is a likely explanation of initial transmission. Richman et al. [1999] cite evidence of this particular herpesvirus in free-ranging African elephants. However, in captivity, it appears to affect young Asian elephants most severely, calling attention to the potential effect of disease on the viability of the captive Asian elephant population.

Our study demonstrates a risk for disease transmission through indirect contact with other specimens in the managed population. Within this context, we examine possible routes of transmission within the North American regional studbook populations for the newly described herpesvirus disease. We also compare the rates of mortality attributed to this disease with mortalities of individuals with no direct or indirect contacts with identified disease cases. These represent the first comprehensive analyses of disease transmission potential and routes for managed populations in North America using advanced computer modeling techniques.

METHODS

We used data from the North American regional studbook for Asian elephants [M. Keele, current to July 1, 1997] and African elephants [D. Olson, current to February 5, 1999]. Data were extracted from the SPARKS [Single Population Analysis and Record Keeping System, ISIS, 1996] databases using an un-compiled Visual D-base program, TYPHMARY, written expressly for this purpose [Thompson, 1999]. Because Richman et al. [1999] suggested that the novel herpesvirus is transmitted cross-generically, we combined the African and Asian databases to permit detection of possible transmission within and between the two species. For this study, the presence of both species at an institution simultaneously is our best indicator of the potential for inter-specific transmission of disease. The SSP has recommended that the

species be housed separately, although this recommendation was issued in the last year for which we consider data. Furthermore, even with separate housing, trunk examination through adjoining spaces is often possible. Therefore, the assumption of contact based on simultaneous occupation of an institution is valid. For purposes of this paper, we consider a direct contact to occur when specimens reside at the same institution simultaneously. Indirect contacts are defined as specimens that had previously been in direct contact with one of two specimens in direct contact. To avoid duplicating the records, the Asian elephant studbook was re-coded for our analysis, putting the prefix X before the studbook number. For this part of the analysis, the data extracted were restricted to the period 1980 through 1997 to accommodate all cases identified in the original study [Richman et al. 1999].

CEFSTAT is an un-compiled D-base program [Thompson, 1997] used to extract data from SPARKS and tally the number of inter-zoo transfers per year. It was written to extract information from SPARKS data sets on the number of births, moves between institutions in North America, imports (from outside North America), wild captures, deaths, neonatal deaths, etc. TYPHMARY then extracts data by tallying each direct contact for each specimen in the population as that specimen moves from institution to institution. Dates and durations of direct contact are recorded specimen by specimen. The resulting data set permits analyses of any and all direct contacts as a function of location and date. For any given specimen, indirect contacts are recorded as the direct contacts experienced by each specimen listed as a direct contact with the index specimen (Fig. 1A). Because this approach could be extended ad infinitum, we give these indirect contacts ordinal nomenclature, e.g., secondary indirect contacts are those animals in direct contact with our primary indirect contacts, who are in direct contact with animals who were in direct contact with the index case in question (Fig. 1B). Intra-institutional redundancies are removed to prevent inflated data. CEFTSTAT and TYPHMARY were extensively tested by direct comparisons with hand-tallied subsets from several studbook databases.

Using the indirect contact data, it was possible to hypothesize transmission of the disease with tertiary contacts. Furthermore, these data allowed us to suggest possible transmission routes, demonstrating two sets of circumstances in the elephant population. These routes link the cases for which we have confirmed histological evidence of this herpesvirus and are demonstrated in a chronological flowchart. Each institution presents several potential routes and directions for infection, but by tracing back to cases of direct exposure to known infected animals, possible transmission pathways can be elucidated. In this figure, cases are numbered, cohort elephants that are potential carriers are represented by pedigree shapes and the hatched shapes denote African elephants. Actual studbook numbers and institution names are withheld by request. With approval from the SSP and participating institutions, the true data will be made available to bona fide researchers.

