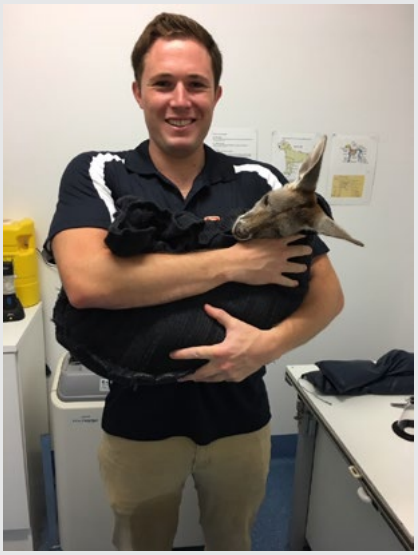

Major Winner Bio

Joe is an English born veterinarian that moved to Sydney to complete his university studies. Joe graduated in 2017 and has since worked in both clinical practice and "human" medical research.

Joe currently works at the Small Animal Specialist Hospital, however, he will soon be moving back to the UK to complete a veterinary cardiology-training program.

Once Joe has completed his Cardiology training program he plans to come back to Australia, where he hopes to live out the rest of his career without ever having to sit another exam again!

MAJOR Winner

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Avian

USE OF INTRALIPID TO PREVENT MYOCARDIAL NECROSIS POST PERSIN TOXICITY IN AN INDIAN RING NECK

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Abstract

Avocado ingestion by birds is a severe and possibly life-threatening toxicity. When a toxic dose is ingested, it is often challenging to perform successful decontamination, and once the toxin is absorbed, there is no known antidote or cure for persin toxicity.

In the case presented here, intralipid therapy was used in the attempt to sequester the persin toxin and prevent myocardial necrosis in a 1-year-old female entire Indian Ringneck Parakeet (*Psittacula Krameri)*, which had been fed >10-15g of Hass Avocado (*Persea Americana*).

On initial physical examination, the patient had a reduced ability to perch, lethargy, and drooping of the neck. Crop lavage was of low yield, and charcoal was administrated before gaining IV access and administering intralipid. Throughout the hospitalisation period, the ringneck developed an arrhythmia and dyspnoea. The dyspnoea resolved with diuretic therapy, and the arrhythmia resolved within 48 hours of intralipid administration, with discharge occurring on the 5th-day post avocado ingestion.

Clinical case

A one-year-old female entire Indian Ringneck Parakeet presented within 30-60 minutes of ingesting >10-15g of Hass Avocado pulp. On initial visual examination, the patient was dull, mildly ataxic, was not perching and appeared to be bowing at the neck. On physical examination, the perching reflex was reduced, the patient was mentally dull and ataxic. On further examination, the heart sounds were normal, regular with a rate >300bpm. Air sac auscultation was unremarkable, and the respiratory rate was 52bpm. The rest of the examination was unremarkable.

Due to the potentially significant dose of persin ingestion and the risk of myocardial necrosis, a crop lavage was performed within 90 minutes of ingestion. The crop lavage produced a small volume of white/yellow material mixed with the instilled water. Subsequently, 1g/kg of activated charcoal was instilled using a crop needle.

Subsequently, the patient was sedated using butorphanol 0.2mg/kg and midazolam 2mg/kg intramuscular (I.M.) injection. While sedated, the feathers were removed from the axillary region and the skin was aseptically prepared. A 26g intravenous catheter was placed within the brachial vein and sutured in place with 4-0 nylon suture.

Intralipid 20%, 2.5mL/kg bolus was initially given over one minute, followed by a C.R.I. running at 0.025mg/kg/min for 6.5h.[1] Concurrently, plasmalyte crystalloid IV fluid was started at a 25mL/kg/day rate, which was increased to 75mL/kg/day once the intralipid was discontinued. The patient was placed in a Brinsea TLC-50 incubator in I.C.U. and monitored actively throughout the treatment period.

The patient's mentation did not improve overnight, and the clinical condition remained static. Later the subsequent day, the patient remained dull and increased respiratory effort and rate were noted. The veterinarian on duty auscultated an arrhythmia and found one vomit/regurgitation in the bedding. Frusemide at 4mg/kg P.O. was given as a one-off dose, improving respiratory effort and rate. Intravenous fluids were discontinued with subcutaneous plasmalyte to be given q12h to maintain 50mL/kg/day fluid requirement.

The patient's demeanor improved throughout the second day, and a further dose of activated charcoal 1g/kg mixed with Emeraid® omnivore 2mL was given via crop needle.

