



ANTINEOPLASTIC AGENTS

Occupational Hazards in Hospitals

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health**



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ANTINEOPLASTIC AGENTS

Introduction

Antineoplastic agents are widely used in cancer therapy because they can inhibit growth by disrupting cell division and killing actively growing cells. These agents can also cause health effects among health care workers who work with them. A summary of these health risks and means for protecting workers are available in a recent NIOSH Alert [NIOSH 2004].

The following list contains commonly used antineoplastic agents and some of the cancers treated by these agents [Rogers 1987; Chabner et al. 1996; Jochimsen 1992; McFarland et al. 2001]:

Alkylating agents (interfere with normal mitosis and cell division)

- *Chlorambucil (Leukeran®)*—breast, lung, ovarian, and testicular cancer; Hodgkin’s disease
- *Cyclophosphamide (Cytoxan®)*—multiple myeloma; breast, lung, and ovarian cancer
- *Carmustine (BiCNU®)*—malignant melanoma, brain tumors

Antimetabolites (interfere with folic acid, purine, and pyrimidine synthesis)

- *Methotrexate (Mexate®)*—leukemia, breast, and lung cancer

- *Fluorouracil (Adrucil®)*—bladder, liver, pancreatic, lung, and breast cancer
- *Mercaptopurine (Purinethol®)*—acute leukemia

Antibiotics (cause single- and double-strand DNA breaks)

- *Actinomycin D (Cosmegen®)*—Kaposi's sarcoma, rhabdomyosarcoma
- *Doxorubicin (Adriamycin®)*—acute leukemia, breast cancer
- *Bleomycin (Bleo®)*—Hodgkins/non-Hodgkins lymphoma, testicular cancer

Natural products (antimitotic agents) (block mitosis and produce metaphase arrest)

- *Vinblastine (Velban®)*—non-Hodgkin's lymphoma, breast and testicular cancer
- *Vincristine (Oncovin®)*—small-cell lung cancer, non-Hodgkin's lymphoma
- *Paclitaxel (Taxol®)*—ovarian and breast cancer

Miscellaneous agents

- *Hydroxyurea (Hydrea®)*—acts as an antimetabolite in S phase; malignant melanoma, metastatic ovarian cancer
- *Estrogens*—interfere with hormone receptors and proteins in all phases of cell cycle; prostate cancer, postmenopausal advanced breast cancer

Some of these antineoplastic agents are also being used for other purposes such as the treatment of nonmalignant diseases. Examples include the use of methotrexate for rheumatoid arthritis [Baker et al. 1987], cyclophosphamide



for multiple sclerosis [Moody et al. 1987], and 5-fluorouracil for psoriasis [Abel 2000].

The purpose of this brochure is to

- make you aware of the adverse health effects of antineoplastic agents,
- describe how you can be exposed to these agents, and
- provide and identify control methods and work practices to prevent or reduce your exposure to antineoplastic agents.

What health effects can be caused by exposure to antineoplastic agents?

The following symptoms and health effects have been reported in hospital workers exposed to antineoplastic agents:

- Abdominal pain
- Coughing
- Dizziness
- Nausea
- Facial flushing
- Vomiting
- Diarrhea
- Skin rashes
- Hair loss
- Adverse reproductive effects such as disruption of menstrual cycle, fetal loss, and birth defects

If you experience any of these health problems when working with antineoplastic agents, report them to your supervisor or safety officer.

Statistically significant genotoxic effects and genetic damage (for example, increased micronuclei formation and increases in sister chromatid exchange and chromosomal aberrations) have been reported in hospital pharmacists and nurses exposed to antineoplastic agents. Little information is available about the risk of cancer related to exposure of hospital workers to antineoplastic agents [Burgaz et al. 1999; McDiarmid et al. 1992; Oestreicher et al. 1990]. However, one case of bladder cancer in a pharmacist was attributed to her routine exposure to antineoplastic agents. Apparently, she had no other exposures to known occupational or environmental carcinogens [Levin et al. 1993]. An undifferentiated carcinoma of the nasopharyngeal type was identified in a nurse who had been employed for 12 years in a clinical oncology department where antineoplastic agents were frequently used (cyclophosphamide, methotrexate, and vincristine, for example) [Gabriele et al. 1993]. Skov et al. [1990, 1992] reported an increased risk for leukemia among Danish physicians and nurses who handled antineoplastic agents.

Who might be exposed to antineoplastic agents in hospitals?

