

# Occupational Dermal Exposure to Cyclophosphamide in Dutch Hospitals: A Pilot Study

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**Introduction:** Several studies have shown that exposure to antineoplastic drugs can cause reproductive toxic effects as well as carcinogenic effects. Presence of these drugs in the urine of hospital personnel has been widely studied and some work has been done on exposure by inhalation. So far, assessment of dermal exposure to antineoplastic drugs has not been extensively studied. In this pilot study we assessed potential and actual dermal exposure for several common hospital tasks. Results were used to derive an optimal measurement strategy for a currently ongoing exposure survey.

**Methods:** Dermal exposure to cyclophosphamide was determined in three Dutch hospitals during five tasks (preparation, decanting urine, washing the patient, removing bed sheets and cleaning the toilet) using pad samples on 10 body locations. In addition, protective medical gloves (worn during the performance of these activities) were collected to estimate potential exposure of the hands. Subsequently, hands were washed to measure actual exposure of the hands. Bulk samples (i.e. application and body fluids) were collected and possible contact surfaces were monitored to assess the amount of cyclophosphamide potentially available for exposure.

**Results:** The results show that hospital personnel (i.e. pharmacy technicians and oncology nurses) are dermally exposed to cyclophosphamide during performance of their daily duties. Exposure occurred predominantly on the hands and sporadically on other body locations (i.e. forehead and forearms). Gloves used during preparation of cyclophosphamide were more contaminated than gloves used in other tasks, however, actual exposure of the hands (underneath the gloves) was highest during decanting of urine of treated patients. Glove samples correlated significantly with handwash samples ( $r = 0.57$ ,  $P = 0.03$ ,  $n = 15$ ). The level of protection from gloves varied between tasks, being highest for gloves used during preparation (median = 98%) and lowest for gloves used during decanting urine (median = 19%).

**Conclusion:** This pilot study demonstrated that dermal exposure to cyclophosphamide is common among hospital personnel. The results showed that hands, forearms and forehead accounted for 87% of the cyclophosphamide total body exposure. Glove samples together with handwash samples enabled estimation of glove efficiency, which appeared to vary strongly between tasks observed.

**Keywords:** antineoplastic drugs; cleaning personnel; cyclophosphamide; dermal exposure; hospital; nurses; pharmacy technicians

## INTRODUCTION

Several studies of hospital workers have shown that

exposure to antineoplastic drugs can cause reproductive toxic effects (Selevan *et al.*, 1985; Stücker *et al.*, 1990) as well as carcinogenic effects (Waksvik *et al.*, 1981; Pohlová *et al.*, 1986; Milkovic-Kraus and Horvat, 1991; Sardas *et al.*, 1991; Goloni-Bertollo *et al.*, 1992; Sessink *et al.*, 1994a). Several biomonitoring studies have corroborated that nurses and

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pharmacy personnel working in a hospital are exposed to these agents (Sessink *et al.*, 1992, 1994b; Ensslin *et al.*, 1994, 1997; Burgaz *et al.*, 1999), but the actual pathways through which exposure occurs are still largely unknown. Exposure surveys focusing on the identification of the relevant exposure pathways are scarce and have mostly focused on exposure to antineoplastic drugs through inhalation (de Werk Neal *et al.*, 1983; McDevitt *et al.*, 1993; Kromhout *et al.*, 2000; Kiffmeyer *et al.*, 2002). These studies failed to prove exposure as an important route of exposure. A few studies focused on the dermal route of exposure and found gloves to be contaminated with antineoplastic agents during the preparation and administration of these drugs (Sessink *et al.*, 1994b, 1997). To our knowledge, no studies on dermal exposure to these hazardous agents during nursing and cleaning tasks have been performed so far, although several authors have suggested that the dermal exposure route is important (McDevitt *et al.*, 1993; Sessink *et al.*, 1994b; Kromhout *et al.*, 2000). Results of a recent study using a fluorescent tracer technique indicated the occurrence of spills during administration of antineoplastic drugs and handling of patient's urine (Kromhout *et al.*, 2000). It therefore seems likely that oncology nurses and cleaning personnel are dermally exposed to antineoplastic drugs, since these antineoplastic drugs are present in the patient's excreta (Ritschel *et al.*, 1981; Heggie *et al.*, 1987; Burgaz *et al.*, 1988; Madsen and Larsen, 1988; Mader *et al.*, 1996). Pharmacy technicians might be exposed to antineoplastic drugs through the skin, due to insufficient protection during preparation of the drugs (Colligan and Horstman, 1990; Connor, 1993; Harrison and Kloos, 1999).