Richman et al. [1999] listed 10 cases from which serum and tissues were obtained (Table 1). Two additional cases were identified as having similar mortality report descriptions; however, tissue samples were not examined. Of the 10 confirmed cases, two are African elephants (2 and 8) and the remaining eight are Asian elephants. Cases were identified by studbook number using information furnished by the article on institution location and using the database for both African and Asian elephants in the North American population. The studbook data also showed an Asian

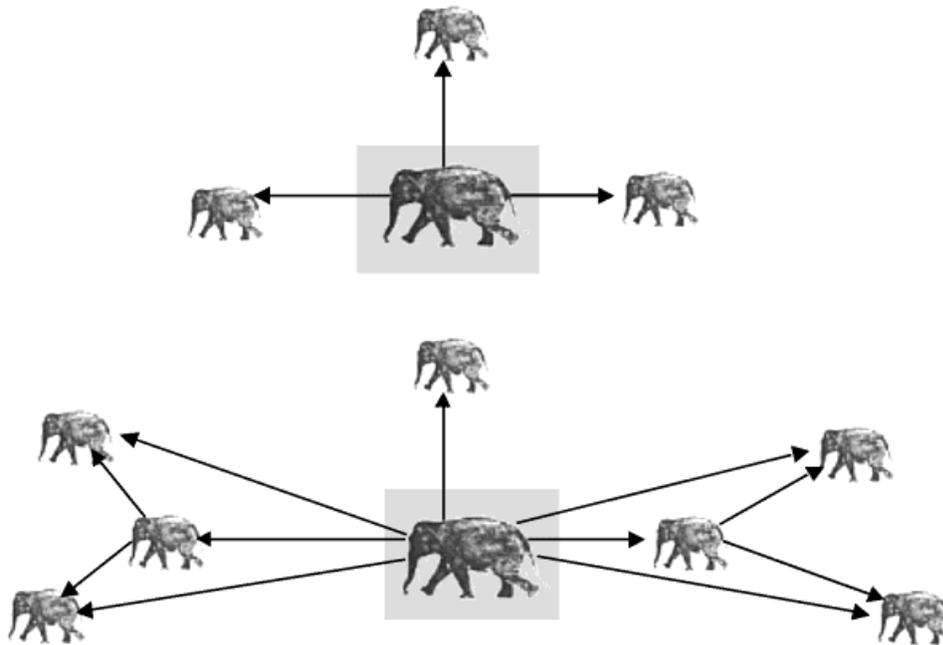


Fig. 1. **A:** Index case elephant (in shaded box) has three direct contacts, denoted by the solid line arrows. **B:** Index case elephant (in shaded box) now has three direct contacts and four indirect contacts, denoted by the dashed-line arrows. [Note that this now creates a series of direct, primary indirect and secondary indirect contacts between the elephants in the diagram].

elephant that was transferred to Europe, where it died of a viral disease. This mortality has since been attributed to the same herpesvirus [R. Montali, personal communication], and this case is included in our analyses as case 13.

A multi-way log-linear regression was used to determine whether our set of cases were any more prone to contacts than cohorts in the population (Table 2).

TABLE 1. Suspected cases of herpesvirus in African and Asian elephants

Case	Species	Birth location	Birth date	Death date	Age at death	Last location
1	Asian	Z	14 Dec 93	26 Apr 95	1Y, 4M, 11D	Z
2	African	Z	3 Nov 95	7 Oct 96	11M, 4D	Z
3	Asian	Z	2 Jul 96	Cured	—	Z
4	Asian	Z	20 Aug 81	26 Jan 83	1Y, 5M, 7D	Z
5	Asian	Wild	~1958	17 Jan 86	~28 Y	Z
6	Asian	Z	1 Feb 84	26 Aug 88	4Y, 6M, 26D	Z
7	Asian	Z	7 Dec 88	2 Sep 91	2Y, 8M, 26D	Z
8	African	Wild	~1981	12 Nov 91	~12Y	Z
9	Asian	Z	26 Jul 91	28 Feb 93	1Y, 7M, 5D	Z
10	Asian	Z	5 Oct 86	26 Nov 93	7Y, 1M, 24D	Z
12	Asian	Wild	1982	25 Dec 87	5Y est.	Z
13	Asian	Z	31 Dec 87	30 Aug 98	10Y, 8M, 32D	Z

Y, year; M, month; D, day.

