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Abstract: Four 3 mo old cheetah littermates were dewormed with levamisole hydrochloride according to the regular deworming regimen of the Peaugres Zoo. Levamisole was administered subcutaneously at a dosage of 5 mg/kg. Shortly after the injection, all four cubs showed severe respiratory distress and seizures, and died within twenty minutes despite attempts at resuscitation.
PRESUMED LEVAMISOLE INTOXICATION IN FOUR CHEETAH CUBS
(Acinonyx jubatus)

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Extended abstract
Four 3 mo old cheetah littermates were dewormed with levamisole hydrochloride according to the regular deworming regimen of the Peaugres Zoo. Levamisole was administered subcutaneously at a dosage of 5 mg/kg. Shortly after the injection, all four cubs showed severe respiratory distress and seizures, and died within twenty minutes despite attempts at resuscitation. At necropsy, the only consistent gross finding in all four cubs was a marked pulmonary oedema. Furthermore thymic haemorrhages were found in one animal. Histologic lesions in the lung included congestion with leukocytostasis, diapedesis of neutrophils into the alveolar lumina, prominent alveolar and interstitial oedema with alveolar foamy macrophages, small intraalveolar hemorrhages, and bronchial mucous hypersecretion.

Levamisole, the Levo-Isomer of dl-Tetramisole, is an antiparasitic drug of the imidazothiazole group that is widely used in the treatment of nematodes as well as an immunomodulator in both humans and animals including mammals, avians, reptiles, and amphibians. It is structurally and physiologically similar to nicotine, and therefore, is able to activate cholinergic receptors in ganglia, in the neuromuscular junction, and in the central nervous system (5, 7). Levamisole has a narrow safety margin, and numerous adverse reactions have been reported in many species including vomitus, diarrhea, hypersalivation, muzzle foaming, dyspnea due to bronchospasms and pulmonary oedema, urination and defecation, depression, tremor, ataxia, paresis, excitation, clonic convulsions, immune-mediated haemolytic anemia, thrombocytopenia, bone marrow depression, cardiac arrhythmias, erythroderma, erythema multiforme, toxic epidermal necrolysis and unexplained deaths (1, 3, 4, 5, 6, 8, 9, 10, 12, 13). Information on pathologic lesions in levamisole intoxications are few and include congestion of the splenic red pulp, neutrophilic infiltration of the lung parenchyma, marked subepicardial petechia, enteritis, acute hepatic degeneration with subcapsular hemorrhages, massive necrosis of the liver, hemorrhages in the thalamus, and perivascular cuffing with mononuclear cells in the CNS (5, 11). In the present case, pathologic lesions were restricted to the lung and to the thymus.

Based on the acute onset and the nature of clinical symptoms as well as the pathologic findings, the death of the cheetah cubs is presumed to be the result of levamisole intoxication. Symptoms of levamisole intoxication are reported to begin within 5 to 15 minutes after administration and reach a peak at approximately 30 minutes (7).

The reason for the intoxication in the present case is not known. In dogs and cats, fatalities have been described with fourfold overdosage of levamisole, and the molecule is considered to be more dangerous when administered parenterally than when given orally (3). In these four cheetahs, the dosage was 5 mg/kg subcutaneously which is within the recommended range in dogs and cats. The injection solution had been prepared by tenfold dilution with sterile physiological solution ten days prior to use in the four cubs and had been stored at room temperature. The same solution had been used previously in other animals without any adverse effects. The storage at room temperature should not have any influence
on the compound, since the recommended storage temperature for levamisole hydrochloride lies between 15 and 30°C (10). It may be possible that an individual susceptibility is responsible for the fatal reaction. In view of the narrow safety margin and the numerous adverse effects reported, levamisole should be used in non-domestic species only if the potential benefits outweigh the risks of the treatment.

Key words: Cheetah, *Acinonyx jubatus*, levamisole, intoxication, adverse drug effect

References