STANDARD OPERATING PROCEDURE
SAFE HANDLING OF CYTOTOXIC DRUGS AND RELATED WASTE
Kate Hill and Andrew Scuffham 2007; Reviewed by Els Acke, Jon Bray, and Steve Crow 2012

1 Purpose
This Standard Operating Procedure (SOP) is designed to ensure the safety of MUVTH staff, students and clients when handling chemotherapeutic agents. The SOP is also designed to meet the requirements of the Occupational Health and Safety Service of the Department of Labour guidelines for the safe handling of cytotoxic drugs and related waste.

Additions and changes made to this SOP in 2012 are mainly based on the ECVIM-CA guidelines for ‘Preventing occupational and environmental exposure to cytotoxic drugs in veterinary medicine’ (2007), and the Queensland Government Workplace Health and Safety Strategy ‘Guide for handling cytotoxic drugs and related waste’ (2005).

2 Responsibility
It is the responsibility of all staff members to ensure their own safety and the safety of others and that no action or inaction will cause harm to themselves or others.

The Veterinarian and Veterinary Nurse in charge of the case have the responsibility to ensure that the procedures are followed as directed. They should abide this SOP at all times, unless animal welfare or safety concerns dictate other treatment. Any alteration to this SOP must be documented and signed by the clinician in charge of the case.

The Veterinarian in charge of the case determines the treatment of the animal on clinical grounds. The Veterinarian treating the animal has the responsibility to ensure that all equipment is prepared and available in accordance with this SOP. A qualified Veterinarian or Veterinary Nurse is responsible for the preparation and administration of all cytotoxic drugs.

As in compliance with Massey University policy, the supervisor and the Management group leader is to ensure that those employees under their control are trained sufficiently in the tasks that are being undertaken. This responsibility includes preparation for emergencies and correct use of personal protective equipment.

The Head of the Institute is to ensure that staff are working in safe environment and that the hierarchy of controls has been placed.

The IVABS Health and Safety coordinator is responsible to investigate any accidents that may occur and make recommendations to the management group leader and the Head of the Institute.
3 Definitions
Biohazard: Hazardous to life
Carcinogenic: An agent which is responsible for the formation of a cancer
Chemotherapy: The treatment of disease by chemical substances
Cytotoxic: Toxic to cells
Extravasation: Leakage of cytotoxic drug from the vein into the surrounding tissue
Mutagenic: An agent capable of producing a mutation
Teratogenic: An agent capable of causing abnormalities in a developing foetus, resulting in birth defects.

4 Introduction
All personnel involved with cytotoxic drugs and related waste have to be aware of the hazards, safe use and protocols associated with handling these materials.

4.1 Routes of exposure
The main routes of exposure to cytotoxic drugs are through the inhalation of drug particles or aerosols, skin absorption, inadvertent ingestion through contact with contaminated food or cigarettes, and needle stick injuries.

Exposure may occur during preparation and administration of the drugs, handling of body fluids from animals receiving cytotoxic drugs, handling and disposal of cytotoxic wastes and related trace contaminated material, and transportation of cytotoxic drugs. Some cytotoxic drugs have a direct irritant effect on the mucous membranes, eyes and skin. Spills onto skin surfaces that have cuts or abrasions and punctures of the skin with a contaminated needle or broken glass can lead to severe soft tissue injury. They should be treated immediately and observed for potential problems.

4.2 Potential effects of exposure
Persons at risk of exposure to cytotoxic drugs and their metabolites include the Veterinarian, Veterinary Nurse, students, the pharmacist or dispensary personnel, animal attendants, the pet owner and family members, and cleaning personnel.

Adverse effects are dependent on dose and exposure time. Staff who are involved in the preparation, administration, or chemotherapy patient care are at greatest risk of exposure. Low level occupational exposure could potentially cause harm to staff and students if adequate precautions are not taken.

Most chemotherapeutic agents are carcinogenic, mutagenic and teratogenic. Serious adverse effects in exposed staff where control measures were inadequate have been reported, including development of cancer, increased
frequency of chromosome damage, and adverse reproductive outcomes (including higher incidence of spontaneous abortion and a higher risk of malformations).

Exposure to cytotoxic drugs can also produce more acute effects, including irritation of skin, eyes and mucous membranes, allergic reactions upon contact with the skin, as well as more subjective symptoms including nausea, dizziness, and headache.

4.3 Work practices
There are no established safe levels of exposure to cytotoxic drugs. Medical opinion is that even small quantities of cytotoxic drugs and their metabolites should be avoided as much as possible. The safest approach therefore is to reduce occupational exposure to levels as low as reasonably achievable. For ease of management, it is best to restrict the number of people performing tasks involving cytotoxic drugs and related waste.

5 Personnel

5.1 Staff training
All personnel involved in any aspect of the handling of cytotoxic drugs must receive adequate training. The training is to include known potential risks, relevant techniques and procedures for their handling, the proper use of personal protective equipment and materials, spill procedures, medical policies, and first aid procedures in the event of accidental skin or eye contact with cytotoxic drugs.

A training and supervision Checklist for Handling Chemotherapeutic Agents is included as appendix I.

The instructor will sign the person off when that person is deemed to be competent. Only those who have been trained in any aspect of the treatment or care can undertake that portion of the treatment or care of the animal. The Head of the Institute or designated person can sign off staff members who are considered competent to train and supervise other staff members. The Head of Institute can also sign off personnel who are deemed to be competent in the handling and usage of cytotoxic drugs, where that person has received training in a recognised training course.

5.2 Personnel who are Pregnant, Breast Feeding or Planning Parenthood
It is recommended that employees who are pregnant, breast feeding, or planning pregnancy should not be exposed to cytotoxic drugs and be offered alternative duties.
6 Recording requirements

6.1 Personnel Register
Each staff member involved in the administration of chemotherapeutics, handling animals or cleaning waste of animals must be recorded in the register. – See appendix II for the personnel register.

6.2 Tracking of Chemotherapeutics
All cytotoxic drugs must be tracked through all stages from delivery to disposal.

See appendix III for the register of tracking chemotherapeutic agents. The register will be kept in the small animal hospital dispensary or a designated site in the oncology ward.

6.3 Case Notes
In each animal’s notes, the following information must be recorded: the date of administration, volume of drug, route of administration (including which vein and which leg), and the veterinarian’s signature or initials. Any extravasation or spillage must be noted.

7 Product information
The material safety data sheet (MSDS) and all other relevant information will be kept in the same location as the register. A file will be kept in the dispensary or ward where chemotherapy drugs are handled.