TABLE 2. Direct and indirect contacts by age for all non-stillborn African and Asian elephants born between 1983 and 1986

	African elephants		Asian elephants		All elephants	
	Direct contacts	Indirect contacts	Direct contacts	Indirect contacts	Direct contacts	Indirect contacts
Dead cases						
Age 1 (0–4.9)	9	100	39	284	48	432
Age 2 (5–9.9)	0	22	14	36	14	72
Age 3 (10–13.9)	0	0	0	0	0	0
Subtotal	9	122	53	320	62	504
Mean (\pm SD)	1.13 \pm 1.642	15.3 \pm 8.97	7.75 \pm 4.138	40.0 \pm 25.3	7.75 \pm 3.37	63.00 \pm 32.3
Other elephants						
Age 1 (0–4.9)	34	631	652	1,980	686	3,297
Age 2 (5–9.9)	21	411	219	1,679	240	2,330
Age 3 (10–13.9)	49	455	420	1,406	469	2,330
Subtotal	104	1,497	1,291	5,065	1,395	7,957
Mean (\pm SD)	2.04 \pm 2.93	29.4 \pm 19.6	25.3 \pm 29.0	99.3 \pm 59.8	27.3 \pm 28.3	156.0 \pm 91.7
Total for all	113	1,619	1,344	5,385	1,457	8,461
Mean for all (\pm SD)	1.92 \pm 2.80	27.44 \pm 19.1	22.8 \pm 27.7	91.3 \pm 59.9	24.7 \pm 27.2	143.4 \pm 91.7

Cases born 1983–1996 (n = 8).

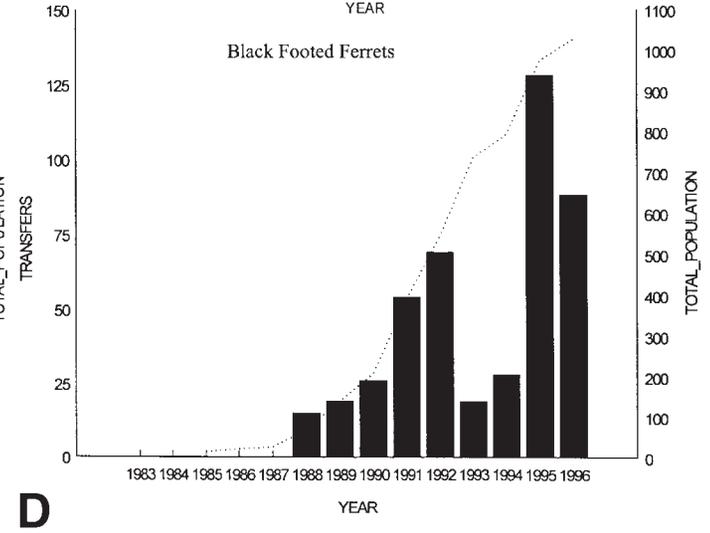
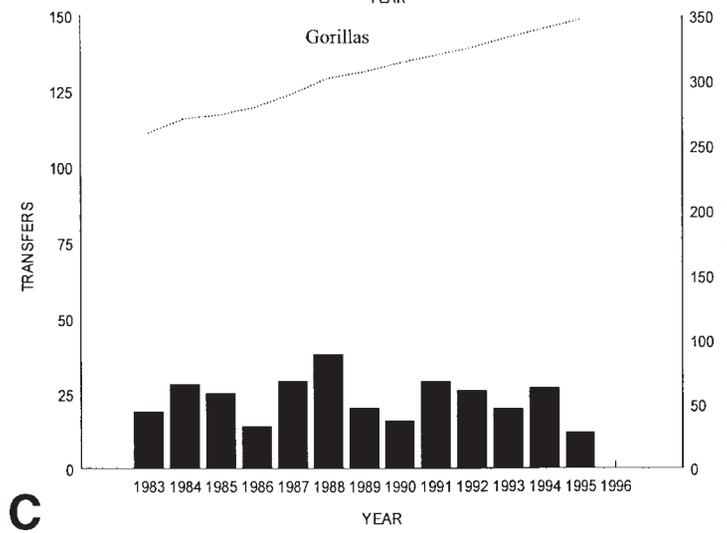
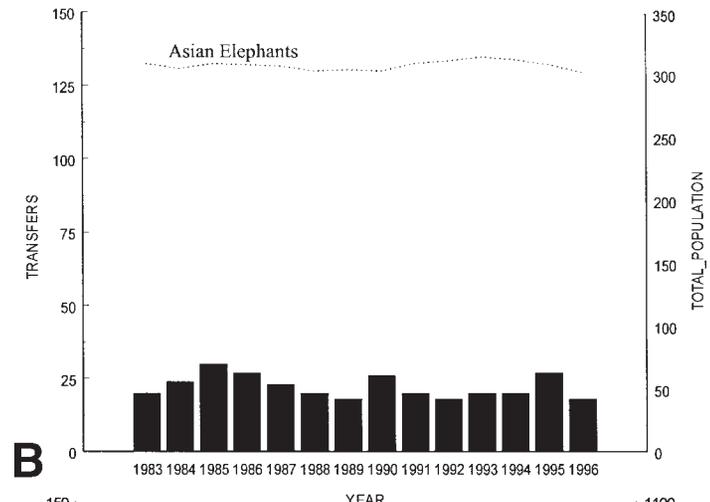
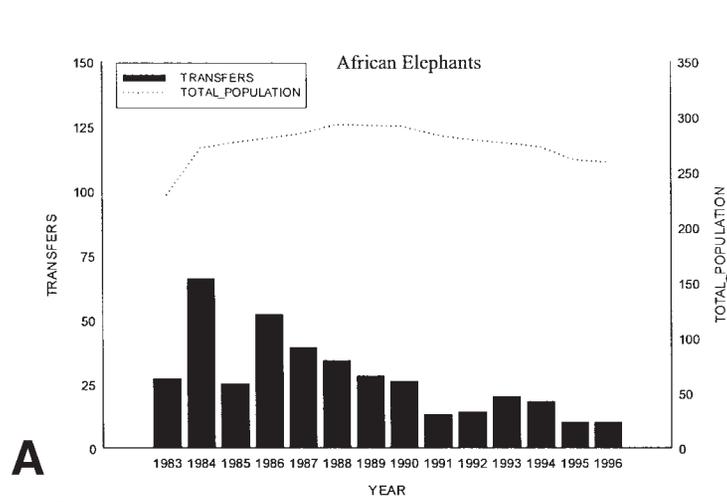
Other elephants, minus stillborns, born in 1983–1996 (n = 59).