The patient's mentation deteriorated on the second night, and on the morning of day 3, the parakeet was again depressed, with a small amount of vomitus dried onto the skin around the nares. Mild green staining around the vent was noted, and the urates were green-tinged. Tachypnoea with mild increased respiratory effort and harsh lung sounds were again recorded. Cardiac auscultation revealed muffled heart sounds with an H.R.>300bpm. TFAST was performed, which showed no pericardial effusion and no pleural

effusion. Frusemide 1 mg/kg q8h P.O. was started in addition to Silybin 50mg/kg q12h P.O.

Bloods to determine if there were hepatic abnormalities were not performed as there was a mild amount of bleeding during catheter removal, and blood draw for liver enzyme testing was deemed of high risk at this stage in time.

Mentation improved significantly on day 4, with demeanor characterized as bright, alert, and responsive. The patient started eating independently, and respiratory effort and sounds were normal. Cardiovascular examination was unremarkable. Frusemide was discontinued, and the patient was kept in for a further 24 hours of monitoring.

Discharge occurred on day 5 with no evidence of cardio-respiratory disease. The patient was discharged with Sylibin 50mg/kg P.O. B.I.D. for seven days, and on a phone call recheck on day 10, the patient was described as bright and as her usual self by the owner.

Discussion

Persin, a larvicidal and antifungal alkanol, is found in the stems, fruit, pip, leaves and skin of the avocado plant, with the Guatemalan strains (such as Hass avocados) being the most toxic.[2, 3] Despite all parts of the plant containing persin, the toxin concentration varies depending on which part of the fruit or plant is eaten (Table 1), with the pulp containing the highest toxin concentration.[2, 4-7] Prospective studies on rabbits fed 150g of avocado leaves showed that those who ate the Fuerte variety died within 12h. On the other hand, rabbits fed leaves from Nabal varieties survived past 12h but succumbed within 24h, and those fed Mexicola varieties showed no ill effects.[8]

Plant matter (freshly harvested Guatemalan variety)	Persin concentration mg/g
Peel	0.6-1.4mg/g
Flesh	1.5-5.8mg/g
Leaves	<0.01-4.5mg/g

Table 1. Persin concentration in mg/g in the different parts of the avocado plant[7, 13]

Avocado toxicity has been shown to cause sterile mastitis secondary to coagulopathic necrosis, interstitial oedema, and desquamation of the acinar epithelium in goats, cattle and mice with acute exposure to 60-100mg/kg persin.[14, 15] Goats and horses have also been shown to develop neck and brisket oedema at 60-100mg/kg.[2, 3, 12, 15] However, sheep exposed to either an acute dose of 100mg/kg or chronic doses of 2.5mg/kg over 32 days develop cardiac insufficiency in controlled experimental models.[3, 8, 16]

Clinical signs in birds are less well defined, with reports suggesting that avian species are more severely affected and often die after short periods of dyspnoea, neck oedema, thigh and abdomen anasarca and cardiac insufficiency.[2, 9, 10, 17]

One of the few designed experiments investigating the effects of persin in birds found that both New Hampshire Hens and Ostriches often developed cardiac insufficiency when they had access to avocado fruit or leaves. On histological examination, it was noted that the myocardium was infiltrated with heterotrophils, there were areas of macrophage proliferation, karyopyknosis, and the myofibres exhibited marked granularity of the sarcoplasm.[9] **Chickens** fed avocado also developed hepatocellular vacuolation and hepatocyte congestion in the liver parenchyma.[9]

A second branch of the same study looked at 2½-month-old **ostriches**, which were fed different parts of the avocado plant (see Table 2). All birds developed listlessness and drooping of the neck two hours before death.[9] Severe anasarca of the neck was evident in the ostriches fed Hass leaves, with mortality occurring within 48 hours.[9] Ostriches fed Fuerte fruit also developed severe hydropericardium, and pericardial oedema was noted in the birds fed the Fuerte foliage.[9] All birds

Product fed	Number of ostriches
Hass foliage 30g/kg	1
Hass fruit 100g/kg	1
Fuerte foliage 75g/kg	1
Fuerte fruit 100g/kg	1
Water (controls)	2

Table 2. Ostrich number and avocado matter fed in the Anna et al (1994) study.[8]

Case reports on persin toxicity in animals are scant, with very few peer-review prospective studies having investigated avocado toxicity in veterinary medicine. Thus far, persin toxicity has been reported in budgerigars, cockatiels, turkeys, chickens, sheep, ostriches, fish, guinea pigs, canaries, rats, rabbits, horses, goats, and cattle, with unconfirmed incidences in dogs.[9-12]

Figure 1. Catheter in place.

