Risk factors associated with development of poxvirus lesions in hospitalized California sea lions

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Objective—To identify risk factors that may predispose California sea lions (*Zalophus californianus*) to development of cutaneous poxvirus nodules during hospitalization in a rehabilitation center.

Design—Retrospective case-control study.

Animals—90 California sea lions admitted to a rehabilitation center.

Procedure—Hospital records of 275 stranded California sea lions admitted to the rehabilitation center between January 1 and December 31, 2002, were reviewed. All California sea lions (n = 18) that developed ≥ 1 cutaneous poxvirus nodule during hospitalization were classified as cases. Seventy-two California sea lions that did not develop poxvirus lesions during hospitalization were randomly selected (control group). The frequencies of various exposure factors prior to admission, at admission, and during hospitalization for cases and control sea lions were compared by use of logistic regression.

Results—California sea lions that had previously been admitted to the rehabilitation center were 43 times as likely to develop poxvirus lesions as sea lions admitted for the first time; those with high band neutrophil counts ($> 0.69 \times 10^3$ bands/μL) at admission were 20 times less likely to develop poxvirus lesions than sea lions with counts within reference limits.

Conclusions and Clinical Relevance—Results suggest that sea lions with a history of prior hospitalization or band neutrophil counts within reference limits at admission were more likely to develop poxvirus lesions during hospitalization. Sea lions with histories of hospitalization should be kept in quarantine and infection control measures implemented to help prevent disease transmission to attending personnel and other hospitalized animals. (*J Am Vet Med Assoc* 2005;227:467–473)

The presence of poxviruses has been confirmed in free-ranging pinnipeds from the northern and southern Atlantic and Pacific oceans, including California sea lions (*Zalophus californianus*),[1,2] harbor seals (*Phoca vitulina*),[3,4] northern fur seals (*Callorhinus ursinus*),[5] grey seals (*Halichoerus grypus*),[6-10] northern elephant seals (*Mirounga angustirostris*),[2] and South American sea lions (*Otaria flavescens*).[11] Poxvirus-induced lesions are pathognomonic. Typically, the lesions are raised, firm cutaneous nodules (≤ 3 cm in diameter) that may ulcerate and suppurate. Poxvirus lesions develop primarily on the head and neck of affected pinnipeds, but lesions have also been reported[4] on the oral mucosa and in the nasal passages and perineal area. In severe cases, cutaneous lesions can become confluent and spread to the thoracic and abdominal regions as well as the flippers. The body of severely affected pinnipeds can be covered by as many as several hundred nodules.[11] Unless the lesions develop on the eyes or in the nostrils or oral cavity, the poxvirus-related mortality rate among captive pinnipeds is usually low[4]; however, the poxvirus-related morbidity rate can be high, especially among young animals.[2] The morbidity and mortality rates associated with poxvirus infections in wild pinnipeds are unknown.

When diseased pinnipeds are found stranded on beaches, they are often transferred to specialized marine mammal clinics for rehabilitation with the intention of subsequent release. Poxvirus infections are a common complication in the rehabilitation of these stranded pinnipeds.[1,2] Poxvirus infections are likely to negatively affect the overall health of the animals and duration of hospitalization and, consequently, increase the cost of maintaining these animals in rehabilitation centers. Poxviruses from pinnipeds are also potential zoonotic agents.[6] Poxvirus infections are therefore also of concern to marine mammal rehabilitation workers.

To our knowledge, very little information is available about the susceptibility of pinnipeds to this common hospital-acquired disease or the factors involved in the transmission and prevention of nosocomial infection; no studies have addressed the epidemiologic features of hospital-acquired poxvirus infections in pinniped rehabilitation centers. The purpose of the study of this report was to identify risk factors that may predispose captive California sea lions to development of cutaneous poxvirus nodules during hospitalization in a rehabilitation center. A better understanding of the predisposing factors for poxvirus infections would be useful in the development of strategies to prevent and manage poxvirus outbreaks in marine mammal rehabilitation centers, which would ultimately contribute to provision of better patient care for hospitalized seals and sea lions.

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Materials and Methods

Study population—Hospital records of 275 stranded California sea lions admitted for rehabilitation to **The Marine Mammal Center (TMMC)** in Sausalito, Calif, between January 1 and December 31, 2002, were considered for inclusion in the study. Sea lions (n = 65) that were hospitalized for < 24 hours were not included in the study because the medical records of these animals were incomplete.