Workers in hospitals who might be exposed to antineoplastic agents include the following:

- Hospital staff who work in areas where solutions of these agents (including agents prepared from crushing or breaking tablets) are prepared, administered, and disposed of

- Pharmacy personnel who prepare the solutions
- Hospital staff in oncology departments and infusion units who administer these solutions
- Hospital staff who dispose of feces, urine, etc. of patients treated with these agents
- Hospital staff who handle bed clothing of patients treated with these agents

When are workers most likely to be exposed to antineoplastic agents in hospitals?

Workers are most likely to be exposed to antineoplastic agents by breathing them, ingesting them unintentionally, or having skin contact with them during the following procedures:


- Counting tablets poured from multidose bottles
- Crushing or breaking tablets to be made into liquid preparations
- Preparing solutions
- Handling solutions
- Administering solutions
- Disposing of solutions
- Disposing of used intravenous (IV) sets or other drug administration equipment
- Cleaning spills
- Disposing of feces, urine, bed clothing, etc. of patients treated with these agents
- Handling soiled bed clothing of patients treated with these agents

Workers can also be exposed to contaminated carpeting.

How can I protect myself from exposure to antineoplastic agents?

Protect yourself by using the following control methods and work practices:

- Prepare these agents in a centralized area restricted to authorized personnel only.
- Prepare these agents in a biological safety cabinet (BSC)—Class II Type B, or Class III. (A BSC with an outside exhaust must be vented away from outside fresh-air intake units.)
- Use syringes and IV sets with Luer-Lok™-type fittings for preparing and administering these agents. Place these syringes and needles in chemotherapy waste containers designed to protect workers from injuries.
- Consider using closed-system drug transfer devices and needleless systems.
- Avoid skin contact. Use a disposable gown made of a lint-free, low-permeability fabric. The gown should have a closed front, long sleeves, and elastic or knit closed cuffs.
- Use good quality, powder-free, disposable gloves that cover the gown cuff (unless the manufacturer of the antineoplastic agent specifies a particular glove material).
- Use two pairs of gloves.
- Change gloves periodically.
- Wear a plastic face shield or splash goggles to avoid contact of eyes, nose, or mouth with these



agents whenever splashes, sprays, or aerosols are generated.

- Remove protective clothing carefully to avoid spreading contamination.
- Attend training classes in safety awareness about the use of and exposure to antineoplastic agents.

For more information about how to protect yourself, refer to NIOSH [2004] and OSHA guidelines for controlling hazardous drugs [OSHA 1999].

Safety Tips

Protect yourself with the following safety tips:

- Do not eat or drink in areas where antineoplastic agents are prepared or administered.
- Become familiar with and be able to recognize sources of exposure to antineoplastic agents.
- Wash hands before using and after removing personal protective clothing such as disposable gowns.
- Handle wastes related to antineoplastic agents separately from other hospital trash. Treat them as hazardous waste.
- Clean up spills immediately using appropriate precautions.
- Learn what written policies your unit has for the safe handling of antineoplastic agents.
- Refer to NIOSH [2004] and OSHA [1999] for further information about emergency procedures in the event of a large spill.

Case Reports

Case 1—While preparing a vincristine solution in a horizontal laminar-flow air hood, a pharmacy technician inhaled an aerosol of the solution. His symptoms included sneezing, hot flashes, swelling of his eye lids, shortness of breath, chest tightness, and congestion. He immediately sought medical attention in the emergency room, where he also complained of slight shortness of breath. He was treated intramuscularly with Benadryl® and instructed to take Benadryl by mouth the next day. By the following morning, all of his symptoms were gone [McDiarmid and Egan 1988].

Case 2—On two separate occasions, a patient care assistant working on the oncology floor of a community teaching hospital developed a red face and rash over the arms, neck, trunk, and hands about 30 minutes after emptying a container of urine into a toilet. On both occasions, she denied having any direct contact with the urine of her two patients, as she had worn a protective gown and nitrile gloves and had followed hospital policy for the disposal of materials contaminated with antineoplastics. She had not worn a mask. The rash subsided after 1 to 2 days. After reviewing records of both hospital patients, her supervisor discovered that each patient had been recently treated with vincristine and Adriamycin®.

The patient care assistant reported that she had no known history of allergies or recent infections, nor did she have symptoms of upper respiratory infection. She also said she had used no medication

or new personal care items, cosmetics, or laundry detergents. She was not pregnant. She recalled that both patient rooms had flowers and balloons, but she said she was not sensitive to these items. No family members or close contacts developed a rash during the period of evaluation. After the patient care assistant was treated with diphenhydramine (Benadryl[®]) and corticosteroids, the symptoms resolved [Kusnetz and Condon 2003].

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More information about antineoplastic agents


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