ALDICARB INTOXICATION IN DOGS

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INTRODUCTION

Although not immune to their effects, the early hunter-gather societies were generally not concerned with pests. It was only with the adoption of the agrarian lifestyle when pest control became important; the increased density of human and animal populations, as well as the cultivation and storage of crops, created an environment where pests could thrive. Even in ancient times, mankind sought ways to control pests.

The Fertile Crescent, also known as the “Cradle of Civilization,” produced some of the earliest documentation of the use of pesticides. As early as 2500 BC, Sumerians were using sulfur to control mites and insects; sulfur was also mentioned by Greek poet Homer around 1000 BC. Chinese writings from 1200 BC told of using mercury and arsenic for the control of body lice. The burning of bitumen was recommended by Roman writer Cato in 200 BC as a method of controlling insects in vineyards.

Centuries later, arsenic mixed with honey was described as an effective method for controlling ants in the 1600’s. With the increasing production of crops in America, farmers in the 19th century found themselves using products such as sulfur, nicotine sulfate, acetoarsenite and calcium arsenite to control insects. Pyrethroids derived from the plant genus Chrysanthemum have also been used for centuries to control insects and lice.

The modern age of pesticides began in the 20th century with the discovery of DDT’s effectiveness in controlling a wide variety of insects, not only those of agricultural importance but also for those who spread human diseases. The development of organochlorines, like DDT were important in World War 2 because of the limited accessibility of pyrethroids and the necessity to protect large numbers of military personnel in tropical climates. Organophosphates became widely studied in Germany in the 1930’s as their neurotoxic properties made them not only good pesticides but also chemical warfare agents. Americans took this knowledge and produced products like parathion and malathion. Carbamates, an organic compound created in the production of urea, is a neurotoxin like the organophosphates although not generally as toxic. Pesticide use increased greatly during the mid-twentieth century because they were effective and helped to greatly increase crop yields by minimizing loss to pests, plus they were easy and inexpensive to mass produce.
Pesticide legislation began in the United States in 1910 with the Federal Insecticide Act (FIA) and regulated the use of properly labeled and unadulterated products. To address the increased production in synthetic pesticides as well as address health and ecologic hazards, the Federal Insecticide, Fungicide and Rodenticide Act was passed in 1947. In 1972 regulatory control over pesticides was transferred from the Department of Agriculture to the newly created Environmental Protection Agency (USEPA). FIRPA has since undergone two major revisions: one in 1988 to require re-registration of pesticides registered prior to 1984, and it was further amended in 1996 by the Food Quality Protection Act.

HAZARD IDENTIFICATION

Aldicarb is a carbamate insecticide. It was owned and produced by Union Carbide, but through several industrial acquisitions is now manufactured by Bayer Crop Science. It is the active ingredient in Bayer’s Temik, which is labeled for professional use only on restricted crops. Aldicarb is sometimes referred to as a “hot” carbamate due to its quick onset of clinical signs. Aldicarb is sold in Mexico and Latin America under the name “Tres Pasitos” as a rodenticide and roach killer; it has been brought illegally into the United States. The name “Tres Pasitos” (three little steps), or “Two Steps” as it is sometimes known by, is thought to refer to the number of steps an animal will take after ingesting the product.

SCOPE OF ASSESSMENT

Because of its effective and rapid kill, aldicarb is sometimes used as bait for killing vermin; it is not unusual for dogs and scavengers to be poisoned by consuming the bait or carcasses. Additionally, aldicarb has been used intentionally to poison domestic and wild animals. Although it may be unusual to see, aldicarb intoxication of dogs has been well documented. Furthermore, aldicarb has been well studied under laboratory conditions in dogs.

PHYSICAL AND CHEMICAL PROPERTIES OF ALDICARB

Aldicarb is a white crystalline solid. It is heat sensitive and unstable under normal conditions. Unlike other car bamates, it is extremely toxic by oral and dermal routes, by liquids and emulsions. Due to this and its instability, it is distributed in granular form. It is not corrosive to plastic or metals. Aldicarb is quickly oxidized and hydrolyzed; aldicarb sulfoxide and aldicarb sulfone are the byproducts of oxidation and are commonly tested for along with aldicarb.
Aldicarb is very water soluble and highly mobile in sandy and loam soils. Its half-life varies greatly (anywhere from one day to several months) depending upon pH, moisture levels, and degradation by bacteria and sunlight. Because of this instability, aldicarb and its metabolites are more likely to be found in ground water than in surface water. It is not at this point considered a bioaccumulator.  