8 Purchase and storage of cytotoxic drugs

8.1 Purchase and drug preparation
Chemotherapy drugs are ordered through the Purchasing Officer. Some of the drugs may be pre-prepared and delivered as a single-dose delivery unit in syringes and double packed when purchased. Pre-prepared drugs will be administered using a PhaSeal® connector which will be attached after unpacking the drug in a Class II, type B2 Biological Safety Cabinet (BSC). Drugs that are delivered in vials or bottles will be only be prepared in the BSC using a closed system (i.e., PhaSeal® or similar product) by the Veterinarian or Veterinary Nurse.

a) The Veterinarian in charge of the case will complete a prescription with the owner’s name, animal’s name, address of owner, veterinarian’s name in writing, and name of drug required, drug concentration, volume and number of syringes/units. See appendix IV for a sample prescription.

b) Commonly used drugs may be kept in stock for immediate use. They are to be stored either in a locked cupboard in the oncology ward or
Dispensary (tablets and capsules that do not require refrigeration) or, for drugs that need refrigeration, in the designated cytotoxic drug refrigerator.

c) When drugs are ordered for a specific animal (i.e., not available in stock), the following policies will apply:
   i) The purchasing officer will provide a quote of the total cost and order the drug. The Massey order will be sent with the prescription and will be signed by an authority.
   ii) The drug order is received by the Purchasing Officer and stored either in a locked cupboard in the Dispensary (tablets and capsules that do not require refrigeration) and for drugs that need refrigeration, in the designated cytotoxic drug fridge. The Veterinarian will be told as soon as practicable of drug’s arrival.
   iii) The Purchasing Officer bills the client for the drug on arrival.

While preparing drugs in the BSC prior to chemotherapy treatment, personal protective equipment as described in section 10 must be worn at all times. Any equipment used during preparation will be disposed of in the correct cytotoxic waste/sharps bin kept within the dispensary.

Manipulation of oral or topical medicines containing cytotoxic drugs should be avoided. Chemotherapy gloves (powder free purple nitrile gloves, Kimberly-Clark®) should be worn when handling tablets or capsules in the BSC. Tablets should not be crushed or divided, and capsules should not be opened. Only designated counting trays can be used if these are needed. A counting tray will be placed in the BSC and should be wiped with a damp tissue after use.

Eating, drinking, chewing gum, applying cosmetics or storing of food is not allowed in any drug preparation or administration area.

8.2 Storage

The cytotoxic drugs will be sent to a person who has been deemed competent for purchasing, receiving and storing cytotoxic drugs (currently the IVABS Veterinary Teaching Hospital purchasing officer). The refrigerator where the cytotoxic drugs are stored shall be labeled with a warning that cytotoxic drugs are held there and kept in the dispensary or designated oncology ward. Material safety data sheets will be stored in the dispensary.

Each drug will be clearly labeled ‘Cytotoxic’. Bottles need to be stored in their original containers in the refrigerator and labeled. Cytotoxic drugs for oral administration that do not need refrigeration will be stored on a designated, labeled shelf in a locked cabinet and packed in a zip-lock or sealable bag.
9 Room Preparation and Personnel

Until a designated oncology ward and treatment room are completed, a consultation room, the diagnostics room, or treatment room 2 will be used for handling and treating the small animal chemotherapy patients. Large animals will be treated in the large animal stocks area or, when general anaesthesia is required, in the recovery box or operating theatre.

There will be no smoking, no eating and no drinking signs placed in the entrance ways, and a sign notifying that cytotoxic drugs are in use will be placed on all entrances to the room. Once a designated oncology ward and treatment room are available, only that space will be used to administer chemotherapy to small animals. The table will be covered with a disposable cover/drape. The administration area (2 meters around the table) shall be cleaned with water and detergent soap (not disinfectant) when the chemotherapy procedures are completed for the day. The room where chemotherapy is administered will not be used for any other purpose until cleaning has been performed. Full personal protective equipment (PPE) should be used while cleaning the area (see section 10).

9.1 Personnel present

Only essential personnel will be present in the room during chemotherapy administration. The cytotoxic drug(s) will be administered by a qualified Veterinarian or qualified Veterinary Nurse. The risks of the procedure will be explained to any observers (veterinary students or veterinary nursing students). Observers can be asked to assist with chemotherapy treatment by helping restrain the patient. Only observers who have read this SOP, are wearing adequate personal protective equipment, and who are experienced with animal restraint techniques will assist.

10 Personal protective equipment (PPE)

The minimum requirements for protective clothing for personnel involved with preparing and administering sterile solutions of cytotoxic drugs should include the following — a protective gown (disposable impermeable long sleeved closed front gown with elastic cuffs), disposable impermeable shoe or boot covers, mask (Sperian 2210 respirator masks®), and purpose-manufactured chemotherapy gloves. Hands must be washed before and after gloves are worn. Gown cuffs should be tucked under the gloves. Gloves should be changed every 30 minutes and removed immediately after overt contamination, or if punctured. Goggles or a visor shall be worn. Double gloving is necessary while dealing with spills of cytotoxic drugs.

Any personnel or students holding an animal that is receiving chemotherapy or cleaning cages where chemotherapy patients have bled, defecated, or voided urine shall also don the above clothing before handling the animal or cleaning the soiled area. Further guidelines on cleaning cages/horse boxes and PPE are described in section 14.2. Personnel or students walking a chemotherapy patient should wear chemotherapy gloves and carefully inspect the kennel before the patient is taken out to ensure no biological waste is present. If the kennel is soiled, full PPE must be
worn, and the animal must be placed in a labeled, clean kennel. For horses, all feet will be picked out prior to walking the horse out of the stall.

10.1 Masks
While normal surgical masks offer protection against the inhalation of powder, they do not necessarily protect against the inhalation of liquids and aerosols. The use of a respirator mask (RPE) is optional and is kept in the radiology drugs cupboard. Respiratory Protective Equipment (RPE) must be worn when dealing with spillages or heavily soiled kennels.

10.2 Eye protection
Eye protection (protective goggles with side shields or visors) shall be worn at all times when preparing and administering cytotoxic drugs or cleaning up spills containing cytotoxic drugs. These should fully enclose the eyes to protect against dust and splashes, and should be washed thoroughly with water after use.

11. Drug administration
Parenteral or oral cytotoxic drugs should be administered only by the Veterinarian, Veterinary Nurse, or owner of the animal in case of oral drugs if clear verbal and written instructions have been given to and discussed with the owner.

11.1 Drug preparation
The focus of drug preparation of cytotoxic drugs should be on operator safety, sterility of the product and protection of the working environment.

Prior to preparation and administration, the patient’s name, the drug name, administration route and dosage should be double checked by the Veterinarian and/or Veterinary Nurse. The Veterinarian and Veterinary Nurse in charge of the small animal cases will also check whether the animal’s blood count and/or biochemistry results are appropriate to go ahead with treatment and whether the animal has received appropriate anti-emetic or antihistamine treatment as required.

The Veterinarian will have checked if MDR1 mutation testing is needed in the canine breed presented for chemotherapy, and if the cytotoxic drug dosage has been adapted as required.

