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Preventing Occupational Exposures to Antineoplastic Drugs in Health Care Settings

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ABSTRACT The toxicity of antineoplastic drugs has been well known since they were introduced in the 1940s. Because most antineoplastic drugs are nonselective in their mechanism of action, they affect noncancerous as well as cancerous cells, resulting in well-documented side effects. During the 1970s, evidence came to light indicating health care workers may be at risk of harmful effects from antineoplastic drugs as a result of occupational exposure. Since that time, reports from several countries have documented drug contamination of the workplace, identified drugs in the urine of health care workers, and measured genotoxic responses in workers. Evidence also exists of teratogenic and adverse reproductive outcomes and increased cancers in health care workers. During the past 30 years, professional organizations and government agencies have developed guidelines to protect health care workers from adverse effects from occupational exposure to antineoplastic drugs. Although many safety provisions were advanced to reduce worker exposure in the 1980s, recent studies have shown that workers continue to be exposed to these drugs despite safety policy improvements. In 2004, the National Institute for Occupational Safety and Health (NIOSH) published an alert reviewing the most recent information available and promoting a program of safe handling during their use. (*CA Cancer J Clin* 2006;56:354–365.) © American Cancer Society, Inc., 2006.

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INTRODUCTION

The toxic effects of anticancer chemotherapy are well known to oncology specialists and to primary care clinicians. Awareness of these effects typically influences treatment plans for patients undergoing cancer therapy to prevent or mitigate adverse outcomes. However, beyond the patient safety concerns arising from the necessary therapeutic use of these drugs, occupational risks to health care workers handling these drugs in the course of their duties still need to be fully addressed.

Worldwide, more than 11 million new cases of cancer are diagnosed each year, and that number is expected to rise to 16 million by 2020.¹ In the United States, the American Cancer Society (ACS) predicts that almost 1.4 million new cancer cases will be diagnosed in 2006.² The National Cancer Institute predicts that this figure will double by the year 2050 because the US population is growing and aging.³ This increased patient load, along with the use of high-dose chemotherapy, combinations of several drugs, and the use of antineoplastic drugs for diseases other than cancer, will increase the potential for exposure of the health care worker to these drugs.

For the past 3 decades, treatment for many of these cancer cases has relied principally on anticancer chemotherapy.⁴ The first such agent, sulphur mustard gas, was observed to cause changes in bone marrow of World War I veterans who were hospitalized many years later. This led to its evaluation as an anticancer agent, and the related, but less toxic, nitrogen mustards were later demonstrated to produce tumor regression in lymphoma patients.⁵ With approximately 100 different antineoplastic drugs now in use⁶ and many more under development, drugs used to treat cancer have opened new avenues, from improving the quality of life of patients with cancer to a complete cure. Addressing these drugs' formidable toxicity profile, however, has been an ongoing campaign for clinicians and, more recently, for the occupational health community.

TABLE 1 Antineoplastic Agents That are Classified as Known or Probable Human Carcinogens⁹

Group 1 (Human Carcinogens)	Group 2A (Probable Human Carcinogens)
Arsenic trioxide	Azacitidine
Azathioprine	BCNU
Chlorambucil	CCNU
Chlornaphazine	Chlorozotocin
Cyclophosphamide	Cisplatin
Myleran	Doxorubicin HCl
Melphalan	<i>N</i> -Ethyl- <i>N</i> -nitrosourea
Semustine	Etoposide
Tamoxifen	Mechlorethamine HCl
Thiotepa	<i>N</i> -Methyl-nitrosourea
Treosulfan	Procarbazine HCl
Mustargen-Oncovin-Procarbazine-Prednisone (MOPP)	Teniposide
Etoposide-Cisplatin-Bleomycin (ECB)	

Adapted from the International Agency for Research on Cancer.⁹

HEALTH HAZARDS OF ANTINEOPLASTIC DRUGS

The majority of antineoplastic drugs are non-selective in their action: they exhibit their effects in both cancerous and noncancerous cells in most organs and body tissues. Known effects in treated patients include hepatic and renal toxicity, cardiotoxicity, hematopoietic toxicity, pulmonary toxicity, immunotoxicity, ototoxicity, dermal toxicity, and particularly injury to tissues with a rapid turnover rate.⁷