RESULTS

Over a similar range of population sizes, African elephants have higher numbers of transfers per year (range, 10–66) than Asian elephants (range, 18–30; Fig. 2A,B). These rates are comparable with those of another large mammal, the western lowland gorilla, over the same time period (range, 12–38; Fig. 2C). Elephants and gorillas are large, long-lived mammals with long inter-birth intervals and small captive populations. Therefore, they require careful planning to transfer. Contrasting these to a smaller mammal species (the black-footed ferret), we see that the larger mammals have relatively low numbers of transfers over approximately the same time period, confirming our assumption (black-footed ferret range, 0–128; Fig. 3D).

In both elephant species during the study period of 1983–1996, direct and primary indirect contacts were surprisingly high (Table 2), even for the young specimens that succumbed to the novel herpesvirus (Fig. 3). During 1980–1996, the infant mortality rate for captive births was also high, both for African and Asian elephants. Of 85 Asian elephants born in captivity, 35 (41.2%) died; of these, 20 (57%) were premature or stillborn. Of only 18 African elephants born in captivity, nine (50%) died, but none were premature or stillborn. Of the 47 indirect contacts between the 12 identified cases in Table 1 and captive elephants that were born between 1980 and 1996, 20 (43%) of the pregnancies resulted in death or stillbirth. Of these con-

Fig. 2. The number of transfers per year for four mammals in SSPs. **A:** African elephants; **B:** Asian elephants; **C:** western lowland gorillas; **D:** black-footed ferrets. The primary y-axis is number of transfers (bars), the secondary is the number of animals living in the population (solid line) at the year (x-axis) of transfer.



tacts, 15 (one African, 14 Asian) were common to two or more cases, and the remaining 32 (5 African and 27 Asian) were traced to seven of the cases. Nine (60%) of the common contacts (one African, eight Asian) died; of these, seven (47%, all Asian) were stillborn. Of the remaining 32 indirect contacts from this cohort, 11 (34%, one African, 10 Asian) also died, and of these, seven (22%, all Asian) were stillborn. Thus, of the 47 total indirect contacts, 30% were stillborn Asian elephants.

