Toxic Times

SPRING 2017 ISSUE

Welcome

Welcome to the Spring edition of Toxic Times.

After the excesses of Christmas and the accompanying determined New Leaf approaches, dietary supplements will once again be in the arsenal of measures of many people to tackle weight loss or health issues.

In the Spring 2016 edition of Toxic Times, we discussed, various dietary supplements which pets may be exposed to in the home, but in this issue, we look at the problems associated with animals ingesting vitamin D analogues and joint supplements.

At the other end of the weight loss spectrum, we also give a brief reminder of the treatment doses for chocolate, given that Easter is on the horizon, and, as we all know, dogs especially have no sense of portion control.

Still on the food theme, we look at tremorgenic mycotoxins, most commonly found in mouldy food, an agent that always features in our Top 10 enquiries received-again, mostly dogs!

A long-overdue return of the Meet the Team series recommences with Mark Van-de-Velde—it's always fun to be able to put a face to the name of the person who is helping you with your enquiry. Mark wrote the highly informative article on tremorgenic mycotoxins, whilst taking time off from crushing his opponents at tennis.

The 2017 CPD dates are listed, with a new location of Newcastle making an appearance.

2017 CPD COURSES

Key Areas Covered (six hours of CPD)

- Case histories for potential poisons cases
- Decontamination for poisons cases
- Toxicology information resources

Cost and Bookings

Standard fee: £295 + VAT
Early bird fee: £250 + VAT*

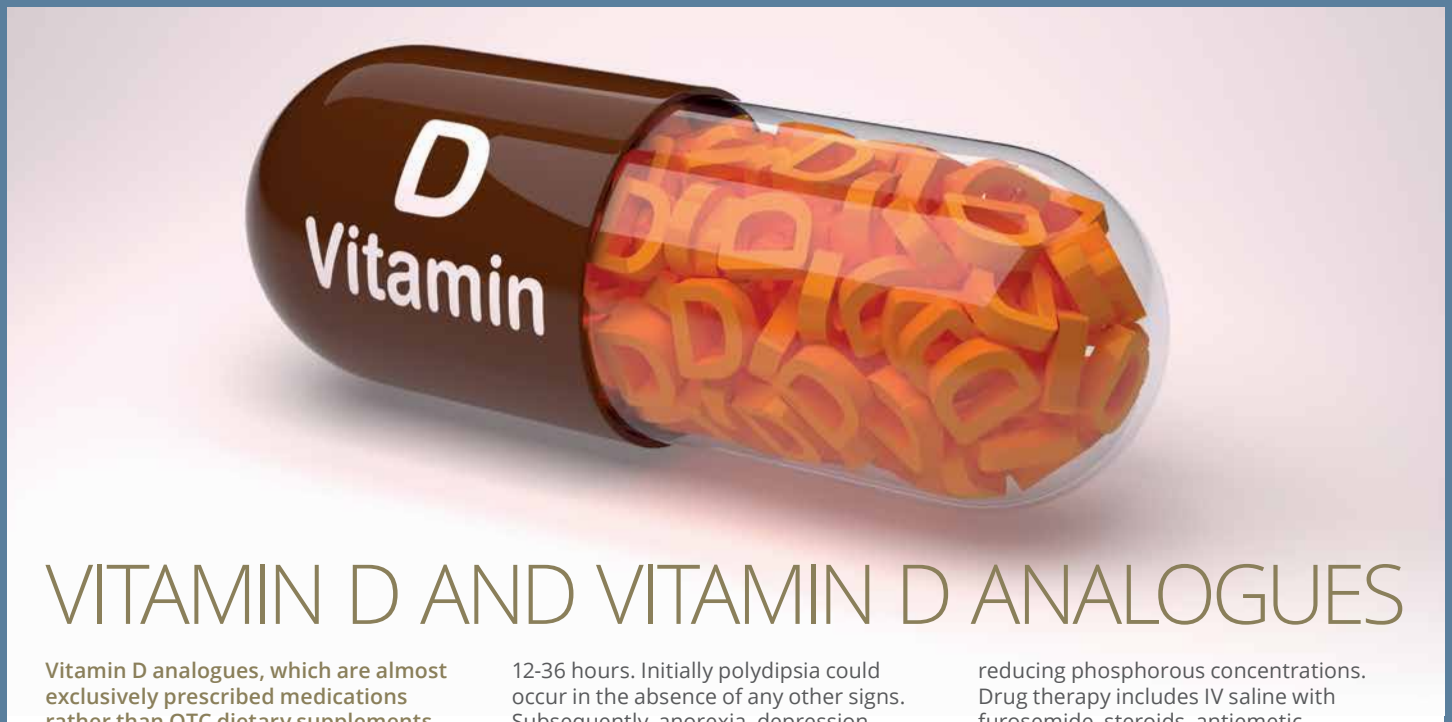
Each delegate will receive course notes and a CPD certificate (equates to 6 hours CPD training). Lunch and refreshments are provided.

