

## Continuing Pharmacy Education

# Managing Cytotoxic Drugs

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### ABSTRACT

**Cytotoxic drugs are used in the management of malignant diseases. They have been found to be carcinogenic, teratogenic and mutagenic. There is growing concern that the handling, preparation, administration and disposal of these substances may constitute an occupational hazard. These guidelines aim to identify, and help avoid or minimize occupational exposure to cytotoxic drugs and related wastes within health care establishments. It is necessary that individuals involved in the use or handling of cytotoxic drugs are made aware of associated matters relating to the safe handling of such drugs.**

**Keywords:** *cytotoxic drugs, occupational exposure, mutagenic, teratogenic, carcinogenic*

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### INTRODUCTION

Cytotoxic drugs are therapeutic agents which are known to be toxic to cells principally through their action on cell reproduction and are primarily intended for the treatment of cancer. Currently there is no established data for safe level of exposure to these drugs. While health care establishment workers involved in the handling of these group of drugs do not receive therapeutic doses, there is concern that unless suitable protective measures are in place, these personnel may be subjected to low level doses in the long term.

Occupational exposure may occur through the inhalation of aerosols and drug particles, skin absorption, ingestion and needle stick injuries resulting from:

- transport of cytotoxic drugs
- cytotoxic drug preparation and administration
- contamination of surfaces with cytotoxic drugs
- handling, transportation and disposal of cytotoxic waste (1-3).

Personnel likely to be involved in these processes are nurses, medical officers and pharmacy staff. The greatest risk of occupational exposure to cytotoxic drugs is during their preparation and administration. The need for safe handling of cytotoxic drugs is not confined to injectable dosage forms only. For example, oral dosage forms may shed respirable dust, and when used to prepare oral suspensions, may distribute dust and fragments. Other aspects of patient care such as spill and waste management may also pose a risk of occupational exposure.

#### Potential effects of exposure

Many published studies are inconclusive and little is known of long term effects of exposure to cytotoxic drugs in health care workers. However, there is sufficient evidence to indicate potential adverse effects as a result of occupational exposure (4-7). Studies have reported the following effects amongst personnel preparing and administering cytotoxic drugs:

- contact dermatitis, local toxic or allergic

reaction, which may result from direct contact with skin or mucous membranes

- cytogenetic abnormalities and mutagenic activity related to biological uptake by exposed personnel
- alteration to normal blood cell counts
- excretion of the drugs or metabolites in the urine in exposed personnel
- symptoms including abdominal pain, hair loss, nasal sores and vomiting
- liver damage
- foetal loss in exposed pregnant women and malformation of the offspring of pregnant women

Although the long term effects of occupational exposure to cytotoxic drugs are inconclusive, it is not appropriate to wait for indisputable evidence of harm.

### **Drug preparation**

In general, the principle focus of safety during cytotoxic drug preparation should be on:

- education and training of personnel
- control of the working environment
- adoption of safe working procedure

Education and training of health professionals in cytotoxic drug preparation and handling is recommended to ensure that safe work practices are understood, developed, implemented and maintained. Use of cytotoxic drug safety cabinet, pharmaceutical isolators and other appropriate equipment is recommended to facilitate safe preparation of cytotoxic drugs and to ensure that products, operator and working environment are protected. In order to provide drug containment and aseptic manipulation, all preparation of cytotoxic drugs should take place in a separate, dedicated cytotoxic safety cabinet or in pharmaceutical isolators.

The health care establishment management is responsible for ensuring that personnel who are designated to perform cytotoxic drug preparation procedures are provided with an accredited level of training, and that they have attained proficiency prior to undertaking preparation procedures (8). Accredited training in drug preparation procedures should be undertaken prior to commencement of duties and when new equipment is introduced or procedures changed. Procedures should be in place to ensure that accredited staff are kept informed of new

developments, such as changes in technology and preparation procedures. Validation of accreditation criteria should occur at intervals no greater than two years.

Personal Protective Equipment should be worn by personnel using an approved cytotoxic drug safety cabinet to prepare cytotoxic drugs:

- long sleeved coverall of impermeable material, e.g. made from bonded polyethylene fibre with a closed front and elasticized cuff, with suitable head protection
- overshoes of a similar impermeable material
- suitable respiratory protection
- long PVC, surgical latex, or purpose manufactured gloves

Special precautions are required for the laundering of used Personal Protective Equipment (garments) which may be contaminated with cytotoxic drugs. The conditions required for the laundering of potentially contaminated items should be established to:

- protect laundry personnel who are involved in this process from cytotoxic drug residue
- prevent contamination of other materials being laundered
- ensure the garments are decontaminated prior to sterilization or reuse

Attention to occupationally related work practice will maximize efficiency and productivity and minimize operator errors. Cytotoxic clean room equipment layout should be designed properly. To determine appropriate work periods the entire task should be assessed taking into consideration the:

- level of concentration and visual control required
- precision of movements
- design of equipment and availability of adjustable furniture, e.g. chairs, stools and foot rests
- aesthetic effects of the working environment

Drugs and its storage area and equipment need to be identified. Intravenous equipment and devices containing cytotoxic drugs should be clearly labelled with a permanent, adhesive and recognizable cytotoxic drug label.

