

## Natural antifungal in avocados believed to cause sudden death in aye-ayes

January 4 2017, by Karl Leif Bates



Grendel, age 6-1/2, fell seriously ill just at the same time as the four aye-ayes that died, but managed to survive and is now on the mend. Credit: David Haring, Duke Lemur Center

A two-month investigation into the sudden deaths of four aye-ayes at the Duke Lemur Center has left just one plausible explanation—avocados.

Lemur Center officials believe that a natural toxin found in avocados the <u>animals</u> ate the previous day set off damage to their heart muscles, resulting in death within 36 hours on Oct. 25 and 26. A fifth animal fell ill, but is now recovering.



Avocado leaves, pits, skin and possibly the fruit contain a toxin called persin that the plant produces as a natural antifungal. Persin is not harmful to humans, but it is known to be an issue for domestic cattle, horses and goats, as well as several species of bird.

It had not been recognized as a threat to lemurs. Avocados have routinely been fed to captive lemurs around the world for years as a highfat supplement, and it's one of the aye-ayes' favorite foods. Duke's affected aye-ayes had received various parts of the fruit, possibly including skins and pits, as part of their standard diet the day before they died.

Lemur Center Operations Director Greg Dye said avocado is now off the menu for all of the Lemur Center's 230 rare and endangered animals.

The mystery that may never be solved is why these animals suddenly died on this particular day. Duke's aye-ayes have eaten the fruit about once a week without incident for the last few years, and on Oct. 24 all 13 of the Lemur Center's aye-ayes had been fed avocados from the same box; five fell ill, eight were fine.

The Lemur Center's exhaustive examination of the deaths has included testing the animals' air and water for bacteria, pathogens and volatile organic compounds, none of which turned up any evidence of a threat. Tissue samples and stomach contents of the dead animals have been analyzed by several labs.

Lemur Center veterinarian Cathy Williams said the Centers for Disease Control in Atlanta is still testing <u>tissue samples</u> for exotic pathogens, but the pattern and timing of the deaths doesn't really fit with an infectious agent.

On post-mortem examination, all four animals were found to have fluid



around the heart. One also had fluid around the lungs, but the other three had normal lungs. All of them had food in the stomach. An animal toxicology lab at Michigan State University subsequently detected persin in the stomach contents of three of the four dead animals. (The fourth could not be tested.)

Persin is known to attack the mitochondria, structures inside a cell that generate energy.

According to Duke veterinary pathologist Jeffrey Everitt, who examined tissue samples under a microscope, all four animals had changes in their heart muscles consistent with the kind of cell injury and cell death known to come from persin. Two of the animals that survived the longest after the Oct. 24 feeding also showed signs of an immune response causing inflammation around the heart. The cause of death for all was ruled "acute cardiac toxicity."

Because they suspected heart injury as the deaths were occurring, the Duke veterinarians collected blood serum from the four animals that was later tested for cardiac troponin, a molecule commonly used to assess humans for heart attacks. The surviving aye-aye who was affected, a male named Grendel, had elevated troponin levels, as did the four that died. The eight unaffected animals had no detectable troponin.

After resting quietly for a week and slowly regaining his strength, Grendel (age 6-1/2) is now reported to be eating and behaving normally. He was the first aye-aye to fall ill on Oct. 25, perhaps because his feeding schedule was slightly ahead of the others.

Because there is little information about the aye-ayes' sensitivity to different foods, Williams and Lemur Center veterinarian Bobby Schopler went back and reviewed necropsy reports for four previous sudden and unexplained aye-aye deaths from across the country, dating



back to 1998. In every case, avocados had been part of the diet, and in one case avocado was present in the stomach contents.

These had been isolated, apparently unrelated cases over nearly two decades at facilities that regularly fed avocados to aye-ayes and the pattern had never been established.

It was the remarkably similar necropsy findings and the sudden death of four animals in a 13-hour span that had the veterinarians immediately looking for an acute cardiac toxin, Schopler said. Despite the remaining unknowns, avocado toxicity is the only hypothesis that fits well, he said. "It's compelling, consistent evidence."

"Avocado toxicity is not a problem for humans, and it occurs sort of randomly in animals, so it really hasn't been studied much," Williams said. There isn't a standard test for persin toxicity and nobody knows what a lethal dose would be, she said. Persin concentrations are known to vary between the hundreds of different strains of the fruit, as well.

Lemur Center staff have played the incidents of Oct. 24 to 26 back in their heads repeatedly since the tragedy.

Video footage from the animals' enclosure showed the stricken aye-ayes behaving normally just hours before they died. But then the two males left their nest boxes around 3 p.m. on Oct. 25 in apparent distress. Sensing trouble, their keepers whisked them to the veterinary suite, but the animals rapidly progressed to shock and death despite receiving IV fluids, oxygen, intubation and attempts at cardiac resuscitation.

Norman Bates, age 7, died at 4 p.m. on the 25th. Merlin, 22, died 20 minutes later. Morticia, 28, a wild-caught aye-aye from Madagascar, mother of seven and a matriarch of sorts for the colony, died just before 1 a.m. on the 26th. Her granddaughter Angelique, 11, Merlin's daughter



and the first aye-aye born to two captive aye-ayes, died just before 5 a.m.

Williams and Schopler sent a bulletin to their international colleagues on Nov. 2 and again on Dec. 12 urging them to stop feeding avocados to ayeayes.

"The only good to come from this tragedy is that we now know to be wary of <u>avocados</u>. Hopefully our recommendation can prevent this from ever happening again, either at the DLC or any other collection that houses aye-ayes," said Lemur Center Director Anne Yoder.

Provided by Duke University

Citation: Natural antifungal in avocados believed to cause sudden death in aye-ayes (2017, January 4) retrieved 18 April 2024 from <u>https://phys.org/news/2017-01-natural-antifungal-avocados-believed-sudden.html</u>

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