Antineoplastic Drug Contamination on the Hands of Employees Working Throughout the Hospital Medication System

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Submitted 3 October 2013; revised 13 February 2014; revised version accepted 17 February 2014.

ABSTRACT

We previously reported that antineoplastic drug contamination is found on various work surfaces situated throughout the hospital medication system (process flow of drug within a facility from initial delivery to waste disposal). The presence of drug residual on surfaces suggests that healthcare workers involved in some capacity with the system may be exposed through dermal contact. The purpose of this paper was to determine the dermal contamination levels of healthcare employees working throughout a hospital and to identify factors that may influence dermal contamination. We selected participants from six hospitals and wiped the front and back of workers’ hands. Wipe samples were analyzed for cyclophosphamide (CP), a commonly used antineoplastic drug, using high-performance liquid chromatography-tandem mass spectrometry. Participants were asked about their frequency of handling antineoplastic drugs, known contact with CP on their work shift, gender, job title, and safe drug handling training. In addition, participants were surveyed regarding their glove usage and hand washing practices prior to wipe sample collection. We collected a total of 225 wipe samples. Only 20% (N = 44) were above the limit of detection (LOD) of 0.36 ng per wipe. The average concentration was 0.36 ng per wipe, the geometric mean < LOD, the geometric standard deviation 1.98, and the range < LOD to 22.8 ng per wipe. Hospital employees were classified into eight different job categories and all categories had some dermal contamination levels in excess of the LOD. The job category with the highest proportion of samples greater than the LOD were those workers in the drug administration unit who were not responsible for drug administration (volunteer, oncologist, ward aide, dietician). Of note, the highest recorded concentration was from a worker who had no known contact with CP on their work shift. Our results suggest that a broader range of healthcare workers than previously believed, including those that do not directly handle or administer the drugs (e.g. unit clerks, ward aides, dieticians, and shipper/receivers), are at risk of exposure to antineoplastic drugs. A review of control measures to minimize antineoplastic drug exposure that encompasses a wide array of healthcare workers involved with the hospital medication system is recommended.

KEYWORDS: antineoplastic drugs; cyclophosphamide; dermal contamination; healthcare workers; hospital medication system
INTRODUCTION

Studies have indicated that occupational exposure to antineoplastic (cytotoxic) drugs can result in adverse health outcomes including genetic damage (Cavall et al., 2005; Sasaki et al., 2008), which could lead to cancer, as well as reproductive effects such as miscarriages (Drantsaris et al., 2005; Fransman et al., 2007). The literature lends evidence that healthcare workers’ exposure to antineoplastic drugs is a result of the transfer of surface load of these drugs to the skin (Sottani et al., 2010) and therefore the primary route of occupational exposure is via dermal contact (Sessink et al., 1994; Fransman et al., 2005; Connor, 2006). Dermal exposure may occur by contacting the drugs directly (i.e. handling manufacturers’ vials and/or drug solutions in intravenous bags) or by indirect contact as a result of touching drug-contaminated surfaces.

Our research team previously conducted a pilot study to assess the potential dermal contamination of select personnel at several local hospital pharmacies and confirmed that both pharmacists and pharmacy technicians had detectable levels of drug contamination on their hands (Hon et al., 2011a). We have since reported that drug contamination is found on work surfaces situated throughout the hospital medication system (process flow of antineoplastic drugs at a facility from initial delivery to final waste disposal) and is not strictly limited to the drug preparation and drug administration areas (Hon et al., 2011b, 2013). Based on our observations of the various healthcare workers who may contact these hospital-wide contaminated surfaces (Hon et al., 2011b), we believe that there is a broad range of job categories that may be at risk of exposure—many of whom have never been previously assessed. To our knowledge, the following job categories are involved with the hospital medication system but have never been previously evaluated for their level of dermal contamination to antineoplastic drugs: pharmacy receivers, transport staff, unit clerks, and other workers in the drug administration unit (volunteers, oncologists, ward aids, and dieticians).