In the 1970s, secondary malignancies were reported in patients who had previously received antineoplastic drugs for other, usually solid tumor malignancies. The most commonly seen secondary malignancies were leukemia and bladder cancer reported after a latency period of several years.⁸ Since that time, a number of the antineoplastic drugs, especially many of the alkylating agents, have been associated with secondary cancers in treated patients.⁹ In support of these findings, numerous laboratory studies have identified these agents as rodent carcinogens and as genotoxic in several test systems.⁹ Table 1 lists the known (Group 1) and probable (Group 2A) human carcinogens among antineoplastic drugs in clinical use. An additional 11 agents are considered to be possible (Group 2B) human carcinogens by the International Agency for Research on Cancer (IARC). Given the nature of these agents and the ability of many of them to actively bind to DNA, RNA, and proteins, it would be expected that many of them are both mutagenic and carcinogenic (Figure 1).

In addition to their mutagenic and carcinogenic properties, many of the antineoplastic drugs have been associated with adverse reproductive effects that have been observed in animals as well as treated male and female patients. Meirow and Schiff¹⁰ have reported teratogenic outcomes in laboratory animals and patients treated with antineoplastic drugs during their pregnancies. Currently, 45 antineoplastic drugs are listed as Pregnancy Category D and 5 are listed as Category X by the Food and Drug Administration (Table 2). Reproductive and developmental effects similar to those observed in patients have been reported in health care workers who are exposed to antineoplastic drugs at considerably lower doses than those administered to patients.^{11,12}

EFFECTS OF OCCUPATIONAL EXPOSURE TO ANTINEOPLASTIC DRUGS

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 potentially exposed to all hazardous drugs exceeds 5.5 million.⁶ These workers include shipping and receiving personnel, pharmacists and pharmacy technicians, nursing personnel, physicians, operating room personnel, environmental services personnel, research laboratory personnel, and workers in veterinary practices where hazardous drugs are used. With the use of antineoplastic drugs expanding into

