Effect of topical dermatologic medications in humans on household pets

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Topical medications such as 5-fluorouracil (5-FU) and calcipotriene are common treatments for dermatological conditions such as actinic keratoses, cutaneous malignancies, and psoriasis.^{1,2} While topical application normally results in minimal systemic absorption in humans, unfortunate side effects and deaths may occur to animals from inadvertent contact with these medications.

Although the intravenous form of 5-FU can be used safely in dogs as chemotherapy, the topical form has been implicated in diarrhea and vomiting (bloody and nonbloody), tremors, lethargy, ataxia, seizures (including status epilepticus), bone marrow suppression, cardiac arrhythmias, and respiratory depression.¹ Clinical manifestations can be seen within 30 to 60 minutes of exposure. The fatality rate can reach 48% to 64%; death can be as early as 7 hours after ingestion. These effects can even be seen in small amounts; toxic doses have been reported at 5 mg/kg, with a minimum lethal threshold of 20 mg/kg and doses of >40 mg/kg reported to be uniformly fatal. In a 2-kg dog, a lethal ingested dose may be as little as 0.8 g of cream.² Mechanisms of exposure have included dogs licking a treated area on owners, biting the ointment tube, and licking fur (as a means of grooming) that has been touched by owners with 5-FU on their hands.¹ While most reports deal with canines, 5-FU has been found to be more toxic in cats.¹ Owners have been reported to apply 5-FU to suspected actinic keratoses on their cats' ears, leading to death when the cat licked the area.² Due to their grooming habits, cats are particularly at risk for ingestion through licking their own bodies or their owners' face and hands, which are common sites of cream application.

Topical calcipotriene, 0.005%, also has a toxic effect on dogs. Snively et al reported that extremely small quantities—<2 g of cream for a 2-kg dog—have caused death.² Within 24 to 72 hours of ingestion, canines may exhibit signs of anorexia, hematemesis, diarrhea, polydipsia, polyuria, depression, and weakness.³ Hypercalcemia can lead to renal failure and soft tissue mineralization, particularly in doses exceeding 40 to 60 µg/kg.³

Ingestion of hydrocortisone creams may cause gastrointestinal upset and occasionally ulcers, hematemesis, and melena in dogs; however, the creams are safe to use topically for dry skin and pruritus. Dermal exposure to topical minoxidil has caused lethargy, dyspnea, hypotension, pulmonary edema, pleural effusions, and cardiac dysfunction in cats and dogs.⁴ Permethrin-containing topical products (flea collars) have caused neurotoxicity, tremors, fasciculations, and hypothermia in cats.⁵ Topical ivermectin is used in veterinary medicine for heartworm prevention, but some dog breeds are sensitive to the drug; upon ingestion, they can suffer from dilated pupils, seizures, tremors, and coma.⁶ To date, there are no published reports of animal deaths from ingestion of topical ivermectin or permethrin intended for human medication use.

Accidental ingestion of topical imiquimod by mice has resulted in cutaneous inflammation via type I interferons.⁷ Ingestion of fodder contaminated with *Euphorbia peplus*, the source for ingenol mebutate, has led to severe systemic complications in lactating goats.⁸ Further studies may help to illustrate whether these effects can manifest in dogs, cats, or other common household pets.

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Toxicities from the topical medications discussed above are well known in the veterinary setting. We hope to raise awareness of these toxicities and encourage providers to educate patients regarding the risks of these unfortunate occurrences to their pets.

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Avocations

Photo taken from the Castelo dos Mouros (Castle of the Moors) in Sintra, near Lisbon, Portugal. The castle dates from the 9th century and is located in the Sierra Sintra. The Palace of Sintra in the Vila of the same name is seen through a window in the Palace. Photo taken by Alejandro C. Arroliga, MD, with a Nikon D 7100. Dr. Arroliga (Alejandro.Arroliga@BSWHealth.org) is chief medical officer of Baylor Scott & White Health.