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TYLOSIN TARTRATE PROMOTES RESOLUTION OF INSECT BITE HYPERSENSITIVITY REACTIONS IN CAPTIVE CRANES

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Previous research has described significant serum protein electrophoretic changes associated with intense periocular swelling in several crane species, typical of Type I hypersensitivity reactions, and thought to be the result of insect bites (Hartup and Schroeder 2006). We reviewed medical records for treatment plans and outcomes from 58 cases of insect hypersensitivity reactions observed in a diverse collection of captive cranes at the International Crane Foundation, Baraboo, Wisconsin. The purpose of this study was to fully describe the epidemiological and clinical characteristics of these cases, and determine the efficacy of treatment of these cases with tylosin tartrate, a macrolide antibiotic.

The mean annual number of cases (± SD) between 2000 and 2011 was 4.8 ± 2.9, and ranged from 1 to 11 cases per year (no cases were found prior to 2000). Cases occurred April to September, but peaked in June (n = 31). Twenty-four cases (41%) occurred in 1 quadrant of the off-exhibit breeding facility. Cases were observed in 6 species present at the facility. The largest number of cases occurred in whooping cranes (*Grus americana*) (n = 24, 41%), followed by Siberian cranes (*G. leucogeranus*) (n = 17, 29%). Forty-eight cranes were affected once, 9 cranes were affected twice, and 1 crane was similarly affected 3 times. Forty-one females (71%) and 17 males (29%) were affected. Female cranes were diagnosed with hypersensitivity reactions more than twice as often as males (odds ratio = 2.41, 95% confidence interval 1.05-5.58; $\chi^2 = 5.19$, $P = 0.02$). The affected cranes ranged in age from 9 days to 33 years old; there was no apparent age predilection.

Clinical signs included unilateral periocular swelling (n = 58, 100%), oculonasal discharge (n = 29, 50%), conjunctivitis (n = 19, 33%), blepharitis (n = 12, 21%), or a punctate wound with or without an attached insect exoskeleton remnant (n = 10, 17%). Cases ranged in severity from mild (minimal periocular swelling only, n = 7, 12%), to moderate (modest periocular swelling with up to 1 additional sign, n = 35, 60%), to severe (large periocular swelling with 1 or more additional signs, n = 16, 28%).

Treatment regimens included non-steroidal anti-inflammatory drugs (NSAIDs, including ketoprofen, carprofen, piroxicam, meloxicam), topical antibiotic ophthalmic ointment with or without hydrocortisone, systemic antibiotics (enrofloxacin, tylosin tartrate), or no treatment. There was no to minimal clinical improvement observed in cases where an NSAID, topical ophthalmic ointment or enrofloxacin were used. Cases typically resolved in 18-29 days when these drugs were used alone or in combination. By comparison, the mean time to resolution of clinical signs was 20 ± 6.8 days in 3 cases where no drugs were used. The mean duration of clinical signs decreased significantly in cases where tylosin tartrate was administered (13.0 ± 8.3 days), either alone or in conjunction with another drug, compared to cases where no tylosin was used (25.2 ± 11.2 days, $t = 4.2$, $P < 0.001$). The mean duration of clinical signs was 9.9 ± 5.4 days in 15 cranes that received tylosin tartrate and no other drug.

Tylosin tartrate produced a significant clinical benefit in these cases, typically shortening the duration of signs of hypersensitivity reactions in cranes by 1 to 2 weeks. The drug is easily delivered in drinking water and may provide a prophylaxis to bacterial infection in these cases. We speculate that modulation of inflammatory mediators and cytokines is responsible for the improvements in clinical signs after treatment with tylosin tartrate. *In vitro* and *in vivo* studies in mammals show macrolide antibiotics such as tylosin modify the host immune and inflammatory responses (Cao et al. 2006). Further work is needed to determine the range of pest species that incite hypersensitivity reactions in cranes, to examine whether affected cranes have lowered breeding success, and to investigate possible prevention strategies.

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