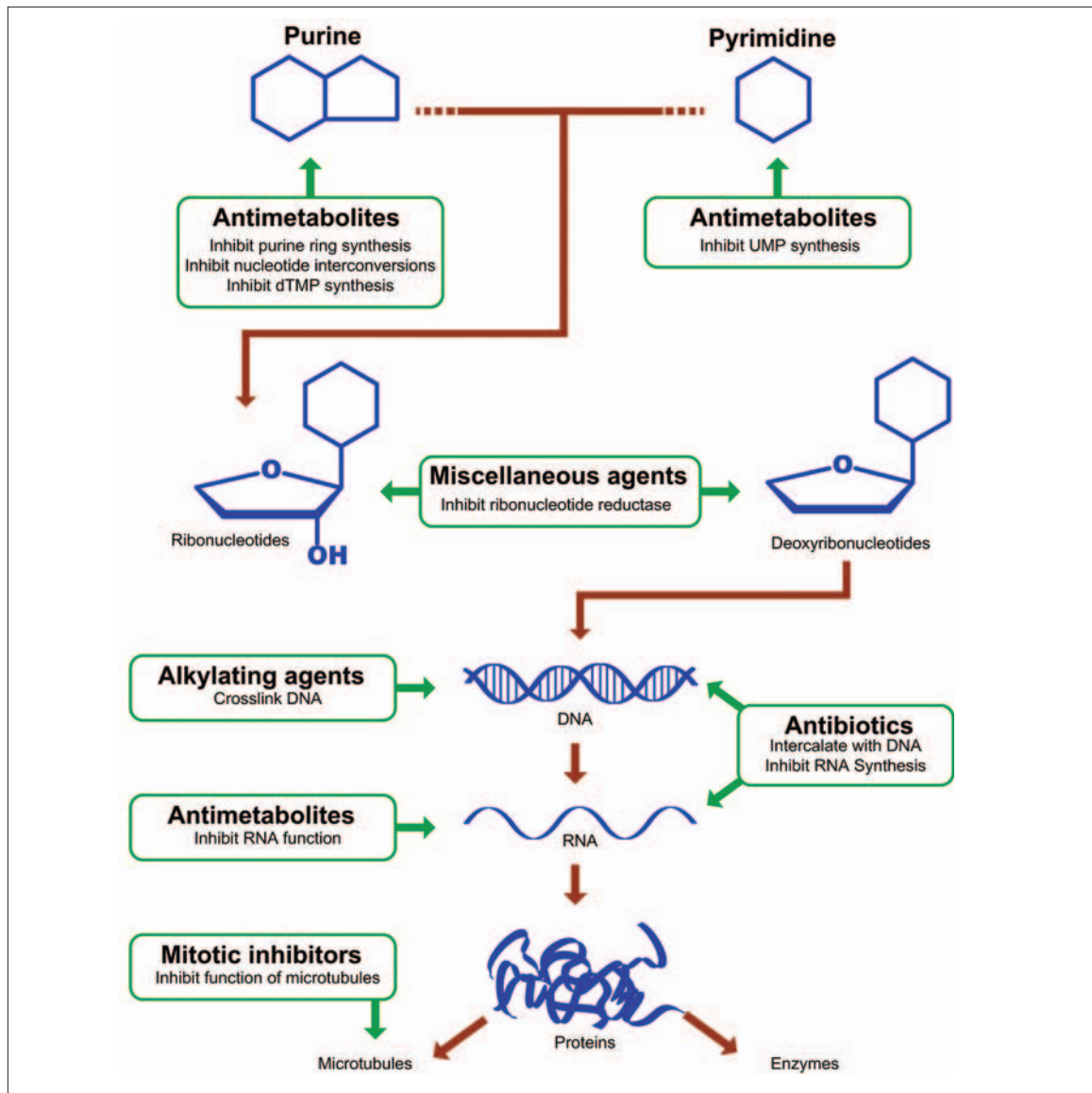


FIGURE 1 Site of Action of Some Antineoplastic Drugs. Adapted from McDiarmid MA.¹³

other specialties, the number of workers who are not properly trained in their safe handling has increased over the past few years.⁶

The first evidence documenting occupational exposure in health care workers was provided by a study by Falck and colleagues.¹⁴ Nurses who prepared and administered antineoplastic drugs had higher indicators of mutagenic substances in their urine compared with nonexposed workers. A dose response was also observed in the urine mutagenicity frequency with additive exposure over the workweek that decreased over the weekend. Although the health consequences of this finding are unknown, this study

suggested that nursing personnel were being occupationally exposed to mutagenic antineoplastic drugs. A 1982 study in the United States demonstrated that pharmacy personnel who prepared injectable antineoplastic agents had detectable concentrations of mutagenic substances in their urine when using a horizontal-flow cabinet (regardless of their use of gloves or masks), whereas no urine mutagenicity was detected after the same personnel wore gloves and used vertical-flow Class II biological safety cabinets (BSC).¹⁵ These findings were supported by numerous studies examining urine mutagenicity, chromosomal aberrations, sister chromatid

TABLE 2 Antineoplastic Agents That are Classified as Pregnancy Category D* or X†¹⁶

Drug	Pregnancy Category	Drug	Pregnancy Category
Arsenic trioxide	D	Imatinib mesylate	D
Azathioprene	D	Interferon alfa-2b	X
Bleomycin	D	Irinotecan HCl	D
Capecitabine	D	Leflunomide	X
Carboplatin	D	Lomustine	D
Carmustine	D	Mechlorethamine HCl	D
Chlorambucil	D	Melphalan	D
Cisplatin	D	Mercaptopurine	D
Cladribine	D	Methotrexate	X
Cyclophosphamide	D	Mitoxantrone HCl	D
Cytarabine	D	Oxaliplatin	D
Dactinomycin	D	Paclitaxel	D
Daunorubicin HCl	D	Pipobroman	D
Docetaxel	D	Procarbazine	D
Doxorubicin HCl	D	Tamoxifen	D
Epirubicin	D	Temozolomide	D
Etoposide	D	Teniposide	D
Floxuridine	D	Thalidomide	X
Fludarabine	D	Thioguanine	D
Fluorouracil	D	Thiotepa	D
Gemcitabine	D	Topotecan	D
Hydroxyurea	D	Tositumomab	X
Ibritumomab tiuxetan	D	Vinblastine sulfate	D
Idarubicin	D	Vincristine sulfate	D
Ifosfamide	D	Vinorelbine tartrate	D

Adapted from the US Food and Drug Administration Center for Drug Evaluation and Research.¹⁶

*D = There is clear evidence of risk to the human fetus, but the benefits may outweigh the risk for pregnant women who have a serious condition that cannot be treated effectively with a safer drug.

