Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings

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Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings
Foreword

The purpose of this Alert is to increase awareness among health care workers and their employers about the health risks posed by working with hazardous drugs and to provide them with measures for protecting their health. Health care workers who prepare or administer hazardous drugs or who work in areas where these drugs are used may be exposed to these agents in the air or on work surfaces, contaminated clothing, medical equipment, patient excreta, and other surfaces. Studies have associated workplace exposures to hazardous drugs with health effects such as skin rashes and adverse reproductive outcomes (including infertility, spontaneous abortions, and congenital malformations) and possibly leukemia and other cancers. The health risk is influenced by the extent of the exposure and the potency and toxicity of the hazardous drug. To provide workers with the greatest protection, employers should (1) implement necessary administrative and engineering controls and (2) assure that workers use sound procedures for handling hazardous drugs and proper protective equipment. The Alert contains a list of drugs that should be handled as hazardous drugs.

This Alert applies to all workers who handle hazardous drugs (for example, pharmacy and nursing personnel, physicians, operating room personnel, environmental services workers, workers in research laboratories, veterinary care workers, and shipping and receiving personnel). Although not all workers in these categories handle hazardous drugs, the number of exposed workers exceeds 5.5 million. The Alert does not apply to workers in the drug manufacturing sector.

The production, distribution, and application of pharmaceutical medications are part of a rapidly growing field of patient therapy. New areas of pharmaceutical development will bring fundamental changes to methods for treating and preventing diseases. Both traditional medications and bioengineered drugs can be hazardous to health care workers who must handle them. This NIOSH Alert will help make workers and employers more aware of these hazards and provide the tools for preventing exposures.

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Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings

Warning!

Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.

Health care workers who work with or near hazardous drugs may be exposed to these agents in the air or on work surfaces, clothing, medical equipment, or patient urine or feces. Hazardous
drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs (see Appendix A of NIOSH Alert: Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings for a List of Hazardous Drugs). The health risk depends on how much exposure a worker has to these drugs and how toxic they are.

**Health care workers should take the following steps to protect themselves from hazardous drugs:**

- Read all information and material safety data sheets (MSDSs) your employer provides to you for the hazardous drugs you handle.
- Participate in any training your employer provides on the hazards of the drugs you handle and the equipment and procedures you should use to prevent exposure.
- Be familiar with and able to recognize sources of exposure to hazardous drugs. Sources of exposure include
  - all procedures involving hazardous drugs (including preparation, administration, and cleaning), and
  - all materials that come into contact with hazardous drugs (including work surfaces, equipment, personal protective equipment [PPE], intravenous [IV] bags and tubing, patient waste, and soiled linens).
- Prepare hazardous drugs in an area that is devoted to that purpose alone and is restricted to authorized personnel.
- Prepare hazardous drugs inside a ventilated cabinet designed to protect workers and others from exposure and to protect all drugs that require sterile handling.
- Use two pairs of powder-free, disposable chemotherapy gloves, with the outer one covering the gown cuff whenever there is risk of exposure to hazardous drugs.
- Avoid skin contact by using a disposable gown made of polyethylene-coated polypropylene material (which is nonlinting and nonabsorbent). Make sure the gown has a closed front, long sleeves, and elastic or knit closed cuffs. Do not reuse gowns.
- Wear a face shield when splashes to the eyes, nose, or mouth may occur and when adequate engineering controls (such as the sash or window on a ventilated cabinet) are not available.
- Wash hands with soap and water immediately before using personal protective clothing (such as disposable gloves and gowns) and after removing it.
- Use syringes and IV sets with Luer-Lok™ fittings for preparing and administering hazardous drugs.
- Place drug-contaminated syringes and needles in chemotherapy sharps containers for disposal.
- When supplemental protection is needed, use closed-system drug-transfer devices, glove bags, and needleless systems inside the ventilated cabinet.
- Handle hazardous wastes and contaminated materials separately from other trash.
- Clean and decontaminate work areas before and after each activity involving hazardous drugs and at the end of each shift.
- Clean up small spills of hazardous drugs immediately, using proper safety precautions and PPE.
- Clean up large spills of hazardous drugs with the help of an environmental services specialist.
Employers of health care workers should take the following steps to protect their workers from exposure to hazardous drugs:

