

Cross-Sectional Evaluation of Surface Contamination with Antineoplastic Drugs in Canadian Health Care Centres

Delphine Hilliquin, Cynthia Tanguay, Sébastien Gagné, Nicolas J Caron, and Jean-François Bussiès

ABSTRACT

Background: Surfaces in health care centres are often contaminated with traces of antineoplastic drugs. Such contamination should be limited as much as possible, to reduce workers' exposure.

Objectives: The primary objective was to monitor environmental contamination with 9 antineoplastic drugs in oncology pharmacy and patient care areas of Canadian health care centres. The secondary objective was to explore the use of sodium hypochlorite as a cleaning agent for cyclophosphamide contamination.

Methods: This cross-sectional evaluation was conducted from January to April 2018. Twelve standardized sites were sampled at each participating centre: 6 in the oncology pharmacy and 6 in patient care areas. Six of the antineoplastic drugs (cyclophosphamide, ifosfamide, methotrexate, gemcitabine, 5-fluorouracil, and irinotecan) were quantified by ultra-performance liquid chromatography – tandem mass spectrometry. For the other 3 antineoplastic drugs (docetaxel, paclitaxel, and vinorelbine), samples were screened for contamination but not quantified. The effect of using sodium hypochlorite as a cleaning agent was evaluated with a Kolmogorov-Smirnov test for independent samples.

Results: Of 202 Canadian centres invited, 79 participated. A total of 887 surface samples were analyzed, 467 from pharmacy areas and 420 from patient care areas. Cyclophosphamide was the drug most often found as a contaminant (32.2% [286/887] of samples positive, 75th percentile of measured contamination 0.0017 ng/cm², 90th percentile 0.021 ng/cm²). The front grille inside the hood (80.8% [63/78] of samples positive for at least one antineoplastic drug), treatment chair armrest (78.9% [60/76]), storage shelf in pharmacy (61.5% [48/78]), and floor in front of the hood (60.3% [47/78]) were the most frequently contaminated surfaces. Cleaning with a sodium hypochlorite solution was highly variable. Among centres that reported using sodium hypochlorite to clean armrests on patient chairs, the concentration of cyclophosphamide was lower (0.00866 versus 0.0300 ng/cm², $p = 0.014$).

Conclusions: Despite growing awareness and implementation of new safe-handling guidelines, surfaces in health care centres were contaminated with traces of many antineoplastic drugs. Providing centres with attainable goals (e.g., 75th to 90th percentile relative to other similar centres) would help in identifying the sampling sites where improvements are needed and in achieving lower surface contamination.

RÉSUMÉ

Contexte : Les surfaces dans les centres de santé sont souvent contaminées par des traces de médicaments antinéoplasiques. Une telle contamination devrait être limitée autant que faire se peut afin de réduire l'exposition des employés à ces produits.

Objectifs : L'objectif principal consistait à mesurer la contamination environnementale provenant de neuf médicaments antinéoplasiques dans la section de la pharmacie oncologique et celle des soins offerts aux patients dans des centres de soins de santé canadiens. L'objectif secondaire consistait à explorer l'action nettoyante de l'hypochlorite de sodium pour éliminer la contamination par la cyclophosphamide.

Méthodes : Cette évaluation transversale a été menée de janvier à avril 2018. Des échantillons ont été prélevés dans douze endroits standardisés de chaque centre participant : six dans la section de la pharmacie oncologique et six dans celle des soins donnés aux patients. La présence de six des médicaments antinéoplasiques examinés (cyclophosphamide, ifosfamide, méthotrexate, gemcitabine, 5-fluorouracil et irinotécan) a été quantifiée par chromatographie liquide à haute performance (HPLC) avec spectrométrie de masse en tandem. Quant aux trois autres échantillons de médicaments antinéoplasiques (docetaxel, paclitaxel et vinorelbine), ils ont été analysés pour rechercher la présence d'une contamination qui n'a pas été quantifiée. L'action nettoyante de l'hypochlorite de sodium a été évaluée à l'aide d'un test de Kolmogorov-Smirnov pour les échantillons indépendants.

Résultats : Sur 202 centres canadiens invités à participer à l'étude, 79 ont répondu à l'invitation. L'analyse a porté sur 887 échantillons de surfaces des lieux sélectionnés : 467 dans la section de la pharmacie et 420 dans la section des soins donnés aux patients. La cyclophosphamide était le médicament contaminant le plus souvent décelé (32,2 % d'échantillons positifs [286/887], 75^e percentile de contamination mesurée 0,0017 ng/cm², 90^e percentile 0,021 ng/cm²). La grille frontale à l'intérieur de la hotte de laboratoire (80,8 % des échantillons [63/78] étaient positifs pour au moins un médicament antinéoplasique), l'accoudoir de la chaise du patient (78,9 % [60/76]), l'étagère de stockage dans la pharmacie (61,5 % [48/78]) et le sol en face de la hotte (60,3% [47/78]) étaient les surfaces le plus souvent contaminées. L'usage d'une solution d'hypochlorite de sodium pour le nettoyage variait grandement d'un centre à l'autre. Dans les centres qui indiquaient utiliser cet agent

Keywords: environmental monitoring, surface contamination, antineoplastic drugs, cyclophosphamide, health care centres, pharmacy

pour nettoyer les accoudoirs des chaises du patient, la concentration de cyclophosphamide sur les accoudoirs était moins élevée (0,00866 contre 0,0300 ng/cm², $p = 0,014$).