The purpose of this study was to assess the dermal contamination levels of the full range of healthcare job categories, with the exception of housekeeping (cleaners), that may be at risk of exposure to antineoplastic drugs because of their involvement with the hospital medication system. In addition, we sought to identify factors such as antineoplastic drug contact frequency and prevention practices that may influence exposure levels. Cyclophosphamide (CP) was used as the marker drug in this study as it has been examined in similar exposure studies (Suspiro and Prista, 2011) and is frequently administered at the participating healthcare facilities. CP is an alkylating agent that causes cancer of the bladder as well as acute myeloid leukemia. Based on these health outcomes, CP is classified as a Group 1 carcinogen (carcinogenic to humans) by the International Agency for Research on Cancer (IARC, 2012).

METHODS

Selection of participants

Approval was obtained from university and hospital ethics boards prior to recruitment of participants. Study participants were employed at six healthcare facilities located in Metro Vancouver that were involved in the earlier phases of this study (Hon et al., 2011b, 2013)—five sites were acute care hospitals and one site was a cancer treatment facility. At all sites, drug preparations were performed in Class II Biological Safety Cabinets that were 100% vented. Closed system drug transfer devices were not employed at any of the participating facilities for either drug preparation or administration.

Participants were selected from those considered at risk of exposure to antineoplastic drugs according to site observations conducted to identify potentially drug-contaminated work surfaces and, in turn, healthcare job categories that contacted such surfaces (Hon et al., 2011b). (Although housekeepers/cleaners were observed to be at risk, they were not included in the study. Further details are found in the Discussion section). Eligible participants were selected by either active recruitment via a mailed letter of invitation or passive recruitment through the distribution of consent to contact forms at departmental meetings. The recruitment methods were dictated by the requirements of the participating hospitals’ research ethics boards. Up to three representatives of each job category per site were invited to participate.

Upon receiving consent from workers to participate in the study, members of the research team contacted each participant via email or telephone to arrange a mutually convenient time to meet at their place of work to collect hand wipe samples. All participants
were given a cash honorarium of $10 each for providing a hand wipe sample.

**Wipe sampling of hands**

Participants were asked to provide hand wipe samples at their convenience during the course of their duties during a work shift. Sampling dates were selected based on availability of research team members and participants’ work schedules. The hand wipe sample collection method was similar to that described previously for collecting wipe samples from work surfaces suspected of having drug contamination (Hon et al., 2011b, 2013). Briefly, the hands of each participant were wiped with a fresh, unused Kimwipe® (Kimberly-Clark, Mississauga, ON, Canada) premoistened with 1.0 ml of 0.1 M ammonium acetate solution (Sigma-Aldrich, Oakville, ON, Canada) using an up-and-down motion starting from the furthest digit away from the medial. The research assistant randomly selected the worker’s hand, either right or left, that was initially wiped. The palm side of the hand was wiped first and then the same wiping procedure was repeated on the back of the hand. Lastly, the webbing between the fingers was wiped to complete sample collection. Once both the left and right hand of a worker was wiped, the wipe was placed in a 20-ml vial and kept in a portable cooler with ice packs.

Participants who were wearing gloves when our research team member arrived to collect the sample were asked to remove them prior to the hand wipe. The research team member wore a new pair of disposable gloves to collect hand wipes from each participant. All collected samples were shipped on ice to the analytical lab within 24 h of sample collection and stored at −20°C until analysis. Both travel and field blanks were collected for quality control purposes.

Sample collection took place between June 2010 and February 2011. Duplicate dermal wipe samples were collected from most participants with at least 3 weeks between collection times. Participants were not made aware of the results from the first round of sampling prior to collection of the second sample.

**Wipe sample preparation and analysis**

The methods employed for preparation and analysis of the wipes were the same as those described for surface wipe samples that we reported earlier (Hon et al., 2013). The stored samples were first thawed and, into each vial, 5.5 ml of 0.1 M ammonium acetate (Sigma-Aldrich, Oakville, ON, Canada) solution was added. In order to extract the drug residue, the wipes were sonicated for 20 min and then placed in a disposable 10-ml syringe used to squeeze the solution out of the wipe into a 20-ml vial. One milliliter of the solution was then extracted and placed into a liquid chromatography vial along with 50 µl of internal standard, D4-cyclophosphamide (Bielefeld University, Bielefeld, Germany).