- Make sure you have written policies about the medical surveillance of health care workers and all phases of hazardous drug handling—including receipt and storage, preparation, administration, housekeeping, decontamination and cleanup, and disposal of unused drugs, contaminated spills, and patient wastes.
- Seek input from workers who handle hazardous drugs when developing these policies and other programs to prevent exposures.
- Prepare a written inventory of all hazardous drugs used in the workplace, and establish a procedure for regular review and updating of this inventory.
- Train workers to recognize and evaluate hazardous drugs and to control exposure to them.
- Provide workers who handle or work near hazardous drugs with appropriate information and MSDSs.
- Provide a work area that is devoted solely to preparing hazardous drugs and is limited to authorized personnel.
- Do not permit workers to prepare hazardous drugs using laminar-flow work stations that move air from the drug toward the worker.
- Provide and maintain ventilated cabinets designed to protect workers and others from exposure to hazardous drugs and to protect all drugs that require sterile handling. Examples of ventilated cabinets include biological safety cabinets (BSCs) and containment isolators designed to prevent hazardous drugs from escaping into the work environment.
- Filter the exhaust from ventilated cabinets with high-efficiency particulate air filters (HEPA filters). Make sure these cabinets are exhausted to the outdoors wherever feasible—well away from windows, doors, and other air-intake locations. Consider providing supplemental equipment to protect workers further—for example, glove bags, needleless systems, and closed-system drug-transfer devices.
- Establish and oversee appropriate work practices for handling hazardous drugs, patient wastes, and contaminated materials.
- Provide workers with proper PPE on the basis of a risk assessment and train workers how to use it—as required by the Occupational Safety and Health Administration (OSHA) PPE standard [29 CFR 1910.132]. PPE may include chemotherapy gloves, nonlinting and nonabsorbent disposable gowns and sleeve covers, and eye and face protection.
- Ensure the proper use of PPE by workers.
- Use NIOSH-certified respirators [42 CFR 84].

  *Note: Surgical masks do not provide adequate respiratory protection.*

- Provide syringes and IV sets with Luer-LokTM fittings for preparing and administering hazardous drugs. Also provide containers for their disposal.
- Consider using closed-system drug-transfer devices and needleless systems to protect nursing personnel during drug administration.
- Periodically evaluate hazardous drugs, equipment, training effectiveness, policies, and procedures in your workplace to reduce exposures as much as possible.
- Comply with all relevant U.S. Environmental Protection Agency/Resource Conservation and Recovery Act (EPA/RCRA) regulations related to the handling, storage, and transportation of hazardous waste.

*Code of Federal Regulations.
Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings

Warning!

Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.

The National Institute for Occupational Safety and Health (NIOSH) requests assistance in preventing occupational exposures to antineoplastic drugs (drugs used to treat cancer) and other hazardous drugs in health care settings. Health care workers who work with or near hazardous drugs may suffer from skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.

Workers may be exposed to hazardous drugs in the air or on work surfaces, clothing, medical equipment, and patient urine or feces. The term hazardous drugs, as it is used in this Alert, includes drugs that are known or suspected to cause adverse health effects from exposures in the workplace. They include drugs used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs. The health risk depends on how much exposure a worker has to these drugs and how toxic they are. Exposure risks can be greatly reduced by (1) making sure that engineering controls such as a ventilated cabinet are used and (2) using proper procedures and protective equipment for handling hazardous drugs.

This Alert warns health care workers about the risks of working with hazardous drugs and recommends methods and equipment for protecting their health. The Alert addresses workers in health care settings, veterinary medicine, research laboratories, retail pharmacies, and home health care agencies; it does not address workers in the drug manufacturing sector. Included in the Alert are five case reports of workers who suffered adverse health effects after being exposed to antineoplastic drugs.

NIOSH requests that employers, editors of trade journals, safety and health officials, and unions bring the recommendations in this Alert to the attention of all workers who are at risk.

For additional information, see NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and other Hazardous Drugs in Health Care Settings [DHHS (NIOSH) Publication No. 2004–165]. Single copies of the Alert are available from the following:

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Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
BACKGROUND

Drugs have a successful history of use in treating illnesses and injuries, and they are responsible for many of our medical advances over the past century. However, virtually all drugs have side effects associated with their use by patients. Thus, both patients and workers who handle them are at risk of suffering these effects. In addition, it is known that exposures to even very small concentrations of certain drugs may be hazardous for workers who handle them or work near them.