Study design—This investigation was designed as a retrospective case-control study. All California sea lions (n = 18) that developed at least 1 pathognomonic, cutaneous, raised pox nodule during hospitalization were classified as cases. A random sample of 72 California sea lions that did not develop poxvirus lesions during hospitalization was selected by use of a random number table; these sea lions were classified as controls (control-to-case ratio, 4:1).

Data collection—All data analyzed in the study were gathered from TMMC medical records of the case and control sea lions. All potential risk factors were categorized as risk factors prior to admission; clinical findings at the time of admission; or clinical findings, procedures, and treatments during hospitalization. Risk factors prior to admission included month of admission, county of stranding (Sonoma, Marin, or Alameda; San Mateo; Santa Cruz; Monterey; and San Luis Obispo or Santa Barbara), sex, age group (pup, yearling, subadult, or adult), and whether the sea lion had previously been admitted to TMMC (readmitted animal). Age classes were defined as follows: pup, < 1 year; yearling, 1 to < 2 years; subadult male, 2 to 8 years; subadult female, 2 to 5 years; adult male, > 8 years; and adult female, > 5 years. Clinical findings recorded at the time of admission included primary clinical finding or problem (trauma, fracture, or entanglement; domoic acid intoxication; infectious disease; malnutrition; neoplasia; or other problems); body condition (considered normal, mildly underweight, or moderately underweight or emaciated); hospital caseload (the total number of California sea lions hospitalized at TMMC at the time of admission to TMMC); sea surface temperature (data obtained from the National Oceanic and Atmospheric Administration satellites and information service, measured at coordinates 37°N, 122.5°W); total serum protein concentration; and counts of WBCs, neutrophils, band neutrophils, eosinophils, and lymphocytes. Clinical findings, procedures, and treatments during hospitalization included use of quarantine, duration of hospitalization (days), housing history (pen B, C, D, E, G, H, or I), signs of anorexia (defined as no spontaneous food consumption for a period > 24 hours), clinical procedures (feeding via orogastric tube, anesthesia, ultrasonography, radiography, and surgery), use of anti-inflammatory (nonsteroidal anti-inflammatory drugs and corticosteroids) and anticonvulsive (phenobarbital) treatments, final diagnosis (trauma, fracture, or entanglement; domoic acid intoxication; infectious disease; malnutrition; neoplasia; or other diagnosis), and discharge status (alive or died during treatment). The number of days after admission that poxvirus nodules were first noted was recorded. Only exposure data (prior to admission, at admission, and during hospitalization) prior to development of pox lesions were included in the analyses.

Statistical analyses—A logistic regression analysis approach was used to model the probability of hospitalized sea lions developing pox lesions as a function of the risk factors evaluated in this study. First, crude **odds ratios (ORs)** and 95% **confidence intervals (CIs)** were calculated for each potential risk factor. Continuous variables (caseload at admission, sea surface temperature, and duration of hospitalization) were categorized into 2, 3, or 4 groups on the basis of their frequency distributions. Clinicopathologic variables were categorized as low, within reference limits, or high on the basis of reference values for stranded weanling sea lions.[12] Adjacent categories of multinomial variables (month of admission,

Table 1—Results of the univariable analysis of risk factors prior to admission associated with development of poxvirus lesions in 90 California sea lions (*Zalophus californianus)* in a rehabilitation facility.

Risk factors prior to admission	No. of cases* (n = 18)	No. of controls† (72)	Crude OR	95% CI	*P* value
Month of admission					
Dec–Feb	1	4	0.85	0.07–9.87	0.89
Mar–May	2	23	0.30	0.05–1.63	0.15
Jun–Aug	10	28	1.21	0.35–4.20	0.75
Sept–Nov	5	17	1.00	Reference	NA
Origin (county)					
Sonoma, Marin, or Alameda	1	9	0.61	0.06–6.34	0.67
San Mateo	3	8	2.06	0.38–11.34	0.40
Santa Cruz	2	15	0.73	0.12–4.60	0.37
Monterey	8	18	2.44	0.64–9.64	0.18
San Luis Obispo or Santa Barbara	4	22	1.00	Reference	NA
Sex					
Male	11	35	1.66	0.58–4.77	0.34
Female	7	37	1.00	Reference	NA
Age group					
Adult	0	18	ND	ND	ND
Subadult	11	22	ND	ND	ND
Yearling	7	30	ND	ND	ND
Pup	0	2	1.00	Reference	NA
Previous admission to facility					
Yes	3	3	4.60	0.95–22.37	0.06
No	15	69	1.00	Reference	NA

A univariable level of significance of $P \leq 0.20$ was required for a potential risk factor to be entered in the multivariable starting model.