In addition, the Veterinarian or Veterinary Nurse administering the cytotoxic drug must be knowledgeable of the immediate side effects of the agent being administered to ensure correct observation and management of potential toxicities. (see ‘Aftershocks of Cancer Therapy: Managing Adverse Effects’ by Thamm and Vail, JAAHA vol 43, 2007 Appendix VII).

An intravenous catheter will be placed if indicated and the animal will be observed closely until the chemotherapy agents have been prepared.
Prepare the room and table as per section 9, don PPE as in section 10.

Prepare all injectable drugs in the BSC in the Dispensary using a closed system (PhaSeal® or similar). While preparing injectable drugs in the BSC, PPE as described in section 10 must be worn at all times. Place a plastic backed absorbent sheet in the BSC. Any contaminated equipment used during preparation will be discarded in the cytotoxic waste bin in the BSC.

Manipulation of oral or topical medicines containing cytotoxic drugs should be avoided. Chemotherapy gloves should be worn when handling tablets or capsules in the BSC. Tablets should not be crushed or divided, and capsules should not be opened. Use tablets in blister or foil packs if possible and avoid using liquids for oral administration.

Eating, drinking, chewing gum, applying cosmetics and storing of food is not allowed in any drug preparation or administration area.

Place the prepared drug and administration device in designated labeled chemotherapy drug container and carry the container with the drug to the administration room.

11.2 Patient and Site preparation

If the animal is fractious, exceedingly nervous, or excited, sedation is strongly recommended prior to administration of intravenous cytotoxic drug administration.

Clip the hair at the desired site of catheter placement and clean the skin aseptically. The hair should be shaved liberally enough to easily visualize the catheter entry site as well as a few centimeters proximally to visualize a potential extravasation.

When using an intravenous catheter it is preferable to use a needle-less closed system such as PhaSeal®. A needle with a Luer-lock 3 way stopcock or a butterfly needle can also be used but is not recommended for intravenous administration, especially if injection volumes are greater than 1ml.

Immobilize the catheter securely, but do not hide the vein proximal to the catheter with tape or bandaging material.

Place a disposable gauze square around the injection port of the catheter or needle.

Place plastic backed absorbent sheets/pads under the injection site.

The preferred sites for indwelling catheters (for chemotherapy) are:

a) cephalic vein
b) lateral saphenous vein
c) medial saphenous (occasionally in dogs or cats but is a less preferable site).

Administration routes for drugs commonly used in veterinary chemotherapy

<table>
<thead>
<tr>
<th>Intravenous-Catheter</th>
<th>Intracavitary</th>
<th>SQ or Intralesional Injection</th>
<th>Oral Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinomycin-D</td>
<td>Carboplatin</td>
<td>Bleomycin</td>
<td>Chlorambucil</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Cisplatin</td>
<td>Cytosine arabinoside</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Carboplatin</td>
<td></td>
<td>L-asparaginase</td>
<td>Hydroxyurea</td>
</tr>
<tr>
<td>Cisplatin</td>
<td></td>
<td>Cisplatin</td>
<td>Lomustine (CCNU)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td></td>
<td></td>
<td>Masitinib</td>
</tr>
<tr>
<td>Cytosine arabinoside</td>
<td></td>
<td></td>
<td>Melphalan</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td></td>
<td></td>
<td>Prednisolone</td>
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<tr>
<td>Doxil</td>
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<td></td>
<td>Prednisone</td>
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<td>Doxorubicin</td>
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<td></td>
<td>Methotrexate</td>
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<td>Gemcitabine</td>
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<tr>
<td>Methotrexate</td>
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<tr>
<td>Mitoxantrone</td>
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<tr>
<td>Mustargen</td>
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<tr>
<td>Vincristine Vinblastine</td>
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<tr>
<td>Vinorelbine</td>
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</tbody>
</table>

11.3 Other preparation

Ensure that there is the appropriate cytotoxic waste sharps bin, and cytotoxic waste bag in the room and that appropriate signs have been placed on the door.

Procedures and the spill kit should be in place for dealing with any spillages that might occur.

Ensure that there is adequate trained assistance to restrain the animal and that each assistant is wearing the required protective clothing.

Ensure a temporary wrap bandage for covering the injection site after removal of the catheter has been prepared in advance.

11.4 Administration and precautions against extravasation

Parenteral drug administration should only be carried out in clearly designated areas. All necessary measures to ensure tranquility and cooperative behavior of the animal treated and for non-disrupted administration of cytotoxic agents must be taken. The Veterinarian or Veterinary Nurse has the right (and responsibility) to not treat the animal if its temperament or behavior does not allow safe administration of the drug. Sedation may be indicated and should be discussed with the owner before the animal is admitted. A consent form must have been signed.
1. Ensure catheter is placed on first attempt (‘First stick’ catheter). Note: start distally and alternate legs for each treatment.
2. Prime the drip set with normal saline before chemotherapy is placed in saline bag and check all connections. When using an infusion pump, check that it is functioning properly and set the desired administration rate.
3. Ideally hold the syringe plunger and the animals’ limb in the one hand.
4. Flush the needle/catheter with 2-10ml of normal saline and check for flash back.
5. Observe for blowing of the vein or leakage from the needle/administration site. If extravasation is observed, stop and replace catheter in a different vein.
6. Slowly inject the drug and check for patency frequently by aspirating on the syringe plunger (checking for "flashback").
7. If the patient demonstrates side effects or any signs of extravasation, or if the equipment fails to function properly, administration must be stopped.
8. When changing syringes while using a butterfly needle, clamp or kink the tubing adjacent to the syringe attachment point to prevent the contents of the catheter from leaking.
9. Following injection of the drug, flush the line or catheter with 2-10 ml of normal saline before withdrawal of the butterfly/needle/catheter.
10. Do not aspirate or check for flash back at this stage.
11. Remove the butterfly/needle/catheter and apply a temporary pressure wrap. Never remove the tubing from an IV bag containing a hazardous drug. Remove the IV catheter, tubing and bag as an intact (connected) unit whenever possible.
12. All potentially contaminated material should be discarded in special waste disposal containers, including gloves and protective gowns.
13. Wash hands with soap and water before leaving the drug administration area.
14. Mark that the drug has been administered and sign off in the case file.

11.5 Extravasation incidents

Leave the catheter or needle in place. Attempt to suck out as much as possible with a separate syringe.

When the needle or catheter is withdrawn, use a 25G or 26G needle and syringe to withdraw any more of the visible subcutaneous bleb.

