SHORT COMMUNICATIONS

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Hematologic and Serum Chemistry Values of Endangered San Joaquin Kit Foxes (*Vulpes macrotis mutica*) with Sarcoptic Mange

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ABSTRACT: A fatal outbreak of sarcoptic mange caused by *Sarcoptes scabiei* in San Joaquin kit foxes (*Vulpes macrotis mutica*) in Bakersfield, California, US is causing the once-stable population to decline. Given the fatality of the disease in this already-endangered species experiencing continued population declines, city-wide interventions are underway. To optimize medical management of mange-infested kit foxes, we documented serum biochemistry and hematology values for 11 kit foxes with mange collected from January–May 2015 and compared them to historical data from 18 healthy Bakersfield kit foxes. Results from kit foxes with mange were consistent with chronic illness and inflammation, protein loss, hypoglycemia, and dehydration. These findings contribute to our understanding of this debilitating, multisystemic disease that can progress to death in individuals without intervention and will aid in the treatment and care of rehabilitated individuals.

Key words: Hematology, San Joaquin kit fox, *Sarcoptes scabiei*, sarcoptic mange, serum chemistry.

Sarcoptes scabiei is a highly infectious parasitic mite with a worldwide distribution and is an emerging concern in wildlife (Kraabøl et al. 2015). Sarcoptic mange in wildlife is likely, but not invariably, fatal (Pence et al. 1983; Nimmervoll et al. 2013) and has caused catastrophic declines of red fox (*Vulpes vulpes*) populations in North America, Europe, and Japan (Morner 1992; Soulsbury et al. 2007; Uraguchi et al. 2014). Mortality in red foxes is often due to strong allergic reaction to the mites, which burrow into the skin where they lay eggs, defecate, shed exoskeletons, and secrete digestive enzymes (Little et al. 1998). This irritation causes hair loss and skin thickening, crusting, and overall fragility while the animal succumbs to wasting, muscle catabolism, and death (Nimmervoll et al. 2013). While red foxes develop antibodies to *S. scabiei*, there is no evidence they develop lasting immunity (Little et al. 1998; Davidson et al. 2008; Nimmervoll et al. 2013).

Recently, the Bakersfield population of San Joaquin kit foxes (*Vulpes macrotis mutica*), an endangered endemic canid in the Central Valley of California, experienced a fatal outbreak of sarcoptic mange (Cypher et al. 2016). Prior to the epidemic, the urban Bakersfield population was stable (Cypher and Frost 1999) and had been well monitored (Cypher et al. 2016). After mange-associated population declines, a city-wide intervention was initiated to trap infested kit foxes and hospitalize individuals requiring treatment. To determine the physiologic parameter alterations associated with mange and aid in medical management of cases to improve survival, we compared serum biochemistry and complete blood cell count (CBC) values for San Joaquin kit foxes with mange to previously published values from apparently healthy Bakersfield kit foxes sampled in 1988–89 (Cypher and Frost 1999).

We conducted this study in the city of Bakersfield (35°22′N, 119°01′W, population 376,380). Work was conducted in accordance with 10(a)1(A) research permit TE825573-2 from the US Fish and Wildlife Service, a Memorandum of Understanding from the California Department of Fish and Wildlife, and University of California–Davis Institutional Animal Care and Use protocol 18179.

We sampled 11 mange-infested kit foxes captured January–May 2015 and taken to the California Living Museum Zoo in Bakersfield

TABLE 1. Fates of 11 mange-infested San Joaquin kit foxes (*Vulpes macrotis mutica*) submitted to the California Living Museum Zoo in Bakersfield, California, USA for rehabilitation in January–May 2015.

ID	Age class	Sex	Mange score	Body condition score
6740	Adult	Female	2	3
6808	Adult	Male	1	3
U241	Adult	Male	2	2
6802	Adult	Male	1	3
6748	Adult	Male	2	2
6580	Adult	Female	2	Unknown
6738	Adult	Female	2	Unknown
6803	Juvenile	Female	2	2
6747	Adult	Female	3	Unknown
6733	Adult	Male	3	2
6734	Adult	Female	1	3