In the current study we measured potential and actual dermal exposure to cyclophosphamide in three Dutch hospitals of: (i) pharmacy technicians during preparation of cyclophosphamide; (ii) oncology nurses during decanting urine, washing the patient and removing bed sheets; (iii) cleaning personnel during cleaning of cancer patient toilets. We also collected bulk samples (application and body fluids) and surface contamination samples to elucidate and quantify strength of exposure sources. The aims of the study were to determine whether dermal exposure to antineoplastic drugs occurred during the performance of oncology-related tasks and to see whether an efficient and effective dermal exposure assessment strategy could be discerned.

## MATERIALS AND METHODS

### *Description of workplaces and tasks*

Cyclophosphamide is one of the many antineoplastic agents that is frequently used in Dutch hospitals. Since cyclophosphamide can be easily absorbed through intact human skin (Hirst *et al.*,

1984) and sensitive analytical techniques are available, exposure to cyclophosphamide was chosen as a measure of exposure to antineoplastic drugs. Dermal exposure to cyclophosphamide was measured in three Dutch hospitals during the performance of five tasks: (i) preparation of antineoplastic drugs in the hospital pharmacy; (ii) decanting patient urine; (iii) washing the patient; (iv) removing the sheets from the patient's bed; (v) cleaning the patient toilet on the oncology ward of the hospital. Preparation of antineoplastic agents was performed in the hospital pharmacy of hospital 1 in a safety cabinet (laminar down flow) by trained pharmacy technicians, wearing an apron and two pairs of latex surgical gloves. Oncology nurses (using nitrile rubber examination gloves) performed the three nursing tasks (decanting urine, washing the patient and removing bedsheets) on the oncology ward of hospital 2. Cleaners, who were not part of the nursing staff, cleaned the patient toilet (using latex examination gloves) in hospitals 1 and 3.

### *Measurements*

In this pilot study four measurements per task were taken. Measurements were taken the morning after cyclophosphamide had been i.v. administered to the patient. For each measurement, 10 cotton pads (10 × 10 cm) were attached with surgical tape to the outside of the (protective) clothing on the torso (front), back, upper arms, forearms, upper legs and lower legs. In contrast to pharmacy technicians, the forearms of nurses and cleaners were not covered by clothing, so pads were attached directly to the skin at that body location. Pads from corresponding body locations (left and right) were pooled and analysed as one sample, which resulted in six pad samples per measurement [torso front, torso back, upper arms (pooled), forearms (pooled), upper legs (pooled) and lower legs (pooled)]. The back of each cotton pad was covered with a piece of plastic (10 × 10 cm) to avoid contamination of the pad from the clothing or skin. Since it was not desirable (for normal patient-nurse interactions) to attach a cotton pad to the head, a wipe sample of the forehead (5 × 3 cm) was taken at the end of the task using two tissues and 10 ml of a 10% isopropanol solution. Medical gloves (if used) were collected (both together in one sample) after performance of the task as a measure of potential exposure of the hands. Subsequently, both hands were washed in a polyethylene bag with 250 ml of a 10% isopropanol solution to assess actual exposure of the hands (Brouwer *et al.*, 2000). Approximately 30 ml of this handwash sample was collected in a polypropylene tube (50 ml) and stored at -20°C prior to analysis. Pads, gloves and forehead wipe samples were stored in polyethylene containers (250 ml) at -20°C prior to analysis.

In addition to the dermal exposure measurements, bulk and surface contamination samples were taken to assess the amount of cyclophosphamide to which hospital personnel could potentially be exposed during the tasks performed. The concentration of cyclophosphamide was determined in patient urine, water (+ soap) after having washed the patient and water (+ detergent) after having cleaned the patient toilet. Wipe samples were taken from the front edge of the safety cabinet in the hospital pharmacy (1170 cm<sup>2</sup>) and the outer urinal (1200 cm<sup>2</sup>) or bedpan (1400 cm<sup>2</sup>) using two tissues and 20 ml of 0.03 M sodium hydroxide solution. Furthermore, the wash cloth (560 cm<sup>2</sup>), an excised section of the towel (100 cm<sup>2</sup>), two excised sections of the bedsheet (2 × 100 cm<sup>2</sup>, corresponding to the back and lower abdomen of the patient, respectively), an excised section of the upper surface of the pillowcase (100 cm<sup>2</sup>) and the cleaning cloth (1600 cm<sup>2</sup>) used for cleaning the toilet were collected for analysis of cyclophosphamide. Before sheets were removed from the bed by the oncology nurse, the entire upper surface of the pillowcase (5082 cm<sup>2</sup>) and two areas (2 × 100 cm<sup>2</sup>) on the sheet (corresponding to the back and lower abdomen of the patient, respectively) were vacuumed to see whether cyclophosphamide was attached to dust particles that could potentially be released from the sheet or pillowcase and thereby causing exposure by inhalation. The two pieces that were cut out of the sheet were located directly next to the two spots on the sheet that were vacuumed. All samples were stored at -20°C prior to analysis. An overview of collected samples per task is given in Table 1.