Vincristine extravasation

- Administer hyaluronidase 300 units via multiple subcutaneous injections into the site of extravasation.
- Apply a warm compress for 15-30min QID for 1-2 days.
- [See article on the use of hyaluronidase by Spugnini, JAVMA Vol 221, No 10 Nov 15, 2002 (Appendix VII)]
Doxorubicin extravasation

- Dilution of doxorubicin will increase the amount dispersed and increase the necrosis injury. Therefore, do not infuse the extravasation site with sterile water, saline or other crystalloid solutions.
- Cold compress for 15-30min QID for 1-2 days and removal of as much drug as possible by aspiration is recommended.
- Dexrazoxane (IV) at 5-10 times the dose of doxorubicin extravasated within 3 hours and repeated at 24h and 48h may be of benefit,
- DMSO may be applied topically (Thamm and Vail, 2007, Appendix VII)

11.6 Non-parenteral cytotoxic drug preparation

All non-parenteral preparations should always be handled with chemotherapy gloves in the BSC and in a manner that avoids skin contact. Tablets and capsules should be tipped from their container directly into a "child safe" medication bottle labeled with cytotoxic drugs and placed in a labeled zip-lock bag. Use the counting tray and spatula labelled for chemotherapeutic drugs only and wipe the tray after use. Chemotherapeutic tablets or capsules should not be cut, broken or pulverized.

12 Spill Management

It is important that all spills are dealt with immediately,

At each site where the chemotherapeutic agents are stored or used, there shall be:

- a chemical spill kit
- adequate supplies of absorbent and cleansing material
- decontamination solution

12.1 Small spills of biological material

Small spills of biological waste should be managed as follows:

- put on chemotherapy gloves wipe up the spill with absorbent material and then discard in a cytotoxic waste container.
- clean the area three times using detergent, then rinse with clear water
- dispose of gloves as cytotoxic waste
- notify the management group leader and head nurse
- an accident report form must be completed

Spills occurring during administration, in storage or transport should be handled using a spill kit using the recommended containment and decontamination procedure.

12.2 Large spills of biological material

Spills of more than 50 ml of body substances or body waste should be handled using a "spill kit".
Spread should be limited by gently covering with absorbent sheets or spill-control pads or pillows.

If a powder is involved, the spill should be contained with damp cloths or towels.

An accident report form must be completed.

12.3 Spillage of cytotoxic drugs

a) In the Safety Cabinet
   - Observe carefully where the cytotoxic drugs were spilled
   - Absorb first the fluid with a dry absorbent towel
   - Clean contaminated area 3 times with a dry tissue in one gloved hand and a tissue with 70% alcohol in the other gloved hand.
   - Always start with the most contaminated area first.
   - Clean area with alcohol tissue and immediately thereafter with dry tissue. Repeat this twice.
   - Dispose all contaminated material in the special waste disposal container.

b) On the floor: a cytotoxic spill kit is used

**Spill kit contents**
Assembled and maintained by Head Nurse.

- 2 x Gown with cuffs and back closure or wrap around closure, made of water impermeable fabric
- 2 x Pair shoe covers
- 2 x 2 Pairs chemotherapy gloves in different sizes
- 1 x Pair goggles
- 1 x full face respirator mask
- 1 x Disposable dust pan (to collect any broken glass)
- 1 x Plastic scraper (to scoop materials into dust pan)
- 1x Large plastic tweezers
- 2 x Plastic backed or absorbable towels
- 2 x Chemical absorbent pads, protective mats (ie bluey or "chemomats")
- 2 x Disposable sponges (one to clean up spill, one to clean up floor after removal of spill)
- 1 x Puncture-proof, leak-proof container (to place all contents in), clearly marked with a biological hazard waste label
- 1 x Container of 70% alcohol for cleaning spill area
- 2 x Large cytotoxic waste disposal bags
- signs to isolate and identify the spill
- Instructions for use
- Incident report form
12.4 Procedures for use of spill kit

Check List
1. Open the spill kit and display spill sign near the spill area. If the spill is out of control, call for help (staff or security) in restricting access to the area. Call for assistance to remove the animals and place them in their kennel.

2. Put on respiratory breathing equipment first, disposable gown, disposable shoe coverings, and protective eyewear.
   Double glove with inner chemotherapy gloves and outer (heavy) utility gloves

3. Prevent the spill from spreading:
   (a) Wait a few seconds for any liquid splashes (aerosols) to settle
   (b) Lay the chemical-absorbent pad over the spill to absorb the liquid and transform it into a gel which is more convenient for disposal
   (c) take care not to touch the spill or to create any splashes (aerosols)
   In case of powder spills, carefully place an absorbent mat over the powder ensuring minimal dust production. Carefully wet the mat prior to placement so the powder dissolves and is absorbed by the mat.

4. Use spill kit box or tweezers to scoop up any broken glass. Place contaminated glass into the cytotoxic waste bin

5. Use spill towels to pick up the remainder of the gel. Repeat several times.
   Use detergent, if necessary, to remove all gel residue

6. Working from the area of least contamination to the greatest, clean with detergent to remove gel residue and then rinse the area with water and dry. Repeat several times

7. All contaminated chemical-absorbent pads and spill towels should be discarded into the cytotoxic waste bag already in use along with any other contaminated disposables. Remove disposable shoe coverings and outer utility gloves and discard them into the plastic waste bag

8. Wearing inner gloves, seal the polythene bag and place into the second polythene bag along with the disposable gown, mask and safety glasses. Remove and discard inner gloves and seal the
9. Dispose of in a specially designated purple cytotoxic waste bag

10. Wash hands thoroughly with soap and water

11. Notify the Management group leader (head nurse) and IVABS Health and Safety coordinator of all spills and personnel contamination’s as soon as possible

12. Complete an Incident Report Form

13. Obtain replacement spill kit.

13  Emergency Procedures
Any person having direct contact with cytotoxic drugs must receive medical attention or advice. Phone the National Poisons Centre 03 4740000 or 0800 764 766 or Massey Medical Centre ext. 5533 or 2787.

The Material Safety Data Sheet (MSDS) must be consulted following any exposure. The MSDS must be taken with the "exposed" person to the medical centre.

The Massey University accident/incident notification form must be filled out as soon as practical.

The Management Group Leader and the IVABS Health and Safety Officer must be informed.

13.1 Contamination of gloves or gowns, or direct skin or eye contact
1. Immediately remove gloves or gown without touching the contaminated area
2. Rinse the affected area of skin and flush thoroughly with copious amounts of cold water. Wash with soap after this.
3. For eye exposure, remove contact lens, immediately flood the affected eye with water, use eye wash bottle and wash eye for at least twenty minutes. A 1-litre bag of sodium chloride 0.9% attached to drip set can be used to flush the eye directly at. Direct the giving set onto the eye and hold eyelids back.
4. Obtain medical attention immediately. Phone Massey Medical Centre (ext 5533).
5. Place gloves and contaminated clothing in cytotoxic waste bag or clothing that is not overtly contaminated should be packaged for laundering.
6. Complete an incident report form.
7. Notify management group leader and IVABS health and safety officer.

13.2 Swallowed or Ingested
Contact Poisons Information Centre 03 4747000 or 0800 764 766?

Receive medical advice
13.3 Inhaled
If dust is inhaled, remove person to fresh air.
Advise them to blow through nose to clear breathing passages. Seek medical attention

14 Patient care
Animal patients receiving cytotoxic drug therapy should be placed in separate cages away from other animals when possible. They will be placed in the dedicated oncology ward (when completed), ward 3 (small dogs and cats) or an outside run (large dogs). Horses will be confined to a single, well-marked stall with biohazard signs affixed to the stall. A sign should be put on the cage, run or stall to indicate that the patient is undergoing cytotoxic drug therapy. A large sign should state "Cytotoxic drugs in use, excreta may be contaminated; authorized personnel only to handle animal and waste".