High-performance liquid chromatography-tandem mass spectrometry using an Agilent Technologies 6410 with a Zorbax XDB-C18 column (Agilent Technologies, Santa Clara, CA, USA) with electro-spray ionization in the positive ion mode was used to analyze the samples. Samples were run at a flow rate of 0.5 ml min−1 with a mobile phase consisting of a gradient of 5 mM ammonium acetate:100% methanol (A:B). A five-point calibration curve was used and a calibration standard was run for every 10 samples for quality control purposes. In addition, method blanks were included in the analysis and duplicate analysis took place every 10th sample. The limit of detection (LOD) was 0.36 ng per wipe, established using the 3:1 signal-to-noise ratio. The method recovery rate was 97% and each resulting sample concentration was adjusted to reflect this with contamination levels reported in nanograms per wipe. In those instances where drug contamination was found in any of the blank samples, the reported results for the corresponding batch of field samples were blank corrected.

**Supplemental data collected on site**

Documented information collected from each participant after hand wipe sample collection included: glove usage prior to sample collection, elapsed time of most recent hand wash up until sample collection, and number of times participant washed their hands on the shift prior to sample collection. Moreover, all participants were asked about contact with CP during the current work shift.

**Self-administered questionnaire**

*Instrument overview*

In addition to the on-site survey mentioned above, participants were also provided with a self-administered questionnaire that included questions related to demographic factors such as gender, job title,
department, and training related to the safe handling of antineoplastic drugs. Furthermore, participants were surveyed regarding the percentage of time spent on a typical work shift handling, preparing and/or administering antineoplastic drugs.

Data analysis
Both untransformed and log-transformed (base e) data were used to examine the distribution of contamination levels. When log-transformed, the measurements exhibited more of a normal distribution than the corresponding untransformed data. Summary statistics [arithmetic mean (AM), geometric mean (GM), geometric standard deviation (GSD), minimum and maximum, and proportion less than LOD] were used to describe the data. Summaries of the dermal contamination levels were stratified by various independent variables from the survey instruments. ‘No’ and ‘don’t know’ responses to pertinent questions from either of the two survey tools were combined into one category and compared with ‘yes’ responses to the same question. Summary statistics were determined using TIBCO Spotfire S+ 8.2 for Windows (TIBCO Software Inc.)

Reporting of results
As with the surface contamination levels reported in a previous publication (Hon et al., 2013), a large proportion of dermal samples had contamination levels less than the LOD (Tables 1 and 2). To address this, we explored ways to prevent the bias that will occur if samples less than the detection limit are omitted or if inappropriate quantitative values are assigned to them (Helsel, 2009). Laboratory-calculated concentrations below the method LOD were available to us. Although these data have a lower signal-to-noise ratio than data above the detection limit, they were based on actual measurements rather than substitute values, a technique often used for exposure data below detection limits (Hornung and Reed, 1990). As there are biases associated with using a substitute value (Ganser and Hewett, 2010), we therefore used the actual analytical data for concentrations below the detection limit for all data analyses.

RESULTS
Characteristics of study population
In total, 115 healthcare workers agreed to participate in the study. It was not possible to calculate a true response rate because of the constraints of the recruitment methods dictated by hospital ethics boards; however, the proportions who participated of those contacted in the six facilities ranged from 55 to 76%. Table 1 presents a summary of the characteristics of the study population. Participants had been in their current job positions for an average of 103 months (range 0–433 months). Workers who had a duty to handle antineoplastic drugs (N = 91) had been handling these agents for an average of 82 months (range 0–336 months).

Summary of contamination levels
Of the 115 participants, 110 supplied a duplicate hand wipe sample, resulting in a total of 225 dermal wipe samples. Only 44 of the samples (20%) were above the LOD of 0.36 ng per wipe (from 42 unique individuals representing all the job categories examined). The AM concentration was 0.36 ng per wipe, the GM < LOD, the GSD 1.98, and the range < LOD to 22.8 ng per wipe. The average dermal contamination levels from workers at acute care hospitals were higher than those from the cancer treatment hospital. When stratified by hospital department, participants from the drug administration units had the highest AM contamination levels (Table 1).