*California sea lions (n = 18) that developed at least 1 pathognomonic, cutaneous, raised pox nodule during hospitalization were classified as cases. †A random sample of California sea lions (n = 72) that did not develop poxvirus lesions during hospitalization was selected by use of a random number table; these sea lions were classified as control animals.

OR = Odds ratio. CI = Confidence interval. NA = Not applicable. ND = Not determined.

county of origin, primary clinical finding, body condition, and final diagnosis) were collapsed whenever it was biologically reasonable to do so and when those categories had similar stratum-specific odds for developing pox lesions. Initial screening of potential risk factors was performed by use of univariable logistic regression. A univariable level of significance of $P \leq 0.20$ was required for a potential risk factor to be entered in a starting model. Variables that passed the initial univariable screening were grouped into 3 subsets for further analysis (risk factors prior to admission, risk factors at admission, and risk factors during hospitalization). A backward stepping approach was used to identify multivariable models for each of the 3 subsets (critical *P* value for retention ≤ 0.10). Variables retained in the multivariable models of the 3 subsets were then included in a single model (critical *P* value for retention ≤ 0.10). Variables that passed the multivariable screening were used to develop the final multivariable model. To identify the best-fitting final multivariable model, a backward model selection procedure was used in a sequential fashion starting with a full model. A model with hierarchical structure was specified by adding terms for biologically plausible interactions between independent variables. The variables for age, month of admission, hospital caseload, and duration of hospitalization were included as required variables in the final model because they can influence the probability of hospitalized sea lions developing poxvirus lesions. The goodness of fit of the multivariable model was explored by use of the Hosmer-Lemeshow goodness-of-fit χ^2 statistic. In the final model, adjusted ORs and 95% CIs were reported. In this study, we used the OR as an epidemiologic measure of association between a risk factor and development of pox lesions. Thus, if a factor was not associated with risk of developing pox lesions, the OR was 1. Risk factors had an OR > 1, and protective factors had an OR < 1. For our purposes, the greater the departure from 1 (either larger or smaller), the stronger the association was between the factor and the odds of developing pox lesions. The upper and lower limits of the 95% CI indicate that we can be 95% confident in the assertion that the true OR falls within this interval.

Results

Between January 1 and December 31, 2002, 275 stranded California sea lions were admitted for rehabilitation to TMMC. The 275 stranded California sea lions included 6 pups, 106 yearlings, 88 subadults, and

Table 2—Results of the univariable analysis of risk factors at admission associated with development of poxvirus lesions in 90 California sea lions in a rehabilitation facility.

Risk factors at admission	No. of cases* (n = 18)	No. of controls† (72)	Crude OR	95% CI	*P* value
Primary clinical finding or problem					
Trauma, fracture, or entanglement	4	27	0.59	0.09–3.89	0.58
Domoic acid intoxication	0	13	ND	ND	ND
Infectious disease	10	20	2.00	0.36–11.24	0.42
Malnutrition	2	4	2.00	0.19–21.04	0.51
Neoplasia or other problem	2	8	1.00	Reference	NA
Body condition					
Moderately underweight or emaciated	13	39	2.33	0.59–9.12	0.21
Mildly underweight	2	12	1.17	0.17–8.19	0.87
Normal for size	3	21	1.00	Reference	NA
Hospital caseload (No. of California sea lions in facility)					
32–44	9	19	2.96	0.79–11.1	0.10
18–31	5	28	1.12	0.27–4.62	0.88
3–17	4	25	1.00	Reference	NA
Sea surface temperature (°C)‡					
14.8–17.3	5	23	1.52	0.37–6.33	0.56
12.6–14.7	9	21	3.00	0.81–11.08	0.09
10.0–12.5	4	28	1.00	Reference	NA
Total protein (g/dL)					
High (10.8–10.86)	0	1	ND	ND	ND
Low (4.8–7.6)	5	29	0.41	0.13–1.30	0.12
Within reference range (7.7–10.7)	13	31	1.00	Reference	NA
Leukocytes ($\times 10^3$ cells/μL)					
High (22.8–44.6)	3	11	0.80	0.19–3.28	0.75
Low (4.8–9.77)	1	8	0.37	0.04–3.19	0.35
Within reference range (9.78–22.8)	14	41	1.00	Reference	NA
Neutrophils ($\times 10^3$ cells/μL)					
High (16.69–39.25)	0 (0)	13 (22)	ND	ND	ND
Low (3.02–5.13)	0 (0)	5 (8)	ND	ND	ND
Within reference range (5.14–16.68)	18 (100)	42 (70)	1.00	Reference	NA
Band neutrophils ($\times 10^3$ cells/μL)					
High (0.69–4.14)	2 (11)	18 (31)	0.28	0.06-1.37	0.10
Within reference range (0–0.68)	16 (89)	41 (69)	1.00	Reference	NA
Eosinophils ($\times 10^3$ cells/μL)					
High (1.48–5.02)	2 (11)	7 (12)	0.95	0.18–5.02	0.95
Within reference range (0–1.47)	16 (89)	53 (88)	1.00	Reference	NA
Lymphocytes ($\times 10^3$ cells/μL)					
Low (0.13–1.17)	3 (17)	16 (27)	0.54	0.14–2.11	0.37
Within reference range (1.18–8.38)	15 (83)	43 (73)	1.00	Reference	NA