14.1 Patient waste
Generally, hospitalization of patients receiving chemotherapy must be kept to a minimum. Patient body substances will be contained in the cage the animal is placed in after treatment with cytotoxic drugs, or outside when dogs are walked.

Although there is no conclusive data available on the pharmacokinetics of most of these drugs in animals, the table shown below has been extrapolated from available data for humans. Note: table courtesy of Dr. Sarah Sheafor of Southpaws Veterinary Referral Center, Springfield, VA.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Urinary Excretion</th>
<th>Biliary Excretion (Vomit/stool)</th>
<th>Estimated clearing time from tissues</th>
<th>Present in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>actinomycin D</td>
<td>yes</td>
<td>yes</td>
<td>36+ hours</td>
<td>yes</td>
</tr>
<tr>
<td>bleomycin</td>
<td>yes</td>
<td>questionable</td>
<td>less than 1 hour</td>
<td>yes</td>
</tr>
<tr>
<td>carboplatin</td>
<td>yes</td>
<td>no</td>
<td>2 - 3 hours</td>
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<td>yes</td>
<td>32+ hours</td>
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<td>5 fluorouracil</td>
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<td>15 minutes</td>
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<td>minimal</td>
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<td>chlorambucil</td>
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<td>less than 12 hours</td>
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<td>melphalan</td>
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<td>5 days</td>
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<td>L-asparaginase</td>
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<td>no</td>
<td>30 hours</td>
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<tr>
<td>vincristine/vinblastine</td>
<td>minimal</td>
<td>yes</td>
<td>24 hours</td>
<td>yes</td>
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</table>
14.2 Cleaning of chemotherapy facilities including preparation and administration area and animal cages

Objective: To prevent exposure of cleaners, employees and other people to cytotoxic agents, taking into account hygienic aspects.

Instruction: The cleaning of kennels following discharge of the patient will be entered into a log book. Date and person responsible will be noted. In addition, the areas cleaned will be noted.

AREAS:  
- Cytotoxic drug preparation facility in Dispensary  
- Cytotoxic drug administration facility in Hospital  
- Special chemotherapy cage in Ward

Recommendations:

- All of the above areas should be regarded as potentially contaminated.
- Staff involved in cleaning of the areas should have received training and education on the health risks associated with cytotoxic drugs and the consequences of ineffective cleaning.
- Personal protective clothing must be worn by staff undertaking cleaning duties in potentially contaminated areas. As a minimum this should include disposable gloves and a chemotherapy gown. Wear face shields if splashing is possible.
- Contaminated disposable items used in cleaning should be disposed of as cytotoxic waste

14.2.1 Equipment
The following equipment is needed to clean the cage:

Personal Protective Equipment (PPE):
Gown  
Protective eyewear  
Disposable particulate respirator mask  
Chemotherapy gloves  
Apron and rubber boots  
Absorbent pads (not for horse boxes)  
Purple polythene bag with seal  
Spill towels (made of granular material) (not for horse boxes)  
Sodium hypochlorite (bleach)  
Virkon

14.2.2 Procedures for cleaning the cage
Generally, care should be taken to prevent generating aerosols when dealing with contaminated body waste and while cleaning any potentially contaminated area. In addition, any bedding used
in the cages for chemotherapy patients should be processed wearing PPE and using designated cytotoxic waste bags. Bedding that may have been exposed to cytotoxic agents needs to be washed at the maximum running capacity for two wash and rinse cycles. After this he laundry can be combined with other non-contaminated items. For horses, all bedding, urine and manure will be disposed as cytotoxic waste. The stall will be emptied and cleaned with Virkon and then procedures as described in 7-11 below will follow.

1. Put on PPE and including chemotherapy gloves
2. Lay absorbent pad over wet excreta
3. When excreta are absorbed, pick up absorbent pad and place in purple polythene bag
4. Pick up faeces with spill towels and place in purple polythene bag
5. Use spill towels and Virkon to rinse the area, repeating several times. Use detergent prior to Virkon if any biological waste was present in the kennel.
6. Fully dry area with absorbent towels and place in purple polythene bag
7. Clean cage with water and bleach avoiding splashes
8. Remove outer gloves and place in purple polythene bag
9. Seal polythene bag and place in second purple polythene bag along with other PPE (gown, and glasses). Do not fill bag more than three-quarters full.
10. Remove and discard inner gloves and seal the second bag
11. Wash hands thoroughly with soap and water.
12. The purple bag is to be taken to the post mortem room for disposal.

15 Outpatient care at home – need to update our instruction

If cytotoxic drugs are prescribed for administration at home, they should be labeled and packaged as described in Section 11.

Care-givers should be informed in writing of the need for special precautions during the usual period that drugs are excreted after treatment.

15.1 Equipment

The following should be available in the patient's home while receiving cytotoxic drug therapy:

- A supply of latex gloves (a pair of gloves is needed for each single use, and then disposed of in household garbage)
- Flushable paper and paper towels for cleaning up biological waste spills
- Detergent
15.2 Administration of oral cytotoxic drugs
Potential problems with ingestion or inhalation by the care-giver and others, and/or of the contaminating of surfaces must be explained. Care-givers are to be advised that they should use a "pill popper" and wear latex gloves when giving the tablet to the animal. The gloves should then be discarded with household garbage.

15.3 Patient waste
Care-givers should try to be aware of the area where the animal urinates so that it can be watered in well to dilute urine. They should be warned to be careful with the use of water so there is no splashing.

Animals should not be walked or allowed to roam in a public place during the period body wastes may be contaminated.

To clean up excreta, scoop onto a non-absorbent implement such as shovel and place in toilet.

Wash the shovel under running water.

Excreta which cannot be picked up should be diluted by hosing (without a jet) until it has been dispersed.

Laundry/disposal of bedding - animal bedding or clothing of the care-giver with traces of contamination should be laundered immediately, and separately from other items.

They should be washed in hot water on the longest running cycle, and double rinsed.

15.4 Cytotoxic spills
A small quantity of patient waste deposited on the floor or on furniture should be dealt with as follows:

1. Put on gloves.

2. Wipe up spill with flushable paper and double flush down the toilet with lid closed, or disposable paper toweling or linen, placing the material in the cytotoxic waste bag

3. Clean area with water and detergent

4. Dispose of cleaning cloth and gloves in household rubbish.

It is best to use flushable paper wherever possible to reduce the amount of contaminated waste to be placed in household garbage.

Interaction with the patient - owners and other family members should exercise careful hygiene practices after handling pets receiving cytotoxic
drugs. The time for particular care is during the period the drugs may be excreted.