Bookings: To reserve a place, please visit the link below and download the booking form.

https://vpisglobal.com/class-based-courses-2017/

Date	Location
March 15th	Birmingham
May 10th	York
June 21st	Bristol
July 19th	Newcastle
September 13th	London
October 4th	Manchester
November 8th	Cambridge

** Early bird discount applies to bookings made up to 8 weeks prior to the course date*



VITAMIN D AND VITAMIN D ANALOGUES

Vitamin D analogues, which are almost exclusively prescribed medications rather than OTC dietary supplements have a really bad reputation in toxicology - with good reason. Some of the vitamin D analogues are extremely toxic - tacalcitol has a potentially lethal dose of <4 mcg/kg in dogs. When dealing with vitamin D you must be certain whether you are dealing with 'plain' vitamin D or with the common analogues of vitamin D3 (colecalciferol or cholecalciferol) or less commonly D2 (calciferol or ergocalciferol). D3 is frequently found in combination with calcium. The dangerous dose of D2 or D3 is > 0.5mg/kg (or 21,000 IU/kg) - given that tablets often contain around 400 IU or less it would be unlikely to be acutely dangerous.

Calciferol and colecalciferol are rapidly absorbed and metabolised by the liver and kidney. The parent compounds and the intermediate metabolites have some limited pharmacological action but the major toxic effects are due to the major metabolite, calcitriol, which enhances resorption of calcium from bone, absorption of calcium from the gut, intestinal calcium transport and proximal renal tubule reabsorption of calcium in the kidney. This gives rise to hypercalcaemia and toxicity.

Calcipotriol is a synthetic derivative of calcitriol, a form of vitamin D. Although it is used in the treatment of psoriasis, and is thus not a dietary supplement, it produces similar effects by the same mechanism. Animals often lick their owner's skin, and extreme care must be taken if these products have been applied to the owner to ensure pets are not put at risk.

If sufficient tablets were taken, the onset of clinical effects for calciferol and colecalciferol would be usually within 12-36 hours. Initially polydipsia could occur in the absence of any other signs. Subsequently, anorexia, depression, weakness, lethargy, recumbency, polyuria, polydipsia, profuse vomiting and diarrhoea could all develop.

As the calcium concentration rises above 3 mmol/L (12 mg/dL) (usually 24-36 hours) there may be severe vomiting, anorexia, constipation, ataxia, dyspnoea, tachypnoea, arching of the back, muscle spasms, twitching and convulsions.

In severe cases of hypercalcaemia, hyperphosphataemia may be present, from 12-72 hours, and deposition of calcium in tissues may cause initial tachycardia, then bradycardia and renal insufficiency (polyuria, azotaemia and hyposthenuria) or renal failure. Haematemesis and haemorrhagic diarrhoea may occur as a result of calcification in the gastrointestinal tract and pulmonary haemorrhage has also been reported. Metabolic acidosis and leucocytosis and thrombocytopenia are occasionally reported, and the commonest causes of fatality are shock and fulminant pulmonary oedema.

Cardiac abnormalities may also be seen on ECG. Hypercalcaemic cardiac failure may occur if the serum calcium concentration exceeds 3.5 mmol/L (14 mg/dL).

These effects are all the result of raising calcium levels due to vitamin D mediated release from bone.

Initial treatment would include emesis - if the dog or cat was seen with a few hours. Activated charcoal probably has no real value in these cases. However the main aim of therapy is to ensure adequate hydration and urine output whilst controlling calcium concentrations and reducing phosphorous concentrations. Drug therapy includes IV saline with furosemide, steroids, antiemetic, gastroprotectants, a phosphate binder and a bisphosphonate. Although lipid emulsion therapy should work (as vitamin D is lipophilic), the ½ life of vitamin D is too long for this to be practical.

Case report to VPIS

Calcipotriol in a dog

A 15 kg cross breed became unwell 20 hours after ingestion of an unknown quantity of Dovonex cream with vomiting and shaking. She presented at 24 hours and was started on IV fluids, maropitant, dexamethasone and furosemide. Laboratory tests found she had renal failure with hypercalcaemia, hyperphosphataemia, hyperglycaemia and hypokalaemia (due to vomiting). She was still producing urine. The next day she was bright in her kennel and wagging her tail but that night she vomited and urinated in the kennel. The next morning she was depressed and was noted to have a swelling under neck. She sounded throaty when lying down but had no breathing difficulties. As the day progressed she became reluctant to sit or stand. She would not drink and continued to vomit. The neck swelling was worse and was thought to be a retropharyngeal injury/abscess from chewing the tube.

