



OCCUPATIONAL DERMAL EXPOSURE TO ANTINEOPLASTIC DRUGS THROUGHOUT THE HOSPITAL MEDICATION SYSTEM AT CANADIAN HOSPITAL PHARMARCIES

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1. Introduction

Antineoplastic drugs are used for treating individuals with cancer. Despite the implementation of control measures, numerous studies have found antineoplastic drug contamination of surfaces in healthcare facilities. Such widespread surface contamination makes the potential for skin contact highly probable. This is noteworthy because dermal absorption is considered the main route of exposure. Occupational exposure to these drug products is known to cause a variety of health effects including genetic damage, adverse reproductive outcomes and cancer (NIOSH, 2004).

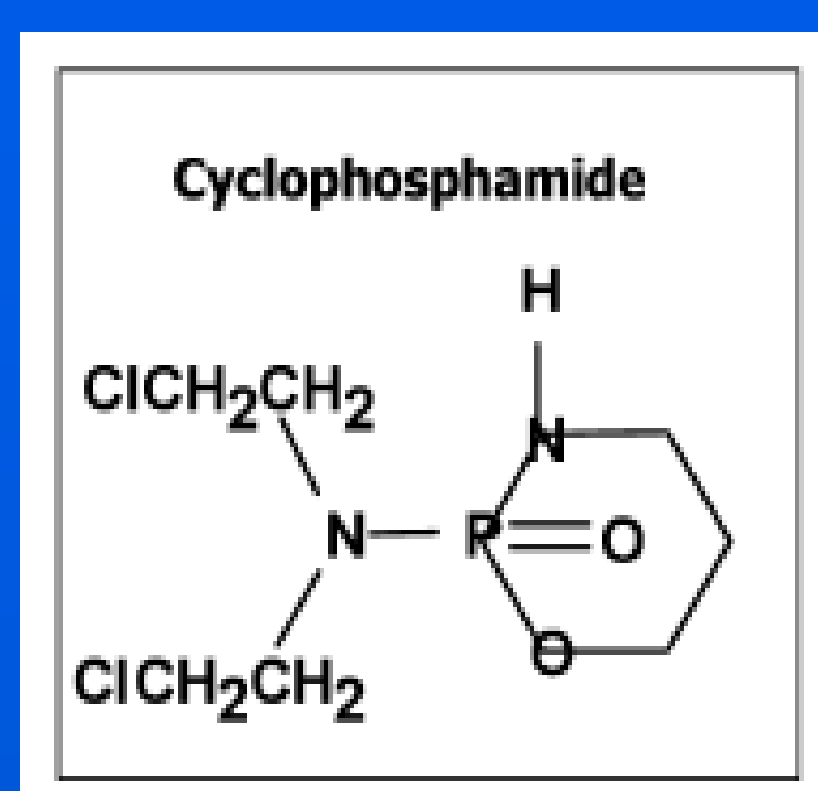
In an earlier study, we demonstrated that drug contamination was found on surfaces located throughout the hospital medication system – the process flow of drugs within a facility from cradle-to-grave (Hon et al., 2011). As such, healthcare workers involved in some capacity with the hospital medication system, such as porters, receivers, and unit clerks, may contact contaminated surfaces and are therefore at potential risk of exposure.

Based on our review of the literature, no single study has simultaneously examined the dermal contamination levels of multiple job categories that are potentially exposed due to their role in the hospital medication system.

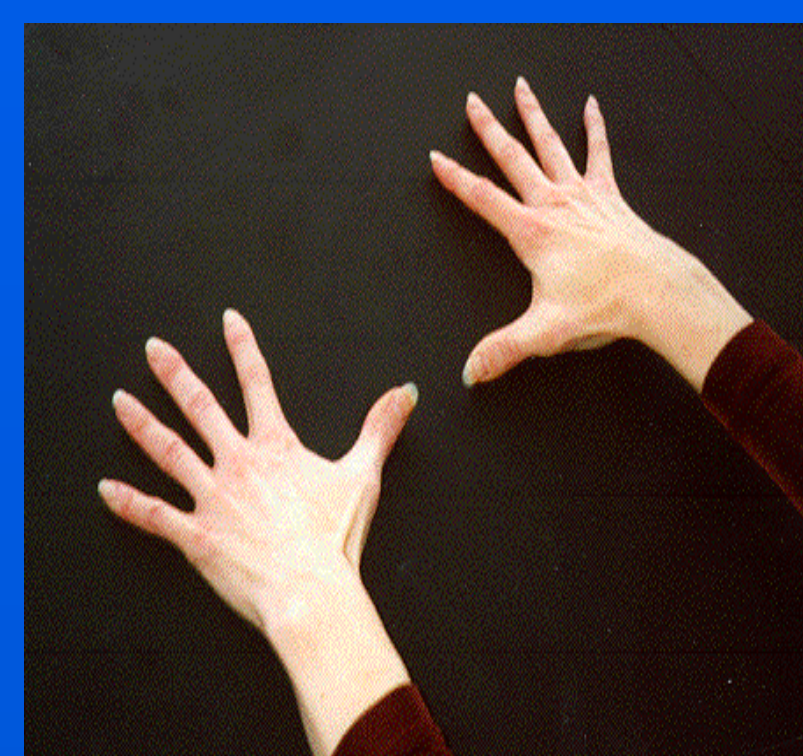
2. Objectives

The main objectives of this study were:

- 1) Quantify the cyclophosphamide contamination levels on the hands of healthcare workers identified as being part of the hospital medication system, and
- 2) Identify factors that are associated with dermal contamination.



