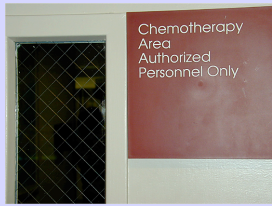


**Safe Handling Practices
Among Handlers of
Antineoplastic Drugs**

*Are drug handlers protecting
themselves from hazards?*



- **Review studies that have shown drugs pose a hazard to health care workers**
- **Discuss sources and routes of contamination**
- **Describe guidelines that are in place and where to find them**
- **Discuss effectiveness of guidelines**
- **Discuss the problem of compliance**

Recently in doing some interviews of pharmacy and nursing staff who work with chemo therapy for the research project I am working on (“Antineoplastic Drug Exposure: Effectiveness of Guidelines”) I became aware of the fact that many of these staff persons were unsure about whether or not safe handling practices of the hazardous drugs they come into contact with were actually necessary, and whether these drugs actually posed a risk. It seems as though in some areas a work culture arises that has a more casual attitude towards these drugs and the standards that are in place to handle them.

In this presentation I would like to touch on the topics presented in this slide:

Recently in doing some interviews of pharmacy and nursing staff who work with chemo therapy for the research project I am working on (“Antineoplastic Drug Exposure: Effectiveness of Guidelines”) I became aware of the fact that many of these staff persons were unsure about whether or not safe handling practices of the hazardous drugs they come into contact with were actually necessary, and whether these drugs actually posed a risk. It seems as though in some areas a work culture arises that has a more casual attitude towards these drugs and the standards that are in place to handle them.

In this presentation I would like to touch on the topics presented in this slide:

Early Studies of Drug Handlers

- **Urine of pharmacy and nursing staff found to be mutagenic**
- **Increased levels of DNA damage in pharmacy and nursing staff**

An early study found that the urine of nurses who handled certain antineoplastic drugs was mutagenic, and this urinary mutagenicity increased during the work week and decreased during the weekend when they were away from work.

Another study found increased mutagenic activity in pharmacy personnel preparing these agents.

Other studies found increased levels of DNA damage in nursing and pharmacy personnel who handled these drugs.

Adverse Reproductive Outcomes

- **Birth defects**
- **Fetal Loss**
- **Infertility**
- **Ectopic pregnancies**
- **Low birth weight**
- **Menstrual dysfunction**

Other early studies, as well as more recent studies, report on adverse reproductive outcomes in workers exposed to antineoplastic drugs. These include increased fetal loss, birth defects, infertility, ectopic pregnancies, low birth weight and menstrual dysfunction among oncology nurses, pharmacy staff and MDs who work with antineoplastics.

Developmental Toxicity and Genotoxicity of Some Common Anticancer Agents

Drug Class	Developmental Toxicity		Genotoxicity
	Animal	Human	
Alkylating Agents	+	+	+
Antibiotics	+	+	+
Antimetabolites	+	+	+
Mitotic Function	+	+	-
Topoisomerase II Function	+	+	

This slide shows that many different classes of antineoplastics, including those on this slide, have demonstrated developmental toxicity as well as genotoxicity in both animal and human studies.

Other health effects

- **Increased risk of leukemia found in Danish studies**
- **Liver disease**

There is much less data regarding cancer occurrence in health care workers who are exposed to antineoplastics. This may be partly due to longer latency period from time of exposure to tumor development. There has been an increased risk of leukemia reported among Danish physicians who were employed at least six months in a department where pts. were treated with anticancer agents, and in oncology nurses (Skov '90 and '92).

Another study reported on the occurrence of liver injury in three head nurses who handled antineoplastic drugs for 6, 8 and 16 years, respectively, as there was an absence of alcohol and drug use by these individuals, their illness was attributed to their exposure to anti cancer drugs (Sotaniemi et al '83)

Sources of Contamination

- **Contaminated vials**
- **Drug preparation and administration**
 - **leaks**
 - **spills**
- **Drug relocation**
- **Spread of spills**

Drug contamination and thus worker exposure can occur in various ways.