Conclusions : Malgré la prise de conscience et la mise en place croissantes de nouvelles lignes directrices en matière de manipulation sécuritaire, les surfaces de certains endroits des centres de santé sont contaminées par des traces de nombreux médicaments antinéoplasiques. La fixation d'objectifs atteignables pour les centres (p. ex., entre le 75^e et le 90^e percentile par rapport aux autres centres similaires) aide à déterminer les sites d'échantillonnage où des améliorations sont nécessaires et à diminuer la contamination des surfaces.

Mots-clés : contrôle environnemental, contamination des surfaces, médicament antinéoplasique, cyclophosphamide, centres de santé, pharmacie

Can J Hosp Pharm. 2019;72(5):377-84

INTRODUCTION

Surfaces in health care centres are often contaminated with traces of antineoplastic drugs, notably cyclophosphamide, gemcitabine, and 5-fluorouracil.^{1,2} Surfaces in centres that handle larger quantities of antineoplastic drugs are generally more contaminated.² All types of surfaces have been documented as being potentially contaminated, from hood surfaces and drug administration areas to pencils and telephones.^{1,2} The causes of this contamination are varied, with inadequate drug handling and spills being the more obvious sources. Other important sources of contamination are health care workers themselves, who inadvertently carry traces of antineoplastic drugs on their hands or gloves.³ Patients treated with these drugs are also an important source of contamination, notably because of contaminated excreta. Over time, working practices have improved worldwide, and many authors have documented a substantial reduction in surface contamination.^{2,4,5} Despite these improvements, trace contamination continues to occur, and few centres are able to avoid all contamination.

Effective and frequent surface cleaning is of the utmost importance to reduce the risk of exposure to these drugs. However, no single cleaning agent can completely remove all antineoplastic drugs from a surface.⁶⁻⁸ Furthermore, no health-based exposure limit has been determined for antineoplastic drugs. Thus, centres strive to reduce as much as possible workers' potential exposure. Performing regular environmental monitoring is recommended by many Canadian organizations.⁹⁻¹¹ To help in compliance with this recommendation, many groups have proposed thresholds based on environmental monitoring data for a particular region or country.^{2,12,13} Comparison of a health care centre's data with these reference values can help the centres to target apparently problematic surfaces.

The primary objective of this study was to monitor environmental contamination by 9 antineoplastic drugs in oncology pharmacy and patient care areas of Canadian health care

centres. The secondary objective was to explore the use of sodium hypochlorite as a cleaning agent for cyclophosphamide contamination.

METHODS

Participating Centres

This cross-sectional evaluation involved a voluntary sample of centres from across Canada. Directors of pharmacy departments in Canadian centres with at least 50 acute care beds were contacted by e-mail on December 8, 2017, with an invitation to participate in a study of surface contamination with antineoplastic drugs (total of 202 directors from the following 11 provinces and territories, listed in alphabetical order: 12 in Alberta, 23 in British Columbia, 13 in Manitoba, 8 in New Brunswick, 2 in Newfoundland and Labrador, 3 in Northwest Territories, 9 in Nova Scotia, 62 in Ontario, 2 in Prince Edward Island, 62 in Quebec, and 6 in Saskatchewan). One reminder was sent by e-mail.

Participating centres applied their local policies and procedures for compounding, administration, surface cleaning, waste management, and any other aspects of drug handling. The pharmacy directors provided data describing their practices for the period April 2017 to March 2018.

Sampling and Analysis

At each centre, surface sampling was conducted on a single day between January and April 2018. Each centre paid for analysis of its samples.

Twelve standardized sampling sites were used: 6 in oncology pharmacy areas and 6 in patient care areas. Any samples from sites that did not match the prespecified sites were excluded from analysis. The 12 sites were selected to represent potential exposure of workers from these areas and to allow comparison with previous studies conducted annually since 2010.² For health care centres located close to the authors' institution, samples were collected by

a single research assistant (D.H.). For centres at locations remote from the authors' institution, samples were collected by an employee at each participating centre. To reduce variability, these employees were trained using a video, descriptions, and photographs of the standardized sampling sites and procedures. Sampling technique and analytical procedures were the same as those previously reported.² Sites were sampled at the end of a workday or in the morning, before surfaces were cleaned.