for care (Table 1). Foxes were live-captured and handled without sedation (Cypher et al. 2016). Sex, weight, body condition, age class, and mange severity score (Pence and Windberg 1994) were recorded, and skin scrapings and blood were collected at intake examination. Mange infestation severity was defined as Class I (mild: lesions present on $\leq$25% of body); Class II (moderate: lesions present on 25–50% of body); or Class III (severe: lesions present on >50% of body). Mange infestation was confirmed by examination of skin scrapings under 400× magnification for mites morphologically consistent with *S. scabiei* (Fain 1968). Blood was collected via jugular venipuncture and placed into a tube containing ethylenediaminetetraacetic acid anticoagulant and a serum separating tube. Blood was allowed to clot and then centrifuged within 24 h for serum collection. Serum chemistries were performed on all 11 sampled foxes using a VetScan® VS2 analyzer (Abaxis, Union City, California, USA) and CBCs were performed on 10 sampled foxes at a commercial laboratory (IDEXX, Sacramento, California, USA).

Data analyses were performed using R (R Development Core Team 2017) and *P*-values of $\leq$0.05 were considered significant. Summary statistics were calculated for each hematologic and serum chemistry parameter and qualitatively evaluated against IDEXX-established normal reference intervals for domestic dogs (*Canis lupus familiaris*) and with published, reanalyzed serum chemistry and CBC values from 18 healthy kit foxes from Bakersfield (Cypher and Frost 1999); both sexes of foxes were represented among mangy and healthy foxes, most of which were adult in both groups. Parameter distributions were tested for normality using the Shapiro-Wilk test. Differences in blood parameters between mange-infested and healthy kit foxes were evaluated using Mann-Whitney *U*-tests. We tested for differences in blood parameters among kit foxes with differing mange severity scores using a Kruskal-Wallis test, followed where indicated by a Dunn's test.

Clinical chemistry (Table 2) and hematologic values (Table 3) were similar among mange-infested foxes regardless of mange score, with the exception of mean corpuscular volume which was significantly elevated in class II individuals. Alkaline phosphatase values in healthy kit foxes were significantly ($P<0.0001$) higher than in mange-infested kit foxes, as were albumin ($P=0.0130$) and glucose ($P<0.0001$). Serum globulins ($P=0.0006$), sodium ($P=0.0200$), and total bilirubin ($P=0.0002$) were elevated in mange-infested kit foxes compared to healthy kit foxes. Mange-infested kit foxes also had higher total white blood cell counts of 21.44 $10^3/mm^3$ ($P=0.0002$), compared to 9.54 $10^3/mm^3$ for healthy kit foxes, with elevations of neutrophils ($P=0.0002$), monocytes ($P=0.0300$), basophils ($P=0.0080$), and band (immature neutrophil) cells ($P<0.0001$), all of which were nearly double the values for healthy kit foxes. Eosinophil counts did not differ between mange-infested and healthy kit foxes. Basophils were detected in mange-infested but not in healthy kit foxes. Few of the values for healthy or mange-infested kit foxes were outside normal reference ranges for domestic dogs except for elevations in mean and median blood glucose levels in healthy kit foxes. All foxes except one (no. U241, which died after a single day in captivity) were released after 28 d in rehabilitation.

TABLE 2. Mean, SD, median, and ranges for serum chemistry for mange-infested and healthy San Joaquin kit foxes (*Vulpes macrotis mutica*) in Bakersfield, California, USA that were captured in January–May 2015. Normal references ranges established by IDEXX for adult domestic dogs (*Canis familiaris*) are provided for reference (IDEXX 2015). Bold values indicate those with significant differences ($P \leq 0.05$) in mean values between mange-infested and healthy kit foxes.

