

Tales from the Hood

Chemo safety and administration

by Kathi L. Smith, RVT, VTS
(Oncology)

An increasing number of clients

are choosing to treat their pets that have been diagnosed with cancer. The safety of the health care team must be made a priority due to the potential health risks associated with the preparation and administration of antineoplastic drugs being used in veterinary medicine.

Background

Antineoplastic drugs have been in clinical use for more than 50 years in human medicine. There are numerous studies in animals and human patients regarding the carcinogenic and toxic properties of these drugs. In animal studies, it has been shown that anti-neoplastic drugs are known to be:

1. Carcinogenic: cancer-causing substances or agents.
2. Teratogenic: causing malformation of an embryo or fetus.
3. Mutagenic: causing gene or chromosomal damage; may also (but not necessarily) act as a carcinogen.
4. Serious organ damage or other toxic manifestation, i.e., cardiotoxicity (doxorubicin), hemorrhagic cystitis (cyclophosphamide), or thrombocytopenia (lomustine).

It wasn't until 1979 that studies were instituted looking at the occupational risks associated with low-dose exposure of these drugs to the health care



The safety of the health care team must be made a priority due to the potential health risks associated with the preparation and administration of antineoplastic drugs being used in veterinary medicine.

workers handling them. The lack of existing exposure records for health care workers, along with the fairly recent interest in occupational exposure to antineoplastic drugs, have made studies on their long-term side effects difficult.

The risk to health care workers using antineoplastic drugs is difficult to monitor due to the inherent toxicity of the drugs, individual susceptibility, concurrent exposure to known carcinogens such as cigarette smoke, and the level (occasional vs. constant) or type (drug or material) of exposure.

There have been studies in oncology nurses that show adverse reproductive outcomes with occupational exposure to antineoplastic drugs. Birth defects, fetal losses, infertility, ectopic pregnancies, low birth weights, and menstrual dysfunctions have been reported.

Workplace studies revealed that the chemotherapeutic drug doxorubicin remained stable on various surfaces for up to 7 weeks, and other studies examined airflow exposure in HEPA filters from cyclophosphamide contamination.

Studies have been done that show that health care workers who wear protective gear (gloves, gowns, and facial shields) are in fact at a lower risk of exposure than those who do not.

In 1986 the Occupational Safety and Health Administration (OSHA) published guidelines for health care workers exposed to low-dose occupational doses of cytotoxic drugs. This was in response to a series of Technical Assistance Bulletins that were developed by the American

Society of Hospital Pharmacists and recommendations from the Federal Occupational Safety and Health Administration, the National Institutes of Health, and the American Medical Association. These guidelines are readily available, and veterinary hospitals that offer chemotherapy to their clients should have formal procedures instituted into their practice. With proper training and protection, chemotherapy preparation and administration can be performed safely.

Methods of exposure

There are several ways that technicians can be inadvertently exposed to antineoplastic drugs.

Inhalation exposure occurs during the mixture and/or administration of cytotoxic drugs. This is due to the aerosolizing of the drug. Studies have been done to measure air levels of cytotoxic drugs (cyclophosphamide) when biological safety cabinets (BSCs) were not in use. Increased levels of the drugs were reported in the HEPA air filter. This is also an opportunity for respiratory exposure to those employees changing the air filters.

Absorption exposure occurs during the absorption of the drug through the skin and mucous membranes. There are case reports (McDiarmid & Egan, 1988) of health care workers that developed severe acute allergic reactions from accidental cytotoxic drug spills.

Ingestion exposure occurs through contact with contaminants such as food, cosmetics, or cigarettes.

Inoculation exposure occurs while recapping needles after drug



Cautions

Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Indications

SENTINEL[®] SPECTRUM[®] (milbemycin oxime/lufenuron/praziquantel) is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*; for the prevention and control of flea populations (*Ctenocephalides felis*); and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Taenia pisiformis*, *Echinococcus multilocularis* and *Echinococcus granulosus*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration

SENTINEL SPECTRUM should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 4.55 mg/lb (10 mg/kg) lufenuron, and 2.28 mg/lb (5 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes.