MECHANISM OF TOXICITY

Acetylcholine (ACh) is a neurochemical present in the synaptic space between nerve cells. It relays signals from the pre-synaptic membrane to the post-synaptic membrane and has both neurotransmitter and neuromodulator functions. Under normal conditions, the acetylcholinesterase (AChE) enzymes are present on the post-synaptic membrane and terminate the transmission. As a carbamate, aldicarb binds with AChE and allows ACh to accumulate in the synapse. This results in over-stimulation of the nerves. With carbamates this binding is only temporary (unlike with organophosphates), but long enough for clinical signs to appear and possibly even lead to death. Clinical signs include increased secretions of eyes, mouth and respiratory tract, gastrointestinal distress due to hypermotility, respiratory depression and bradycardia. Hypoxia mainly due to respiratory paralysis is the usual cause of death.

Acetylcholinesterase Mechanism of Action and Inhibition

Aldicarb is readily absorbed through the gut; it is easily absorbed through the skin if combined with oil or organic solvents. Elimination occurs rapidly (hours to days), mainly through urine excretion but also
through feces, lactation and a very small amount through expiration. Aldicarb metabolism appears to be consistent throughout most animal species that have been studied and is considered highly toxic for most mammalian species.  

IN VIVO STUDIES

Laboratory studies have been conducted with individual and combination exposure to aldicarb and its metabolites. The toxicant was generally delivered in bolus form or as part of the diet. One study looked at smoke inhalation of aldicarb-treated tobacco to assess possible toxicity via inhalation. Dogs in these studies have been observed for clinical signs of intoxication (tremors, vomiting, decreased food intake and changes in body weight). AChE levels in plasma and red blood cells were measured as that is the best indicator of toxicity. Post-mortem examination was routinely done and included gross and microscopic pathology. The following is a summary of the early aldicarb studies conducted in dogs:  

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects/Groups</th>
<th>Toxicant</th>
<th>Dosage *</th>
<th>Length</th>
<th>NOAEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weil &amp; Carpenter, 1973</td>
<td>2 beagle/sex</td>
<td>aldicarb</td>
<td>0, 0.2, 0.3, 0.7</td>
<td>7d</td>
<td>&gt;0.07</td>
</tr>
<tr>
<td>Weil &amp; Carpenter, 1974c</td>
<td>4 beagles/sex</td>
<td>aldicarb</td>
<td>0, 0.2, 0.3, 0.7</td>
<td>100d</td>
<td>0.3 mg/kg/d</td>
</tr>
<tr>
<td>Weil &amp; Carpenter 1966c</td>
<td>3 beagles/sex</td>
<td>aldicarb</td>
<td>0, 0.025, 0.05, 0.1</td>
<td>5d/wk x 2yrs</td>
<td>0.1 mg/kg/d</td>
</tr>
<tr>
<td>Hamada 1985</td>
<td>1 dog/sex</td>
<td>aldicarb</td>
<td>0, 1, 3, 10, 30, 100 ppm</td>
<td>14d</td>
<td></td>
</tr>
<tr>
<td>Hamada 1987b</td>
<td>1 dog/sex</td>
<td>aldicarb</td>
<td>0, 0.1, 0.3, 1, 3, 10 ppm</td>
<td>14d</td>
<td>0.096 mg/kg/d</td>
</tr>
<tr>
<td>Hamada 1991</td>
<td>6 beagles/sex</td>
<td>aldicarb</td>
<td>0, 0.35, 0.7, 2 ppm</td>
<td>5wks</td>
<td>0.2 mg/kg/d</td>
</tr>
<tr>
<td>Hamada 1988</td>
<td>5 beagles/sex</td>
<td>aldicarb</td>
<td>0, 1, 2, 5, 10 ppm</td>
<td>52 wks</td>
<td>0.027 mg/kg/d</td>
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<tr>
<td>Weil &amp; Carpenter 1968b</td>
<td>3 beagles/sex</td>
<td>aldicarb sulfoxide</td>
<td>0, 0.0625, 0.125, 0.25, 0.5</td>
<td>5d/wk x 3mos</td>
<td>0.25 mg/kg/d</td>
</tr>
<tr>
<td>Weil &amp; Carpenter 1968c</td>
<td>3 dogs/sex</td>
<td>aldicarb sulfone</td>
<td>0, 0.2, 0.6, 1.8, 5.4</td>
<td>5d/wk x 90d</td>
<td>5.4 mg/kg/d</td>
</tr>
<tr>
<td>Hamada 1985a</td>
<td>1 dog/sex</td>
<td>aldicarb sulfone</td>
<td>0, 3, 10, 30, 100, 300 ppm</td>
<td>2 wks</td>
<td></td>
</tr>
<tr>
<td>Hamada 1987a</td>
<td>6 beagles/sex</td>
<td>aldicarb sulfone</td>
<td>0, 5, 25, 100 ppm</td>
<td>1 yr</td>
<td>0.54 mg/kg/d</td>
</tr>
</tbody>
</table>

* Doses were in mg/kg/d unless otherwise noted.