15.5 Information for care-givers

Owners or other care-givers of animals receiving cytotoxic drug therapy will need to be provided with written information on the following:

1. Hazards of cytotoxic drugs
2. Precautions to be taken while caring for animal patients during the time the drug may be excreted
3. Reasons for taking precautions in the handling of cytotoxic drugs
4. Waste precautions to take with interaction between the animal and people in the home - small children, the aged and women who are pregnant or breast feeding,
5. How to store cytotoxic drugs at home
6. Equipment which may be needed for the animal's care at home
7. Route of excretion of drugs and how to dispose of body waste
8. Emergency procedures for accidental exposure or accidental ingestion of cytotoxic drugs by children (e.g. ring poisons information immediately- this is staffed round the clock) and gain emergency advice
9. Disposal of drugs no longer needed by returning to the Veterinary Teaching Hospital

See appendix V for the information sheet.

16 Cytotoxic waste

All waste generated during the preparation and use of cytotoxic drugs and the cleaning up of spills must be segregated, packaged, and disposed of in accordance with specifications outlined in the NZS 4304:1990 Healthcare waste management. All containers for cytotoxic waste should be colour coded purple and marked with a symbol indicating cytotoxic waste.

16.1 Personal Protective Clothing

All personnel involved in the routine handling of cytotoxic waste should wear appropriate protective clothing, whether the waste appears properly packaged or not. This should be removed immediately if contamination is suspected and disposed of accordingly.

16.2 Materials

Any materials that have been used in the preparation and administration of cytotoxic drugs, such as gloves, gowns, are to placed in a double purple labeled cytotoxic waste bag. Both bags are to be sealed. Sharps, syringes and needles, and items of the closed administration system, are to be placed in an impenetrable purple cytotoxic waste container specified for the purpose.

The containers are to be taken to the post mortem room and placed in a medical waste bin. Notify the PM room technician of the waste.
16.3 Waste Storage

Storage of cytotoxic waste in healthcare establishments should be in a dedicated, secure area which can also be easily cleaned and maintained. Waste bins should be seal-able. The waste is stored in the PM room medical waste bin annex.

17 References


Appendix I: Training and Supervision Checklist for Handling Chemotherapeutic Agents

Name of Employee: .................................................................

Position: ......................................................................................

Instructor to sign each section

<table>
<thead>
<tr>
<th>Task</th>
<th>Date read and Understood SOP</th>
<th>Date competent to work Under supervision</th>
<th>Date Competent to perform tasks</th>
<th>Competent to train and Supervise other personnel</th>
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</thead>
<tbody>
<tr>
<td>Understand potential risks</td>
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<tr>
<td>Purchasing and ordering chemotherapeutic agents</td>
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<tr>
<td>Handling Spills</td>
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<tr>
<td>Storing of the drugs</td>
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<td>First Aid treatment for accidental injection</td>
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<td>First Aid treatment for accidental eye contact</td>
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<td>Administrating cytotoxic agents</td>
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<td>Cleaning Cages</td>
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## Appendix II: Personnel Register

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<th>Animal details</th>
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<th>Time spent with drugs, waste or animal waste</th>
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## Appendix III: Tracking of Chemotherapeutics

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<th>Ordered by</th>
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<th>Animal’s name</th>
<th>Client’s surname</th>
<th>Case number</th>
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Appendix IV: Prescriptions

The Clinician in charge of the case will complete a prescription with the owners name, animals names, address of owner, clinicians name in writing, qualifications, name of drug required, strength, volume and number of syringes.

Date: ...........................................................

Owner: ........................................................... Animal: ..............................................................

Case No: .................................................................................................................................

Drug: ........................................................... Concentration: ..................................................

Amount (no. of tabs/caps): ........................................................................................................

Instructions: ...............................................................................................................................
Appendix V: Cytotoxic Drugs Used Commonly in Veterinary Practices

Carboplatin
Chlorambucil
Cisplatin
Cyclophosphamide
Cytarabine (cytosine arabinoside)
Doxorubicin
Epirubicin
Gemcitabine
Hydroxyurea
Idarubicin
L-Asparaginase
Lomustine (CCNU)
Melphalan
Methotrexate
Mitoxantrone
Vincristine
Vinblastine
Vinorelbine
Appendix VI: Sample owners information sheet

Advice Sheet for Clients with Pets Being Treated With Cytotoxic Drugs

General Information
Your pet has been prescribed one or more chemotherapeutic drugs as part of his/her treatment regime. Chemotherapy means the treatment of disease by chemical agents. The drugs that are used are “cytotoxic”, meaning that they will kill actively dividing cells, such as cancer cells. As such they have the potential to damage normal cells and may cause signs of illness and are potentially dangerous for people contacting them.

Safe Handling and Use of Cytotoxic Drugs

Personnel handling cytotoxic drugs, waste or animal waste have had the following problems reported:

- Dermatitis
- Cell abnormalities
- Abnormal blood cell counts
- Excretion of the drugs in urine
- Abdominal pain
- Hair loss
- Nasal sores
- Vomiting
- Liver damage
- Increased miscarriage rate
- Congenital abnormalities

Precautions

Taking precautions as outlined below, will reduce the risk to yourself and others from the hazardous effects of cytotoxic drugs.

1. Store your pet's drugs away from the reach of any children and from any other drugs (human or animal) that you have stored in your house. Do not store them near to food storage or food preparation areas.

2. Keep your pet's drugs in the container in which they have been dispensed to you, and do not transfer them to another type of container.

3. Use the latex gloves provided when giving you pet its medication. Always use the pill popper to treat the animal, if you accidentally make skin contact with the tablets then wash your hands thoroughly with soap and water. Do not crush or cut the tablets.

Patient waste

1. You should try to be aware of the area where the animal urinates so that it can be watered in well to dilute urine. Try to be careful with the use of water so there is no splashing.
2. Animals should not be walked or allowed to roam in a public place during the period body wastes may be contaminated. This may be up to 48 hours or more after each treatment.
3. Animals should not be walked or allowed to roam in a public place during the period body wastes may be contaminated. This may be up to 48 hours or more after each treatment.
4. Wash the shovel under running water.
5. Excreta which cannot be picked up should be diluted by hosing (without a jet) until it has been dispersed.
6. Laundry/disposal of bedding - animal bedding or your own clothing with traces of contamination should be laundered immediately, and separately from other items.
7. They should be washed in hot water on the longest running cycle, and double rinsed
8. For cats using a litter pan, dispose of litter twice daily. Wear gloves when handling the litter pan or pan liners.

**Cytotoxic spills**
A small quantity of patient waste (excreta, urine or vomit) deposited on the floor or on furniture should be dealt with as follows:

1. Put on gloves.
2. Wipe up spill with flushable paper and double flush down the toilet with lid closed, or disposable paper toweling or linen, placing the material in the cytotoxic waste bag.
3. Clean area with water and detergent.
4. Dispose of cleaning cloth and gloves in separate double bag in household rubbish or you can bring the sealed bag into the clinic and we will dispose of it for you safely.