For drug storage, the quantities of cytotoxic drugs stored in pharmacy departments, wards,

clinics and satellite pharmacies should generally be restricted to the quantities for short term use. A dedicated area for the storage of cytotoxic drugs should be provided in pharmacy departments and storage areas. Use of a dedicated area facilitates quick and efficient containment and management of a spill.

Oral solid cytotoxic doses should be individually packaged. Automatic tablet counters, or other equipment which may generate particulate matter, should not be used in the packaging of cytotoxic drugs. If a prepared therapy has to be transported on-site, it should be in a transport container which is of sufficient strength to prevent leakage of its contents and should be securely closed and labelled with cytotoxic warnings. Cytotoxic drugs should not be transported in pneumatic automated tube systems.

Standard operating procedures for the preparation of cytotoxic drugs should be documented and should include:

- using specially dedicated equipment in a pharmacy to provide containment of powder where there is a requirement for compounding cytotoxic preparations
- operational specifications for the use of cytotoxic drug preparation facilities including cytotoxic drug safety cabinet
- initial and ongoing validation of operator competence
- reconstitution procedures
- routine and emergency cleaning and decontamination protocol
- spill management
- maintenance and certification of equipment and facilities
- availability of drug safety information
- documentation and records
- maintenance of daily records
- labelling and packaging for transport internally or externally

Health care establishments which are unable to provide facilities, equipment and training to employees, should not undertake to provide a cytotoxic drug service. Alternative arrangements could include:

- purchase and supply of the prepared cytotoxic drug in a single dose delivery unit.
- establishment of supply arrangements with a health care institution which has the required facilities, equipment and trained personnel

to provide prepared cytotoxic drug doses.

### **Drug administration**

Nursing, medical and other personnel may be involved in administering oral, parenteral and topical cytotoxic drugs. A number of factors influence their level of risk of exposure to cytotoxic drugs during administration. Exposure may occur due to contamination from solid or liquid spills or splashes and needle stick injuries.

Many factors contribute to the risk of exposure, including:

- poor technique, improperly used or inappropriate equipment
- patient behaviour, when it increases the difficulty of administration, for example, if the patient is uncooperative
- the route of administration, for example, the risk of splashes in the eyes of the operator or assistant during an intrathecal injection is increased owing to the proximity of the face to the injection site
- an inappropriate working environment

It is important that practitioners identify the level risk, then use appropriate work practices and Personal Protective Equipment to minimize the risks.

All staff administering cytotoxic drugs should be appropriately trained (9) in the following aspects of cytotoxic drug handling and demonstrate proficiency prior to commencing duties:

- potential occupational hazards
- approved work practice
- specialized operator techniques
- waste containment and handling
- spill management techniques
- proper use of Personal Protective Equipment

The following Personal Protective Equipment should be considered for use during administration of cytotoxic drugs:

- a particulate respirator type mask
- a long sleeved gown of impermeable material
- safety spectacles or goggles
- long PVC, surgical latex, or purpose manufactured gloves

Personal Protective Equipment should be removed following completion of procedures and appropriately cleaned or disposed of.

## **Spill management**

Strategically, small spills that occur on-site and during transportation should be managed by the health care establishment. Procedures must specify under what conditions emergency services should become involved. Spill containment should be the principle role of health personnel in gross spill management, pending the attendance of the emergency spill management team.

Procedures should be established for small spills. The management should ensure that safe work practices are developed, understood, implemented and maintained by all personnel who handle cytotoxic drugs and who may be involved in spill management. Training in spill containment and decontamination procedures should be provided to personnel likely to be involved in spill management including:

- pharmacy personnel
- store personnel
- nursing and medical personnel
- cleaners
- waste collectors

Spill kits should be located so that they are readily available for immediate use at all sites where cytotoxic drugs and waste are handled, stored and transported.

Standard operating procedures for spill management should specify:

- the trained personnel approved for spill management
- spill strategies for specific location, e.g. wards, or in transit
- procedures for using decontamination solutions
- where and how to obtain decontamination solutions
- who is responsible for providing and maintaining spill management supplies
- the personnel protective equipment to be used

## **Waste management**

Cytotoxic waste includes any residual drug following patient treatment and the material associated with the preparation or administration of cytotoxic drugs such as sharps, syringes, IV infusion sets and containers, ampoules, vials and disposable gowns, caps and gloves and swabs

and materials used to clean and contain spills. All cytotoxic waste need proper identification, segregation and containment. An easily identifiable symbol that denotes cytotoxic materials can be used. Containers and plastic bags to contain cytotoxic waste should be:

- of any selected colour, e.g. purple
- marked "CYTOTOXIC WASTE"
- placed in a rigid-walled container for transport to a designated storage area

All sharps should be:

- placed in a rigid-walled containers
- labelled "CYTOTOXIC SHARPS"
- disposed of according to recommended procedures

## **Personnel management**

Little is known about the long term effects of occupational exposure to low level doses of cytotoxic drugs. Therefore the primary focus of safety during use of cytotoxic drugs must be on the control of the working environment and safe work practices.