†X = There is clear evidence that the medication causes abnormalities in the fetus. The risks outweigh any potential benefits for women who are (or may become) pregnant.

exchanges, and other endpoints in studies of pharmacists and nurses who handle antineoplastic drugs.¹⁷⁻¹⁹

Surveys have associated workplace exposures to antineoplastic drugs with acute health effects, primarily in nurses. These included hair loss, headaches, acute irritation, and/or hypersensitivity,¹² as well as adverse reproductive outcomes (including infertility, spontaneous abortions, and congenital malformations).

A meta-analysis of 14 studies performed from 1966 to 2004 in the United States and Europe described an association between exposure to antineoplastic drugs and adverse reproductive effects in female health care workers.²⁰ The most common reproductive effects found in these studies were increased fetal loss,^{21,22} congenital malformations,²³ low birth weight and congenital abnormalities,²⁴ and infertility.²⁵ With the meta-analysis, no significant association was detected between exposure to antineoplastic drugs and congenital malformations and stillbirths. However,

a significant association was identified between exposure and spontaneous abortions. A number of other endpoints had elevated responses, but were not statistically significant. A study from China that was not included in the meta-analysis reported a significant decrease in full-term births and significant increases in premature birth, spontaneous abortion, and congenital malformations in nursing personnel who were exposed to antineoplastic drugs.²⁶ A recent study by Martin²⁷ documented learning disabilities in the children of nurses who had handled antineoplastic drugs during the course of their employment.

The adverse effects found in many of these studies occurred before the adoption of safe handling guidelines promoted by the Occupational Safety and Health Organization (OSHA) and professional organizations in the mid-1980s. However, these studies document the plausibility of occupational exposure sufficient to cause clinically significant adverse outcomes in routinely exposed workers.

Taking advantage of the vital records data linkage systems available in Denmark, two reports have addressed the link between cancer occurrence and 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 to 1987.²⁸ The same group²⁹ found an increased risk of leukemia in physicians employed for at least 6 months in a department where patients were treated with antineoplastic drugs. However, the increase was not statistically significant. Despite the small number of cases observed, the biological relevance of these excess hematopoietic malignancies is underscored in light of the commonly observed hematopoietic second malignancies observed in treated patients.⁸ These two studies^{28,29} examined workers' exposure to antineoplastic drugs before safe handling guidelines were in place, however, and no contemporary studies have examined cancer outcomes in similar populations.

SOURCES AND INDICATORS OF OCCUPATIONAL EXPOSURE

Exposure of health care providers to antineoplastic drugs is varied, and the routes of exposure are typically inhalation, dermal, or oral. Workers may be exposed by inhalation via droplets, particulates, and vapors when they create aerosols, generate dust by crushing tablets, and clean up spills. Dermal exposure may occur when workers touch contaminated surfaces during the preparation, administration, or disposal of hazardous drugs, and oral exposure may occur from hand-to-mouth contact. Accidental injection with an antineoplastic drug, although rare, has been documented. Table 3 lists activities that may result in exposures through inhalation, skin contact, ingestion, or injection.⁶

Dermal contamination can arise from drug residues on the outside of drug vials.³⁰⁻³⁸ Thus, the environment of health care personnel may be contaminated even before antineoplastic drug reconstitution has begun. Since the early 1990s, numerous studies have been published that have demonstrated contamination of the workplace with antineoplastic drugs.^{18,19,30,31,38-60} Typically, two to five "marker" drugs are sampled and

analyzed in pharmacies and patient treatment areas. Studies from several countries have shown contamination of surfaces of biological safety cabinets, countertops, floors, equipment, and most surfaces in areas where patients are treated. In all studies, at least one of the drugs was detected. In many studies, all drugs were detected, indicating that other drugs for which analyses were not performed were most likely present.