Contamination levels by job and gender
When stratified by job category, three of the job categories had average dermal contamination levels in excess of the LOD—porters, nurses and those working in patient units not tasked with drug administration (volunteer, oncologist, ward aide, dietician). Of these three groups, the highest average contamination level belonged to those other workers in the drug administration unit (volunteers, oncologists, ward aides, and dieticians). In addition, the volunteers, oncologists, ward aides, and dieticians, as a whole, had the highest proportion of samples in excess of the LOD. The maximum reported dermal concentration of every job category examined exceeded the LOD of 0.36 ng per wipe.

When stratified by gender, female participants had a higher average dermal contamination level than males (Table 1).

Contamination levels by antineoplastic drug contact and preventive measures
We asked participants if they had ever received safe drug handling training. The proportion of samples
greater than LOD was virtually identical between those who had received training and those who did not. In addition, the maximum recorded dermal concentration level between those who were trained and those who were not was also similar (Table 2).

Participants who reported that they do not have a duty to handle antineoplastic drugs had an almost equal proportion of samples greater than LOD compared to those who do have a duty. Those who stated that they never handle antineoplastic drugs on their work shift had a similar proportion of samples in excess of the LOD compared to those who handle antineoplastic drugs at least 25% of the time on their shift (Table 2).

When asked if they handled or came into contact with CP at least once during their work shift, 63 of the participants (28%) reported that they had. However, the maximum reported dermal contamination level of 22.8 ng per wipe was from an individual who stated that they had no contact with CP on the work shift (Table 2).

### Table 1. Dermal CP contamination levels of healthcare workers involved with the hospital medication system, stratified by job and demographic variables: summary statistics and percent of samples greater than detection limit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subcategory</th>
<th>N</th>
<th>% &gt; LOD</th>
<th>AM (ng per wipe)</th>
<th>GM (ng per wipe)</th>
<th>GSD</th>
<th>Max (ng per wipe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital type</td>
<td>Cancer center</td>
<td>44</td>
<td>27.3</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>3.98</td>
<td>4.04</td>
</tr>
<tr>
<td></td>
<td>Acute care hospital</td>
<td>181</td>
<td>17.7</td>
<td>0.44</td>
<td>&lt;LOD</td>
<td>1.40</td>
<td>22.8</td>
</tr>
<tr>
<td>Department</td>
<td>Pharmacy</td>
<td>91</td>
<td>15.4</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>2.66</td>
<td>9.29</td>
</tr>
<tr>
<td></td>
<td>Drug administration</td>
<td>115</td>
<td>24.3</td>
<td>0.66</td>
<td>&lt;LOD</td>
<td>1.46</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>19</td>
<td>10.5</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.18</td>
<td>4.55</td>
</tr>
<tr>
<td>Job title</td>
<td>Pharmacist</td>
<td>40</td>
<td>10.0</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>4.15</td>
<td>1.49</td>
</tr>
<tr>
<td></td>
<td>Pharmacy receiver</td>
<td>12</td>
<td>25.0</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.09</td>
<td>1.27</td>
</tr>
<tr>
<td></td>
<td>Pharmacy technician</td>
<td>45</td>
<td>17.8</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.42</td>
<td>9.29</td>
</tr>
<tr>
<td></td>
<td>Porter</td>
<td>11</td>
<td>9.1</td>
<td>0.40</td>
<td>&lt;LOD</td>
<td>1.25</td>
<td>4.55</td>
</tr>
<tr>
<td></td>
<td>Nurse (includes LPN)</td>
<td>64</td>
<td>26.6</td>
<td>0.77</td>
<td>0.36</td>
<td>1.46</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Transport (includes biopacker, transporter, and shipper/receiver)</td>
<td>8</td>
<td>12.5</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.05</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Unit clerk</td>
<td>24</td>
<td>16.7</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.31</td>
<td>2.03</td>
</tr>
<tr>
<td></td>
<td>Others in drug admin unit (volunteer, oncologist, dietician, ward aide)</td>
<td>21</td>
<td>28.6</td>
<td>1.32</td>
<td>0.504</td>
<td>1.64</td>
<td>22.4</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>180</td>
<td>22.2</td>
<td>0.45</td>
<td>&lt;LOD</td>
<td>1.43</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>45</td>
<td>8.9</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>3.85</td>
<td>4.55</td>
</tr>
</tbody>
</table>