Dosage Schedule

Body Weight	Milbemycin Oxime per chewable	Lufenuron per chewable	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	46 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	115 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	230 mg	114 mg	One
50.1 to 100 lbs.	23.0 mg	460 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables			

To ensure adequate absorption, always administer SENTINEL SPECTRUM to dogs immediately after or in conjunction with a normal meal.

SENTINEL SPECTRUM may be offered to the dog by hand or added to a small amount of dog food. The chewables should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole. Care should be taken that the dog consumes the complete dose, and treated animals should be observed a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

Contraindications

There are no known contraindications to the use of SENTINEL SPECTRUM.

Warnings

Not for use in humans. Keep this and all drugs out of the reach of children.

Precautions

Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention.

Prior to administration of SENTINEL SPECTRUM, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. SENTINEL SPECTRUM is not effective against adult *D. immitis*.

Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Do not use in puppies less than six weeks of age.

Do not use in dogs or puppies less than two pounds of body weight.

The safety of SENTINEL SPECTRUM has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime and lufenuron alone.

Adverse Reactions

The following adverse reactions have been reported in dogs after administration of milbemycin oxime, lufenuron, or praziquantel: vomiting, depression/lethargy, pruritus, urticaria, diarrhea, anorexia, skin congestion, ataxia, convulsions, salivation, and weakness.

To report suspected adverse drug events, contact Virbac at 1-800-338-3659 or the FDA at 1-888-FDA-VETS.

Information for Owner or Person Treating Animal

Echinococcus multilocularis and *Echinococcus granulosus* are tapeworms found in wild canids and domestic dogs. *E. multilocularis* and *E. granulosus* can infect humans and cause serious disease (alveolar hydatid disease and hydatid disease, respectively). Owners of dogs living in areas where *E. multilocularis* or *E. granulosus* are endemic should be instructed on how to minimize their risk of exposure to these parasites, as well as their dog's risk of exposure. Although SENTINEL SPECTRUM was 100% effective in laboratory studies in dogs against *E. multilocularis* and *E. granulosus*, no studies have been conducted to show that the use of this product will decrease the incidence of alveolar hydatid disease or hydatid disease in humans. Because the prepatent period for *E. multilocularis* may be as short as 26 days, dogs treated at the labeled monthly intervals may become reinfected and shed eggs between treatments.

Manufactured for: Virbac AH, Inc.
P.O. Box 162059, Ft. Worth, TX 76161

NADA #141-333, Approved by FDA
© 2015 Virbac Corporation. All Rights Reserved.
SENTINEL and SPECTRUM are registered trademarks of Virbac Corporation.
02/15

administration. Recapping needles should be discouraged for this reason.

Clinical exposure is probably the most common source of exposure and can be associated with needle withdrawal from a pressurized vial, drug transfers from different containers, opening of glass ampules, expulsion of air from drug-filled syringes, equipment failure or improperly set up equipment, exposure to excreta from patients that have received cytotoxic drugs, and crushing or breaking of tablets or capsules of cytotoxic drugs.

Equipment for preparing and administering chemotherapeutics

A Class II vertical laminar flow BSC should be part of any facility that administers antineoplastic drugs. These devices ensure that aerosolized particles are properly vented away from the veterinary technician preparing the drug, and that containment is made easier in the event of an accidental spill. BSCs can be found relatively inexpensively.

Closed double-membrane systems for drug transfer, such as Equashield, PhaSeal, or OnGuard, are excellent for use with multi-dose drug vials. They ensure that drug aerosolization does not occur and that the drug vial maintains the correct amount of pressurization. They also prevent the possibility of absorption exposure.