Log-linear analysis demonstrates that the identified cases were at no greater contact risk than their cohorts. The mean number of direct and indirect contacts for case specimens that died and cohorts that survived differed significantly among ages and between species (Table 2; log-linear analysis, $P < 0.001$), with significantly fewer contacts for specimens that died and for African elephants. However, younger specimens that died had more contacts than older specimens, whereas older specimens that lived had fewer contacts than younger specimens (Table 2).

Tracing the direct and indirect contacts for elephants in Table 1 confirmed that although institutions may have kept both species simultaneously, there were in fact no direct contacts between any of the cases identified in the study. However, in cases 1, 6, 7, and 8 (Table 1), there had been many cross-species direct contacts (Fig. 3A). In many cases, the number of indirect contacts for each case show more than a 10-fold increase over direct contacts (Fig. 3B). This continues to rise as more indirect contact levels are added.

Figure 4 shows the two possible routes of transmission of this herpesvirus within the North American regional studbook populations of elephants. The first case that appears chronologically is case 5 in P1 during the period 1958–1961; it was there concurrently with three cohorts whose studbook death notes seem to describe the pathology of the herpesvirus and others that are not included for reasons of space and discontinuity in our routes. Elephants held at this institution concurrently may have transmitted the disease to case 5, or contracted it from case 5 or, equally plausibly, from another animal that was infectious. What we can ascertain from the records is that some elephants died, as portrayed by the thick-bordered shapes in the flowchart. Case 5 was transferred to an institution in Canada eventually, where she died (Table 2). As we follow the arrows (Fig. 4), the male does not move further because he died at P1. The Asian female cohort was transferred to Z2, where it encountered a male, who in turn was transferred to Z4 to sire case 10. He was also at Z3, where he may have contracted the virus when he contacted another male African elephant, which died of an unidentified infection. At Z3, there are two potential female Asian elephant carriers who may have contracted the virus and later exposed case 4 to it at Z5 the early 1980s. From the point of origin at P1, elephants that may have been infected radiated out to varying locations across North America such as Z1, where they may have indirectly infected many animals, including cases 6, 7, and 13. At Z11, the possibility of contacting an infected individual was quite high, with three siblings all contracting the viral disease.

In this central part of the diagram, there is a dichotomy of transmission patterns. The lower branch suggests African elephant carrier possibilities, involving an African elephant death as we trace through the institutions P2, P3, and P4. It is likely that the disease was initially introduced from the wild population by importing elephants to a private institution and that the central part of the diagram is a possible point of re-introduction of the virus from the wild in the early 1980s. This central transmission pathway emphasizes the low morbidity of the disease because it seems to travel innocuously, with clinical signs striking only young elephants [Richman et al., 1999].

