Administering Chemotherapy: Is It Safe for Pregnant or Breast-feeding Veterinary Technicians?

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In the veterinary field, women are often the main care providers. Because of exposure to toxins in their workplaces, female veterinary professionals should be concerned about the safety of their fetuses during pregnancy and their infants while breast-feeding.

Anticancer drugs are cytotoxic. Most of these agents have properties that also make them mutagenic, carcinogenic, and teratogenic. How toxic are these drugs? How might these drugs interfere with conception and carrying a fetus to term? Does the handling of cytotoxic drugs by female veterinary staff members during lactation cause problems for their breast-feeding infants?

Assessing the Risks
Unfortunately, there is little comprehensive information in the human or veterinary literature about the risks to health care providers who handle cytotoxic drugs. For personnel who do not administer cytotoxic drugs but who enter the preparation and administration areas, the risk of exposure may be lower than for personnel who prepare and administer these agents. Several safety recommendations highlight the issue of contamination within the work area, particularly surface contamination. According to the Oncology Nursing Society’s (ONS’s) Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, “Even when all recommended precautions are used, the potential for exposure cannot be completely eliminated. Therefore, an additional level of precaution is suggested for those most vulnerable to the reproductive and developmental effects of hazardous drugs.”

According to the American Society of Health-System Pharmacists, “… workers may be exposed to a hazardous drug at many points during its manufacture, transport, distribution, receipt, storage, preparation, and administration, as well as during waste handling and equipment maintenance and repair. All workers involved in these activities have the potential for contact with uncontained drug.” When incidental environmental exposures are considered, the potentially contaminated area may be much larger than expected. The National Institute for Occupational Safety and Health (NIOSH) has stated that it “… measured detectable concentrations of one to five hazardous drugs in various locations such as biological safety cabinet (BSC) surfaces, floors, counter tops, storage areas, tables and chairs in patient treatment areas, and locations adjacent to drug-handling areas … Such widespread contamination of work surfaces makes the potential for skin contact highly probable in both pharmacy and patient areas.” Thus, despite work practice guidelines for handling hazardous drugs in health care settings, workers are being exposed to cytotoxins and may experience serious health effects. The use of personal protective equipment (PPE), ventilation cabinets, and needleless systems and the prohibition of nonessential staff from contact with hazardous materials decrease the likelihood of exposure but do not remove all risk.

Biohazard Exposure During Pregnancy
The three phases of pregnancy are embryogenesis, organogenesis, and fetal development (TABLE 1). Biohazard
exposure at each phase has different effects on the fetus. Embryogenesis begins at fertilization of the ova and lasts approximately 2 weeks. Cell damage during this phase either is repaired, allowing growth to continue, or results in fetal death. During organogenesis, the fetus forms connective tissue, organs, and other body systems. Organogenesis lasts from day 15 to day 84 of gestation. Damage to the fetus during this phase results in fetal death or irreparable malformation. During the final phase, fetal development (day 85 through birth), damage to the fetus results in functional defects instead of visible physical malformation of the fetus, the main effects are mental and growth retardation as well as shortening of the length of gestation.

**Effects of Chemotherapy**

Because chemotherapy affects rapidly dividing cells and fetuses have a very high rate of cell division, fetuses are highly sensitive to the effects of chemotherapy. In children, the most common adverse effects of intrauterine exposure to chemotherapy are growth retardation and head and limb anomalies.4 Because fetuses have a high metabolic demand and fluid is exchanged through the placenta, transfer of drugs between pregnant women and their fetuses is inevitable. If a pregnant woman has contact with hazardous chemotherapy drugs—whether by ingestion, inhalation, skin contact, injection, or other routes—these drugs may enter the fetus through the placenta.

**Recommendations for Veterinary Technicians**

What does the above information mean for veterinary technicians? Currently, there are no clear guidelines regarding exposure to cytotoxic drugs for veterinary technicians who are pregnant, attempting to become pregnant, or breast-feeding. Despite information that describes the hazards and their effects, recommendations are subject to personal interpretation. Each technician is responsible for reviewing the available recommendations regarding biosafety to decide what is safe for her and her fetus or infant. The tolerable level of risk may vary among individuals. At a minimum, it is recommended that veterinary technicians who care for oncology patients and are attempting to become pregnant, are pregnant, or are breast-feeding should always wear appropriate PPE in the workplace when exposure to cytotoxic drugs is possible (e.g., when cleaning up after patients, during or after drug administration). The ONS’s official statement to hospitals includes the following: “Alternate duty that does not include cytotoxic preparation or administration must be made available to both men and women involved in planning a pregnancy when requested.”5