The following 6 antineoplastic drugs were quantified: cyclophosphamide, ifosfamide, methotrexate, gemcitabine, 5-fluorouracil, and irinotecan. Samples were also screened for the following 3 antineoplastic drugs, but these drugs were not quantified: docetaxel, paclitaxel, and vinorelbine. These 9 drugs were chosen for our study because they are among the most frequently used in Quebec and because a cost-effective analytical method existed. Quantification and detection of antineoplastic drugs in sampling extracts were performed by ultra-performance liquid chromatography – tandem mass spectrometry (Acquity UPLC chromatographic system coupled with Xevo TQ-S tandem mass spectrometer; Waters Corporation, Milford, Massachusetts). Chromatography was carried out on a C18 Acquity UPLC HSS T3 column (2.1 × 100 mm, 1.8 µm; Waters Corporation). All tests were performed at the Institut national de santé publique du Québec, with the same equipment. The limits of detection and quantification are presented in Table 1. The limit of detection was used as the reporting limit.

Data Analysis

The proportion of positive samples was calculated. A sample was considered positive for a particular drug if the value was above the limit of detection and if the quantifier peak was within the maximum tolerance of the mean calibrator for confirmatory criteria (signal/noise ratio > 3, retention time ±0.02 min, quantifier/qualifier ion ratio ±20%). Descriptive statistical analyses (which generated percentiles) were carried out with SPSS software (IBM Statistics for Windows version 20.0, IBM Corporation, Armonk, New York). For the purpose of calculations, values that fell between the limit of detection and the limit of quantification were assigned a value corresponding to the limit of quantification divided by 2,¹⁴ and values that fell below the limit of detection were assigned a value corresponding to the limit of detection divided by 2.¹⁵

Subanalyses were performed to explore the effect on cyclophosphamide concentration of cleaning with a sodium hypochlorite solution. The following practices were also evaluated: antineoplastic drug usage, removal of outer packaging, cleaning of vials after receipt, use of closed-system drug transfer devices, and priming of antineoplastic IV tubing in the pharmacy. Results were compared with a Kolmogorov-Smirnov test for independent samples. A *p* value less than 0.05 was considered statistically significant.

Table 1. Limits of Detection and Quantification

Antineoplastic Drug	Limit of Detection (ng/cm ²)	Limit of Quantification (ng/cm ²)
Cyclophosphamide	0.0010	0.0033
Docetaxel	0.30	0.30
5-Fluorouracil	0.0400	0.1400
Gemcitabine	0.001	0.001
Ifosfamide	0.004	0.0055
Irinotecan	0.0030	0.006
Methotrexate	0.0020	0.0060
Paclitaxel	0.04	0.1200
Vinorelbine	0.01	0.0120

Communication of Results

After completion of the study, each participating centre was given access to a secure website from which they could retrieve their 2018 results, as well as historical results, if they had participated in sampling in previous years. Sites with values higher than the global Canadian 75th and 90th percentiles were highlighted with a colour code (orange for values between the 75th and 90th percentiles and red for values above the 90th percentile), so that centres could target their corrective measures to surfaces with the most contamination (Figure 1).

RESULTS

Overall, 79 centres from 4 provinces were recruited in 2018 (Table 2). A total of 15 centres had participated in all 8 studies since 2010, and all of these used more than 250 g of cyclophosphamide annually.

In the current study, samples from a total of 887 surfaces were analyzed: 467 in pharmacy areas and 420 in patient care areas. An additional 61 samples were excluded from the analysis because the sampling locations did not match the standardized sampling sites or sampling was not completed. The 3 drugs used in the largest quantities (cyclophosphamide, gemcitabine, and 5-fluorouracil) were also the ones most often detected on surfaces (Table 3).

The proportion of samples with a positive result for at least 1 antineoplastic drug was similar in pharmacy areas (46.9%) and patient care areas (42.4%) (Table 4). The front grille inside the hood (80.8% [63/78]), armrest of patient treatment chair (78.9% [60/76]), storage shelf in pharmacy (61.5% [48/78]), and floor in front of the hood (60.3% [47/78]) were the most frequently contaminated sites, and the contaminating drugs were found at higher concentrations (Table 4).

Cleaning with a sodium hypochlorite solution was highly variable among participating centres. Few centres used this cleaning solution on the armrests of patient treatment chairs (16.0% [12/75]), whereas it was more commonly used on the floor in front of the hood (39.5% [30/76]) and on the front grille of the hood (79.7% [63/79]). The concentration of sodium