Most studies involving air sampling for antineoplastic drugs have detected little to no airborne contamination with these agents.⁶ Studies have typically reported drugs present in only a small percentage of samples and then usually at low concentrations. However, this may be related to problems with the methodology used in the early studies.⁶¹ A recent study by Mason in the United Kingdom reported significant concentrations of several drugs in both personal and area air samples.⁶² Drug particulates can become airborne after the drying of contaminated areas. Vaporization of antineoplastic agents has also been reported with various drugs such as carmustine, ifosfamide, thiotepa, and cyclophosphamide.^{53,63}

Inadvertent ingestion may be an additional route of exposure. When food or beverages are prepared, stored, or consumed in work areas, they may easily become contaminated with airborne particles of antineoplastic drugs. Likewise, hands, cigarettes, cosmetics, and chewing gum can be contaminated. A potential source of exposure is direct skin contact when a spill or leak occurs and a large volume of drug is released to the environment.

As an indicator of internal worker exposure to antineoplastic drugs, 19 studies have measured some of the same marker drugs used in environmental sampling in the urine of health care workers.^{30,39,41-43,56,57,62,64-74} All but two of the studies detected one or more of the drugs in the urine. Four studies reported the presence of antineoplastic drugs in the urine of workers who were not preparing the drugs, indicating secondary exposure from environmental contamination.^{30,41,71,73}

Because many of the antineoplastic drugs are genotoxic by nature, biomarkers for genotoxic agents have been used to monitor worker exposure to these drugs.¹⁷⁻¹⁹ Biomarkers for a number of endpoints such as urine mutagenicity,

TABLE 3 List of Hazardous Drug Handling Activities in Workers⁶

Activity	Primary Group of Workers Exposed
Handling drug-contaminated vials	Pharmacists, pharmacy technicians
Reconstituting powdered or lyophilized drugs and further diluting either the reconstituted powder or concentrated liquid forms of hazardous drugs	
Expelling air from syringes filled with hazardous drugs	
Compounding potent powders into custom-dosage capsules	
Administering antineoplastic drugs by intramuscular, subcutaneous, or intravenous (IV) routes	Nursing personnel
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	
Handling body fluids or body-fluid-contaminated clothing, dressings, linens, and other materials	
Handling contaminated wastes generated at any step of the preparation or administration process	
Counting out individual, uncoated oral doses and tablets from multidose bottles	Pharmacists, pharmacy technicians, nursing personnel
Unit-dosing uncoated tablets in a unit-dose machine	
Crushing tablets to make oral liquid doses	
Contacting measurable concentrations of drugs present on drug vial exteriors, work surfaces, floors, and final drug products (bottles, bags, cassettes, and syringes)	Pharmacists, pharmacy technicians, nursing personnel, housekeeping personnel
Handling unused antineoplastic drugs or antineoplastic drug-contaminated waste	
Decontaminating and cleaning drug preparation or clinical areas	
Performing certain specialized procedures (such as intraoperative intraperitoneal chemotherapy) in the operating room	Physicians, nursing personnel, operating room personnel
Transporting infectious, chemical, or hazardous waste containers	Nursing personnel, housekeeping personnel, waste disposal personnel
Removing and disposing of personal protective equipment after handling hazardous drugs or waste	Pharmacists, pharmacy technicians, nursing personnel, housekeeping personnel
Performing repairs or maintenance on biological safety cabinets or isolators used to prepare antineoplastic drugs	Maintenance personnel, biological safety cabinets certification personnel

Adapted from the National Institute for Occupational Safety and Health.⁶

chromosomal aberrations, micronuclei, sister chromatid exchange, and DNA damage have been used in more than 100 research studies in health care settings where antineoplastic drugs are prepared and administered. Because of their nonspecific nature, these biomarkers can only be used as an indicator of exposure to a genotoxic agent and may be influenced by extraneous sources of exposure, especially tobacco smoke. However, many properly controlled studies have demonstrated a significant difference in the outcomes of these biomarkers in workers exposed to antineoplastic drugs compared with control populations.^{17,75-81}

This evidence highlights the critical need to reduce exposure to all hazardous drugs in the health care environment. Efforts must be made to reduce occupational exposure to concentrations as low as reasonably achievable. A combination of exposure control methods can be applied to achieve this goal.