LPN, licensed practical nurse; LOD = 0.36 ng per wipe.
Participants who wore at least one pair of gloves immediately prior to sample collection had a higher proportion of samples greater than the LOD compared to workers who did not wear gloves. We asked participants to recall their most recent hand wash prior to sample collection. Those workers who indicated that they washed their hands <10 min prior to sample collection had the highest proportion of samples exceeding the LOD. Of note, the maximum dermal contamination level was recorded for an individual who reported hand washing <10 min prior to sample collection. Lastly, we asked individuals how

Table 2. Dermal CP contamination levels of healthcare workers involved with the hospital medication system, stratified by antineoplastic drug contact and preventive measures: summary statistics and percent of samples greater than detection limit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subcategory</th>
<th>N</th>
<th>% &gt; LOD</th>
<th>AM (ng per wipe)</th>
<th>GM (ng per wipe)</th>
<th>GSD</th>
<th>Max (ng per wipe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe drug handling training</td>
<td>Yes</td>
<td>118</td>
<td>19.5</td>
<td>0.36</td>
<td>&lt;LOD</td>
<td>2.42</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>107</td>
<td>19.6</td>
<td>0.37</td>
<td>&lt;LOD</td>
<td>1.42</td>
<td>22.4</td>
</tr>
<tr>
<td>Has a duty to handle antineoplastic drugs</td>
<td>Yes</td>
<td>178</td>
<td>19.7</td>
<td>0.43</td>
<td>&lt;LOD</td>
<td>1.43</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>47</td>
<td>19.1</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>3.75</td>
<td>4.55</td>
</tr>
<tr>
<td>Percentage of time handling antineoplastic drugs</td>
<td>&lt;25%</td>
<td>106</td>
<td>17.9</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.35</td>
<td>7.51</td>
</tr>
<tr>
<td></td>
<td>&gt;25%</td>
<td>74</td>
<td>21.6</td>
<td>0.52</td>
<td>&lt;LOD</td>
<td>1.46</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>45</td>
<td>20.0</td>
<td>0.58</td>
<td>&lt;LOD</td>
<td>3.99</td>
<td>22.4</td>
</tr>
<tr>
<td>Contacted CP on shift (by any means)</td>
<td>Yes</td>
<td>63</td>
<td>25.4</td>
<td>0.54</td>
<td>&lt;LOD</td>
<td>1.31</td>
<td>9.29</td>
</tr>
<tr>
<td></td>
<td>No/don’t know</td>
<td>162</td>
<td>17.3</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>2.20</td>
<td>22.8</td>
</tr>
<tr>
<td>Number of gloves worn immediately prior to sample collection</td>
<td>0</td>
<td>202</td>
<td>18.8</td>
<td>0.36</td>
<td>&lt;LOD</td>
<td>2.01</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>19</td>
<td>26.3</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.76</td>
<td>1.80</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>33.3</td>
<td>2.91</td>
<td>1.71</td>
<td>2.05</td>
<td>9.29</td>
</tr>
<tr>
<td>Elapsed time since most recent hand wash (prior to hand wipe)</td>
<td>&lt;10 min ago</td>
<td>77</td>
<td>24.7</td>
<td>0.93</td>
<td>0.40</td>
<td>1.50</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>10–30 min ago</td>
<td>71</td>
<td>12.7</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>2.99</td>
<td>4.55</td>
</tr>
<tr>
<td></td>
<td>31–60 min ago</td>
<td>43</td>
<td>20.9</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.44</td>
<td>9.29</td>
</tr>
<tr>
<td></td>
<td>60+ min ago</td>
<td>34</td>
<td>20.6</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.19</td>
<td>2.13</td>
</tr>
<tr>
<td>Number of times hands washed on shift (up until hand wipe)</td>
<td>0 (start of shift)</td>
<td>6</td>
<td>66.7</td>
<td>0.57</td>
<td>0.52</td>
<td>1.17</td>
<td>2.13</td>
</tr>
<tr>
<td></td>
<td>1–2</td>
<td>43</td>
<td>18.6</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>4.04</td>
<td>1.74</td>
</tr>
<tr>
<td></td>
<td>3–4</td>
<td>64</td>
<td>15.6</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>1.38</td>
<td>4.55</td>
</tr>
<tr>
<td></td>
<td>5+</td>
<td>112</td>
<td>19.6</td>
<td>0.77</td>
<td>0.38</td>
<td>1.39</td>
<td>22.8</td>
</tr>
</tbody>
</table>