The term hazardous drugs was first used by the American Society of Hospital Pharmacists (ASHP) [ASHP 1990] and is currently used by the Occupational Safety and Health Administration (OSHA) [OSHA 1995, 1999]. Drugs are classified as hazardous if studies in animals or humans indicate that exposures to them have a potential for causing cancer, developmental or reproductive toxicity, or harm to organs. Many hazardous drugs are used to treat illnesses such as cancer or HIV infection [Galassi et al. 1996; McInnes and Schilsky 1996; Erlichman and Moore 1996]. See Appendix A for examples of hazardous drugs and a full discussion of criteria used to define and classify them as hazardous.

Although the potential therapeutic benefits of hazardous drugs outweigh the risks of side effects for ill patients, exposed health care workers risk these same side effects with no therapeutic benefit. Occupational exposures to hazardous drugs can lead to (1) acute effects such as skin rashes [McDiarmid and Egan 1988; Valanis et al. 1993a,b; Krstev et al. 2003]; (2) chronic effects, including adverse reproductive events [Selevan et al. 1985; Hemminki et al. 1985; Stücker et al. 1990; Valanis et al. 1997, 1999; Peelen et al. 1999]; and (3) possibly cancer [Skov et al. 1992].

Guidelines have been established for handling hazardous drugs, but adherence to these guidelines has been reported to be sporadic [Valanis et al. 1991, 1992; Mahon et al. 1994; Nieweg et al. 1994]. In addition, measurable concentrations of some hazardous drugs have been documented in the urine of health care workers who prepared or administered them—even after safety precautions had been employed [Ensslin et al. 1994, 1997; Sessink et al. 1992b, 1994a,b, 1997; Minoia et al. 1998; Wick et al. 2003]. Environmental studies of patient-care areas have documented measurable concentrations of drug contamination, even in facilities thought to be following recommended handling guidelines [Minoia et al. 1998; Connor et al. 1999; Pethran et al. 2003].

The numbers and types of work environments containing antineoplastic drugs are expanding as these agents are used increasingly for nonmalignant rheumatologic and immunologic diseases [Baker et al. 1987; Moody et al. 1987; Chabner et al. 1996; Abel 2000] and for chemotherapy in veterinary medicine [Rosenthal 1996; Takada 2003]. This Alert summarizes the health effects associated with occupational exposure to these agents and provides recommendations for safe handling.

POTENTIAL FOR WORKER EXPOSURE

Workers may be exposed to a drug throughout its life cycle—from manufacture to transport and distribution, to use in health care or home care settings, to waste disposal. The number of workers who may be exposed to hazardous drugs exceeds 5.5 million [U.S. Census Bureau 1997; BLS 1998, 1999; NCHS 1996]. These workers include shipping and receiving personnel, pharmacists and pharmacy technicians, nursing personnel, physicians, operating room personnel, environmental services personnel, and workers in veterinary practices where hazardous drugs are used. This Alert addresses workers in health care settings, veterinary medicine, research laboratories, retail pharmacies, and home health care agencies; it does not address workers in the drug manufacturing sector.

CONDITIONS FOR EXPOSURE

Both clinical and nonclinical workers may be exposed to hazardous drugs when they create aerosols, generate dust, clean up spills, or touch contaminated surfaces during the preparation, administration, or disposal of hazardous drugs. The following list of activities may result in exposures through inhalation, skin contact, ingestion, or injection:

- Reconstituting powdered or lyophilized drugs and further diluting either the reconstituted powder or concentrated liquid forms of hazardous drugs [Fransman et al. 2004]
• Expelling air from syringes filled with hazardous drugs
• Administering hazardous drugs by intramuscular, subcutaneous, or intravenous (IV) routes
• Counting out individual, uncoated oral doses and tablets from multidose bottles
• Unit-dosing uncoated tablets in a unit-dose machine
• Crushing tablets to make oral liquid doses [Dorr and Alberts 1992; Shahsavarani et al. 1993; Harrison and Schultz 2000]
• Compounding potent powders into custom-dosage capsules
• Contacting measurable concentrations of drugs present on drug vial exteriors, work surfaces, floors, and final drug products (bottles, bags, cassettes, and syringes) [McDevitt et al. 1993; Sessink et al. 1992a,b, 1994b; Minoia et al. 1998; Connor et al. 1999, 2002; Schmaus et al. 2002]
• Generating aerosols during the administration of drugs, either by direct IV push or by IV infusion
• Priming the IV set with a drug-containing solution at the patient bedside (this procedure should be done in the pharmacy)
• Handling body fluids or body-fluid-contaminated clothing, dressings, linens, and other materials [Cass and Musgrave 1992; Kromhout et al. 2000]
• Handling contaminated wastes generated at any step of the preparation or administration process
• Performing certain specialized procedures (such as intraoperative intraperitoneal chemotherapy) in the operating room [White et al. 1996; Stuart et al. 2002]
• Handling unused hazardous drugs or hazardous-drug-contaminated waste
• Decontaminating and cleaning drug preparation or clinical areas
• Transporting infectious, chemical, or hazardous waste containers
• Removing and disposing of personal protective equipment (PPE) after handling hazardous drugs or waste

EXPOSURE ROUTES

Exposures to hazardous drugs may occur through inhalation, skin contact, skin absorption, ingestion, or injection. Inhalation and skin contact/absorption are the most likely routes of exposure, but unintentional ingestion from hand to mouth contact and unintentional injection through a needlestick or sharps injury are also possible [Duvall and Baumann 1980; Dorr 1983; Black and Presson 1997; Schreiber et al. 2003].

A number of studies have attempted to measure airborne concentrations of antineoplastic drugs in health care settings [Kleinberg and Quinn 1981; Neal et al. 1983; McDiarmid et al. 1986; Pyy et al. 1988; McDevitt et al. 1993; Sessink et al. 1992a; Nygren and Lundgren 1997; Stuart et al. 2002; Kiffmeyer et al. 2002; Larson et al. 2003]. In most cases, the percentage of air samples containing measurable airborne concentrations of hazardous drugs was low, and the actual concentrations of the drugs, when present, were quite low. These results may be attributed to the inefficiency of sampling and analytical techniques used in the past [Larson et al. 2003]. Both particulate and gaseous phases of one antineoplastic drug, cyclophosphamide, have been reported in two studies [Kiffmeyer et al. 2002; Larson et al. 2003].

Since the early 1990s, 14 studies have examined environmental contamination of areas where hazardous drugs are prepared and administered at health care facilities in the United States and several other countries [Sessink et al. 1992a; Sessink et al. 1992b; McDevitt et al. 1993; Pethran et al. 1998; Minoia et al. 1998; Rubino et al. 1999; Sessink and Bos 1999; Connor et al. 1999; Micoli et al. 2001; Vandenbroucke et al. 2001; Connor et al. 2002; Kiffmeyer et al. 2002; Schmaus et al. 2002; Wick et al. 2003]. Using wipe samples, most investigators 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. All of the studies reported some level of contamination with at least one drug, and several reported contamination with all the drugs for which assays were performed. Such widespread contamination of work surfaces makes the potential for skin contact highly
probable in both pharmacy and patient areas.

**EVIDENCE FOR WORKER EXPOSURE**

Evidence indicates that workers are being exposed to hazardous drugs and are experiencing serious health effects despite current work practice guidelines. Protection from hazardous drug exposures depends on safety programs established by employers and followed by workers. Factors that affect worker exposures include the following:

- Drug handling circumstances (preparation, administration, or disposal)
- Amount of drug prepared
- Frequency and duration of drug handling
- Potential for absorption
- Use of ventilated cabinets *
- PPE
- Work practices

The likelihood that a worker will experience adverse effects from hazardous drugs increases with the amount and frequency of exposure and the lack of proper work practices.

Worker exposures have been assessed by studies of biological markers of exposure. No single biological marker has been found to be a good indicator of exposure to hazardous drugs or a good predictor of adverse health effects [Baker and Connor 1996]. Sessink and Bos [1999] noted that 11 of 12 studies reported cyclophosphamide in the urine of health care workers tested, indicating continued exposure despite safety precautions.

