LEAD POISONING IN A DOG

J H WILLIAMS* and M C WILLIAMS**

ABSTRACT
A case of lead poisoning caused by ingestion of a lead roof-washer is described in a one-year-old, spayed Fox Terrier bitch, presented with nervous signs, and basophilic stippling of red blood cells. Blood concentrations of lead were in the low toxic range. Radiography of the abdomen revealed radio-dense objects in the stomach, which on gastrotomy included a lead roof-washer. Prior to removal of the foreign bodies, the dog showed remarkable improvement on non-specific symptomatic treatment alone, and recovered well after surgery, only to die unexpectedly several hours later. Concentrations of lead in the liver and kidneys were extremely high, and histology revealed typical intracellular inclusions and organ degeneration. In the light of these findings, it is suggested that all cases of suspected or confirmed lead poisoning be given specific chelation therapy.

Key words: Poisoning, lead, dog.

INTRODUCTION
Lead poisoning in dogs has been comprehensively researched, reported and reviewed in the literature1-10, but despite being regarded as a "common" poisoning elsewhere, lead poisoning in dogs has not been reported in the Republic of South Africa. Twenty-eight cases of lead poisoning in dogs and cats were reported at Broken Hill Mine Township in Zambia6. It was found that the lead content of soil in the area where cases occurred, was high. In houses where some of the cases occurred, smelter ash (high in lead) from the mine was invariably distributed on their driveways. Cases where older dogs were involved, animals presented with clinical signs of restlessness and abdominal pain and occasionally with vomiting and/or diarrhoea which was sometimes bloodstained. Younger animals often showed intermittent bouts of nervous signs characterised by anxiety, hyperexcitability, fear, hysteria, continuous barking and convulsions.

The incidence of lead poisoning in dogs is reportedly seasonal6 with most cases occurring in summer and autumn. This may be due to a decrease in faecal and urinary excretion of lead which occurs at high environmental temperatures8, and/or increased amounts of vitamin D produced, following prolonged exposure to sunlight, thus promoting intestinal absorption of ingested lead8. There is probably no breed predilection, although in one survey Poodles were highly represented8. Most affected dogs are younger than one year old, this age-group being most prone to chewing and eating various oddments which could include lead-containing materials such as certain paints (no longer the threat it was in the first half of this century), linoleum and building materials8. Other specific sources mentioned include weights, toys, fishing sinkers, golf balls, putty, lead-glazed containers used as receptacles for water or food8, batteries and solder8. A source of possibly-increasing importance is atmospheric lead from vehicles combusting leaded gasoline (which prevails in very high concentrations at dog-nose level on busy streets9,9). It could be expected that cats, due to their grooming behaviour, might also ingest lead-containing fallout on their coats, in addition to inhaling it in congested urban areas.

The presenting clinical signs recorded in lead-poisoned dogs7,8 include gastrointestinal dysfunction (anorexia, abdominal pain, vomition, diarrhoea or constipation); nervous disorders (clonic-tonic convulsions, hysteria, tremors, nervousness, behavioural changes, champing fits, paraplegia, muscle spasms, hyperaesthesia, blindness, deafness, retraction of the eyeballs with resultant protrusion of the nictitating membranes, Horner's syndrome, photophobia, miosis, incoordination and rarely, oesophageal paralysis) and pallor of the mucous membranes. Convulsions, if present, may show an extreme variation in frequency and duration. Sometimes there is weakness, weight loss and sialosis. Very occasionally there is a Burtonian line on the gums and in a few young dogs with active growth plates, there may be radiographic or post mortem evidence of "lead lines" in the metaphyses of long bones9. Radiographically these lead lines appear as densely sclerotic bands, 2-4 mm wide and, if present, are most easily visualised in the distal radius and ulna. In some animals mild proteinuria7,8 casts and occasionally glycosuria7,9 may be seen, but often urinalysis and blood urea concentrations are normal7. There may be excess concentrations of urobilinogen7,9 and delta amino levulinic acid5,7 in the urine.