Repeated bloods showed that renal parameters has deteriorated and she had hypoproteinaemia (presumably due to urinary loss). She had severe hypercalcaemia, hyperphosphataemia and hyperkalaemia. She was euthanized 52 hours post-ingestion. The vet felt the poor outcome was due to late presentation in this case.

KING
IMAGE CREDIT: THE WHITE HORSE VETERINARY CLINIC, CALNE

Tremorgenic mycotoxins in dogs

Rotting food stuff often consists of many different potential fungal metabolites which can be harmful to our pets. Ingestion of a variety of mouldy foods, including bread, walnuts, almonds and peanuts, as well as general rubbish around the family home, have all been associated with the presence of tremorgenic mycotoxins.

Tremorgenic mycotoxin poisoning in dogs typically presents as an acute onset of generalized tremors, sometimes of sufficient severity to resemble a seizure. Such cases may be very serious and often require hospitalization. Dogs are more commonly affected than other species because of their tendency to scavenge.

The most common signs reported to the Veterinary Poisons Information Service (VPIS) include hypersalivaton, excessive panting, pyrexia, nystagmus, mydriasis, hypersensitivity, and ataxia. The time of onset of tremors after ingestion varies from 30 minutes to 3 hours. Dogs may also experience gastrointestinal disturbances such as vomiting and diarrhoea.

Treatment is usually symptomatic and supportive care. Seizure control is the most crucial aspect of emergency care and many anticonvulsant drugs such as diazepam or methocarbamol can be used to reduce tremor activity, although diazepam alone may not be effective in controlling mycotoxin- induced tremors.

Lipid infusion is increasingly being used in the management of tremorgenic mycotoxin poisoning due to the lipophilic nature of these fungal metabolites and should be considered for any animal at risk of serious toxicity. Given intravenously, it can lead to dramatic improvements in clinical condition, reduce the amount and duration of treatment with other drugs and reduce the overall hospitalization time. It is simple, easy to administer and cost-effective. For more information on how to source lipid emulsions (Intralipid® 20%) visit the VPIS website.

The prognosis is generally good for mildly affected dogs that respond to prompt treatment and seizure control measures. Dogs that experience prolonged seizures or develop aspiration pneumonia have a more guarded prognosis. Clinical signs generally have a short duration, with full recovery seen in most dogs within 24-72 hours.

A dog called King (bodyweight 40kg) ingested a mouldy chicken pie and presented to the veterinary practice with severe muscle twitching, vomiting and hyperaesthesia to noise and touch. A gastric lavage was performed (which was unsuccessful), and intravenous diazepam was given to control the twitching. However, due to persistent neurological signs of 10-12 hours, a course of intravenous lipid infusion was administered. Following the lipid infusion, the patient steadily improved and made a full recovery within one week. A sample was submitted for toxicological analysis, which confirmed exposure to the tremorgenic toxins: Penitrem A and Roquefortine.

Summary

Dogs with suspected tremorgenic mycotoxicosis should receive routine blood tests, muscle relaxants and anticonvulsant drugs to control tremor activity. Following prompt treatment, the prognosis is good and most dogs make a speedy recovery. Lipid infusion therapy can be considered in dogs that fail to respond to other therapies. Avoidance of exposure is the only preventive measure. Inquisitive pets that are prone to scavenge or ingest rubbish or leftovers should have their access to these temptations restricted by owners.

Joint Supplements

Joint supplements commonly contain chondroitin (a glycosaminoglycan, which is a structural component of cartilage) and glucosamine, which is a naturally occurring amino-sugar; it is a precursor for the biosynthesis of the glycosaminoglycans and proteoglycans of the cartilage matrix. It is widely used for the relief of joint pain and stiffness, to improve joint movement and flexibility. There may be present a variety of other ingredients, such as green -lipped mussel extract, a rich source of nutrients, including glycosaminoglycans, such as chondroitin, vitamins, minerals and omega-3 triglycerides.

There is insufficient information to determine a toxic dose of a joint supplement. Liver toxicity has been reported after 20-240 tablets (Khan et al., 2010).

An emetic and/or activated charcoal should be considered, particularly after a large ingestion. Gastrointestinal signs can occur within 1-3 hours, with recovery usually occurring within 12-48 hours.

Usually only diarrhoea (often watery) is present, sometimes accompanied by vomiting and abdominal discomfort.