Courtesy of Turci et al. (2003)



Cyclophosphamide was used as the marker drug in the study as it is frequently administered at the participating sites and it is a known human carcinogen (Class I IARC).

3. Methodology

Selection of participants

Potential participants were recruited from five acute care hospitals and one cancer treatment facility. Up to three representatives from each of the following job categories were recruited to participate: pharmacy technician, pharmacy receiver, pharmacist, nurse, volunteer, unit clerk, oncologist, ward aide, dietician, porter and shipper/receiver. These job categories were chosen because they were considered at risk of contacting drug contaminated surfaces (Hon et al., 2011).

Hand wipe samples

Ethics approval was obtained prior to collecting hand wipe samples from workers. The front and back of both of the participants' hands were wiped using a Kimwipe™ that had been moistened with 0.1 M ammonium acetate solution. Duplicate dermal wipe samples were collected from most participants with at least three weeks' lag between collection times.

Wipe sample preparation and analysis

Wipes were analyzed for cyclophosphamide by high-performance liquid chromatography-tandem mass spectrometry using a C18 column. The mobile phase consisted of a gradient of 5 mM ammonium acetate: 100% methanol (A:B). The limit of detection was 0.356 nanograms per wipe.

Supplemental data collection

After a hand wipe was collected, participants were surveyed regarding the type and frequency of contact with cyclophosphamide during the work shift, the number of gloves worn immediately prior to sample collection, and hand hygiene practices immediately before sample collection as well as during the work shift. Participants were also asked to complete a questionnaire related to their knowledge, attitudes, training and usual protective measures with respect to antineoplastic drugs.

Statistical analysis

Both untransformed and ln-transformed data were used to examine the distribution of dermal contamination levels. Summary statistics (arithmetic mean, geometric mean, geometric standard deviation, minimum and maximum, and proportion less than detection limit) were used to describe the samples. Bivariate analyses were performed to examine the relationship between contamination levels (ln-transformed) and each of the independent variables separately using one-way ANOVA (for categorical variables) or simple linear regression (for continuous variables). All independent variables with $p < 0.20$ from the bivariate analyses and those with a strong *a priori* hypothesis for exposure were then offered into a multiple linear regression model with the ln-transformed dermal contamination levels serving as the dependent variable. A manual backwards stepwise approach was employed to identify those variables that were significantly associated with the dependent variable. Independent variables in which one or more categories had $p < 0.05$ were retained in the final model. Statistical analyses were performed using R v 2.13.1.

4. Results and Discussion

A) Summary of cyclophosphamide dermal contamination levels (ng/wipe) of various healthcare job categories throughout the stages of the hospital medication system



Stage: Drug Delivery				
Job title	N	Mean	Max	% < LOD
Transport	8	< LOD	4.55	87.5



Stage: Drug Preparation				
Job title	N	Mean	Max	% < LOD
Pharmacist	40	< LOD	1.49	90.0
Pharmacy receiver	12	< LOD	1.27	75.0
Pharmacy technician	45	< LOD	9.29	82.2



Stage: Transport to ward				
Job title	N	Mean	Max	% < LOD
Porter	11	0.404	4.55	90.0



Stage: Drug Administration				
Job title	N	Mean	Max	% < LOD
Unit clerk	24	< LOD	2.03	83.3
Nurse	64	0.767	22.8	73.4
Others in unit*	21	1.32	22.4	71.4

* Includes volunteers, oncologists, ward aides, dieticians

B) Coefficients, standard errors and p-values for final multiple linear regression model showing factors associated with dermal contamination (ln-transformed)

Variable	Subcategory	N	Coeff.	Std Error	p-value
Intercept			0.665	0.185	0.00
Type of hospital	Cancer treatment	44	Ref		
	Acute care	181	0.272	0.118	0.02
Job title	Pharmacist	40	Ref		
	Pharmacy receiver	12	0.309	0.220	0.16
	Pharmacy technician	45	0.200	0.147	0.17
	Porter	11	0.583	0.236	0.01
	Nurse	64	0.284	0.137	0.04
	Transport	8	0.874	0.286	0.00
	Unit clerk	24	0.294	0.177	0.10
	Others in drug admin unit	21	0.625	0.194	0.00
Sex	Female	180	Ref		
	Male	45	-0.307	0.128	0.02
Duty to handle antineoplastic drugs?	No	47	Ref		
	Yes	178	0.393	0.142	0.01

We also found detectable levels of cyclophosphamide on the hands of workers even though they were wearing gloves prior to sample collection suggesting that the drugs may permeate through or the participant may have self-contaminated. Glove usage and hand washing practices amongst healthcare workers appears to vary from person-to-person. None of the cleaning agents used for hand washing appeared to be more effective than any other in removing drug residual.

5. Conclusions

This study confirms our hypothesis that, since antineoplastic drug contamination is present on surfaces throughout the hospital medication system, numerous job categories are at risk of exposure. Our results found that additional healthcare job categories, besides pharmacy personnel and nurses, had detectable levels of cyclophosphamide on their hands. Factors associated with dermal contamination were the type of hospital, job title, sex of worker, and whether the worker has a duty to handle antineoplastic drugs.

6. References

- NIOSH (2004) Alert – Preventing Occupational Exposure to Antineoplastic Drugs and Other Hazardous Drugs in Health Care Settings DDHS (NIOSH) Publication #2004-165..
- Hon et al. (2011) Safety and Health at Work 2:273-281.
- Turci et al. (2003) Journal of Chromatography B 789: 169-209.

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