It is best to use flushable paper wherever possible to reduce the amount of contaminated waste to be placed in household garbage.

Owners and other family members should exercise careful hygiene practices after handling pets receiving cytotoxic drugs. The time for particular care is during the period the drugs may be excreted which is within the 48 hours after each dose is given.

Depending on the individual drug your pet is being treated with it may be present in your pet’s urine. If your pet urinates inside then please take the same precautions listed above when clearing it up. The drug is normally excreted from the animal within 48 hours after treatment, but this is dependent on the drug which is being used.

Pregnant or breast feeding women, small children and older persons should avoid contact with the drugs and the animal waste during treatment.

If there is any accidental exposure or accidental ingestion of the drugs by children, medical advice must be sought immediately.

**Phone the National Poisons Centre at 03 474 4000 or 0800 764 766**
If you have any drugs left that you have not administer to your pet, please bring them into the clinic for us to dispose of for you, **DO NOT DISPOSE OF THEM IN YOUR HOUSEHOLD RUBBISH.**

If you have any questions about your pet's health or his treatment please so not hesitate to contact us on 06 354 4508.
Appendix VII

Use of hyaluronidase for the treatment of extravasation of chemotherapeutic agents in six dogs

Enrico P. Spagnuolo, DVM

Use of hyaluronidase for the treatment of extravasation of chemotherapeutic agents is a complication of chemotherapy for various malignancies. Extravasation of chemotherapy agents into soft tissues is a common complication that can cause severe tissue damage and development of deep ulcers. Debridement, excision, and skin grafting may be required for healing. If intervention treatments are not promptly instituted, infection and other complications may result. A high incidence of hyaluronidase around the site immediately after extravasation and then at weekly intervals may promote recovery with minimal fibrosis.

A 10-year-old female boxer dog was referred for treatment of mediastinal lymphoma. The dog had been treated previously with 3 cycles of doxorubicin plus cyclophosphamide, resulting in complete remission of the tumor for a period of 10 weeks. Physical examination revealed that the dog was in considerable respiratory distress. Radiography confirmed the presence of a large mediastinal mass. Results of a CBC, bone marrow aspiration biopsy, and abdominal ultrasonography did not indicate other organ involvement with lymphoma. Results of serum biochemical analyses were within reference ranges. At this time, the dog was treated with a mechlorethamine/vincristine/procainamide-prednisone combination protocol, and complete remission of the tumor was achieved after 1 cycle of chemotherapy. The treatment regimen was scheduled to be repeated for a year. During the fifth month of therapy, extravasation of mechlorethamine (3 ml, 3 mg) and vincristine (0.7 ml, 0.7 mg) occurred. Despite the use of an IV catheter placed in the right cephalic vein, because of a sensation of increased resistance at the beginning of the chemotherapy administration, it was estimated that extravasation of the entire volume of chemotherapeutic agents had occurred. The day after treatment, the dog was returned to the clinic because of marked lameness and swelling of the right forelimb. Because of the cranial location of the limb, a 10-cm strip of soft tissue extending proximally from the carpus was swollen; with a 4-cm central indurated area; the dog would bear weight on the right forelimb and showed signs of pain upon palpation. The dog was treated, according to recommendations in the literature, with 300 units of hyaluronidase diluted with 6 mL of saline (0.9% NaCl) solution administered subcutaneously by use of 0.25-in. injections with a 25-gauge needle around the extravasation area. Care was taken to infiltrate the central induration. No other measures were taken to control the consequences of the extravasation. The infiltration was repeated 3 and 14 days later. The amount of swelling decreased by approximately 50% during the day after the first infiltration of hyaluronidase. The lameness improved greatly during the same period. Gradual resolution of the swelling occurred during the following 20 days (a further reduction of approximately 30% after the second infiltration treatment, with resolution of the swelling within a few days after the third and last treatment). The lameness completely resolved after the second dose of hyaluronidase. The resultant fibrosis of the cephalic vein was considered mild and was localized cranially to a region 10 cm proximal to the carpus. Intravenous chemotherapy was continued as per protocol at the end of the third week following the extravasation event, and the tumor was known to be in remission after 2 years.

A 10-year-old female Boxer dog was referred for treatment of non-weight-bearing lameness and swelling of the soft tissues of the right forelimb extending 12 cm above the carpus, caused by extravasation of vincristine (0.8 ml, 0.8 mg, according to the referring veterinarian) that occurred during the treatment for a transmissible venereal tumor. Signs of mild pain were elicited during palpation of the forelimb; otherwise, the dog was quiet, alert, and responsive. The transmissible venereal tumor appeared to be in complete remission. The dog was treated with hyaluronidase once per week as described for 4 weeks. Five days after the first infiltration of hyaluronidase, swelling of the forelimb was reduced by approximately 50%. Four days after the second dose of hyaluronidase, the dog was able to bear weight on the affected limb. After the last treatment, only a mild fibrosis was present at the site of extravasation. Fourteen months after the extravasation event, the dog was doing well and neither the transmissible venereal tumor nor the leg swelling had recurred.

A 3-year-old male American Pit Bull Terrier was referred for evaluation and treatment of multicentric stage IV lymphoma. Previous treatment with combination chemotherapy had been unsuccessful. The dog was treated with a mechlorethamine/vincristine/procainamide-prednisone protocol. Extravasation of vincristine (0.7 ml, 0.7 mg) and mechlorethamine (3 ml, 3 mg) occurred during the second cycle of chemotherapy.
because of poor condition of the dog's peripher al
vascularization. As a result of the extravasation event, erythema
and extensive swelling of the left hind limb developed
during the following day. Palpation of the swollen region of
the limb induced aggressive behavior and yelping. Six
injections of 100 units of hyaluronidase were adminis-
tered to the dog, beginning immediately after the occur-
rence of the drug leakage. One week after the first treat-
ment, the swelling had decreased by approximately 40% and
continued to decrease during the following treat-
ment. After the final injection, signs of pain were
resolved completely, and erythema had decreased by
approximately 60%. The mild residual adverse effect was
rash erythema of the affected limb that resolved in a
month after the last injection of hyaluronidase. Three
months after the extravasation event, the dog had con-
tinued to receive chemotherapy with partial remission
of the innumerable and with no episodes of leg swelling or
laxness.