*aInformation collected from participants while on site. Total N is 225 because responses may vary between the two sampling dates; LOD = 0.36 ng per wipe.
many times they washed their hands on their shift up until the time of sample collection. The maximum dermal contamination level was recorded for an individual who reported hand washing at least five times on the work shift. Of note, dermal contamination was observed in four of six samples that were collected at the start of a worker’s shift.

**DISCUSSION**

This study quantified the dermal contamination levels of a wide array of healthcare workers involved with the hospital antineoplastic drug medication system. We examined a total of eight different job categories, some of whom, such as volunteers, dieticians, unit clerks, and pharmacy receivers, have not been assessed previously. The study aimed to determine the contamination levels of these various job categories during a work shift, without focus on any particular task. Overall, the majority of our samples (80%) were below the analytical detection limit. However, the maximum measured dermal contamination levels in each of the eight different job categories were all above the LOD of 0.36 ng per wipe. This confirms our earlier hypothesis that, because drug contamination is present on surfaces located throughout the hospital medication system, a wide range of job categories are at risk of dermal contact with antineoplastic drugs (Hon et al., 2013). Job categories found to be at risk of indirect exposure via contaminated surfaces included healthcare workers who are not responsible for drug preparation and/or drug administration, such as porters, ward aides, dieticians, and pharmacy receivers. Because these employees are not expected to have direct exposure, they usually do not have the same level of formal training related to the safe handling of antineoplastic drugs and, therefore, may not be aware of the proper precautionary measures.

It has long been considered that pharmacists and nurses are the highest risk cohorts for occupational exposure to antineoplastic drugs because of their duties related to drug preparation and drug administration, respectively (McDiarmid et al., 2010). However, we found that other job categories working within the drug administration unit (volunteers, oncologists, dieticians, and ward aides) had not only the highest average dermal contamination levels but also the highest proportion of samples in excess of the LOD. Although it is not surprising that participants who had a duty to handle antineoplastic drugs had higher levels of dermal contamination than those who did not, what is surprising is that the proportion of samples greater than LOD was similar in the two groups. Similarly, regardless of whether or not a worker received safe drug handling training, the proportion of samples above LOD was the same.

The maximum reported level of dermal contamination was from a worker who had no known contact with CP during his/her work shift. This finding is consistent with other occupational exposure studies that suggest that a worker does not necessarily have to work with antineoplastic drugs to have detectable levels of contaminant (Sessink et al., 1994; Mader et al., 1996; Pethran et al., 2003). This is important from a risk management perspective because unintentional occupational exposure to antineoplastic drugs should never occur due to the risks associated with these hazardous agents (Friese et al., 2012).

Our results indicated that those who worked in acute care hospitals had higher dermal contamination levels than those employed at the cancer treatment hospital. This difference may be related to the fact that the cancer treatment hospital had more stringent education/training with a broader range of workers being educated due to the specialized nature of the facility. However, with only one cancer treatment hospital participating and a smaller proportion of samples greater than LOD from the participating acute care facilities, additional studies are needed to confidently generalize this result.