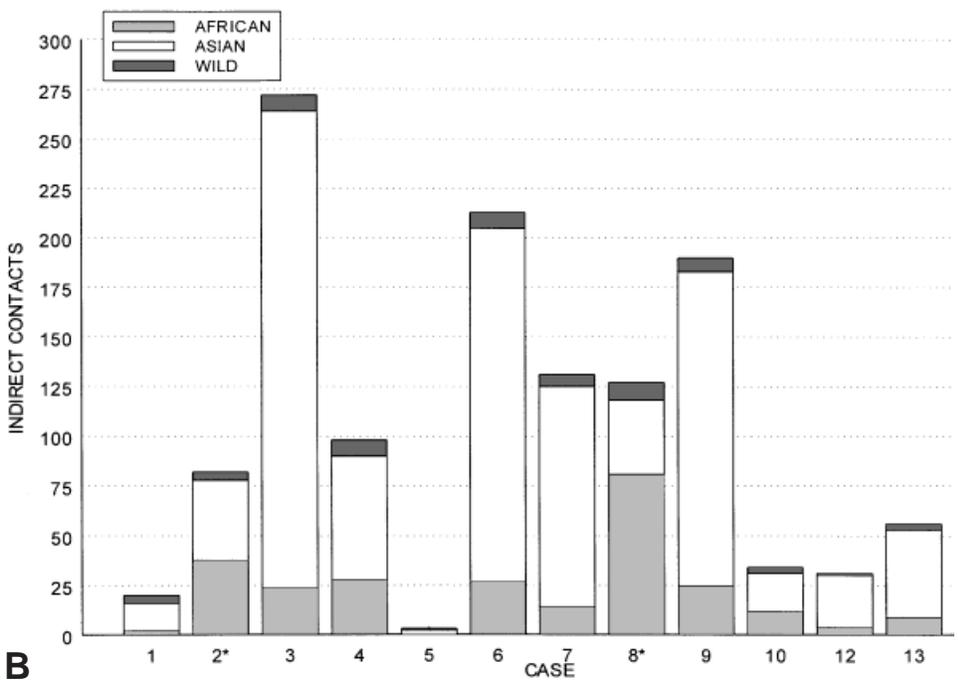
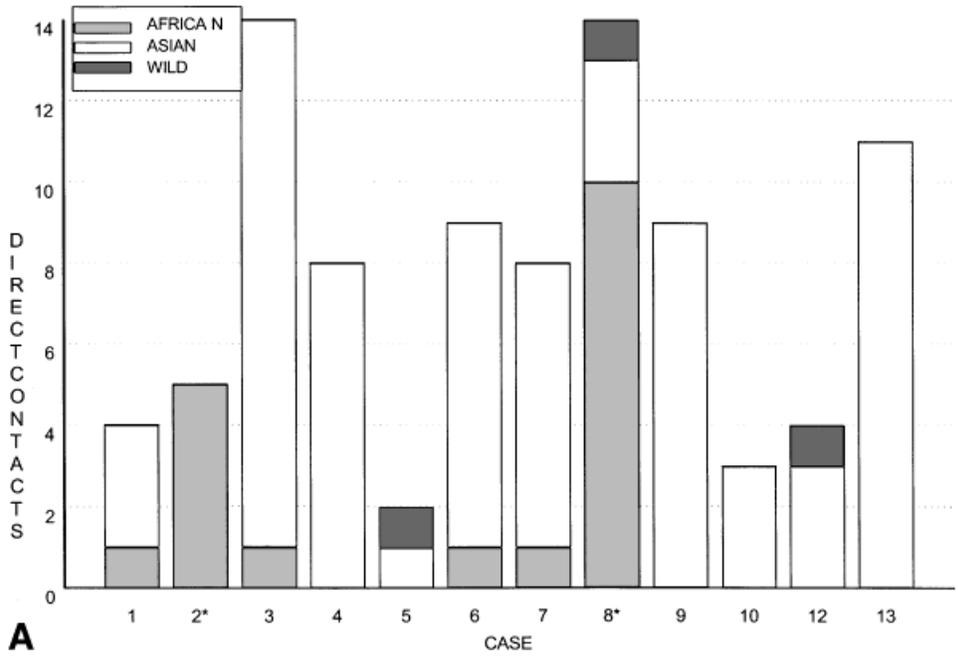


Fig. 3. The number of direct (A) and indirect (B) contacts for the 12 cases. The three possible categories of contact are African elephants, Asian elephants, and wild contacts in the instance of initial importation. (Note the different scales.) Cases 2 and 8 are African elephants.