A 3 year-old male Beagle was affected by extrava-
sation of doxorubicin during treatment of multilocular
stage III lymphoma at our institution. The dog was
quiet, alert, and responsive after the event; but phys-
ical examination revealed signs of inflammation of the
right forelimb, and signs of intense pain were elicited
upon palpation. A box area of swelling on the medial
aspect of limb, approximately 5 cm above the elbow
was observed, the site of the swelling, as measured
with a caliper, suggested a volume of approximately
10 ml. A box 6 cm in diameter of 15 ml (3,3-dichloro-2-hydroxymethyl-2-nitroso-pierin-3-yl (DHN3)), the recom-
trated treatment for doxorubicin extravasation, was
taken. Injections of 2 ml of hyaluronidase was
administered by use of 6 injections around the extrava-
sation site. According to recommendations in human medici-
ne, the area of injection was treated with 0.9% saline solu-
tion. The extravasation site was treated with
weekly injections of 30 units of hyaluronidase for
approximately 6 weeks. Moderate cutaneous ery-
thema at this site was eradicated. The dog was cleared
from the site after a month and was treated by the dog
breeding to that site. An area of skin, 3 cm in diameter
was treated. The erythema treated during a
period of 2 weeks. The swelling resolved after the fourth
injection of hyaluronidase, without treatment. Treatment
without hydration was performed. When treated with
hyaluronidase, the dog continued to be treated and
the affected limb did not improve. Local irritation
with doxorubicin (2 ml, 20 mg) was added to the
injection protocol at the time of the second dose of
hyaluronidase. Deesmesereuse biopsy was injected in a
periosteal area around the extravasation site, immediately prior to injection of hyaluronidase. The combina-
tion treatment further decreased the swelling and signs of inflammation, resulting in improved limb
condition. Treatment of the limb was discontinued after 4
injections of hyaluronidase with 3 with deesmeser-
sel. Two months after the last administration there was
substantial fibrosis (2 X 3 cm) localized at the site of
the initial nodal swelling, but the function of the limb
was preserved. No signs of pain were elicited during
physical examination.

An 11 year-old male mixed-breed dog was referred
for treatment of a large multinodular lymphoma. The dog
was quiet, alert, and responsive and had received sup-
portive therapy at another institution. The condition of
the dog's peripheral veins was very poor, fragility of the
left cephalic vein contributed to the extravasation of
doxorubicin (approximately 0.5, 0.5 ml, 40 mg) during induction
chemotherapy. An area approximately 4 cm above the
left carpus was affected, the signs of pain shown by the
dog suggested that extravasation of the entire limbs had
occurred. The extravasation site was promptly injected
with hyaluronidase (110 units) in a perineural pat-
tern. The dog was sent home and treated with pedi-
mucr according to the lymphoma protocol (30 mg/m2
for 7 days, then 28 mg/m2 for 7 days, then 10 mg/m2 for
7 days). The dog developed mild lameness of the left
forelimb and began licking the extravasation site. These
problems resolved without additional therapy within 10
days of the extravasation event. Because the dog's lam-
eness had almost resolved by the time of the second
appointment and the extravasation site did not show
signs of an adverse reaction, the second dose of
hyaluronidase was not administered. During several
appointments, the extravasation site appeared normal
and the owner reported no signs suggestive of pain or
discomfort. However, the patient was euthanized after 5
weeks because of poor results of the dose of
chemotherapy.

A 28 year-old male Labrador Retriever with stage
IV multicentric lymphoma was affected by extrava-
sation of doxorubicin as a result of accidental removal
of a catheter from the left cephalic vein during the third
chemotherapy cycle. The amount of extravasated drug
was approximately 10 ml, 20 mg. As estimated from the
duration of symptoms and the volume of extravasated
drug-saline solution. The extravasation site was treated
with weekly injection of 30 units of hyaluronidase for
approximately 4 weeks. Moderate cutaneous ery-
thema at this site was eradicated. The dog was cleared
from the site after a month and was treated by the dog
breeding to that site. An area of skin, 3 cm in diameter
was treated. The erythema treated during a
period of 2 weeks. The swelling resolved after the fourth
injection of hyaluronidase, without treatment. Treatment
without hydration was performed. When treated with
hyaluronidase, the dog continued to be treated and
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injection protocol at the time of the second dose of
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tion treatment further decreased the swelling and signs of inflammation, resulting in improved limb
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substantial fibrosis (2 X 3 cm) localized at the site of
the initial nodal swelling, but the function of the limb
was preserved. No signs of pain were elicited during
physical examination.

During the past decade, the demand for
chemotherapy, management of malignancies in
companion animals has increased, resulting in pro-
longed survival times and improved quality of life of
pets with neoplasia. The use of antineoplastic drugs is
not without risk for patients because of a reported lack
of target cell specificity. The toxic effects frequently
reported in the literature are systemic; the drugs and
their metabolites can induce a wide range of adverse
effects. Limited information is available regarding the
cytopathic effects of extravasation of chemotherapeutic
agents, and treatment options in veterinary medicine
are anecdotal and not well defined. The prevalence of
extravasation of chemotherapeutic drugs in veterinary
practice has not been determined; however, data
available from humans indicate the prevalence ranges
from 0.1 to 6.9%, although an accurate measure has
proven difficult. Venous leakage of many anti-

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Injuries from drugs such as doxorubicin and melphalan for which the drug has been recommended, these include topical administration of diclofenac sodium, or intraperitoneal administration of 5-Fluorouracil for doxorubicin, and peritoneal instillation of sodium thiosulfate for melphalan. The results of chemotherapy treatment are comparable when achieved with other chemotherapeutic drugs, vinca alkaloids, and taxanes, that have different mechanisms of action resulting in complete prevention of cutaneous ulcers.

In these dogs, hyalurondase was administered weekly and clinical signs (swelling, erythema, signs of pain) were no longer observed, with or without on treatment. The number of hyalurondase treatments required to achieve this effect varied among dogs. The optimal hyalurondase treatment interval is not known, and local hyalurondase infiltration administered once per week may be unnecessarily frequent. For the treatment of extractions, high concentrations of DNA-binding drugs have been measured at the extractions site by use of high performance liquid chromatography. Drug extractions attributed to behavioral problems in 2 dogs reported here, in each condition of the peripheral veins of 2 dogs, and to the use of a butterfly needle instead of a polyethylene catheter for the administration of chemotherapy in another dog.

To avoid extractions, when administering a potentially cytotoxic agent, all possible precautions must be taken, such as ensuring patency of IV catheters, monitoring the injection site carefully, and using patient restraint or sedation when necessary. Although the occurrence of extractions with chemotherapy agents can be decreased by application of acceptable precautions, such events result in serious adverse reactions, the treatment of which can be highly distressing. Weekly percutaneous infiltration of extractions with hyaluronidase was used with success in these 6 dogs. Hyalurondase appears to be a safe treatment and may play an important role in the prevention or reduction of local reactions induced by extractions of chemotherapeutic agents.
References
Aftershocks of Cancer Chemotherapy: Managing Adverse Effects

Most cytotoxic chemotherapy protocols used in small animals are designed to have a low risk of adverse effects; however, adverse events can occasionally occur. Timely and appropriate management of adverse events greatly increases client satisfaction and the likelihood of a successful treatment outcome. This article presents guidelines for the management of chemotherapy-associated hematological and gastrointestinal disturbances, extravasation injury, and anaphylaxis.