Liver damage (Khan et al., 2010) and multi-organ dysfunction has been reported in dogs (Khan et al., 2010; Nobles and Khan, 2015) after ingestion of joint supplements. The onset of elevated liver enzymes has been reported as 24 to 48 hours in most cases but occurred within 10-12 hours in two cases. The cause of hepatotoxicity is unknown. Liver toxicity has not been reported in any VPIS cases where follow up has been available.

Khan SA, McClean MK, Gwaltney-Brant S. 2010 Accidental overdose of joint supplements in dogs. J Am Vet Med Assoc 236 (5):509-510.

Nobles IJ, Khan S. 2015 Multiorgan dysfunction syndrome secondary to joint supplement overdosage in a dog. Can Vet J 56(4):361-4

MEET THE TEAM

Name: Mark Van-de-Velde

Job Title: Information Scientist

How long have you worked for VPIS?
I started working for the VPIS in November 2015 shortly after graduating from University. I have now been working here for over a year!

What do you most like about your job?
I think having the ability to help a poisoned animal in some small part by providing advice to vets is the most rewarding thing about my job. Also, I like that every day is unique as we receive so many different enquiries which vary depending on the kind of poisons encountered.

I enjoy contributing to our monographs which serve as guides when answering poisoning enquiries. I also write pieces for the VPIS E-newsletter and Toxic Times which I find very fulfilling.

What do you most dislike about the job?
Working the night shifts every month, especially the ones on the weekends.

What is your most memorable VPIS telephone enquiry?
There are so many but one of the most memorable, saddest enquiries I received was on one of my night shifts. An 8 week old Chihuahua puppy weighing only 480g was treated by a breeder with a malathion louse powder (an organophosphate insecticide). After the new owners returned home the puppy suddenly became unwell with depression, diarrhoea, constricted pupils, collapse and convulsions. Despite everyone's best efforts and intensive nursing, the tiny puppy did not recover. She developed multiple hypoglycaemic episodes and other complications with her blood results.

Do you / did you have a pet / pets?
I have a family cat back home in Loughborough, called Norbit who I try to visit often! Also uncle to two great dogs; Mani the Pug and Alfie the Labrador-collie cross.

What are your hobbies / other interests?
I like the usual things really: chilling out/ watching TV, going to the movies, gym and the occasional music festival (recent ones have been Parklife and SW4).

I really enjoy my tennis as well. I began playing at the age of 8. I am currently slaying at the local tennis league in London; hoping to win tickets this year to tournaments such as Queens and Wimbledon!

Favourite food?
Fish & Chips with curry sauce!

Where is the most unusual place you have ever visited?
The ancient Mayan ruins of Chichen Itza, located on Mexico's Yucatan Peninsula was pretty cool! It was a long hot day in the middle of nowhere but well worth the trip. There was so much culture and history about the ancient civilization that existed thousands of years ago.

Favourite quote:
One of my favourite quotes given to me by my Dad is:

"Do not go where the path may lead, go instead where they is no path and leave a trail."

CHOCOLATE: A REMINDER

It's that time of year again: shops bursting with tempting chocolatey comestibles, eggs in every shape and size, chocolate bunnies, chicks, ducklings and even carrots... Easter!

It's worth remembering that dogs (in particular) have no sense of portion control and will eat any or all that is put in front of them- or possibly more correctly, what they unearth around the home.

Here is a reminder of our chocolate treatment doses, but below are 2 sadly fatal cases involving dark chocolate and drinking chocolate powder:

White Chocolate	No treatment required, as insufficient quantities of theobromine present
Milk Chocolate	Treat for amounts of ≥ 14g/kg
Dark Chocolate	Treat for amounts of ≥ 3.5/kg
Cocoa Powder	Treat for amounts of ≥ 0.5g/kg
Drinking Chocolate	Treat for amounts of ≥ 40g/kg

Dark chocolate in a dog
A 14 year old, 8kg West Highland white terrier stole and ingested Sultans Plain Chocolate Covered Stem Ginger containing a total of 70g of dark chocolate. He developed diarrhoea and abdominal distension within 8 hours and was stomach tubed to relieve the distention. He was also given IV fluids but developed severe pancreatitis with intractable pain and refused to eat. He was euthanized at 72 hours.

Drinking chocolate in a dog
A 10 year old collie broke into a kitchen cupboard and ingested 500g of Cadbury's Drinking Chocolate during the afternoon. About 12 hours later (during the night) the owner called the veterinary surgery because the dog was 'acting oddly'. The vet advised they bring the dog into the practice in the morning. At 16 hours the dog developed convulsions and was dead on arrival at the surgery 17 hours post-ingestion.

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