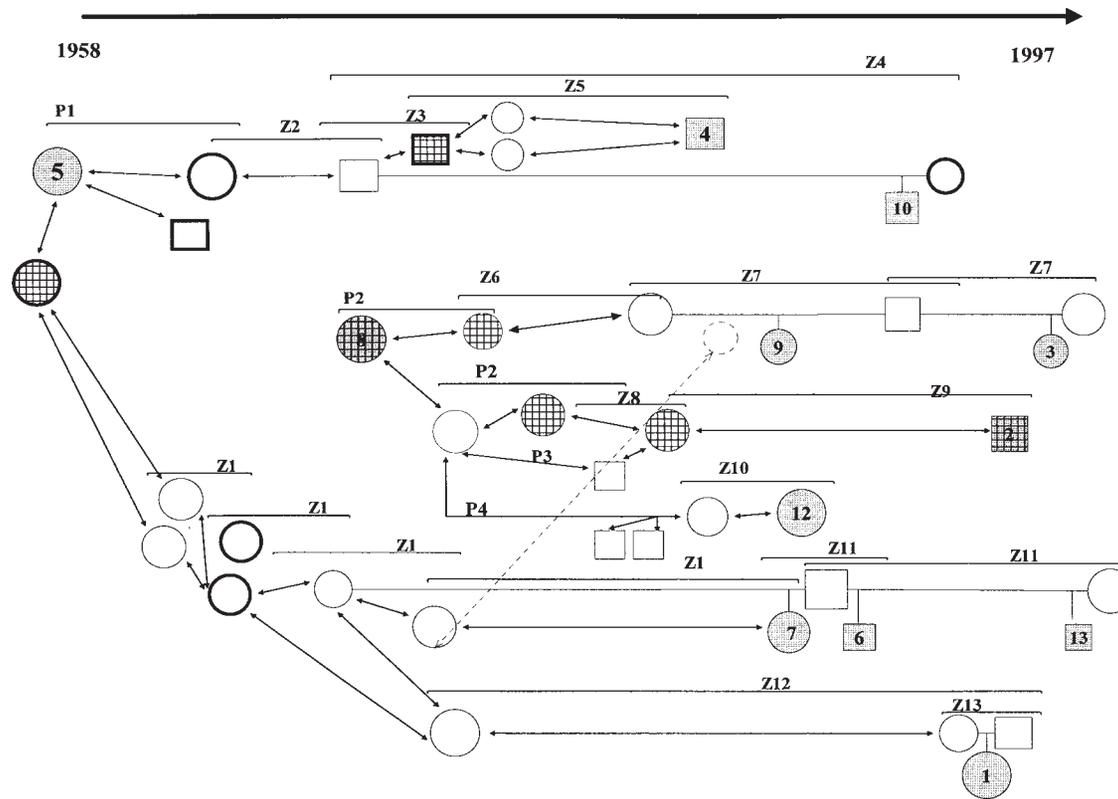


Fig. 4. Possible transmission routes for the novel herpesvirus disease, moving through the captive North American populations of elephants. Shaded shapes are cases, as numbered, 1 to 13; shapes with thicker outlines are elephants that we suspect died of the herpesvirus. Hatched individuals are African elephants; all others are Asian elephants. As with pedigree charts, females are circles, males are squares, and solid connecting lines with descendants are per pedigree format. Solid lines with arrow connections demonstrate direct contacts. Brackets with institution codes (Z, zoo; P, private parties) denote simultaneous occupation of a location.

DISCUSSION

This study examining the possible contacts in a population of two species often housed together in institutions gives us some insight into the disease transmission risks involved in small population management. Although there is a low frequency of movement in large animals, it can still allow a large number of potential disease exposures. Thus, concerns are well founded that movement of specimens between institutions, such as those cooperating in an AZA SSP program, poses substantial risks of disease transmission. For a disease such as this novel herpesvirus, which seems to normally manifest itself as an endemic, non-infectious disease with low morbidity in African elephants, disease management is greatly complicated by the large number of direct and indirect contacts that are typical of specimens in the North American elephant populations. In addition, because the circumstances under which the disease becomes infectious and even fatal are not clear, this further complicates identification of risk levels and the route of transmission.

However, the possible contact routes for the disease gave us insight into the level of contacts achieved in small population management. Clearly the use of stud-book databases to identify the scope of contacts, as well as specific contacts, is a potentially powerful tool for the study of disease risk in managed populations. The sheer number of indirect contacts produced by the moves of individual elephants in the population (e.g., 272 indirect disease transmission possibilities in less than 2 years for case 3) could not readily be assessed from paper records. Moreover, construction of potential transmission routes puts these contacts in the temporal perspective necessary to identify potential new cases of a disease and/or specimens that are or were at high risk of developing the disease sometime in the future. Although we have described (Fig. 4) what we believe to be the simplest route of transmission, more complex routes are clearly possible.