Summary report for United Kingdom Ministry of Agriculture, Fisheries and Food  
USEPA Integrated Risk Information System

Clinical signs of aldicarb intoxication were only noticed in dogs given the very highest doses. Measurement of plasma AChE was done usually 24-48 hours after the last exposure. Since aldicarb is metabolized and excreted so rapidly, these tests would not have accurately expressed AChE inhibition during the period of toxicity; due to this, these NOAEL’s are no longer considered adequate for regulatory purposes. Studies done more recently have used methods designed to maximize detection of AChE levels, resulting in a NOAEL of 0.2-0.3mg/kg/d.
In some of the original studies, there were gross changes noted: decreased body weight, as well as decreased testicular size and increased adrenal size in males. Extended exposure at low levels does not cause apparent disease; even the LD50 bolus dose, when given daily as part of the dogs’ diets, was not lethal and caused only minor disease. Because aldicarb is apparently metabolized the same in all laboratory animals, following reproductive studies, carcinogenic studies and immunotoxic studies in rats and mice it has been determined that there are no chronic effects of aldicarb exposure and it is not a teratogen, carcinogen or immunotoxin.

AGRICULTURAL AND ENVIRONMENTAL STUDIES

Because of its ability to move in soil, concerns have been raised over the potential of aldicarb to contaminate drinking water sources. In 2005, Bayer Crop Science tested 1,673 drinking wells. These wells were located in 9 different areas of the United States where aldicarb was widely used, and within 300m of fields that had been treated at least once between 2002 and 2005. Only 10 of those wells tested were positive for residue using gas chromatography, and levels were between 1.0 and 2.9 micrograms/Litre. The USEPA Health Advisory Limit at that time was 10 micrograms/Litre. Bayer concluded that using aldicarb according to label instructions was adequate at preventing potable well contamination.

A 2002 study looked for the presence of aldicarb in water in canals draining citrus groves in southern Florida. Application of aldicarb was permitted between January 1 and April 30 in Florida. 457 water samples were collected between mid-May, 2001 and mid-August, 2002. Aldicarb, A. sulfoxide and A. sulfone were detected in 20 samples, with concentrations ranging from <0.16 to 4.97 ng ml (-1).

The half-life for aldicarb in pond water is between 5 to 10 days. Aldicarb is considered moderately toxic to fish and exhibits little bioaccumulation. Recently, USEPA published an aquatic risk assessment of aldicarb as part of a re-registration process. Using models, they looked at 30 years of peak pond residue levels of aldicarb and its metabolites in areas where the pesticide had been used for a variety of crops. Taking the risk curves into account along with incident reports, they concluded that exposure risk to freshwater fish and invertebrates is minor.

In the past, aldicarb was commonly applied to many crops, including sugar beets, potatoes, onions, cotton, beans, strawberries and citrus fruits. Although most cases of human intoxication occur in agricultural workers where the pesticide is being applied, aldicarb has been identified as the culprit in several pesticide food poisoning events. Outbreaks related to contaminated cucumbers and watermelons in the United States and Canada were reported in the 1970’s and 1980’s. Incorrect storage and labeling was blamed for an accidental food poisoning incident that occurred in Louisiana in 1998. Aldicarb had been stored in a container labeled “black pepper” and was mistakenly added to a cabbage salad and caused illness in 14 people. In 2007 the US Food and Drug Administration (FDA) issued a recall for fresh ginger imported from China to northern California after aldicarb sulfoxide residues were detected in the California Department of Public Health monitoring program. In 2010, in response to continued USEPA concerns, Bayer Crop Science agreed to voluntarily phase out production of its product Temik; its use in potatoes and citrus was immediately stopped with a total phase out required by 2015.
EXPOSURE ASSESSMENT

It is estimated that 80% of aldicarb intoxications in food animals are related to improper storage and handling. Pesticide containers may be mislabeled and be inadvertently added to feedstuffs or the pesticide could be transported in vehicles prior to carrying feed. Additionally, large animals may become intoxicated when grazing on pastures or croplands that are excessively or recently treated with the pesticide. 15