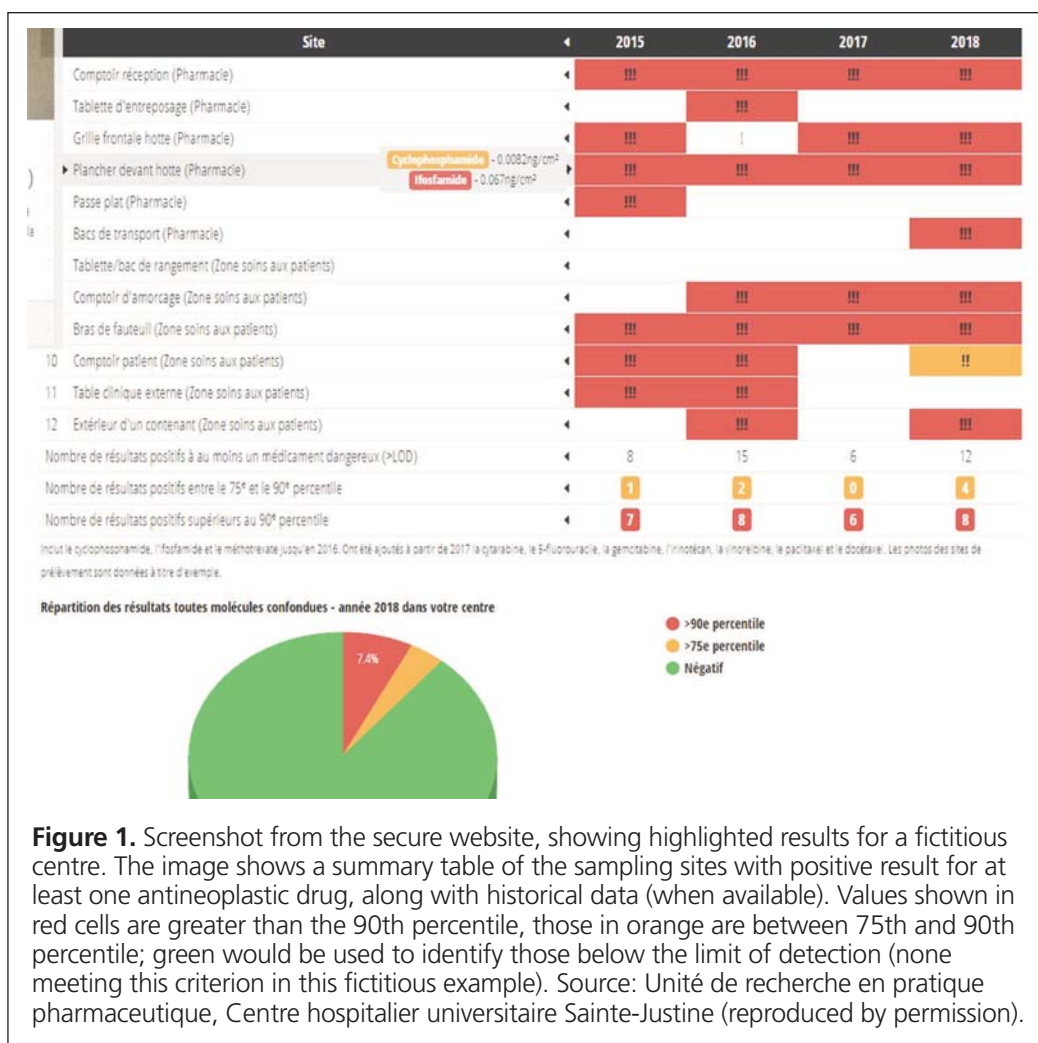


Figure 1. Screenshot from the secure website, showing highlighted results for a fictitious centre. The image shows a summary table of the sampling sites with positive result for at least one antineoplastic drug, along with historical data (when available). Values shown in red cells are greater than the 90th percentile, those in orange are between 75th and 90th percentile; green would be used to identify those below the limit of detection (none meeting this criterion in this fictitious example). Source: Unité de recherche en pratique pharmaceutique, Centre hospitalier universitaire Sainte-Justine (reproduced by permission).

hypochlorite varied between 0.6% and 10%, with concentrations in the range of 2% to 2.4% being the most common (e.g., for front grille of the hood, this concentration was used by 87.5% [49] of the 56 centres reporting these data). The frequency of cleaning with sodium hypochlorite was also highly variable, from many times a day to once a year. For example, monthly cleaning of the front grille of the hood with sodium hypochlorite was reported by 36 (57.1%) of 63 centres. Centres that reported cleaning a particular surface with a sodium hypochlorite solution tended to have lower cyclophosphamide concentrations on that surface than did centres not performing such cleaning, although the difference was significant only for the armrest of patient treatment chairs (Table 5).

The centres with the greatest use of cyclophosphamide had the highest level of contamination: those that reported using 250 g or more of this drug per year had higher concentrations of cyclophosphamide than those that reported using less than 250 g (75th percentile 0.0060 ng/cm² versus less than limit of detection; $p < 0.001$). Centres that used a closed-system drug transfer device for at least 90% of drug preparations did not have lower contam-

ination (75th percentile of cyclophosphamide 0.0017 ng/cm² versus 0.0029 ng/cm², $p = 0.20$), nor did the centres that primed at least 90% of their lines in the pharmacy (0.0017 versus 0.0037, $p > 0.99$). Centres that removed the outer packaging and those that cleaned vials upon receipt tended to have lower surface contamination, but this difference was significant only for cleaning vials upon receipt (0.0017 versus 0.0084, $p = 0.026$).

DISCUSSION

In this study, nearly half of surfaces sampled in 79 Canadian centres were contaminated with 1 of the 9 antineoplastic drugs analyzed, and one-third were contaminated with cyclophosphamide. Contamination was mostly found on front grilles inside hoods, armrests of patient treatment chairs, storage shelves, and floors in front of the hoods. The 75th percentile of cyclophosphamide concentration was 0.0017 ng/cm², and the 90th percentile was 0.021 ng/cm². There was high variability in methods among centres that used sodium hypochlorite cleaning solutions for decontamination.