Haematological changes include basophilic stippling of erythrocytes, which may be "punctuate" or "reticular", and the presence of immature (especially nucleated) erythrocytes, in the absence of severe anaemia. These changes are considered almost pathognomonic for lead poisoning in dogs7,5,8,9 but are not always present5. Pale mucous membranes may be noticeable despite a relatively normal packed cell volume. This is due to reduced haemoglobin concentration of erythrocytes. Lead disrupts heme synthesis at several points and interferes with normal maturation of red cells9, leading to decreased oxygen-carrying capacity and increased fragility. Globin synthesis is
also partially inhibited, contributing to a decreased red cell life-span. The enzymes most sensitive to inhibition by lead, are delta amino levulinic acid dehydratase (ALAD) and ferrochelatase. Amino levulinic acid concentrations have been measured in the urine (U-ALA) as an indicator of lead poisoning in dogs, but results have been variable. Due to these biochemical disruptions, a mild to moderate normocytic and hypochromic anaemia may be present. Anisocytosis, poikilocytosis and polychromatophilia often occur. Some dogs show mild to moderate leucocytosis, usually attributable to absolute neutrophilia and a left shift. Lymphopaenia, eosinopaenia and monocytopenia are other findings in these animals although a few animals have absolute leukopaenia, but monocytes and eosinophils. Erythrocyte sedimentation rate is normal and Coombs' tests are negative.

Reports on bone marrow changes vary. Increases in segmented neutrophils and megaloblastic series cells, and increased myeloid-erythroid ratios (M:E), which decreased once lead administration had ceased, were reported in experimental dogs. Bone marrow sections from 15 naturally-occurring cases showed hyperplastic bone marrow, especially of erythroid elements.

An increased protein concentration in cerebrospinal fluid in lead-poisoned dogs is occasionally seen.

Electro-encephalographic (EEG) abnormalities are usually intermittent, generalised, high amplitude, slow wave activity, which although not diagnostic for lead poisoning, may differentiate encephalopathy from encephalitis. The slow waves vary from 1 to 4 cycles per second, with amplitudes of 100 μV to greater than 200 μV in moderately to severely affected dogs. The EEGs were recorded with the animals lightly anaesthetised in one study, and non-sedated in another series.

Zook et al. state that the diagnosis of lead poisoning in dogs is fairly accurate when based on the history, clinical signs, radiography, haematological manifestations and clinical response to chelation therapy. Confirmation of the diagnosis is most meaningfully performed by measuring blood and urine concentrations compared before, and 24 h after, the initiation of calcium disodium ethylene diamine tetra-acetate (CaEDTA) therapy. Diagnostically-significant values quoted are 35 microgram or more per 100 ml of blood and 75 μg or more per l of urine before treatment and 821 μg or more per l of urine 24 h after the start of chelation therapy. Normal blood lead concentrations in dogs are quoted as ranging from 0.02 to 0.05 mg 100 ml−1, but a few dogs with concentrations of 0.04 to 0.05 mg 100 ml−1 did actually have lead poisoning. Usually concentrations of 0.06 mg 100 ml−1 or more, are considered to be diagnostic for poisoning. There does not, however, seem to be a correlation between the concentration of lead in the blood and the severity or character of clinical signs, but dogs with very high blood levels tend to recover slowly and are more likely to have recurrences after termination of treatment.

Postmortally, liver specimens are the most reliable source for lead determination. Samples should be collected some distance from the gall-bladder or major bile ducts, since lead is concentrated in bile and may be imbibed into the parenchyma after death. Diagnostic levels of lead in liver (wet mass) are quoted as 3.6 μg or more per gram. It has been shown that neither freezing of tissues for a few months, nor storage in 10% neutral buffered formalin for up to 5 years, affected the lead content of the stored liver tissue. Kidney tissue is sometimes also analysed, but considerably more lead is found in the renal cortex, than in the medulla and hence uniform sampling is difficult.

In contrast to humans, hair-analysis in dogs gives unreliable results due to variable growth rates and seasonal shedding. A value of 88 μg or more per gram of hair has nevertheless been quoted as diagnostic for dog hair.