Accidental exposure in dogs and cats is usually related to miscalculation or misapplication of the product to the wrong species. Pesticides are routinely labeled for use in healthy adult animals, and those who are sick or stressed may suffer ill effects. Aldicarb has also been used to maliciously poison pets, especially dogs that are more likely to ingest adulterated food material. 15

Dogs can be accidently exposed when they eat poisoned bait intended to kill wild predators like coyotes and foxes. There are sites on the internet where information on product (Temik) as well as dosage (8 tiny granules) is published for creating bait. Unfortunately, without the evidence of bait it may be very difficult to determine exactly how much aldicarb was ingested and whatever was ingested will be readily absorbed. Due to rapid onset and progression of signs, a clinician may need to make a presumptive diagnosis of carbamate toxicity rather than wait for laboratory confirmation.

CLINICAL SIGNS OF ALDICARB INTOXICATION

Carbamates work by interfering with the enzyme acetylcholinesterase (AChE) and permitting acetylcholine (ACh) to accumulate in the synapse between nerves. Decreased levels of AChE permit increased transmission of nerve impulses. Since aldicarb is readily and quickly distributed throughout the body (thus the term “hot” carbamate), clinical signs are related to the organ systems where ACh is a neurotransmitter. Signs include:

- Skeletal muscle and motor neurons – twitching, tremors, ataxia, weakness and paralysis,
- Gastrointestinal – increased salivation, nausea, hypermotility and diarrhea,
- Respiratory – increased bronchial secretions, bronchial constriction and dyspnea,
- Cardiac – bradycardia and hypoxia,
- Ocular – increased lacrimation and miosis,
- Urinary – increased micturition, and
- Central Nervous System – seizure activity and centrally mediated respiratory. 15

TREATMENT OF ALDICARB INTOXICATION

If exposure to this pesticide is known and very recent (which is seldom the case in dog poisonings), emesis may be induced and activated charcoal can be given to prevent absorption. Atropine sulfate is given at higher than anesthetic levels to reverse and decrease the severity of signs. Anti-convulsive medications like diazepam are used for seizure control; diphenhydramine and methocarbamol are used to control skeletal muscle signs. Systemic acidosis can be treated with intravenous sodium bicarbonate or respiratory ventilation. Supportive care, especially for respiratory depression, is very important. Although the onset of aldicarb toxicity is very fast and the signs can be quite severe, the neurologic
effects and signs of toxicity are reversible and complete recovery can happen in a period of hours or a few days.  

LITERATURE REVIEW OF ALDICARB POISONING IN DOGS

In 2011, the Veterinary Emergency and Critical Care Society produced a retrospective, observational study of aldicarb poisoning in 15 dogs. These were dogs that were owned by clients and presented to an urban referral hospital. Eleven of the dogs were admitted to the hospital and 10 survived. This study found that treatment of aldicarb toxicity was very effective and that the average patient was discharged within one day.  

The Veterinary Diagnostic and Investigational Laboratory at the University of Georgia’s College of Veterinary Medicine released the results of a decade-long retrospective study in 1999. From 1988 through 1998, 162 cases of aldicarb intoxication were positively identified; although there were several domestic species involved, dogs represented the largest numbers of cases. From examination of stomach contents, it appeared that most cases were malicious and that the toxin had been given with bait in the form of hamburger, hotdogs and ham. At that time aldicarb was widely used as a pesticide on crops in Georgia, with its accessibility making it more likely to be used as the agent of poisoning.  

Aldicarb was implicated in a string of poisoning incidents in the Yellowstone and Salmon National Park regions of the United States in 2004 and 2005. Dog cases included some that were visiting the parks and wildlife regions and others that were residents of the area. In addition to the dogs, investigators found a dead wolf, fox, coyote and three magpies. Forensic evidence showed that the aldicarb granules had been mixed with elk meat and used as bait, presumably to kill wolves. Further evidence led to the arrest of a vocal anti-wolf activist; he was convicted under the Endangered Species Protection Act and sentenced to 6 days in jail and banned from public lands for 2 years.  

Reports out of South Africa note that not only has aldicarb been used for malicious poisoning, but that there has been criminal activity associated with it as well. Aldicarb was available be purchased through illegal channels as a rat poison. There were many cases where family dogs were poisoned days before the family’s residence was robbed; presumably this was done in order to allow the perpetrators easier access to the building. In Gauteng province in 2003 there were a reported 97 victims, nearly all dogs. Another criminal activity where aldicarb has been used was the adulteration of watering holes by wildlife poachers.  