Harrison [2001] reported that six different drugs (cyclophosphamide, methotrexate, ifosfamide, epirubicin and cisplatin/carboplatin) were detected in the urine of health care workers by 13 of 20 investigations. Two recent studies have documented antineoplastic drugs in the urine of pharmacy and nursing personnel [Pethran et al. 2003; Wick et al. 2003]. Pethran and coworkers collected urine samples in 14 German hospitals over a 3-year period. Cyclophosphamide, ifosfamide, doxorubicin, and epirubicin (but not daunorubicin or idarubicin) and platinum (from cisplatin or carboplatin) were identified in urine samples from many of the study participants. A U.S. investigation demonstrated that use of a closed-system device for 6 months reduced both the concentration of cyclophosphamide or ifosfamide in the urine of exposed health care workers and the percentage of samples containing these drugs [Wick et al. 2003]. Hazardous drugs have also been documented in the urine of health care workers who did not handle hazardous drugs but were potentially exposed through fugitive aerosols or secondary contamination of work surfaces, clothing, or drug containers [Sessink et al. 1994b; Mader et al. 1996; Pethran et al. 2003].

*A ventilated cabinet is a type of engineering control designed to protect workers. Examples includes BSCs and isolators designed to prevent hazardous drugs inside of the cabinet from escaping into the work environment. See the glossary in Appendix B for additional descriptions of engineering controls.

**EVIDENCE FOR HEALTH EFFECTS IN WORKERS**

By the 1970s, the carcinogenicity of several antineoplastic drugs in animals was well established [Shimkin et al. 1966; Weisberger 1975; Schmahl and Habs 1978]. Likewise, a number of researchers during this period linked the therapeutic use of alkylating agents in humans to subsequent leukemias and other cancers [Harris 1975, 1976; IARC 1979]. Many health care professionals began to question the safety of occupational exposure to these agents [Ng and Jaffe 1970; Donner 1978; Johansson 1979].

**Mutagenicity**

A number of studies indicate that antineoplastic drugs may cause increased genotoxic effects in pharmacists and nurses exposed in the workplace [Falck et al. 1979; Anderson et al 1982; Nguyen et al. 1982; Rogers and Emmett 1987; Oestricher et al. 1990; Fuchs et al. 1995; Ündeğer et al. 1999; Norppa et al. 1980; Nikula et al. 1981].
Developmental and Reproductive Effects

A recent review of 14 studies described an association between exposure to antineoplastic drugs and adverse reproductive effects, and 9 studies showed some positive association [Harrison 2001]. The major reproductive effects found in these studies were increased fetal loss [Selevan et al. 1985; Stücker et al. 1990], congenital malformations depending on the length of exposure [Hemminki et al. 1985], low birth weight and congenital abnormalities [Peelen et al. 1999], and infertility [Valanis et al. 1999].

Cancer

Several reports have addressed the relationship of cancer occurrence to health care workers’ exposures to antineoplastic drugs. A significantly increased risk of leukemia has been reported among oncology nurses identified in the Danish cancer registry for the period 1943–1987 [Skov et al. 1992]. The same group [Skov et al. 1990] found an increased, but not significant, risk of leukemia in physicians employed for at least 6 months in a department where patients were treated with antineoplastic drugs.

CURRENT STANDARDS AND RECOMMENDATIONS

Currently, no NIOSH recommended exposure limits (RELs), OSHA permissible exposure limits (PELs), or American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLVs ®) have been established for hazardous drugs in general. An OSHA PEL and an ACGIH TLV have been established for soluble platinum salts [29 CFR † 1910.1000; ACGIH 2003]. However, these standards are based on sensitization and not on the potential to cause cancer. A PEL, an REL, and a TLV have also been established for inorganic arsenic compounds, which include the antineoplastic drug arsenic trioxide [29 CFR 1910.1018; NIOSH 2004; ACGIH 2003]. A workplace environmental exposure level (WEEL) has been established for some antibiotics, including chloramphenicol (AIHA 2002). Some pharmaceutical manufacturers develop risk-based occupational exposure limits (OELs) to be used in their own manufacturing settings, and this information may be available on material safety data sheets (MSDSs) or from the manufacturer [Sargent and Kirk 1988; Naumann and Sargent 1997; Sargent et al. 2002].