Dogs which die from lead poisoning may show few gross changes at necropsy apart from meningeal congestion, occasional white “lead-lines” in the metaphyses of immature dogs, abnormally reddened bone marrow and foreign material in the gastrointestinal tract. Microscopic changes are more specific and consistent, especially in the brain, metaphyses, kidneys, liver and bone marrow. Lead encephalopathy is characterised by dilatation of blood vessels, swelling and necrosis of endothelial cells, haemolysis and necrosis of some arterioles and occasionally thrombosis of capillaries. There may be oedema, fibrin and haemorrhage around these damaged vessels. Vascular necrosis of neurons and gliosis may be present in the cerebral cortex. If nervous signs have persisted for more than a week, endothelial cells and new capillaries may proliferate in the cortical gray matter. The “lead-lines” in immature metaphyses consist of heavily-mineralised cartilaginous trabeculae covered with a thin layer of bone extending from the epiphyses towards the diaphyses. In most dogs characteristic, eosinophilic, acid-fast, nuclear inclusions are found in renal and hepatic epithelial cells. The bone marrow, especially the erythroid element, is hyperplastic. Less common lesions include random necrosis of striated muscle fibres and peripheral neuropathy. The latter lesion is thought to be the cause of megaesophagus following lead-induced vagal neuropathy. Suppression of ovarian follicles and spermatogenesis, and haemosiderosis of the liver and spleen have also been observed.

The approach to treatment of lead-poisoned dogs varies. Some researchers recommend that patients exhibiting moderate clinical signs with no immediate threat to life, are best treated conservatively (by removal of unabsorbed lead from the digestive tract by means of laxatives, enemas, emetics or surgery), and only those with severe blood or nervous derangements should receive specific chelation therapy. Others, however, advise specific chelation therapy as soon as a diagnosis is made, in addition to prompt removal of the source of lead from the gut. In a recent experimental study it was shown that in the absence of chelation therapy, following oral dosing of lead, several months were required for the blood lead concentrations to return to pre-dosing levels. It was also demonstrated that at this point there were
still large amounts of lead in the bones, which would probably require several more years to eliminate.

Dilmercaprol\textsuperscript{5}, calcium disodium ethylene diamine tetra-acetate (CaEDTA)\textsuperscript{2,10} and penicillamine\textsuperscript{5} can be used as chelating agents. CaEDTA has proved to be the most effective and has fewer adverse side-effects when compared to the others. CaEDTA forms complexes with circulating lead, leading to rapid excretion in the urine\textsuperscript{2} and significant clinical improvement usually occurs within 24 to 48 h\textsuperscript{2,7,8}. Shortly after commencement of treatment with CaEDTA, both nucleated and stippled red blood cells decrease rapidly in the peripheral blood and are usually absent after 5 d. Additional 3-5d courses of CaEDTA at weekly intervals have been recommended if blood lead concentrations are still high or if clinical signs recur\textsuperscript{2,10}.

Recommended dosages of CaEDTA, routes and regimens vary eg. 22 mg kg\textsuperscript{-1} body weight 4 times daily for 4 to 5 d administered intravenously, subcutaneously or intraperitoneally after dilution in 5% dextrose\textsuperscript{2}; 100 mg kg\textsuperscript{-1} CaEDTA divided into 3 portions administered subcutaneously over 12 h (at 4-hourly intervals) after similar dilution in 5% dextrose solution, for 5 d; per os administration of CaEDTA tablets at 100 mg kg\textsuperscript{-1} divided 3 times daily for 5 d; 110 mg kg\textsuperscript{-1} divided into 4 equal portions subcutaneously after dilution with 5% dextrose to a concentration of 10 mg CaEDTA ml\textsuperscript{-1} for 5 d\textsuperscript{3}; and one source\textsuperscript{6} recommends 110 mg kg\textsuperscript{-1} d\textsuperscript{-1} but not exceeding 2 gm d\textsuperscript{-1} total dose, similarly diluted and administered subcutaneously 4 times daily.

Sedatives\textsuperscript{6,7,8} (eg.barbiturates), anticonvulsants\textsuperscript{5}, dexamethasone\textsuperscript{8} and mannitol\textsuperscript{8} may be given as supportive treatment, in conjunction with chelation therapy. Intravenous infusion of amino acid and glucose solutions may assist in re-establishing an adequate nutritional state in individuals with prolonged anorexia or severe nervous signs\textsuperscript{5}. Whole blood transfusions may also be considered\textsuperscript{8}.