Vials can arrive contaminated which may occur through breakage in shipping.

The process of preparation itself may allow the drug to be released by spills or leaks into the environment undetected.

Once these spills or leaks occur they may be spread.

Routes of exposure

- **Dermal**
- **Oral**
- **Inhalation**
 - **Vapors**
 - **Particulates (droplets, dust)**

When work surfaces are contaminated the worker may be exposed to the drug through these routes: through the skin, by oral ingestion or by inhalation. Air sampling has detected very small particulates of the drugs in the surrounding air that can be inhaled. In addition many of these drugs have been shown to vaporize, increasing the risk of inhalation.

1986 OSHA Guidelines

- **Employed hierarchy of control technologies to mitigate worker exposure**
 - **engineering controls**
 - **administrative and work practice controls**
 - **personal protective equipment (PPE)**
- **Enforced under the OSHA “General Duty” clause - to provide a safe and healthful work environment**

In 1986 the Occupational Safety & Health Administration recognizing through surveys that there was little standardization in the use of engineering controls and personal protective equipment when handling antineoplastics published its first set of drug handling guidelines.

1995 OSHA Hazardous Drug Guidelines

- **ASHP definition of a hazardous drug**
- **Includes agents in tablet form**
- **Includes aerosolized agents**
- **Hazard Communication Standard**
- **Updated Appendix with source listed**
- **Reproductive Hazards Policy**
- **Enlarges domain of drugs considered**

Subsequent surveys of U.S. cancer centers and oncology clinics revealed a wide variation in work practices, equipment or training for personnel preparing CD's.

One study done in 1993 reported on air and surface cyclophosphamide sampling results in a hospital oncology pharmacy where OSHA guidelines were in place. Results revealed air samples with rare detectable drug, but multiple surface wipe samples with measureable drug concentrations.

These sorts of findings and the continued lack of standardization resulted in revised guidelines. These guidelines adopted the American Society of Hospital Pharmacists (ASHP) definition of hazardous drugs which includes antineoplastic and non-antineoplastic drugs. Other updates and additions include those on this slide.

Studies show that guidelines are effective

- **DNA damage significantly lower in nurses:**
 - **Who apply the necessary individual safety protections**
 - **Used more than one type of protective equipment**
 - **Worked in well-ventilated area**

If adhered to, studies show that these guidelines are effective in protecting workers.

One study (Undeger et al, '99) looked at the work characteristics of exposed nurses and the use of PPE. DNA damage was observed, this damage was found to be significantly lower in nurses who applied the necessary individual safety protections during their work.

Another study (Fuchs et al '95) compared DNA damage in 10 oncology nurses not using recommended safety precautions to controls, higher levels of damage were found in the nurses. After applying recommended precautions there was a statistically significant decrease in the level of DNA damage to the level of controls.

Another study (Kopjar '01) found that DNA damage was lower in exposed subjects who used more than one type of protective equipment and who worked in a well-ventilated safety cabinet..

Studies show that guidelines are effective

- **Nurses with positive mutagenicity tests:**
 - **Handled more drug**
 - **Used less skin protection**
 - **Had more skin contact**

And finally, in a 4th study (Labuhn '98) it was found that among nurses who prepared and administered antineoplastics, those with positive mutagenicity tests handled more doses of the drugs, used less skin protection and had more skin contact with the drugs than those with negative tests

Where to find guidelines:

- **Occupational Safety and Health Association:**
http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html
- **American Society of Health-System Pharmacists**
- **Oncology Nurses Association**

The OSHA guidelines for the safe handling of hazardous drugs are extensive and can be found on their web site at this address. In addition the professional associations for the Oncology nurses and hospital pharmacists have guidelines that are available to their members.

In Summary:

- **Reviewed studies that have shown drugs pose a hazard to health care workers**
- **Discussed sources and routes of contamination**
- **Described guidelines that are in place and where to find them**
- **Discussed effectiveness of guidelines**
- **Encouraged close compliance to standards**