SAFE HANDLING GUIDELINES

When the risk to the health of exposed workers first became a recognized safety concern, the Society of Hospital Pharmacists of Australia

TABLE 4 Characteristics That Define Hazardous Drugs^{6,90,92}

Carcinogenicity
Teratogenicity or other developmental toxicity
Reproductive toxicity
Organ toxicity at low doses
Genotoxicity
Structure and toxicity that mimics existing hazardous drugs

Adapted from the National Institute for Occupational Safety and Health,⁶ the Occupational Safety and Health Administration,⁹⁰ and the American Society of Health-System Pharmacists.⁹²

published safe handling guidelines in 1981.⁸² Several organizations and government agencies in the United States also published guidelines for the safe handling of hazardous drugs, starting with the American Society of Health-System Pharmacists (ASHP) in 1985,⁸³ and including the Oncology Nursing Society (ONS),⁸⁴ the National Institutes of Health (NIH),^{85,86} the National Study Commission on Cytotoxic Exposure,⁸⁷ and the American Medical Association's Council on Scientific Affairs.⁸⁸ OSHA issued safe handling guidelines in 1986.⁸⁹ These guidelines were expanded in 1995 to include all hazardous drugs.⁹⁰

The ASHP Technical Assistance Bulletin of 1990 first used the term "hazardous drug" to address other pharmaceuticals that posed a hazard to workers, but were not used in cancer therapy.⁹¹ They proposed a schema whereby a drug could be qualitatively characterized as hazardous based on its inherent toxicity. These characteristics generally relate to carcinogenicity, genotoxicity, teratogenic, or reproductive hazards and are listed in Table 4. Two-thirds of the approximately 140 hazardous drugs that have been identified are classified as antineoplastic/cytotoxic agents. The remainder includes some hormonal agents, immunosuppressants, antiviral medications, and monoclonal antibodies.⁶

Although guidelines for safe handling have been in place since the mid-1980s in the United States, subsequent reports indicate that workplace contamination and worker exposure were continuing where antineoplastic drugs were being prepared and administered.^{46,57} Therefore, the National Institute for Occupational Safety and Health (NIOSH) developed an alert that addressed safe handling issues for all hazardous drugs.⁶ Other safe handling guidelines have been

TABLE 5 Hierarchy of Industrial Hygiene Control⁹⁴

Elimination of the hazard or substitution with a less hazardous chemical (this is not feasible in health care)
Engineering controls (the use of biological safety cabinets, isolators, or closed systems)
Administrative controls (training and education programs; availability of material safety data sheets; established work practices, policies, and surveillance)
Personal protective equipment (the use of protective gloves, gowns, respiratory protection, and eye protection)

Adapted from Soule RD.⁹⁴

updated by professional organizations in this time frame, including the ASHP⁹² and the ONS.⁹³

CONTROL OF EXPOSURE

The basic occupational health approach to minimize exposure to any workplace hazard is a hierarchy of industrial hygiene control methods. This approach has achieved success across many industrial settings.⁹⁴ The elements of this hierarchy include elimination or substitution of the hazard, engineering controls, administrative controls, and personal protective equipment (PPE), (Table 5) and can be applied to the health care setting.

RECOMMENDATIONS FOR SAFE HANDLING OF ANTINEOPLASTIC DRUGS

NIOSH, ASHP, and ONS have current guidelines for the safe handling of hazardous drugs that are based on sound occupational health principals and professional standards of practice. Considerable concurrence exists between the various recommendations and also with the OSHA guidance of 1999.⁹⁰ The highlights from the NIOSH recommendations presented in Table 6 generally reflect the hierarchy of control technologies. More detailed recommendations can be found at www.cdc.gov/niosh/docs/2004-165/.