Table 2. Characteristics of Participating Centres

Characteristic	No. (%) of Centres (n = 79)	
Province		
Quebec	64	(81.0)
Ontario	9	(11.4)
New Brunswick	5	(6.3)
Manitoba	1	(1.3)
Participation in previous multicentre surveillance studies by same research team		
0–7 studies	64	(81.0)
8 studies	15	(19.0)
Size of oncology clinic		
<i>No. of inpatient beds</i>		
< 15	57	(72.2)
≥ 15	21	(26.6)
Data missing	1	(1.3)
<i>No. of outpatient stretchers, chairs, beds</i>		
< 15	48	(60.8)
≥ 15	30	(38.0)
Data missing	1	(1.3)
Antineoplastic preparations/year		
< 4000	32	(40.5)
≥ 4000	40	(50.6)
Data missing	7	(8.9)
Cyclophosphamide used/year (g)		
< 250	38	(48.1)
≥ 250	40	(50.6)
Data missing	1	(1.3)
Removal of outer packaging upon receipt		
Yes	68	(86.1)
No	11	(13.9)
Cleaning of vials after receipt		
Yes	64	(81.0)
No	15	(19.0)
Use of closed-system drug transfer device*		
Yes	26	(32.9)
For ≥ 90% of preparations	17	NA
For < 90% of preparations	9	NA
No	53	(67.1)
Priming of antineoplastic IV tubing		
In pharmacy (for ≥ 90% of preparations)	59	(74.7)
In health care unit (for ≥ 90% of preparations)	18	(22.8)
Other†	2	(2.5)

NA = not applicable (proportion not calculated for this subgroup).

*The following devices were used: ChemoClave System (ICU Medical Inc, San Clemente, California), *n* = 18; Phaseal (Becton, Dickinson and Company, Franklin Lakes, New Jersey), *n* = 4; Equashield (EquaShield Medical, Port Washington, New York), *n* = 2; Tevadaptor (Teva Medical, Petha Tikva, Israel), *n* = 1; and Texium (BD, Franklin Lakes, New Jersey), *n* = 1.

†For 2 centres, neither the pharmacy nor the health care unit performed ≥ 90% of priming.

Environmental Contamination in Canadian Hospitals

These results were similar to those obtained in 2017: the proportion of contaminated samples remained constant, and the same sites were the most frequently contaminated.² The 75th percentile of cyclophosphamide concentration declined, from

0.0040 to 0.0017 ng/cm², which confirms previous observations that practices improve over the years.^{2,4,5} Although Dugheri and others⁵ observed a reduction over time in the proportion of positive samples (from 11.7% in 2010 to 1% in 2017), the reduction that we observed was not as marked, for instance, from 52% of samples positive for cyclophosphamide in 2008–2010¹⁶ to 32% in the current study. This difference may be partly explained by differences in sampling sites, study methods, and handling practices.

Effect of Cleaning

Considering the importance of surface cleaning in the elimination of persistent traces of antineoplastic drugs, we explored the effect of cleaning with a sodium hypochlorite solution. This cleaning solution was chosen for investigation because it has previously been shown as the most effective cleaning agent for a variety of antineoplastic drugs.^{6,7} We hypothesized that surfaces with more thorough routine cleaning might have lower residual contamination, leading to less contamination at the end of the workday. However, the aim of the current study was not to test cleaning efficacy, especially given that surfaces were sampled after a workday, before cleaning. Even surfaces that have been cleaned may be contaminated with antineoplastic drugs immediately after cleaning.⁸ The cleaning practices of centres that did not use sodium hypochlorite were not investigated.

There was tremendous variability in cleaning practices with sodium hypochlorite. Some centres used this solution for daily cleaning, but it was mostly used on a weekly or monthly basis, to perform more thorough cleaning. Indeed, the *Ordre des pharmaciens du Québec* recommends monthly deactivation of the hood with sodium hypochlorite followed by thiosulfate, in addition to daily cleaning with water and detergent and disinfection with alcohol.¹¹ The armrests of patient treatment chairs were seldom cleaned with sodium hypochlorite, perhaps because a disinfecting product is often prioritized for use when oncology patient care areas are cleaned.⁸ Centres that did use sodium hypochlorite to clean treatment chair armrests had significantly lower contamination. This promising result will need to be confirmed by further studies. The concentration of sodium hypochlorite used for cleaning was also variable. Preliminary results have suggested that less concentrated solutions are equivalent in effectiveness, and using more dilute solutions would help to alleviate the disadvantages of sodium hypochlorite, notably its corrosive action on some surfaces and the unpleasant odour for workers and patients.¹⁷

The other working practices that were evaluated led to results similar to those reported previously.² The centres that used more antineoplastic drugs had greater levels of surface contamination, but the other practices were not associated with significantly lower concentrations of cyclophosphamide. Conflicting results were obtained for centres that removed the outer packaging and those that cleaned the vials upon receipt, given that the difference was