Breast-feeding women who wear PPE may consider themselves to be safe, especially if they only handle pre-compounded drugs or clean up bodily wastes or chemotherapy administration devices. However, the American Society of Health-System Pharmacists has made the following statement2:

Several studies have shown floor contamination and the ineffectiveness of cleaning practices on both floors and surfaces. … Studies in the 1990s, using analytical methods significantly more specific and sensitive than the Ames test, indicated that environmental and worker contamination occurs in workplace settings despite the use of controls recommended in published guidelines, including the use of Class II BSCs [biologic safety cabinets]. The exact cause of contamination has yet to be determined. Studies have shown that (1) there is contamination on the outside of vials received from manufacturers and distributors, (2) work practices required to maximize the effectiveness of the Class II BSC are neglected or not taught, and (3) the potential vaporization of hazardous drug solutions may reduce the effectiveness of the high-efficiency particulate air (HEPA) filter in providing containment. Studies of surface contamination have discovered deposits of hazardous drugs on the floor in front of the Class II BSC, indicating that drug may have escaped through the open front of the BSC onto contaminated gloves or the final product or into the air.

The ONS’s position is that any nurse handling chemotherapy during pregnancy or breast-feeding is at risk for exposure, regardless of whether PPE is worn.7 Several chemotherapy drugs have been found in breast milk; therefore, to protect infants, these drugs should not be handled by breast-feeding mothers (TABLE 2).1 In a study of two cases in which breast-feeding mothers were exposed to cyclo-

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</tr>
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<td>Day 85–birth</td>
<td>Functional defects</td>
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1. **TABLE 2**

2. **TABLE 1** Phases of Pregnancy and the Effects of Biohazards

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TABLE 2 Effects of Chemotherapy Drugs on Breast-feeding Infants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Possible Neonatal Effects</th>
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</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Immunosuppression, growth retardation, carcinogenesis, neutropenia</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Immunosuppression, growth retardation, carcinogenesis</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Immunosuppression, growth retardation, carcinogenesis</td>
</tr>
<tr>
<td>Methotrexate</td>
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phosphamide, both infants were found to be neutropenic.6 Unfortunately, studies on the effect of chemotherapy drugs on breast-feeding are scarce, so it is unclear how harmful these drugs are to infants. However, significant potential for cytotoxic drug transfer into breast milk should not be discounted. According to the American Academy of Pediatrics, four cytotoxic drugs (i.e., cyclophosphamide, cyclosporine, doxorubicin, methotrexate) have been proven to interfere with the cellular metabolism of breast-feeding infants.7 These drugs induce immunosuppression and neutropenia in infants and may also inhibit growth and cause carcinogenesis.7 It is critical to note that pharmacologic or chemical agents that do not appear in the literature of the American Academy of Pediatrics may also be transferred into human milk and affect infants. Therefore, exclusion of certain pharmacologic or chemical agents from TABLE 2 indicates only that no relevant reports were found in the current literature.

When a chemotherapy agent is used, a material safety data sheet (MSDS) can provide basic information on managing a spill and the possible adverse effects if exposure occurs. MSDSs describe cytotoxic chemotherapeutics as having carcinogenic, genotoxic, teratogenic, or mutagenic effects. Many drugs used in clinical oncology have more than one of these effects, all of which can negatively affect fetuses and breast-feeding infants. Most cancers develop as a result of either random, but significant, gene mutations or damage to a cell’s DNA from environmental carcinogens such as radiation and chemicals. Carcinogenic refers to agents that transform normal cells into malignant cells. Chemicals that cause these mutations are called chemical carcinogens. Genotoxic refers to agents (i.e., chemical, physical, biologic) that can damage genetic material, such as DNA, possibly leading to mutation. Teratogenic refers to agents that can cause fetal malformation (developmental defects). Mutagenic refers to agents (e.g., chemicals, ultraviolet light, radioactive elements) that can induce or increase the frequency of mutation in an organism.

Based on the available information about cytotoxicity, should veterinary technicians risk exposing their fetus or breast-feeding infant? It is suggested, but not required, that veterinary technicians avoid work that increases the risk of cytotoxic exposure while pregnant or breast-feeding.1 Because of the inconvenience of wearing PPE and the lack of education about adverse cytotoxic effects, pregnant or breast-feeding veterinary technicians may not take adequate precautions to protect themselves or their fetuses or infants. Oncologic staff members, whether in human or veterinary medicine, are at higher risk for adverse cytotoxic effects than their patients because of daily exposure to chemotherapy drugs. At the 2009 annual congress of the ONS, the effects of these hazardous drugs on pregnant and breast-feeding nurses were discussed.8 The ONS emphasized that cytotoxic drugs have adverse effects on the reproductive system, including menstrual dysfunction, infertility, miscarriage, fetal abnormalities, premature labor, and effects that lead to learning disabilities in children. In addition, the ONS stated that “… multiple studies have reported an increase of cancer cases in nurses, physicians and pharmacists who work with hazardous drugs.”9 In 2006, a study found that 75% to 100% of vials of cyclophosphamide, 5-fluorouracil, and doxorubicin were extremely contaminated with cytotoxic drugs before arriving from the distributor.8