We found instances of dermal contamination among the small number of workers in our study who were wearing gloves immediately prior to sample collection (N = 22). This may be the result of skin contamination before donning of gloves (e.g. dermal contact with a drug-contaminated surface), self-contamination due to improper doffing techniques (Casanova et al., 2008, 2012), or permeation of the drug products through gloves. Several studies have indicated that permeation of antineoplastic drug through gloves does indeed occur, including through nitrile, the most common glove material worn by our subjects (15/22 or 68%) (Connor, 1999; Wallemacq et al., 2006). Under working conditions, the durability of gloves may change resulting in leakage (Kerr et al., 2004; Phalen and Wong, 2012). It would therefore be valuable to test various combinations
of glove material (during the course of normal duties) to ensure that users are adequately protected.

Our results also indicated that individuals had dermal contamination at the start of their work shift. There are two possible reasons: (i) residual drug from a previous shift due to ineffective hand washing or (ii) dermal contact with a contaminated hospital surface prior to any work activities. These results are consistent with our previous finding that, even though a surface was reportedly cleaned, it had little impact on the residual drug contamination levels (Chu et al., 2012).

A review of the literature found a proposed dermal occupational exposure limit (DOEL) for CP of 4 ng cm$^{-2}$ (Bos et al., 1998) or 3360 ng per wipe using an average surface area for both hands of 840 cm$^2$ (Lee et al., 2007). None of the dermal contamination levels in the current study exceeded this DOEL. However, it is important to mention that this DOEL was established based on absorption of CP on a daily basis; as our study design was cross-sectional, we are unable to ascertain a worker’s exposure over a full day. Regardless, it is our opinion from an occupational hygiene perspective that the collection of hand wipes should be complementary to surface sampling to evaluate occupational exposure to antineoplastic drugs. Surface sampling is a suitable tool to identify surfaces and/or objects that may be contaminated and, in turn, can lead to identification of healthcare workers who may come into contact with these surfaces. However, in order to quantify a worker’s true exposure level, collecting wipe samples from the hands of a worker is more appropriate than surface wipes.

Limitations of the current study need to be addressed. We were unable to recruit housekeepers (cleaners) into the study because the contract company that employed the housekeepers declined to participate. Cleaners are responsible for removing the cytotoxic waste bins from the various departments at each facility as well as cleaning of patient lavatories and are therefore known to be at risk of exposure to antineoplastic drugs (Fransman et al., 2005; Hedmer et al., 2008). As this study was cross-sectional in nature, the findings are only representative of the point in time when samples were collected; cumulative occupational exposure to antineoplastic drugs, if any, was not evaluated. Our sampling strategy was based on convenience sampling, which allowed assessment of exposure throughout a day, but does not allow comparison to task-based exposure levels assessed in other similar studies (Fransman et al., 2004, 2005). The dermal wipe sampling method may have resulted in measurements that underestimated actual exposure as CP may have absorbed through the skin (Hirst et al., 1984). The recovery rate of the skin sampling method employed is not known. We analyzed for only one antineoplastic drug. However, since CP has been found to have relatively high permeability through the skin (Odraska et al., 2011), is a known human carcinogen, and was frequently used in the study hospitals, we believe that it is an important antineoplastic drug for dermal exposure monitoring. Lastly, we were unable to quantify the amount of CP handled and/or contacted. Although we attempted to ask this information from participants, the reported amounts were not considered reliable because a majority of participants were unable to answer this question and, those who did respond, merely provided an estimate.

**CONCLUSIONS**

Our study has demonstrated dermal contamination to antineoplastic drugs of a broad range of healthcare job categories working throughout the hospital medication system. These findings are consistent with our earlier suggestion that there is likely an underestimate of the total number of healthcare workers at risk of exposure to antineoplastic drugs (Hon et al., 2011b). Based on the results of the current study and our earlier finding that contamination is found on surfaces situated throughout the hospital medication system (Hon et al., 2013), we believe that it is important to consider all at-risk healthcare workers when designing control measures, including medical surveillance (Chalupka, 2013), to minimize exposure to antineoplastic drugs.

**FUNDING**


**ACKNOWLEDGEMENTS**

We appreciate the time and cooperation of all participants and their respective facilities. We would like to recognize the assistance of the Dr Winnie Chu from University of British Columbia who led the team responsible for sample analyses. Lastly, we are indebted to the following individuals who helped to collect samples for the study: Jennifer Shum, Pearl Siganporia, and Sarah Chiarello.
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