developed cardiomyopathies, and histopathology showed hydropic degeneration to fragmentation and rhabdomyolysis of myocardial fibres.[9] As with the chickens, the myocytes of ostriches fed avocado plant matter had sarcoplasms with increased granularity, myofibrillolysis and eosinophil infiltration.[9] Heart histopathology cross-sectional examination also showed eosinophilic cytoplasm and pyknotic nuclei of the myofibres, with heterotrophil infiltration.[9, 18] A similar finding of hydropericardium has also been seen in caged birds.[10]

Our patient ingested >10-15g of pulp, placing the consumed dose of persin between 18.5mg/kg and 107mg/kg, depending on the toxin concentration within that specific fruit.[2, 4-7]

Standard decontamination procedures (crop lavage and charcoal therapy) were administered; however, the owner was highly invested in this parakeet and wanted to try everything possible. With decontamination, the prognosis was still determined to be poor due to the potentially large dose of avocado ingested, and due to the dull presentation, bowing head and ataxia, which in many studies have been described as end-stage clinical signs antecedent to death.[1, 8, 9, 15] As a result, based on the chemical properties of the persin toxin, we suggested trialling intralipid therapy (I.L.T.), which the owner approved of despite being warned of the possible risks and off—label nature of the treatment.[19]

Intralipid, a soybean-oil fat emulsion, has been used in human medicine since the 1970s to treat life-threatening toxicosis caused by fat-soluble toxins.[20] Due to the unknown aetiology of many toxicities in veterinary medicine, and the lack of easily accessible extracorporeal therapies, I.L.T. is often initiated earlier or when conventional therapies are unsuccessful.[20] The objective of I.L.T. therapy is to increase energy production, thus altering the kinetics of persin and creating a lipid sink that can sequester lipophilic toxins within the intravascular space.[20]

The lipophilicity of a chemical is based on its LogP value, where P is the partition coefficient of the toxin.[19] The partition coefficient is a measure of how soluble a compound is between a lipophilic (octanol) and a hydrophilic (water) solution. The higher the LogP, the more lipophilic a compound is, although the lipophilicity depends on the acidity of the contained solution.[19] As a result, LogD is often used in medical chemistry, where the D represents the partition coefficient of a chemical at physiological pH of 7.4, again with partition coefficients varying in states of acidemia or alkalosis.[20, 21] Persin with a LogP and D of 5.98 indicates that the toxin is ~955,000 times more soluble in the lipid phase than the aqueous one.[19]

To the author's knowledge, the use of I.L.T. has not been used in Ring Necks before with one reported use of intralipid in a goose with suspected oleander toxicity.[22] Parakeets can consume soybeans without known side effects, and only a low dose C.R.I. was used out of concerns of hepatic lipid congestion, anaphylaxis and increased plasma oncotic pressure.[20]

The patient tolerated I.V. intralipid therapy without issues at the time of administration. While in hospital, the patient did develop signs of acute cardiorespiratory disease; however, this did resolve with diuretic therapy before discharge, and these symptoms were not apparent on recheck. No reports exist that suggest persin toxicity is reversible or self-limiting, with mortality seen in all birds that developed myocardial necrosis.[3, 4, 6, 8-10] At this time, without histopathology, we cannot determine whether the signs were secondary to persin myocardial toxicity or by volume overload caused by the intralipid itself.[8, 21] An immune reaction towards the intralipid could cause an increase in pulmonary microvascular permeability resulting in non-cardiogenic pulmonary oedema; however, this would not have been responsive to frusemide therapy.[23]

Our patient did develop green urates, a common sign associated with liver disease in birds, although this remains unconfirmed due to the lack of blood work and imaging.[9, 10]

Limitations include the case number and our inability to determine whether the arrhythmia and the dyspnoea seen during hospitalization were due to the acute side effects of the persin toxin or secondary to iatrogenic causes.[20, 21, 23] Furthermore, the response of intra-lipid by other species of birds may vary significantly compared to what was seen in our case. **However, despite the limitations of this report, we now have early-stage evidence to suggest that Parakeets can tolerate low dose IV intralipid therapy.**

We hypothesize that intralipid can reduce the cardiotoxic risk profile of avocado ingestion based on the chemical analysis of persin. As a result, this report can be used as a base on which to build further studies in the use of intralipid on lipophilic toxins in birds, and it can provide the basis for justifying a prospective study that investigates the use of I.L.T. in avocado toxicity.

Conflicts of interest

The author and owners of the patient involved have no conflicts of interest.

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COMMENT COURTESY OF

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Avocado toxicosis is widely reported but predominantly anecdotally. The toxic effect is well known, but usually presented as a cause of death. In fact, I have had many bird owners declare adamantly that avocado is not toxic. It is pleasing to see the author not only successfully treated the patient, but expands on the toxic principles of avocado, the differences between different types of avocado and plant parts, the course and clinical signs of the toxicosis, and then presents a novel treatment protocol (for birds) that warrants further investigation.