However, there are variables that need to be considered in determining occupational hazards of cytotoxic drugs to an individual:

- chemical properties of the drugs
- the susceptibility of the individuals to the drug's toxic effects
- cofactors such as dietary habits, smoking and natural or manmade environment contamination
- type of exposure, e.g. skin contact, inhalation, ingestion

It is important that the health status of employees is monitored. There is currently no biological health assessment technique that is sufficiently specific to adequately predict the effects of exposure to cytotoxic drugs. Employers should investigate and use the most appropriate and recent method of health surveillance available and ensure that baseline data are collected. Records should be maintained of all health assessment and biological monitoring results related to occupational cytotoxic drug exposure. One purpose of these records is to facilitate retrospective studies to assess risk of exposure to employees.

Where any form of health surveillance is undertaken, confidentiality should be ensured. Requirements such as employee consent, record

retention and security should be achieved and maintained. Employees should receive duplicates of health surveillance test as soon as available. Employees who are pregnant, breast-feeding or planning parenthood and involved in the preparation or administration of cytotoxic drugs should be informed of the risks of reproductive effects and possible effects on foetal development. Personnel required to perform these may elect to not to do so. In such cases appropriate and suitable alternative duties must be provided.

Employees should report any effects of, or exposure to cytotoxic drugs related to handling of the drugs or contaminated waste. The report should be made to the supervisor through the normal workplace incident reporting procedures. Any near miss incident or accident involving the handling of either cytotoxic drugs or waste, should be investigated to determine the cause. Appropriate action to prevent a recurrence should be determined and taken. A listing of personnel approved to undertake cytotoxic drug preparation and administration should be maintained.

The management is responsible for maintaining, in perpetuity (e.g. 25 years minimum), the following records for employees handling cytotoxic drugs:

- accreditation or training status and type and extent of training period

- record of time spent in the preparation and administration of cytotoxic drugs
- activity logs including name of the drug and activity undertaken)
- protective equipment used (e.g. cytotoxic drug safety cabinet, Personal Protective Equipment)
- unusual equipment (e.g. for managing spills).

In view of the long latency for some toxic effects, each employee should receive, on termination of employment, a statement indicating the cytotoxic drugs used and results of any biological monitoring carried out.

## CONCLUSION

Although there are many reports and studies that have been carried out to show the relationship between cytotoxic exposure and risk to health, it is still difficult to confirm it. This is perhaps due to the small sample size, difficulty in quantifying exposure or protection used and latency period between exposure and health effects. Despite these limitations, there is enough information to warrant prudent action when handling cytotoxic drugs. Therefore, the safe handling of cytotoxic drugs is an issue that must be addressed in health care settings.

**See next page for the CPE questions**



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## Continuing Pharmacy Education questions:

Study the questions below and send your answers (only one of A, B, C and D is correct) to the MPS-CPE Secretariat at the Malaysian Pharmaceutical Society, P.O. Box 158, Jalan Sultan, 46710 Petaling Jaya, Selangor. You may earn up to 2 CPE points.

1. **The most common routes of occupational hazard from handling cytotoxic drugs are**
  - A. accidental injection, gastric absorption
  - B. direct contact, gastric absorption
  - C. inhalation, direct contact
  - D. mucosal absorption, inhalation
  
2. **Potential effects of exposure to cytotoxic drugs in health care personnel are**
  - A. contact dermatitis and cardiotoxicity
  - B. foetal loss or malformation in pregnant women
  - C. liver damage and phlebitis
  - D. extravasation at the injection site
  
3. **The greatest risk of occupational exposure of cytotoxic drugs is during**
  - A. preparation and transportation
  - B. administration and disposal
  - C. preparation and administration
  - D. transportation and disposal
  
4. **The advantage of having a dedicated area for storage of cytotoxic drugs in pharmacy departments is to**
  - A. facilitate searching of stock
  - B. facilitate quick and efficient containment and management of spill
  - C. provide proper stock management
  - D. provide better control and monitoring of cytotoxic drugs usage
  
5. **Standard operating procedures for preparation of cytotoxic drugs should include those below, EXCEPT**
  - A. documentation and record
  - B. reconstitution procedures
  - C. maintenance and certification of equipment
  - D. potential hazard of cytotoxic drugs
  
6. **The following are the variables that can be considered in determining occupational hazards of cytotoxic drugs to health personnel, EXCEPT**
  - A. chemical properties of the drugs
  - B. toxic effects of the cytotoxic drugs
  - C. type of exposure
  - D. cofactors such as dietary habit