Table 3. Surface Contamination and Reported Annual Use of Antineoplastic Drugs

Antineoplastic Drug	No. (%) of Positive Samples (n = 887)	Contamination (ng/cm ²)*			Reported Use (g/year)†	
		75th percentile	90th percentile	Max	Median	Max
Cyclophosphamide	286 (32.2)	0.0017	0.021	2.4	251	1 900
Gemcitabine	167 (18.8)	<0.001	0.0043	8.5	302	3 210
5-Fluorouracil	74 (8.3)	<0.0400	<0.0400	210	1756	10 660
Ifosfamide	47 (5.3)	<0.004	<0.004	3.0	12	2 800
Methotrexate	37 (4.2)	<0.0020	<0.0020	2.6	4.35	5 997
Irinotecan	19 (2.1)	<0.0030	<0.0030	0.33	47.75	1 560
Paclitaxel	5 (0.6)	NA	NA	NA	40.35	604
Vinorelbine	1 (0.1)	NA	NA	NA	3	280
Docetaxel	0 (0)	NA	NA	NA	10	390

Max = maximum, NA = not applicable (drug not quantified).

*For all drugs, the minimum level of contamination was below the limit of detection.

†Based on data for 78 centres.

Table 4. Contamination by Sampling Site

Sampling Site	No. (%) Positive for ≥ 1 Antineoplastic Drug	No. (%) Positive for Cyclophosphamide	Cyclophosphamide Concentration (ng/cm ²)		
			75th percentile	90th percentile	Maximum
Pharmacy areas					
Front grille of hood (n = 78)	63 (80.8)	50 (64.1)	0.022	0.19	1.3
Floor in front of hood (n = 78)	47 (60.3)	43 (55.1)	0.015	0.11	0.78
Storage shelf (n = 78)	48 (61.5)	36 (46.2)	0.0042	0.015	0.082
Trays used for drug delivery (n = 78)	24 (30.8)	8 (10.3)	<0.0010	0.0017	0.026
Service hatch or counter for post-preparation validation (n = 78)	22 (28.2)	11 (14.1)	<0.0010	0.019	0.039
Shipment reception counter (n = 77)	15 (19.5)	6 (7.8)	<0.0010	<0.0010	0.07
Subtotal (n = 467)	219 (46.9)	154 (33.0)	0.0034	0.020	1.3
Patient care areas					
Armrest on patient treatment chair (n = 76)	60 (78.9)	56 (73.7)	0.030	0.098	1.1
Exterior surface of antineoplastic drug container (n = 68)	29 (42.6)	17 (25.0)	0.0014	0.032	2.4
Counter used for priming or validation (n = 75)	24 (32.0)	17 (22.7)	<0.0010	0.0017	0.0091
Counter in patient room (n = 58)	25 (43.1)	19 (32.8)	0.0017	0.018	0.068
Counter in outpatient clinic (n = 71)	20 (28.2)	14 (19.7)	<0.0010	0.0017	0.055
Storage shelf (n = 72)	20 (27.8)	9 (12.5)	<0.0010	0.0017	0.79
Subtotal (n = 420)	178 (42.4)	132 (31.4)	0.0017	0.022	2.4
Total (pharmacy and patient care areas) (n = 887)	397 (44.8)	286 (32.2)	0.0017	0.021	2.4

significant only for the latter. The low concentrations measured on surfaces and the descriptive approach of this study limit the generalizability of these findings.

Contaminated Surfaces to Be Targeted for Action

Centres that participated in our study could access their own results through a study-specific website and could easily identify the surfaces with the greatest contamination, through colour coding (see Figure 1). These are the sites that should be prioritized for corrective measures. We agree with others that this pragmatic method is helpful for centres looking to reduce surface contamin-

ation.^{12,13} Considering the improvements that we have observed over the years (since 2010), our approach is to update the target values each year. In addition, target values should be established at the regional level, taking into account differing regulations and working practices. For instance, the 90th percentiles for cyclophosphamide and gemcitabine obtained for Canada in 2018 were 0.021 and 0.0043 ng/cm², respectively, whereas Sottani and others¹² reported 90th percentiles in Italian hospitals of 3.6 and 0.9 ng/cm², respectively.

In addition to prioritizing surfaces according to threshold values, failure mode and effects analysis could be conducted to identify and score the risks of occupational exposure. Le and

Table 5. Effect of Cleaning with Sodium Hypochlorite Solution

Surface Cleaned*	Cyclophosphamide Concentration (ng/cm ²), as 75th Percentile	p Value†
Armrest on patient treatment chair‡		0.014
Cleaned with sodium hypochlorite (n = 12)	0.00866	
Not cleaned with sodium hypochlorite (n = 63)	0.0300	
Front grille of hood		0.59
Cleaned with sodium hypochlorite (n = 63)	0.0205	
Not cleaned with sodium hypochlorite (n = 16)	0.130	
Floor in front of hood‡		0.90
Cleaned with sodium hypochlorite (n = 30)	0.00833	
Not cleaned with sodium hypochlorite (n = 46)	0.015	

*Grouped results for any cleaning frequency and use of sodium hypochlorite solution with any concentration.