A univariable level of significance of $P \leq 0.20$ was required for a potential risk factor to be entered in the multivariable starting model.

‡Data from the National Oceanic and Atmospheric Administration satellites and information service, measured at coordinates 37°N, 122.5°W.

See Table 1 for remainder of key.

Table 3—Results of the univariable analysis of risk factors during hospitalization associated with development of poxvirus lesions in 90 California sea lions in a rehabilitation facility.

Risk factors during hospitalization	No. of cases* (n = 18)	No. of controls† (72)	Crude OR	95% CI	*P* value
Quarantine					
Yes	6	29	1.10	0.35–3.57	0.85
No	8	43	1.00	Reference	NA
Length of hospitalization (d)					
46–174	7	9	18.67	2.00–173.77	0.001
27–45	3	18	4.00	0.38–41.70	0.21
5–26	3	21	3.43	0.33–35.51	0.28
1–4	1	24	1.00	Reference	NA
Housed in pen B					
Yes	8	21	3.24	1.03–11.16	0.04
No	6	51	1.00	Reference	NA
Housed in pen C					
Yes	10	26	4.42	1.34–14.63	0.01
No	4	46	1.00	Reference	NA
Housed in pen D					
Yes	11	42	2.62	0.69–9.93	0.15
No	3	30	1.00	Reference	NA
Housed in pen E					
Yes	1	2	2.69	0.69–9.93	0.15
No	13	70	1.00	Reference	NA
Housed in pen G					
Yes	10	60	2.12	0.59–7.69	0.25
No	4	12	1.00	Reference	NA
Housed in pen H					
Yes	4	13	1.71	0.47–6.25	0.41
No	10	59	1.00	Reference	NA
Housed in pen I					
Yes	4	17	1.29	0.36–4.68	0.69
No	10	55	1.00	Reference	NA
Anorexia					
Yes	6	40	0.60	0.19–1.91	0.38
No	8	32	1.00	Reference	NA
Tube feeding					
Yes	8	27	2.22	0.70–7.02	0.17
No	6	45	1.00	Reference	NA
Administration of NSAIDs					
Yes	8	7	4.31	1.38–13.49	0.01
No	6	55	1.00	Reference	NA
Administration of corticosteroids					
Yes	4	24	0.80	0.23–2.83	0.73
No	10	48	1.00	Reference	NA
Administration of phenobarbital					
Yes	5	13	2.52	0.74–8.60	0.13
No	9	59	1.00	Reference	NA
Anesthesia					
Yes	6	18	2.25	0.70–7.27	0.17
No	8	54	1.00	Reference	NA
Ultrasonography					
Yes	1	8	0.62	0.07–5.32	0.65
No	13	64	1.00	Reference	NA
Radiography					
Yes	5	14	2.30	0.68–7.83	0.85
No	9	58	1.00	Reference	NA
Surgery					
Yes	1	5	1.00	0.11–9.69	0.97
No	13	67	1.00	Reference	NA
Final diagnosis					
Trauma, fracture, or entanglement	5	24	1.15	0.19–7.00	0.88
Domoic acid intoxication	2	15	0.73	0.09–6.23	0.77
Infectious disease	6	19	1.70	0.30–10.24	0.54
Malnutrition	3	3	5.50	0.64–47.47	0.15
Neoplasia or other problem	2	11	1.00	Reference	NA
Discharge status					
Released alive	14	39	2.96	0.91–9.59	0.07
Died during hospitalization	4	33	1.00	Reference	NA

A univariable level of significance of $P \leq 0.20$ was required for a potential risk factor to be entered in the multivariable starting model.