Aldicarb is frequently the choice when trying to control feral dogs and other wild canids. The state of South Carolina reports 6 to 12 poisoning cases each year. Bayer’s Temik is the pesticide most commonly reported to have been used. Three prized hunting dogs were killed in 2009 by a man trying to keep coyotes away from his horses. In 2010 a Hampton County man pleaded guilty to tainting hamburger meat with aldicarb resulting in the deaths, not only of the foxes he intended to kill, but also a pet dog and cat and several vultures. He told authorities he got the idea off of the internet and then stole the pesticide from a nearby farm. A small community of mobile homes lost 4 dogs to aldicarb poisoning after the manager of a local turkey hunt operation put out meat bait to kill feral dogs. In Lee County in 2011 three hunting dogs were poisoned and died after consuming meat mixed with aldicarb. Their owners were exposed to the pesticide while trying to help their dogs had to be decontaminated at a local hospital; one 13 year old boy was ill and hospitalized overnight.
RISK CHARACTERIZATION

The risk for aldicarb intoxication must be broken down into likely and possible scenarios. Potential exposure to aldicarb, when used as a pesticide following proper label instructions, would occur mainly through ingestion. Sources of the pesticide would include contaminated surface or ground water or food produced from meat, vegetables, fruits or grains containing residue. Due to the studies cited above, it seems that intoxication via water is unlikely. Exposure due to food contamination is not likely because most pet food processing would break down the pesticide. Dermal exposure could be possible if dogs were allowed access to recently treated land (hunting dogs or herding dogs), but again is not likely.

The most likely scenarios for aldicarb poisoning in dogs continues to be from ingestion of adulterated meat, whether as collateral damage from trying to control wildlife or due to malicious intention to kill the pet. Wherever aldicarb is in use or is available through illegal channels, it will be used by people as a poison, and must be on the list of rule-outs for dogs exhibiting signs of toxicity.

RISK MANAGEMENT

The most obvious step to decrease canine exposure to aldicarb has already been taken by Bayer Crop Science with their decision to voluntarily discontinue production of Temik. Despite educational materials provided by Bayer and agricultural extension services, and in the face of regulations regarding access and handling, there has been a willingness to obtain and use this product illegally. Steps that may need to be taken in the future may include:

- Discovery and promotion of pesticides that only affect the pests they are targeting (like Insect Growth Regulators),
- Development of ways to produce and distribute pesticides in such a manner where they cannot be removed from their original and labeled packaging,
- Enact regulations requiring that individuals who handle pesticides have been trained in their proper use and are certified,
- Increased enforcement of laws aimed at illegal importation of pesticides and off-label use, and
- Improved communication with the public about the proper uses and dangers of pesticides.

CONCLUSION AND COMMENTS

There are several lessons to be learned by looking at the history and uses of aldicarb.

First, there is a wide range of reactions to the use of pesticides. Since the book “Silent Spring” was published in the 1960’s, there was attention to the harmful and long-term effects on humans and the environment. This led to the banning of DDT and many other insecticides. While this caution is necessary and commendable, one consequence is the increase in vector-borne diseases like malaria. There is a need for pesticides and regulatory agencies to look at all sides of public health issues in decision-making processes. There needs to be a balancing act between efforts made in research and development of new pesticides and protection of human and non-human health and the environment.

At the other end of the spectrum is a distinct casualness in the way many people approach pesticides, similar to how many view antibiotics. One need only walk into a local discount store to find shelves full of all manner of products for humans and pets. Internet-based pet supply and pharmaceutical
companies make a large profit on pesticides. Flea, tick and heartworm products, that have until recently been sold only by prescription from veterinarians, will soon be sold over-the-counter or by human pharmacies. Unfortunately, most pet owners do not understand information given on product packaging which can lead to inappropriate handling and usage. Retail and pharmaceutical sales persons are not trained but are often in the position of giving advice to pet owners. This situation will increase the likelihood that there will be pets poisoned by misuse; furthermore resistance in insects and nematodes is of increasing concern.

Although aldicarb intoxication by ingestion of pet food products is very unlikely, there are increasing numbers of products imported into the United States from other countries. The United States has effectively banned aldicarb from being used in domestic products, and although they can exert some pressure on WTO trading partners, there must be increased vigilance in monitoring items from non-compliant countries.

Lastly, the internet is providing access to knowledge and products, and this has been and will be a problem. The question becomes: Who is responsible for monitoring the internet? There will need to be coordination and cooperation between industry, government and law enforcement agencies for any efforts to be effective. Veterinarians and the animal health industry continues to play a vital role in educating pet owners and the public in general to the proper uses, benefits and hazards that pesticides play in our lives.