	Mange			Healthy[a]			Normal dogs
Blood analytes (units)	*n*	Mean (SD)	Median (range)	n	Mean (SD)	Median (range)	Range
Albumin (g/dL)	**11**	**2.4 (0.7)**	**2.6 (1.4–3.5)**	**18**	**3.1 (0.3)**	**3.1 (2.5–3.4)**	2.3–4.0
Alkaline phosphatase (U/L)	**11**	**24.7 (9.4)**	**26.0 (5–35)**	**18**	**88.4 (42.6)**	**78.0 (41–209)**	23–212
Alanine transferase (U/L)	11	76.6 (41.4)	60.5 (47–182)	—	—	—	10–125
Amylase (U/L)	11	222.0 (64.6)	223.0 (139–324)	—	—	—	500–1500
Total bilirubin (mg/dL)	**11**	**0.3 (0.1)**	**0.3 (0–0.4)**	**18**	**0.1 (0.1)**	**0.1 (0.1–0.3)**	0.0–0.9
Blood urea nitrogen (mg/dL)	11	28.8 (24.6)	22.0 (14–97)	18	20.7 (4.5)	21.5 (12–30)	7–27
Calcium (mg/dL)	11	9.3 (0.9)	9.1 (0–10.6)	18	9.4 (1.1)	9.2 (8.1–11.6)	7.9–12.0
Phosphate (mg/dL)	11	5.4 (0.9)	5.3 (4.2–6.8)	18	5.5 (1.2)	5.9 (3.3–7.2)	2.5–6.8
Creatinine (mg/dL)	11	0.7 (0.4)	0.7 (0.3–1.6)	18	0.8 (0.2)	0.7 (0.6–1.3)	0.5–1.8
Glucose (mg/dL)	**11**	**100.9 (28.1)**	**112.0 (<10–131)**	**18**	**163.3 (21.1)**	**165.0 (115–193)**	74–143
Sodium (mEq/L)	**11**	**155.9 (7.7)**	**152.0 (147–165)**	**18**	**148.3 (4.5)**	**149.0 (141–155)**	144–160
Potassium (mEq/L)	11	4.7 (0.8)	4.9 (2.8–5.6)	18	4.5 (0.3)	4.5 (4–5)	3.5–5.8
Total protein (g/dL)	11	6.4 (0.8)	6.4 (5.3–7.7)	18	5.8 (0.5)	5.8 (4.7–6.4)	5.2–8.2
Globulin (g/dL)	**11**	**4.0 (0.9)**	**3.7 (2.3–6.0)**	**18**	**2.7 (0.4)**	**2.6 (1.9–3.5)**	2.5–4.5

[a] The dashes (—) in some cells represent values that were not reported for healthy foxes in Cypher and Frost (1999).

Several serum chemistry and CBC parameters in mange-infested foxes were consistent with chronic disease and inflammation, starvation, and dehydration, including: 1) neutrophilia/leukocytosis and hyperglobulinemia typically associated with inflammation, infection, and parasitism; 2) hypoalbuminemia (with normal blood urea nitrogen and alanine transferase) most likely secondary to dermatopathy; and 3) hypernatremia associated with dehydration. Eosinophilia was consistent with the considerable flea, cestode, and nematode infestations common in this species (Riner et al. 2018). Protein loss was associated with dermatopathy, although we could not rule out gastrointestinal and renal loss without additional clinical testing. In the absence of changes in hemoglobin concentration and red blood cell count, hypernatremia is often attributed to renal disease. Glomerulonephritis was found in mange-infested kit fox carcasses (Cypher et al. 2016); however, renal insufficiency was not observed in our case series given the normal creatinine and blood urea nitrogen values we obtained. Moreover, renal lesions have not been observed in mange in other species (Nimmervoll et al. 2013). Hypernatremia probably reflected inadequate water consumption and possibly vomiting and diarrhea.

Our observations of hypoalbuminemia, hyperglobulinemia, and hypoglycemia could have been consistent with hepatic disease. However, hepatic disease was not diagnosed in any mange-infested kit fox carcasses (Cypher et al. 2016). The cause of the elevated bilirubin was unknown. The hypoglycemia may have been associated with starvation or sepsis, although we saw little evidence for the latter. Hypoglycemia in mange-infested foxes was particularly profound: healthy and mangy foxes were handled similarly, and yet healthy foxes showed stress-associated hyperglycemia whereas mange-infested foxes did not (Wingfield and Romero 2001). Thus, we expected the value for

TABLE 3. Mean, SD, median, and ranges for hematologic parameters for mange-infested and healthy San Joaquin kit foxes (*Vulpes macrotis mutica*) in Bakersfield, California, USA that were captured in January–May 2015. Normal references ranges established by IDEXX for all life stages of domestic dogs (*Canis familiaris*) are provided for reference (IDEXX 2017). Bold values indicate those with significant differences ($P \leq 0.05$) between mange-infested and healthy kit foxes.