Absorbent mats with a leak-free plastic backing prevent contamination

of the work surface in the event of an accidental spill from the injection port. Disposable diapers can be used if chemo safety mats are unavailable.

Using resealable plastic bags for used chemotherapy administration materials will help eliminate possible aerosolization or contamination of the drugs after they are disposed of in the hard waste chemotherapy containers.



Personal protection should always include the use of face shields that cover the entire face if a BSC is unavailable. Dust particle face masks and safety goggles should only be used as a last resort due to the potential risk of exposure. Surgical masks should never be used because they do not protect against the breathing of aerosolized drugs.

Powder-free chemo gloves should be used instead of latex exam gloves as they are made of a thicker material.

Disposable, solid front, moisture barrier gowns with cuffs should be worn to prevent accidental exposure to skin or clothing. Gloves should be worn both under the cuff and over the cuff to ensure that no bare skin of the wrist or forearm is exposed. Gowns can be worn several times before disposing if proper preparation techniques are maintained. Those staff members that are assisting during chemotherapy administration should also wear protective gear.

Luer lock-style syringes should be utilized instead of slip tip syringes. This will help eliminate accidental separation of the needle from the syringe, thus preventing a chemo spill situation.

Gauze 4x4s soaked with alcohol are used for covering the injection port, which will help prevent aerosolization at the injection port. Porous white tape is better for anchoring catheters in place because it's not as

sticky as some of the other brands and is easier to remove.

Due to the regulated nature of disposal of cytotoxic waste, proper waste containers are required. There must be one for all soft waste items, which include gloves, gowns, tape, gauze, and absorbent mats. Waste such as syringes, bottles, vials,

Prior to treating a patient with a chemotherapeutic agent, there are protocols that should be in place to prevent problems during the administration.

needles, indwelling IV catheters, butterfly catheters, IV drip sets, and fluid bags need to be in a yellow chemotherapy hard waste container.

Chemotherapy preparation

Preparing chemotherapeutic agents should ideally be done away from the general flow of traffic, preferably in a separate, isolated room with a BSC on a counter at waist level. Unfortunately, most hospitals are unable to accommodate all of the above recommendations. However, steps can be taken to ensure the safety of the veterinary technician preparing cytotoxic drugs and other staff members in the immediate area.

Antineoplastic drugs should be prepared in a low-traffic area that is away from windows, doorways, or drafts. This will help eliminate secondary exposure to the rest of the staff.

Syringes should not be filled more than two-thirds full to prevent the plunger from separating from the syringe barrel, and prime IV drip sets prior to adding antineoplastic drug to fluid bags. This can be prevented with the use of closed systems such as Equashield, PhaSeal, or OnGuard.

Veterinary technicians who prepare the cytotoxic drugs should *never* eat, drink, apply makeup, or smoke in any of the areas where these drugs are prepared.

Any drawers or cabinets that contain chemotherapeutic agents must be labeled properly. All antineoplastic

drugs that require refrigeration must be kept in their own refrigerator. No other drugs, food, beverages, or other products are allowed in the chemotherapy refrigerator.

Chemotherapy administration

Prior to treating a patient with a chemotherapeutic agent, there are protocols that should be in place to prevent problems during the administration:

1. Identify the patient to be treated.
All patients should have ID bands to prevent mix-ups.
2. Check for the current weight (treatment day weight, not last week's).
3. Choose drug to be administered.
4. Calculate dose and ask another person to cross check.
5. Choose appropriate administration materials (butterfly vs. indwelling catheter).

Veterinary technicians should always wash their hands prior to preparing and administering chemotherapeutic drugs. This helps prevent absorption of any drug that may have inadvertently contaminated the skin.

Choosing the peripheral vein used for the administration is a personal choice. The veins typically used are the cephalic, and lateral (dogs) or medial (cats) saphenous. Other sites may be used, but these are the most common. Some facilities are still using

central indwelling catheters that are surgically placed into the jugular vein for long-term use.