The ONS, NIOSH, and most human medical institutional guidelines assert that biologic safety cabinets or compounding aseptic containment isolators should be used to compound chemotherapeutic agents. These devices should be vented externally and undergo routine cleaning. In addi-
Glossary

Carcinogenic:—agents that transform normal cells into malignant cells
Cytotoxic:—inducing cell damage
Genotoxic:—inducing DNA damage
Intrauterine:—within the womb
Mutagenic:—causing genetic mutation
Teratogenic:—inducing fetal development and malformation

Even when all recommended precautions are used, the potential for exposure cannot be completely eliminated. Therefore, an additional level of protection is suggested for those most vulnerable to the reproductive and developmental effects of hazardous drugs. Employers should allow employees who are actively trying to conceive or are pregnant or breastfeeding to refrain from activities that may expose them and their infant to reproductive health hazards such as chemical, physical, or biologic agents. Alternate duty that does not include hazardous drug preparation or administration must be made available upon request to both men and women in the aforementioned situations or who have other medical reasons for not being exposed to hazardous drugs. The employee has the responsibility of notifying the employer of the specific situation (e.g., pregnancy, preconception, breastfeeding).

According to these recommendations, health care workers should be given choices to avoid workplace activities that increase their risk of exposure to cytoxins. However, veterinary technicians are ultimately responsible for reviewing the current data and making a personal decision about acceptable risk. While there are regulations and guidelines for handling cytotoxic drugs during pregnancy and breastfeeding, there are no laws to guide institutions in their regulations. For the many veterinary technicians who decide to continue caring for patients undergoing chemotherapy, consistent use of PPE (nonpermeable gowns and double gloves) is strongly recommended because PPE has been shown to significantly reduce the risk of exposure to hazardous drugs. Knowing more about these drugs and their adverse effects as well as being knowledgeable about PPE can benefit all veterinary technicians, not only those who are pregnant or breast-feeding. If veterinary technicians suspect that they might be at risk for cytotoxic exposure, they should remove themselves from the situation. They should also remember that chemotherapy-free areas do not exist in an oncology ward.

Conclusion

For human nurses and veterinary technicians, there are no specific safety guidelines for pregnancy or breast-feeding. However, the ONS has made the following statement:

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References

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1. Cytotoxic agents have properties that
   a. are beneficial to cells.
   b. make them mutagenic, carcinogenic, and teratogenic.
   c. aren’t harmful.
   d. make them dangerous only to dogs and cats.

2. Exposure to cytotoxic agents can occur during drug
   a. transportation.
   b. administration.
   c. handling.
   d. all of the above

3. Cytotoxic damage to cells during embryogenesis can
   a. cause fetal death.
   b. enhance growth.
   c. result in irreparable malformation.
   d. retard growth.

4. Chemotherapy affects
   a. cancer cells only.
   b. tissue, not cells.
   c. rapidly dividing cells.
   d. noncancerous cells only.

5. PPE should be worn
   a. only during administration of chemotherapy.
   b. only during pregnancy.
   c. only while breast-feeding.
   d. whenever cytotoxic exposure is possible.

6. Cytotoxic contamination has been found
   a. only in BSCs.
   b. only on the gloves of those who handle chemotherapy drugs.
   c. on floors.
   d. only on chemotherapy vials.

7. The ONS has stated that
   a. PPE is all that is needed to protect a pregnant or breast-feeding nurse.
   b. all nurses are at risk when handling chemotherapy drugs, even when all recommended precautions are used.
   c. there is no need for PPE.
   d. pregnancy or breast-feeding is not a concern for handlers of chemotherapy drugs.

8. Carcinogenesis
   a. changes normal cells into malignant cells.
   b. only affects breastmilk.
   c. occurs only in the womb.
   d. is a harmless process.

9. Many drugs used in clinical oncology are
   a. carcinogenic.
   b. mutagenic.
   c. genotoxic.
   d. all of the above

10. For compounding chemotherapeutic agents, closed-system transfer devices
    a. should be used in addition to PPE and a BSC.
    b. can be used without other safety measures.
    c. can be used without a BSC.
    d. are not needed.