Adherence to recommended work practices and the use of engineering controls and PPE has been shown to substantially reduce worker exposure to antineoplastic drugs. However, several factors, such as increased workload, understaffing, improper training, budgetary constraints, more complex treatment regimens, use in non-oncology

TABLE 6 NIOSH Recommendations for Safe Handling of Antineoplastic and Other Hazardous Drugs⁶

Activity	Recommendations
Receiving and storage of drugs	<p>Wear PPE* suitable for task being performed</p> <p>Properly label all hazardous drugs</p> <p>Store and transport drugs in proper containers</p>
Preparation and administration of drugs	<p>Evaluate drug preparation and administration policies</p> <p>Wear suitable PPE, including double gloves for task being performed</p> <p>Limit access to areas where drugs are prepared</p> <p>Use proper engineering controls when preparing drugs</p> <p>Wash hands with soap and water before donning and after removing gloves</p> <p>Prime intravenous tubing in a ventilated cabinet</p> <p>Use needleless or closed systems when preparing and administering drugs</p> <p>Do not disconnect tubing from an intravenous bag containing a hazardous drug</p> <p>Dispose of used materials in the appropriate container</p>
Ventilated cabinets	<p>Perform all preparations with hazardous drugs in a ventilated cabinet designed to reduce worker exposure</p> <p>Do not use supplemental engineering controls as a substitute for a ventilated cabinet</p> <p>When asepsis is required, select a cabinet designed for both hazardous drugs containment and aseptic processing</p> <p>Horizontal laminar-flow clean benches should not be used for preparation of hazardous drugs</p> <p>Properly maintain engineering controls as required by the manufacturer</p>
Routine cleaning, decontamination, housekeeping, and waste disposal	<p>Use suitable PPE for the task being performed</p> <p>Establish periodic cleaning routines for all work surfaces and equipment used where hazardous drugs are prepared or administered</p> <p>Consider used linen and patient waste to be contaminated with the drugs and/or their metabolites</p> <p>Separate wastes according to institutional, state, and federal guidelines and regulations</p>
Spill control	<p>Manage spills according to written policies and procedures</p> <p>Locate spill kits in areas where exposures may occur</p> <p>Adhere to Occupational Safety & Health Administration (OSHA) respiratory protection program</p> <p>Dispose of spill material in a hazardous chemical container</p>
Medical surveillance	<p>Participate in medical surveillance programs at work, or see your private health care provider if one does not exist</p> <p>Medical surveillance should include the following:</p> <ul style="list-style-type: none"> • Reproductive and general health questionnaires • Complete blood count and urinalysis • Physical examination at time of employment and annual health status questionnaire review • Follow up for workers who have shown health changes

Adapted from the National Institute for Occupational Safety and Health.⁶

*PPE = personal protective equipment.

specialities, and others can adversely affect how these drugs are handled.

The use of safe handling practices for antineoplastic and other hazardous drugs in some primary areas can dramatically reduce the potential exposure of health care workers to these drugs. These include receipt and storage of drugs, drug preparation, administration of the drug to the patient, transportation of the drug, and drug waste handling, including patient waste, drug

waste, and laundry. In addition to the recommendations in Table 5, the following is a summary of some of the highlights of safe handling guidelines that have been described in greater detail elsewhere.^{6,90,92,93}

General Precautions

Only individuals trained in the safe handling of antineoplastic drugs should be involved in their handling. Retraining and competency testing

should be done at least on a yearly basis. This training should include the location and use of spill kits, fit-testing and training for respirators, and sources of safety information (Material Safety Data Sheets, Standard Operating Procedures, OSHA, NIOSH, ASHP, ONS websites) for all employees handling antineoplastic drugs.^{6,92,93,95}

Receipt and Storage of Antineoplastic Drugs

As described above, drug vials received from manufacturers are often contaminated on the outside of the vial.^{30–38} Studies have shown that from a few vials to all the vials in a shipment may be contaminated. The contamination is not typically associated with vials being broken during shipment.³⁷ Obviously when vials are broken during shipment, much higher concentrations of contamination must be dealt with. It is recommended that shippers of antineoplastic drugs place them in zippered plastic bags inside rigid, sealable shipping containers. Containers should be opened carefully and closely inspected on arrival. Personnel unpacking drug vials should wear gloves recommended for handling antineoplastic drugs and respiratory protection to protect themselves from dermal and inhalation exposures. Antineoplastic drugs should be stored in a well-ventilated area separate from other drugs.^{6,92}