A population approach to this study allowed us to trace the disease as it may have spread through the population of elephants in North America. Although the number of second-order indirect contacts (those in direct contact with first indirect contacts) was staggering, it allowed us to hypothesize a simple and likely transmission route based on the presence of animals at or passing through the same zoos or private institutions (Fig. 4). As pointed out by Richman et al. [1999], there are institutions that have had cases many years apart; there are also animals that have contacted each other more than once at different institutions. The simple transmission route that we developed is chronologically possible and logistically feasible given the locational data in the studbook. However, it was constructed largely by linking mortalities identified by Richman et al. [1999] and assumes a relatively linear unidirectional route of transmission. More convoluted routes are possible, with the most complex scenario being that the disease is widespread within the captive populations and is either asymptomatic or goes unreported unless mortality results.

Richman et al. [1999] posit a high rate of early mortality in captive-bred elephants. In re-examining the data using an alternate source, we find that this is slightly more severe than they attest to. Their synopsis of infant birth and mortality data obtained from AZA printed studbooks is that "between 1983 and 1996, 34 Asian elephants were born in North America...seven of these animals have died with lesions attributed to the endotheliotropic herpesvirus disease" [p 1173]. Extraction of all birth data from the SPARKS databases for this time period reveals 75 Asian elephant births in North America, of which 31 died before 1996. Fourteen of those

deaths were stillbirths, and 16 others are due to bacterial or viral infections, environmental and/or behavioral conditions, or unknown causes. Richman et al. [1999] provided histological evidence suggesting that the virus is additionally responsible for stillbirths; thus mortality due to this disease may be greater than initially indicated. The captive births of African elephants during this time period are just as discouraging with seven births, of which there were five deaths (none were stillborn but three did not even survive a week).

The presence of indirect links between the cases in this study also raises the issue of inconspicuous carrier animals. Although the data do not yield a consistent picture of carrier elephants, it is plausible that adult female Asian elephants, displaying non-pathogenic herpetic lesions, can pass on the virus through intimate contact. Based on this supposition, we can recommend histological investigation of additional specimens (Fig. 4) that died “in the right place at the right time.” These specimens not only present possible new cases for investigation but may also have infected their institutional cohorts and are continuing to do so. This allows us to make precautionary recommendations for animal enclosures and assist veterinarians further in containing this disease. Richman et al. stipulate that the herpesvirus strain in the wild African elephant population remains essentially latent, although displaying “external herpetic lesions.” Asian elephants develop a fatal endothelial disease from this same strain in the early years of life, which the authors attribute to a cross-species infection by the African strain. In fact, a latent vaginal virus disease was described for a mixed species herd in 1983 [Leach, 1983], in which an African elephant appeared to have a non-irritant blister-causing virus. They also noticed that two of the Asian elephants had a similar syndrome but with apparently different pathology. That this ongoing, slow-cycling, vaginal blister disease was the same virus is unclear, but the elephants described are prime candidates for carriers. In this case, we would recommend that the two species be separated and monitored.

The viability of captive populations of endangered species is often measured in terms of demographic and genetic analyses, but with a novel disease in the elephant population that could affect infant mortality to such a degree, we realize that disease risk must play a larger role in management decisions. Asian elephants are somewhat successful at breeding in captivity, but the captive African elephant population still must be stocked with wild-caught animals, which not only provides repeated opportunities for foreign pathogens to enter this small captive population but is both logistically and financially costly.

CONCLUSIONS

1. Extraction of data from electronic SPARKS studbook databases offers an important, novel approach to assessing potential routes of disease transmission and identifying specimens with potential exposures to infectious diseases within captive populations.
2. Our analyses reveal surprisingly high levels of direct and indirect contacts within and between the North American captive elephant populations. This suggests that, even for species with relatively low rates of inter-zoo transfers, the risk of disease transmission is very high.
3. Although elephants have relatively few inter-zoo transfers compared with other species in captive populations, the intricacy of our simplest route of

transmission emphasizes how complex the potential routes of disease transmission can be, even when virtually all of the potential contacts are known.

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