†Kolmogorov-Smirnov test for independent samples (2 groups).

‡Some centres did not report their cleaning practice for specific surfaces: for armrest of patient treatment chair, n = 4; for floor in front of hood, n = 3.

others¹⁸ used this approach to rank their corrective measures and succeeded in reducing their risk score over 5 years. They implemented a specific training program, posted the requirements for personal protective equipment, and reviewed cleaning practices.

Strengths and Limitations

For each participating centre, sampling occurred at the end of a single workday and might not represent the risk of exposure on all days. The results obtained from the 79 centres were comparable to those obtained in previous years, which supports the conclusion that they are representative of surface contamination in Canadian health care centres. For centres remote from the authors' location, sampling was not done by the same research assistant, which might have biased the results; however, care was taken to train staff members at these locations, in an attempt to ensure uniformity of the sampling technique. Participation was voluntary, and each centre paid for its own analyses, which might have introduced participation bias. Most of the participating centres were from Quebec, so the results are more representative of practice in that province. In a previous study, we showed that there was no significant difference between Quebec and other Canadian provinces in terms of contamination of health care centres.¹⁹ The standards of the National Association of Pharmacy Regulatory Authorities²⁰ were directly inspired by the Quebec standards¹¹; therefore, as these standards are adopted by each province, improvements may be observed in the future.

The sampling method had good limits of detection, which were comparable to other published methods.²¹ The chemical analysis was not blinded.

Not all working practices were investigated; for example, we did not inquire about the use of other cleaning agents. Although these preliminary results are interesting, they should be interpreted with caution, and the usefulness of sodium hypochlorite as a

cleaning agent must be confirmed in other studies. No methods were applied to control for type 1 error associated with conducting multiple statistical tests.

CONCLUSION

Contamination of surfaces with antineoplastic drugs persists in Canadian health care centres. Over the past few years, improvements have been observed, but trace contamination occurred each year. Attainable goals based on results from many similar centres (e.g., 75th and 90th percentiles of concentration) can help facilities to identify the specific sampling sites where attention is needed to attain the least possible contamination and reduce the risk of workers' exposure. Optimizing cleaning methods may help in achieving this objective.

References

- Hon CY, Teschke K, Chu W, Demers P, Venners S. Antineoplastic drug contamination of surfaces throughout the hospital medication system in Canadian hospitals. *J Occup Environ Hyg*. 2013;10(7):374-83.
- Chauchat L, Tanguay C, Caron NJ, Gagné S, Labrèche F, Bussièrès JF. Surface contamination with ten antineoplastic drugs in 83 Canadian centers. *J Oncol Pharm Pract*. 2019;25(5):1089-98.
- Hon CY, Teschke K, Demers PA, Venners S. Antineoplastic drug contamination on the hands of employees working throughout the hospital medication system. *Ann Occup Hyg*. 2014;58(6):761-70.
- Sottani C, Porro B, Comelli M, Imbriani M, Minoia C. An analysis to study trends in occupational exposure to antineoplastic drugs among health care workers. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2010;878(27):2593-605.
- Dugheri S, Bonari A, Pompilio I, Boccalon P, Tognoni D, Cecchi M, et al. Analytical strategies for assessing occupational exposure to antineoplastic drugs in healthcare workplaces. *Med Pr*. 2018;69(6):589-604.
- Querquau Lamerie T, Nussbaumer S, Décaudin B, Fleury-Souverain S, Goossens JF, Bonnabry P, et al. Evaluation of decontamination efficacy of cleaning solutions on stainless steel and glass surfaces contaminated by 10 antineoplastic agents. *Ann Occup Hyg*. 2013;57(4):456-69.
- Roland C, Adé A, Ouellette-Frève JF, Gagné S, Caron N, Bussièrès JF. Pilot study evaluating the efficacy of four cleaning solutions and two types of mops in delimited areas of a floor contaminated with cyclophosphamide. *Pharm Technol Hosp Pharm*. 2017;2(3):99-106.
- Viegas S, de Oliveira AC, Carolino E, Pádua M. Occupational exposure to cytotoxic drugs: the importance of surface cleaning to prevent or minimise exposure. *Arb Hig Rada Toksikol*. 2018;69(3):238-49.