U.S. Environmental Protection Agency (EPA) regulations under the Resource Conservation and Recovery Act (RCRA) [42 USC ‡ 6901–6992] apply to the management of hazardous wastes, which include nine antineoplastic drugs [40 CFR 260–279].

OSHA

OSHA originally published guidelines for antineoplastic drugs in 1986 [OSHA 1986]. Current OSHA standards and guidelines that address hazardous drugs include the following:

- Hazard communication standard [29 CFR 1910.1200]
- Occupational exposure to hazardous chemicals in laboratories standard [29 CFR 1910.1450]
- OSHA Technical Manual; Section VI, Chapter 2: Controlling Occupational Exposure to Hazardous Drugs [OSHA 1999]. Main elements of these 1999 OSHA guidelines include the following:
  - Categorization of drugs as hazardous
  - Hazardous drugs as occupational risks
  - Work area
  - Prevention of employee exposure
  - Medical surveillance
EPA

EPA/RCRA regulations require that hazardous waste be managed by following a strict set of regulatory requirements [40 CFR 260–279]. The RCRA list of hazardous wastes was developed in 1976 and includes only about 30 pharmaceuticals, 9 of which are antineoplastic drugs. Recent evidence indicates that a number of drug formulations exhibit hazardous waste characteristics [Smith 2002]. OSHA [1999] and ASHP [1990] recommend that hazardous drug waste be disposed of in a manner similar to that required for RCRA-listed hazardous waste. Hazardous drug waste includes partially filled vials, undispensed products, unused IVs, needles and syringes, gloves, gowns, underpads, contaminated materials from spill cleanups, and containers such as IV bags or drug vials that contain more than trace amounts of hazardous drugs and are not contaminated by blood or other potentially infectious waste. Published EPA guidelines are as follows:


**Additional Guidelines**

Additional guidelines that address hazardous drugs or the equipment in which they are manipulated include the following:

- Centers for Disease Control (CDC) and National Institutes of Health (NIH). Primary Containment for Biohazards [CDC/NIH 2000]. Provides guidance on the selection, installation, testing, and use of BSCs.

- NIH. Recommendations for the Safe Handling of Cytotoxic Drugs [NIH 2002]. Includes recommendations for the safe preparation and administration of cytotoxic drugs.


- Oncology Nursing Society. Chemotherapy and Biotherapy Guidelines and Recommendations for Practice [Brown et al. 2001]. Provides complete guidelines for the administration of antineoplastic drugs, including safe handling guidelines.

- Oncology Nursing Society. Safe Handling of Hazardous Drugs [Polovich 2003]. Includes proper handling guidelines for hazardous drugs.

- United States Pharmacopoeia. Chapter <797> Pharmaceutical Compounding— Sterile Preparations [USP 2004]. Details the procedures and requirements for compounding sterile preparations and sets standards applicable to all settings in which sterile preparations are compounded.

- National Sanitation Foundation (NSF) and American National Standards Institute (ANSI). NSF/ANSI 49–2002 Class II (Laminar Flow) Biosafety Cabinetry [NSF/ANSI 2002]. Addresses classification and certification of Class II BSCs and provides a definition for Class III BSCs.


CASE REPORTS

The following cases illustrate the range of health effects reported after exposure to antineoplastic drugs:

Case 1

A female oncology nurse was exposed to a solution of carmustine when the complete tubing system fell out of an infusion bottle of carmustine, and all of the solution poured down her right arm and leg and onto the floor [McDiarmid and Egan 1988]. Although she wore gloves, her right forearm was unprotected, and the solution penetrated her clothing and stockings. Feeling no sensation on the affected skin areas, she immediately washed her arm and leg with soap and water but did not change her clothing. A few hours later, while at work, she began to experience minor abdominal distress and profuse belching followed by intermittent episodes of nonbloody diarrhea with cramping abdominal pain. Profuse vomiting occurred, after which she felt better. The nurse went to the emergency room, where her vital signs and physical examination were normal. No specific therapy was prescribed. She felt better the following day. Carmustine is known to cause gastric upset, and the investigators attributed her gastrointestinal distress to systemic absorption of carmustine.