Antineoplastic Drug Preparation

Procedures for drug preparation can vary from one institution to the next. In some locations, BSCs are used for antineoplastic drug preparation, whereas others use isolators. A horizontal laminar flow clean bench should never be used for antineoplastic drug preparation, as this design results in significant exposure of the worker and work area.¹⁵ For preparing antineoplastic drugs, a Class II or Class III BSC or an isolator intended for asepsis and containment is required.⁶ When a Class II BSC is used, NIOSH recommends that it be a Class II, 100%-vented cabinet whenever possible. Drug preparation should be done in a controlled environment where access is limited to authorized personnel. BSCs and isolators should be free from clutter, properly cleaned, and maintained to ensure maximum efficiency and to reduce exposure of personnel. Personnel should follow all recommendations for PPE.^{6,90,92}

All waste should be segregated and disposed of according to hospital policy and state and federal regulations that apply.⁹⁶

Antineoplastic Drug Administration

Detailed guidelines for the administration of antineoplastic drugs have been developed by the ONS,⁹³ and additional recommendations have been published by others.^{6,90} Although administration of antineoplastic drugs can take several forms, some general recommendations should be stressed. PPE that is appropriate for the task being performed should be used. Needleless systems should be used whenever possible. If intravenous tubing is not primed in the pharmacy, it should be primed with a solution other than the drug, or by the backflow method, and tubing and administrative sets should remain intact for disposal. As in the pharmacy, all waste should be segregated and disposed of according to hospital policy and state and federal regulations that apply.⁹⁶

Antineoplastic Drug Transportation

Drugs within an institution should be transported in zippered plastic bags placed in containers that protect them. Containers should be labelled to identify the contents as hazardous. Personnel who transport the drugs should be aware of emergency procedures in case of a spill and have access to spill kits.

Antineoplastic Drug Waste Handling

Each institution should have a policy for segregation of waste materials resulting from antineoplastic drug preparation and administration. Some states have their own regulations for disposal of hazardous waste, and federal regulations apply to some medications.^{6,92,96} Personnel collecting and transporting waste materials in institutions should wear recommended PPE and follow institutional policies. All materials that come in contact with the drugs and patient waste (urine, blood, sweat, feces, and vomit) should be considered to contain the drugs and/or their metabolites and should be handled as hazardous. These materials include used vials and intravenous sets, syringes, gloves, gowns, bedpans, linen, underpads, and similar materials and must

be disposed of accordingly. Many institutions have special requirements for linen handling, such as double washing and washing contaminated linen separately from other linen.⁹⁵

Medical Surveillance

Medical surveillance involves collecting and interpreting data to detect changes in the health status of working populations potentially exposed to hazardous substances.⁶ The elements of a medical surveillance program are used to establish a baseline of workers' health and then monitor their future health as it relates to their potential exposure to hazardous agents. Medical surveillance is one element of a comprehensive approach to minimizing worker exposure and should be used as part of a safety and health program that includes engineering controls, good work practices, and PPE.

Employers should ensure that health care workers who are exposed to hazardous drugs are routinely monitored as part of a medical surveillance program.^{90,92,93} This includes workers who directly handle hazardous drugs, such as nurses, pharmacists, and pharmacy technicians. In addition, other workers (eg, nurses' aides) who may come directly into contact with patient wastes within 48 hours after a patient has received a hazardous drug should be included in a medical surveillance program.

SUMMARY

The toxicity of anticancer chemotherapy has been well known since its initial clinical use. Indeed, it has often been these drugs' toxic side effects that have limited their therapeutic value. The risk-benefit equation for a cancer patient often determines these drugs' appropriate use despite acknowledged side effects. Although these drugs present the same potential toxicities to exposed health care workers, that risk-benefit ratio is altered. A balance must be achieved to continue the use of these beneficial drugs in patients, while assuring the health of personnel administering them. A body of guidance now exists on how to achieve this goal. Much of the new guidance revisits the long standing elements of a comprehensive safe handling program and reminds us that the risk remains and our vigilance is required, but that a harmonized safe handling approach has been adopted that assures minimal risk to workers who provide lifesaving therapies to their patients.

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