Blood analytes (units)	Mange			Healthy[a]			Normal dogs
	n	Mean (SD)	Median (range)	*n*	Mean (SD)	Median (range)	Range
White blood cells (10^3/mm^3)	**10**	**21.4 (10.6)**	**20.0 (10.3–45.2)**	**16**	**9.5 (2.0)**	**9.3 (6.4–13.9)**	5.5–16.76
Red blood cells (10^6/mm^3)	10	7.5 (2.1)	7.5 (3.9–10.4)	16	7.9 (1.2)	7.7 (5.8–10.0)	5.65–8.87
Hemoglobin (g/dL)	10	12.0 (3.4)	11.8 (6.5–16.5)	16	12.4 (2.4)	13.0 (8.2–15.6)	13.1–20.5
Hematocrit (%)	10	37.9 (9.7)	37.6 (23–51.8)	16	38.7 (7.7)	38.9 (28–55.2)	37.3–61.7
Mean corpuscular volume (fL)	10	51.3 (6.6)	52.5 (41–59)	16	48.9 (4.9)	49.0 (43–60)	61.6–73.5
Mean corpuscular hemoglobin (pg)	10	16.0 (1.0)	16.5 (14.4–17.3)	16	15.9 (3.1)	15.2 (12.5–25)	21.2–25.9
Mean corpuscular hemoglobin concentration (g/dL)	10	31.6 (3.2)	31.9 (27.1–38.0)	16	32.4 (5.0)	31.2 (27.8–49)	32–3
Nucleated red blood cells (per 100 WBC)	10	8.7 (1.5)	9.0 (7–10)	—	—	—	0–2
Reticulocytes (10^3/mm^3)	10	96.8 (50.3)	91.0 (27–177)	—	—	—	10–110
Platelets (per µL)	10	403.4 (120.2)	442.0 (259–585)	—	—	—	148–484
Neutrophils (per µL)	**10**	**17,110.0 (8,808.3)**	**14,940.0 (8,487–36,612)**	**16**	**8,137.5 (1,014.5)**	**8,250.0 (5,800–9,700)**	2,940–12,670
Bands (per µL)	**10**	**1,289.6 (997.6)**	**771.0 (358–2,712)**	**16**	**43.8 (126.3)**	**0 (0–500)**	0–170
Lymphocytes (per µL)	**10**	**2,452.6 (1,972.5)**	**1,739.5 (292–5,832)**	**16**	**1,268.8 (919.2)**	**1,100.0 (200–3,600)**	1,060–4,950
Monocytes (per µL)	**10**	**812.8 (437.5)**	**822.0 (0–1,431)**	**16**	**450.0 (236.6)**	**500.0 (0–900)**	130–1,150
Eosinophils (per µL)	10	230.8 (316.0)	83.5 (0–904)	16	93.8 (123.7)	0 (0–400)	70–1,490
Basophils (per µL)	**10**	**9.2 (18.0)**	**0 (0–58)**	**16**	**0**	**0**	0–100

[a] The dashes (—) in some cells represent values that were not reported for healthy foxes in Cypher and Frost (1999).

mange-infested foxes to be elevated, but the actual results showed reductions in blood glucose levels.

We acknowledge this study had a small sample size and that there was an extended period of time between when data were collected from healthy kit foxes (Cypher and Frost 1999) and when samples were collected from foxes with mange for this study. However, our results indicated a similar pathogenesis of mange in kit foxes, as occurred in bobcats (*Lynx rufus*) and other canids (Pence et al. 1983; Little et al. 1998; Davidson et al. 2008; Serieys et al. 2013), although our findings that values in both healthy and mangy kit foxes generally remained within canine reference ranges implies that caution is necessary when using canine values to interpret data for canids such as kit foxes. In each of these studies, blood chemistry values of mangy coyotes (*Canis latrans*), domestic dogs, and bobcats remained within normal, taxon-specific reference ranges. Nevertheless, trends in abnormalities were detected by comparing mange-affected animals with unaffected conspecifics. Across species, hypoalbuminenia is a consistent finding for mange-infested bobcats, coyotes, and kit foxes when animals with mange are compared to healthy individuals of the same species (Pence et al. 1983; Serieys et al. 2013). The marked leukocytosis of mange-infested kit foxes has also been reported in domestic dogs, red foxes, and bobcats (Arlian et al. 1995; Little et al. 1998; Serieys et al. 2013).

Our study identified particular blood values that appear to be altered during mange infestation of kit foxes and should be considered if rehabilitation is going to be successful. Blood glucose should be supported as rapidly as possible. Animals should be hydrated and protein requirements supported while broad-spectrum antibiotics and antiparasitic drugs are administered. Importantly, blood chemistry and hematologic values did not appear to become progressively disordered with progression of mange, implying that delaying treatment for the results of diagnostic tests or for fear of causing stress to the animal by drawing blood or other hands-on procedures on intake are not warranted.

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