9. *Prevention guide: safe handling of hazardous drugs*. Montréal (QC): Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales; 2008 [cited 2017 Dec 21]. Available from: http://www.asstas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf
10. Chapter 18: Environmental monitoring. In: *Compounding: guidelines for pharmacies*. Ottawa (ON): Canadian Society of Hospital Pharmacists; 2014.
11. *Norme 2014.02 : Préparation de produits stériles dangereux en pharmacie*. Montréal (QC): Ordre des pharmaciens du Québec; 2017 [cited 2017 Dec 21]. Available from: www.opq.org/fr-CA/publications/normes-de-pratique-et-lignes-directrices/
12. Sottani C, Grignani E, Oddone E, Dezza B, Negri S, Villani S, et al. Monitoring surface contamination by antineoplastic drugs in Italian hospitals: performance-based hygienic guidance values (HGVs) project. *Ann Work Expo Health*. 2017;61(8):994-1002.
13. Dugheri S, Bonari A, Pompilio I, Boccalon P, Mucci N, Arcangeli G. A new approach to assessing occupational exposure to antineoplastic drugs in hospital environments. *Arb Hig Rada Toksikol*. 2018;69(3):226-37.
14. Commission directive 2009/90/CE of 31 July 2009. Article 5: calculation of mean values. In: *Official Journal of the European Union*. Brussels (BE): European Union; 2009 [cited 2017 Feb 25]. Available from: <http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:201:0036:0038:EN:PDF>
15. Hornung RW, Reed LD. Estimation of average concentration in the presence of nondetectable values. *Appl Occup Environ Hyg*. 1990;5(1):46-51.
16. Bussièrès JF, Tanguay C, Touzin K, Langlois E, Lefebvre M. Environmental contamination with hazardous drugs in Quebec hospitals. *Can J Hosp Pharm*. 2012;65(6):428-35.
17. Soubieux A, Palamini M, Tanguay C, Bussièrès JF. Evaluation of decontamination strategies for cyclophosphamide. *J Oncol Pharm Pract*. 2019 Aug; 107815521986593.
18. Le LMM, Reitter D, He S, Bonle FT, Launois A, Martinez D, et al. Safety analysis of occupational exposure of healthcare workers to residual contaminations of cytotoxic drugs using FMECA security approach. *Sci Total Environ*. 2017;599-600:1939-44.
19. Poupeau C, Tanguay C, Caron NJ, Bussièrès JF. Multicenter study of environmental contamination with cyclophosphamide, ifosfamide, and methotrexate in 48 Canadian hospitals. *J Oncol Pharm Pract*. 2018;24(1): 9-17.
20. *Model standards for pharmacy compounding of hazardous sterile preparations*. Ottawa (ON): National Association of Pharmacy Regulatory Authorities; 2016 [cited 2017 Dec 21]. Available from: https://napra.ca/sites/default/files/2017-09/Mdl_Stnds_Pharmacy_Compounding_Hazardous_Sterile_Preparations_Nov2016_Revised_b.pdf
21. Marie P, Christophe C, Manon R, Marc M, Charleric B, Patrice V. Environmental monitoring by surface sampling for cytotoxics: a review. *Environ Monit Assess*. 2017;189(2):52.

Delphine Hilliquin, DPharm, is a Research Assistant with the Unité de recherche en pratique pharmaceutique, Centre hospitalier universitaire Sainte-Justine, Montréal, Québec. At the time of the study, she was also a student in the DPharm program at Université Angers in Angers, France.

Cynthia Tanguay, BSc, MSc, is Coordinator with the Unité de recherche en pratique pharmaceutique, Centre hospitalier universitaire Sainte-Justine, Montréal, Québec.

Sébastien Gagné, MSc, is a Chemist with the Centre de toxicologie du Québec, Institut national de santé publique du Québec, Québec, Québec.

Nicolas J Caron, PhD, is a Chemist with the Centre de Toxicologie du Québec, Institut national de santé publique du Québec, Québec, Québec.

Jean-François Bussièrès, BPharm, MSc, MBA, FCSHP, FOPQ, is Head of the Unité de recherche en pratique pharmaceutique, Centre hospitalier universitaire Sainte-Justine, and Clinical Professor with the Faculty of Pharmacy, Université de Montréal, Montréal, Québec.

Competing interests: None declared.

Address correspondence to:

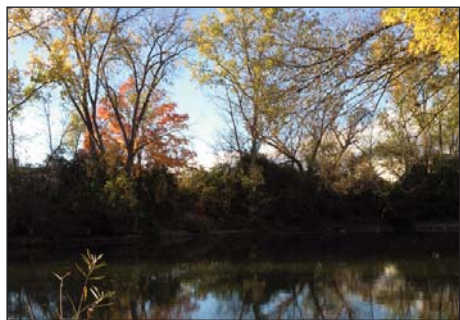
Jean-François Bussièrès
Pharmacy Department
Centre hospitalier universitaire Sainte-Justine
3175, Côte-Sainte-Catherine
Montréal QC H3T 1C5

e-mail: Jf.bussieres@sss.gouv.qc.ca

Funding: None received. Each participating centre paid for analysis of its own samples.

Acknowledgements: The authors would like to thank the centres that participated in the 2018 study.

ON THE FRONT COVER



Autumn in London, Ontario

This issue's cover photograph was one of several taken by Linda Hooper during a walk home from the London Health Sciences Centre, University Hospital, where she works as a Drug Information Specialist. Linda used her iPhone 5 to capture the image. Being from Northern Ontario, Linda has a deep appreciation for the fall colours and enjoys the opportunity to walk home when the weather permits. "I like to think that most everywhere is within walking distance if you have the time, and I like to make the time!"

The *CJHP* would be pleased to consider photographs featuring Canadian scenery taken by CSHP members for use on the front cover of the Journal. If you would like to submit a photograph, please send

an electronic copy (minimum resolution 300 dpi) to publications@cshp.pharmacy.