If properly and timeously treated, most dogs suffering from lead poisoning recover rapidly and completely\textsuperscript{2}. The overall mortality in the USA is probably more than 15% including cases which receive no medical attention and those where the condition is misdiagnosed or the animals are euthanased or incorrectly treated\textsuperscript{1}.

CASE REPORT
A one-year-old, spayed, vaccinated, Fox Terrier bitch with a body mass of 7kg was presented in a recumbent state. The dog was showing paddling limb-movements and salivation. According to the owner the animal had shown similar clinical signs approximately 2 weeks previously. The dog’s appetite and water intake had apparently been normal throughout.

A physical examination revealed generalised tonic-clonic convulsions, galloping movements which worsened when the animal was handled, sialosis and mydriasis. The nictitating membranes were retracted halfway across the eyes. There was a marked head-tilt to the right with immediate severe ataxia and falling to that side when the dog was placed in sternal recumbency. The pulse rate was 190 beats min\textsuperscript{-1}, the respiration rate 60 min\textsuperscript{-1} and rectal temperature 39°C. The mucous membranes were moderately pale and the dog was slightly dehydrated.

Examination of a peripheral blood-smear, revealed clear basophilic stippling in several erythrocytes. In addition to basophilic stippling of red cells, there were also many immature and nucleated cells. Haematological findings are presented in Table 1. Electro-encephalographic (EEG) examination (performed under general anaesthesia) and examination of cerebrospinal fluid on the second day revealed no abnormalities.

On Day 3, a blood lead concentration of 0.04 mg 100 ml\textsuperscript{-1} was established. On Day 4, examination of peripheral blood-smears still revealed evidence of regenerative anaemia and basophilic stippling. Radiographic examination of the skull and abdomen clearly demonstrated 2 roundish, highly radiodense objects of differing size in the stomach region (Fig. 1).

A presumptive diagnosis of lead poisoning was based on the clinical and radiographic findings, the haematological picture and the suspicious blood lead concentrations. A gastroscopy was performed and the diagnosis confirmed when a lead roof-washer was removed from the stomach, together with a one-cent and a five-cent coin (Fig. 2).

During the first 24 h after admission, the dog was kept under general barbiturate anaesthesia, but thereafter was not sedated apart from a short period of general anaesthesia during which the EEG was performed and CSF collected. On admission, the dog had been rehydrated with a polyionic isotonic fluid and maintained on intravenous fluid. Two injections of atropine sulphate were given on Day 1 in an attempt to control sialosis. On the third day, a parenteral feeding preparation containing multivitamins, electrolytes, essential amino acids and fatty acids was administered in the drip.

When the dog awoke from the barbiturate sedation, continual, slow, head movements to the left and back while lying on her right side, were observed. No muscle twitches or head movements were observed while the animal was asleep.

By Day 3, there was an improvement in the dog’s appetite, head movements were less marked and the dog seemed to be aware of its surroundings. By Day 4, it was able to lie in sternal recumbency. At this stage the drip was removed and a milk powder preparation administered per stomach tube although the patient did try to lap from a bowl.

Following the gastroscopy performed on Day 4, the dog recovered well from anaesthesia and sat up on her own during the same evening. She was treated with intravenous fluids, whole fresh blood and an antibiotic injection, but died unexpectedly during the night. At no stage was CaEDTA treatment given, because this was not considered to be necessary because of blood lead concentrations which had not seemed remarkably elevated.

Necropsy findings included mild generalized cyanosis; slight diffuse meningeal congestion of the brain; acute, diffuse hepatic degeneration; moderate splenomegaly, with focal disseminated splenic parenchymal suggilations; and severe focal pulmonary haemorrhage with focal disseminate alveolar emphysema. There was mild serosanguinous ascites. The small intestines showed a few scant-
tered areas of mucosal hyperaemia and there was severe hyperaemia of the colonic mucosa and the presence of meleena.