NSAIDs = Nonsteroidal anti-inflammatory drugs.

See Table 1 for remainder of key.

Table 4—Results of the multivariable analysis of risk factors associated with development of poxvirus lesions in 90 California sea lions in a rehabilitation facility.

Risk factor	No. of cases* (n = 18)	No. of controls† (72)	Adjusted OR	95% CI	*P* value
Age group					
Pup, yearling	7	32	2.09	0.28–15.75	0.11
Subadult	11	40	1.00	Reference	NA
Month of admission					
Sept–Nov	5	17	1.09	0.02–61.05	0.96
Jun–Aug	10	28	0.37	0.00–29.19	0.66
Mar–May	2	23	0.05	0.00–4.33	0.19
Dec–Feb	1	4	1.00	Reference	NA
Previous admission to facility					
Yes	3	3	43.48	1.67–1,129.51	0.02
No	15	69	1.00	Reference	NA
Hospital caseload (No. of California sea lions in facility)					
32–44	9	19	16.49	0.81–336.01	0.07
18–31	5	28	6.74	0.46–97.67	0.16
3–17	4	25	1.00	Reference	NA
Band neutrophils (X 10^3 cells/μL)					
High (0.69–4.14)	2	18	0.05	0.00–0.66	0.02
Within reference range (0–0.68)	16	41	1.00	Reference	NA
Duration of hospitalization (d)					
46–174	7	9	8.96	1.53–52.44	0.01
1–45	7	63	1.00	Reference	NA

A value of $P \leq 0.05$ was considered significant.
See Table 1 for key.

75 adults. Of these, 15 (5%) California sea lions had previously been admitted. Eighteen of 275 (6.5%) sea lions developed poxvirus nodules (**Tables 1 and 2**). Of the 90 California sea lions included in this study, there were 44 (49%) females and 46 (51%) males; 70 (78%) were subadults or adults. No pups or adults were diagnosed with pox lesions; only yearlings and subadults were affected. The mean ± SE number of days between admission to the hospital and development of pox lesions was 25 ± 18 days. The duration of hospitalization of cases (median, 47 days; range, 4 to 83 days) and control sea lions (median, 20 days; range, 1 to 174 days) differed significantly ($P < 0.001$). Three of the 18 cases and 3 of the 72 control sea lions had previously been admitted to TMMC. These 3 readmitted cases developed pox lesions 23 and 42 days after their initial release from TMMC. Among the 18 cases, 14 were discharged alive; among the 72 control sea lions, 39 were discharged alive. This difference between the groups was not significant ($P = 0.07$; **Table 3**).

Sixteen of the 35 variables examined in univariable analyses had values of $P \leq 0.20$ and were included in the multivariable analysis. Age, month of admission, hospital caseload, and duration of hospitalization were forced into the final model because they can influence the probability of hospitalized sea lions developing poxvirus lesions. The 2 other variables that were retained in the final model were readmission status and concentration of band neutrophils (**Table 4**). Addition of 2-way interaction terms did not contribute to the final model for risk of developing pox lesions; therefore, these terms were removed from the model. The *P* value of the Hosmer-Lemeshow statistic was 0.77, which supported the overall goodness-of-fit of the model.

In the multivariable analysis, California sea lions that had previously been admitted to TMMC were 43 times as likely to develop poxvirus lesions than sea lions admitted for the first time (OR = 43.4; 95% CI = 1.6 to 1,129.5; $P = 0.02$). California sea lions with high counts of band neutrophils ($> 0.69 \times 10^3$ bands/μL) at the time of the initial examination were 20 times less likely to develop pox lesions than sea lions with band neutrophil counts that were within reference limits (OR = 0.05; 95% CI = 0.0 to 0.6; $P = 0.02$).

Discussion

The objective of the study of this report was to identify risk factors that may predispose California sea lions to the development of poxvirus lesions during hospitalization in a rehabilitation center, thereby providing data that might be used to improve patient care for hospitalized seals and sea lions. Results of our study suggest that sea lions with a history of prior hospitalization were more likely to develop poxvirus lesions during hospitalization at the rehabilitation center. Sea lions with high counts of circulating band neutrophils at the time of admission were less likely to develop poxvirus lesions. The variables of age, month of admission, hospital caseload, and duration of hospitalization were retained in the final logistic regression model because the morbidity rate associated with poxvirus infections is higher in younger than in older pinnipeds,[2] the summer months are associated with a high hospital caseload, and the duration of hospitalization can affect the probability of sea lions developing poxvirus lesions. With regard to California sea lions, the caseload at TMMC is typically highest between June and August of each year. During those months,