#### Analysis of samples

Pad, glove, wipe and cloth samples were extracted with 160 ml of 0.03 M sodium hydroxide solution and subsequently analysed for cyclophosphamide using gas chromatography-tandem mass spectrometry (GC-MSMS) as described previously (Sessink *et al.*, 1993). Liquids were directly analysed for cyclo-

phosphamide using the same GC-MSMS method. The described analytical method had a detection limit of 0.1 ng/ml.

#### Quality assurance

For each kind of sampling material one field blank sample per task was taken. All blank samples were below the instrument detection limit (IDL) of 0.1 ng/ml, so the limit of detection (LOD) and limit of quantification (LOQ) could not be calculated. Therefore, the limit of detection (LOD) was treated as equivalent to the IDL of 0.1 ng/ml.

Liquid samples (handwash sample, urine, washing water and cleaning water) were split and analysed in duplicate to determine the assay variation. The total coefficient of variation (CV<sub>1</sub>) was 39% (*n* = 16) for handwash samples, 44% (*n* = 4) for washing water samples and 8% (*n* = 4) for urine samples.

Spike samples were taken to calculate the recovery of cyclophosphamide for the analysed matrices. A 20, 50, 100 and 200 ng cyclophosphamide series was spiked in duplicate on or in the sampling materials. Subsequently, the samples were extracted with 160 ml of 0.03 M sodium hydroxide solution and the samples were analysed for cyclophosphamide using GC-MSMS as previously described (Sessink *et al.*, 1993). For the dermal exposure samples, the average recoveries were 58% for gloves, 100% for handwash solution, 100% for pads and 100% for forehead wipe samples. Subsequently, measured concentrations on the gloves were corrected for the average recovery.

#### Statistical analysis

The data were analysed using SAS statistical software (version 8.02; SAS institute, Cary, NC). In situations where sample values were less than the LOD, two-thirds of the LOD was substituted for sample values. Median levels were calculated using Proc Univariate. Because of the small number of samples per task, we could not determine whether the results approximated a log-normal or a normal distribution.

Table 1. Collected dermal exposure samples, bulk samples and surface contamination samples per task

	Preparation	Decanting urine	Washing patient	Removing sheets	Cleaning toilet
Dermal exposure samples	Gloves (latex)	Gloves (nitrile)	Gloves (nitrile)	Gloves (nitrile)	Gloves (latex)
	Handwash	Handwash	Handwash	Handwash	Handwash
	Forehead wipe	Forehead wipe	Forehead wipe	Forehead wipe	Forehead wipe
	6 pad samples	6 pad samples	6 pad samples	6 pad samples	6 pad samples
Bulk samples and surface contamination samples	Wipe sample front edge of safety cabinet	Patient's urine	Patient's washing water	Piece of pillowcase	Cleaning water
		Wipe sample outer urinal or bedpan	Washing cloth	2 pieces of bed sheet	Cleaning cloth
			Towel	Vacuum sample pillowcase	
				Vacuum sample bed sheet	

Table 2. Median cyclophosphamide exposure levels at each body location per task (ng/cm<sup>2</sup>/min) with the number of detectable samples ( $n > \text{LOD}$ ) in parentheses

Sample	<i>n</i>	Pharmacy technician Preparation ( $n > \text{LOD}$ )	Oncology nurse			Cleaning personnel Cleaning toilet median ( $n > \text{LOD}$ )
			Decanting urine median ( $n > \text{LOD}$ )	Washing patient median ( $n > \text{LOD}$ )	Removing sheets median ( $n > \text{LOD}$ )	
Gloves	4	0.45 (3)	0.006 (2)	0.03 (4)	<0.0009 (0) <sup>a</sup>	0.008 (2)
Handwash	4	0.002 (3)	0.02 (3)	0.003 (3)	<0.0008 (0)	<0.001 (0)
Forehead	4	0.01 (2)	<0.109 (0) <sup>a</sup>	<0.036 (1) <sup>a</sup>	0.05 (2)	<0.047 (0)
Torso (front)	4	<0.001 (1)	<0.016 (0)	<0.005 (0)	<0.004 (0)	<0.007 (0)
Back	4	<0.001 (1)	<0.016 (1)	<0.005 (0)	<0.004 (0)	<0.007 (0)
Upper arms	4	<0.0005 (1)	<0.008 (0)	<0.003 (0)	<0.002 (0)	<0.004 (0)
Forearms	4	0.001 (2)	<0.008 (0)	<0.003 (0)	<0.002 (0)	<0.004 (0)
Upper legs	4	<0.0005 (0)	<0.008 (0)	<0.003 (0)	<0.002 (0)	<0.004 (0)
Lower legs	4	<0.0005 (0)	<0.008 (0)	<0.003 (0)	<0.002 (0)	<0.004 (0)

*n*, number of measurements per task; LOD, limit of detection.