Toxicological examination of samples of liver and kidney were found to have 129,5 and 390 µg of lead respectively per g of tissue, determined on a wet basis by atomic absorption (Perkin-Elmer BP5000 Instrument).

Histologically, the kidney glomeruli showed moderate widening of Bowman’s spaces with aggregated globules of eosinophilic material lining the periphery in many glomeruli. Some tubules were lined with degenerating epithelial cells which had granular eosinophilic cytoplasm and showed variable nuclear pyknosis. Other tubules had dilated lumens with flattened epithelial cells. Aggregated eosinophilic globules were present in the lumen of some tubules. Many of the tubule epithelial cells had enlarged, vesicular nuclei with chromatin margination. These nuclei contained one to a few large, pale, acid-fast chromatin granules. The inclusions were noted in especially the dilated tubules with flattened epithelium. Hepatocytes in the liver sections showed moderate widening of Bowman’s spaces with aggregated globules of eosinophilic material lining the periphery in many glomeruli. Many glomeruli were found to have small nuclear inclusions which were acid-fast, but could also be seen in Haematoxylin-eosin stained sections.

A few small foci of myofibre vacuolation and necrosis were observed in the myocardium. Mild fibrosis accompanied these lesions. There was moderate congestion of meningeal blood vessels, and widespread, variable neuronal degeneration and scattered necrotic neurons were found in the brain. No significant lesions were found in the lung and spleen.

**DISCUSSION**

In this case there was a poor correlation between lead concentrations in the blood and lead concentrations in kidney and liver samples. Blood concentrations were in the lower positive range while large concentrations of lead were present in the kidneys and liver. This would suggest that specific chelation therapy should be instituted from the outset, even if the patient shows clinical and haematological improvement with conservative treatment. This applies also to cases (as in this one) where the source of poisoning has been removed.

Such high organ-concentrations of lead would probably have required several courses of chelation therapy to eliminate most of the lead. Ideally, monitoring of urine and blood lead concentrations before and after chelation therapy should be done to ascertain efficacy of the treatment. Basophilic stippling of red cells is not very specific in humans and certain other animal species, but it appears to be virtually diagnostic of lead poisoning in dogs; hence if laboratory facilities are not available to determine blood levels of lead, stippled red cells, together with other suggestive clinical signs, allows for a presumptive diagnosis of lead poisoning to be made and specific (and supportive, if necessary) treatment to be instituted.

**ACKNOWLEDGEMENTS**

The authors gratefully acknowledge the assistance of Mr Minhey of the Department of Toxicology at the Veterinary Research Institute, Miss Anneline van Heerden and Professor J van Heerden. Miss M Stiemens is thanked for her typing of the manuscript.

**References**

6. Scott H M 1963 Lead poisoning in small animals. The Veterinary Record 75: 830-833

**Table 1: Haematological changes in a dog with lead intoxication**

<table>
<thead>
<tr>
<th></th>
<th>DAY 1</th>
<th>DAY 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin g</td>
<td>164</td>
<td>70</td>
</tr>
<tr>
<td>Red cell count</td>
<td>6.57</td>
<td>3.28</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.43</td>
<td>0.22</td>
</tr>
<tr>
<td>Mean volume fl</td>
<td>67</td>
<td>66</td>
</tr>
<tr>
<td>White count</td>
<td>37.5</td>
<td>12.1</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>0.65</td>
<td>0.76</td>
</tr>
<tr>
<td>(immature)</td>
<td>0.27</td>
<td>0.12</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>0.08</td>
<td>0.07</td>
</tr>
<tr>
<td>Monocytes %</td>
<td>0</td>
<td>0.05</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytes 1</td>
<td>Normal Normal</td>
<td></td>
</tr>
<tr>
<td>Polychromatophilia</td>
<td>4+</td>
<td></td>
</tr>
<tr>
<td>Normoblasts</td>
<td>3+</td>
<td></td>
</tr>
<tr>
<td>Basophilic stippling</td>
<td>2+</td>
<td>+</td>
</tr>
<tr>
<td>Reticulocytosis</td>
<td>4+</td>
<td></td>
</tr>
</tbody>
</table>