After choosing the appropriate vein, shave the injection site (remember that hair grows much slower in cancer patients) and prepare aseptically with soft, cotton gauze material. Contact time of the cleaning agent on the skin is more effective as an antimicrobial agent than the physical scrubbing. This will also help prevent irritation to the injection site tissue. Patients are also less likely to lick the area after administration if it is not irritated. Dogs can form lick granulomas, and care must be taken to prevent secondary bacterial infections from occurring. Using the lateral saphenous instead of the cephalic will usually help in these patients.

Place the absorbent mat under the patient's leg to absorb any cytotoxic drugs that might accidentally spill. Proper restraint is critical when administering antineoplastic drugs. There should always be another technician or tech assistant to help restrain the patient. If necessary, sedation should be used to prevent any possibility of perivascular injection of the drug(s).

Extravasation of certain chemotherapeutic drugs will cause severe tissue necrosis, sometimes requiring amputation of the affected limb. It is for this reason that administration should always be via a "clean stick." Second attempts in the same vein can be done only if it is proximal to the first attempt.

There are several schools of thought on how often the same vein can be used. Some follow the "use it till you lose it" approach, while others



rotate veins with each treatment. Once again, this is a personal choice. Following the placement of the butterfly or indwelling catheter, flush thoroughly with ≈ 12 ml of 0.9% saline to ensure the catheter is properly situated. Heparinized saline should not be used due to the fact that heparin can precipitate with certain chemotherapeutic agents (doxorubicin).

Just prior to the initiation of the chemotherapy, place an alcohol-soaked 4x4 or cotton ball over the injection port. As discussed earlier, this will help eliminate aerosolization of the drug. Administer the chemotherapeutic agent(s) at the appropriate time interval for those particular drugs. Certain drugs, such as vincristine or vinblastine, can be given as a bolus. Other drugs, such as doxorubicin, must be given slowly over a longer period of time.

Following the chemotherapeutic administration, flush with another

0.9% saline injection to eliminate the escape of any of the drug perivascularly after the needle or catheter has been removed. Place a pressure wrap to prevent hematoma formation.

Place all contaminated hard supplies (syringe, needles, catheters, bottles) into a resealable plastic bag and place into the appropriate hard waste yellow chemotherapy container. Gloves and absorbable mats go into the soft chemotherapy waste containers. Always wash your hands after completion of any chemotherapeutic administration.

Accidental chemotherapy spills

In the event of a chemotherapy spill, there are very important steps that must be followed to ensure the safety of the veterinary health care staff.

1. Restrict the contaminated area from the rest of the staff (only the person performing the spill clean up should be in the immediate area).

2. The clean-up person should wear protective gear (gown, gloves, face shield or mask, and goggles).
3. Mop up all liquid spills with absorbent disposable towels or pads.
4. Collect powder spills with damp (water- or alcohol-soaked) disposable towels or pads.
5. Rinse the contaminated area with water, then wipe area again.
6. Small spill (<3 ml): wipe with 70% alcohol 4x4s.
7. Large spill (>3 ml): clean with detergent—*not bleach!*
8. Place in appropriate chemo soft waste container.
9. Wash your hands following spill clean up.

Conclusion

Chemotherapy safety is everyone's responsibility. Establishing standard operating procedures will ensure the safety of your veterinary health care staff and your patients. ✨

Note: This paper was originally presented at the AAHA Austin 2016 conference. It has been edited for length and style. To access the original paper with references, please refer to aaha2016.conferencespot.org.



Kathi Smith, RVT, VTS, works as a senior oncology technician at Portland Veterinary Specialists in Portland, Maine. She graduated in 1979 from Cosumnes River College in Sacramento, Calif. She has worked at referral hospitals in Sacramento and in the oncology, cardiology, and ophthalmology departments at UC-Davis and is a licensed technician in California and Maine.