Case 2

A 39-year-old pharmacist suffered two episodes of painless hematuria (blood in the urine) and was found to have cancer (a grade II papillary transitional cell carcinoma) [Levin et al. 1993]. Twelve years before her diagnosis, she had worked full time for 20 months in a hospital IV preparation area where she routinely prepared cytotoxic agents, including cyclophosphamide, fluorouracil, methotrexate, doxorubicin, and cisplatin. She used a horizontal laminar-flow hood that directed the airflow toward her. Because she was a nonsmoker and had no other known occupational or environmental risk factors, her cancer was attributed to her antineoplastic drug exposure at work—though a cause and effect relationship has not been established in the literature.

Case 3

A 41-year-old nurse who had worked on an oncology ward for 13 years suffered from nasal discharge, difficult breathing, and attacks of coughing 1 to 2 hours after beginning work [Walusia et al. 2002]. During the third year of her employment on the ward, she developed difficult breathing while away from work. Her total IgE was low, and specific IgE antibodies to common agents and skin prick tests to common allergens (including latex) were all negative. The patient was subjected to a number of single-blind bronchial challenge tests with antineoplastic drugs, and she was monitored by spirometry and peak expiratory flow measurements. On the basis of clinical findings, the investigators concluded that the evidence was consistent with a diagnosis of allergic asthma.

Case 4

A malfunctioning BSC resulted in possible exposure of nursing personnel to a number of antineoplastic drugs that were prepared in the BSC [Kevekordes et al. 1998]. Blood samples from the nurses were analyzed for genotoxic biomarkers 2 and 9 months after replacement of the faulty BSC. At 2 months, both sister chromatid exchanges (SCEs) and micronuclei were significantly elevated compared with those of a matched control group. At 9 months, the micronuclei concentrations were similar to those of the 2-month controls. SCEs were not determined at 9 months. The investigators concluded that the elevation in biomarkers had resulted from the malfunctioning of the BSC, which resulted in worker exposure to the antineoplastic drugs. They also concluded that the subsequent replacement with a new BSC contributed to the reduced effect seen with the micronucleus test at 9 months.

Case 5

A 41-year-old patient-care assistant working on an oncology floor developed an itchy rash approximately 30 minutes after emptying a commode of urine into a toilet [Kusnetz and Condon 2003]. She denied any direct contact with the urine, wore a protective gown and nitrile gloves, and followed hospital policy for the disposal of materials contaminated with antineoplastic drugs. The rash subsided after 1 to 2 days. Three weeks later, she had a similar reaction approximately 1 hour after performing the same procedure for another patient. Upon investigation, it was found that both hospital patients had recently been treated with vincristine and doxorubicin. The patient-care assistant had no other signs or symptoms and reported no changes in lifestyle and no history of allergies or recent infections. After treatment with diphenhydramine (intramuscular) and oral corticosteroids, her symptoms disappeared. Although the cause could not be definitely confirmed, both
vincristine and doxorubicin have been associated with allergic reactions when given to patients. The aerosolization of the drug present in the urine may have provided enough exposure for symptoms to develop.

CONCLUSIONS

Recent evidence summarized in this Alert documents that worker exposure to hazardous drugs is a persistent problem. Although most air-sampling studies have not demonstrated significant airborne concentrations of these drugs, the sampling methods used in the past have come into question [Larson et al. 2003] and may not be a good indicator of contamination in the workplace. In all studies involving examination of surface wipe samples, researchers have determined that surface contamination of the workplace is common and widespread. Also, a number of recent studies have documented the excretion of several indicator drugs in the urine of health care workers. Results from studies indicate that worker exposure to hazardous drugs in health care facilities may result in adverse health effects.

Appropriately designed studies have begun and are continuing to characterize the extent and nature of health hazards associated with these ongoing exposures. NIOSH is currently conducting studies to further identify potential sources of exposure and methods to reduce or eliminate worker exposure to these drugs. To minimize these potentially acute (short-term) and chronic (long-term) effects of exposure to hazardous drugs at work, NIOSH recommends that at a minimum, employers and health care workers follow the recommendations presented in this Alert.

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DHHS (NIOSH) Publication Number 2004–165

September 2004