harbor seals and northern elephant seals are often also hospitalized at TMMC. At present, the species specificity of the pinniped poxviruses is unknown, but poxvirus infection could be transmitted from those hospitalized seals to hospitalized California sea lions during those months if the latter are susceptible. A high hospital caseload is typically associated with an increased infection pressure from horizontally transmitted diseases and, as a result, an increased incidence of hospital-acquired infections.[13] When the caseload of California sea lions is high, higher numbers of both susceptible sea lions and infected sea lions are likely to be present in the hospital, compared with the numbers present at other times. Also, when the caseload is high, sea lions are housed in larger groups; consequently, more direct contact between infected and noninfected individuals is possible. As a result, pathogens are more easily transmitted, which may account for the increased incidence of poxvirus infections during periods when the caseload is high.

In the present study, California sea lions with a history of prior hospitalization at TMMC were more likely to develop poxvirus lesions. Two explanations may be considered for the observed association between a history of prior hospitalization and high risk of poxvirus infection. First, the incubation period of the infection may correspond to the time between initial release and restranding of the animals. Sea lions may be exposed to the poxvirus during their initial hospitalization at TMMC but develop clinical disease only during their subsequent hospitalization. The 3 affected, readmitted sea lions developed poxvirus lesions 23 to 42 days after their initial release. The incubation period of poxvirus infections in seals has been suggested to be between 3 and 8 weeks[2]; however, this remains to be confirmed. The incubation periods of other mammalian poxvirus infections range from 48 hours to 14 days.[14-16] Alternatively, the health of sea lions that are readmitted for rehabilitation may be more severely compromised than the health of sea lions that have not been admitted before. These more severely compromised sea lions are likely to be more susceptible to secondary infections, such as poxvirus infections. The fact that sea lions readmitted to TMMC in our study were at high risk for development of poxvirus lesions suggests that those sea lions should be kept in a separate pen. In other species, transmission of poxviruses requires either direct transmission or indirect transmission via fomites. Other infection control measures to help prevent the transmission of poxviruses from those sea lions to handlers and other hospitalized animals should therefore include the strict separation of sea lions with poxvirus lesions from those without, the use of designated animal-handling equipment for each pen, and the use of disposable protective gear (eg, gloves and towels) for handling individual animals.

Hospitalized California sea lions with high counts of circulating band neutrophils at the time of admission were less likely to develop poxvirus lesions than sea lions with band neutrophil counts that were within reference limits. This may suggest that animals with acute inflammatory processes are more protected against poxvirus infections because the immune system is already upregulated. In various species, it is known that the host response to an infection with 1 organism can activate the immune system, thereby increasing the general level of resistance to other agents.[17-20] This augmentation of immunity against infection may be initiated by a specific, adaptive immune response. However, the nonspecific protective effect is mediated via nonspecific modulators of immune function (eg, granulocyte colony-stimulating factors and interferons) and subsequently effected by nonspecific, innate immune cells such as granulocytes, mast cells, macrophages, and natural killer cells.[17,19] Innate interferon-mediated antiviral mechanisms do play an important role in controlling poxvirus infections[21,22]; interferons limit the spread of poxviruses by inducing an antiviral state in uninfected cells and directing nonspecific immune cells to sites of viral replication. Therefore, the high counts of circulating immature granulocytes detected in California sea lions without poxvirus lesions may be an indicator of augmented innate immune activity, in which case any infecting poxvirions would be effectively combated before clinical disease develops.

No signs of poxvirus disease were detected in pups and adult sea lions at TMMC. Two explanations can be considered for the lack of clinical signs in pups and adult sea lions: low frequency of sea lion pups admitted to TMMC and acquired immunity among adults. Only 6 sea lion pups were admitted to TMMC in 2002. Numbers of hospitalized pups are usually low because the pups are born on islands off Southern California. The pups remain on the rookeries and do not frequent the coastline of the mainland until they are at least 6 months of age.[23] The fact that none of the 75 hospitalized adult sea lions developed pox lesions may suggest that adults may have previously acquired immunity against poxviruses and hence were protected against reinfection. It is possible that exposure to poxviruses in wild California sea lion populations is a common event. However, the prevalence of poxvirus infections in wild California sea lions is unknown, and results of a serologic survey for antipoxvirus antibodies in California sea lions would help determine the reason that adult sea lions did not have clinical signs of poxvirus infection in our study.

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