<sup>a</sup>One sample missing,  $n = 3$ .

Therefore, differences in exposure levels among tasks were tested by calculating exact *P*-values using the non-parametric Wilcoxon rank sum test. Spearman correlation coefficients were calculated to examine the relationship between gloves and handwash samples.

## RESULTS

Both handwash and forehead contamination levels reflect the actual exposure of these body parts, whereas gloves reflect potential exposure of the hands. The sum of the glove and the handwash samples equals the total potential exposure of the hands during each task (minus uptake by the skin). Pads were attached to the clothing (potential exposure) and directly to the (uncovered) skin of the forearms and cleaning and personell (actual exposure). One oncology nurse did not use gloves while removing the bed sheets, so one glove sample is missing for that particular task. One forehead wipe sample was missing for both 'decanting urine' and 'washing the patient'.

Table 2 shows median exposure levels per body location per task in nanograms per square centimetre per minute (ng/cm<sup>2</sup>/min) and the number of detectable samples ( $n > \text{LOD}$ ) per task per body location. The results show that pharmacy technicians and oncology nurses were dermally exposed to cyclophosphamide and that cleaning personnel only had detectable levels of cyclophosphamide on the gloves. The percentage of positive samples ( $n > \text{LOD}$ ) per task were 36% for preparation, 17% for decanting urine, 23% for washing the patient, 6% for removing bed sheets and 6% for cleaning the toilet (Table 2). For two measurements during removing bed sheets exposure of the forehead only and not of the hands or any other body part occurred. For all other measurements exposure of the hands mainly occurred (51%

of glove and handwash samples were above the LOD). Furthermore, 28% of forehead wipe samples were above the LOD and sporadically other body parts (<10% of samples exceeded the LOD) were also exposed to cyclophosphamide (Table 2). In total, 87% of all positive samples ( $n > \text{LOD}$ ) were measured as hand samples (gloves + handwash) together with the forehead wipe sample and the pads on the forearms.

In Table 3 median exposure levels of the hands are presented both as potential (glove samples) and actual (handwash samples) exposures. Outer gloves (potential exposure of the hands) of pharmacy technicians seemed to be more highly contaminated ( $P = 0.147$ ) with cyclophosphamide during preparation of the drug compared with the other tasks measured, while handwash samples (actual exposure of the hands) appeared to be significantly ( $P = 0.005$ ) higher during decanting urine compared with the other tasks (Table 3). The sum of the glove and the handwash samples equals the total potential exposure of the hands during each task (minus uptake by the skin). From these results it was possible to calculate the level of protection the gloves gave against cyclophosphamide, which appeared to be higher ( $P = 0.009$ ) for preparation of the drug (98.5%) and lower ( $P = 0.018$ ) for decanting urine (19.3%) compared with the other tasks (Table 3). Glove samples were moderately correlated with handwash samples (Spearman correlation,  $r = 0.52$ ,  $P = 0.02$ ,  $n = 19$ ) when measurements of all tasks were combined.

Table 4 shows the results of the bulk and surface contamination samples. These results confirm that patients i.v. treated with cyclophosphamide excrete cyclophosphamide unmetabolized via their excreta (i.e. urine and sweat) the morning after the drug had been administered (Table 4). The concentration of cyclophosphamide in the urine of the patients was 850–1500 times lower than the concentration handled

Table 3. Median and range of task duration, cyclophosphamide (CP) exposure levels on the hands and glove level of protection (%) per task

	n	Oncology nurse						Cleaning personnel			
		Pharmacy technician			Oncology nurse			Cleaning personnel			
		Preparation		Decanting urine		Washing patient		Removing sheets		Cleaning toilet	
	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	
Task duration (min)	4	100	100–130	6.5	5–10	20	15–25	25	15–25	15	10–20
Gloves (ng/cm <sup>2</sup> /min)	4	0.45 <sup>c</sup>	<0.0002–1.19	0.006 <sup>d</sup>	<0.003–0.02	0.03 <sup>d</sup>	0.01–0.03	<0.0009 <sup>d</sup>	<0.0009 <sup>d</sup>	0.008 <sup>e</sup>	<0.001–0.03
Handwash (ng/cm <sup>2</sup> /min)	4	0.002	<0.0002–0.03	0.02	<0.003–0.05	0.003	<0.001–0.02	<0.0008	<0.0008	<0.001	<0.003–0.03
Total hands (ng/cm <sup>2</sup> /min) <sup>a</sup>	4	0.45	<0.0004–1.22	0.03	<0.007–0.05	0.03	0.02–0.04	<0.002	<0.002	0.01	<0.003–0.03
Glove level of protection (%) <sup>b</sup>	4	98.5 <sup>f</sup>	97.8–99.6	19.3 <sup>f</sup>	5.5–58.5	92.4	29.1–95.6	100 <sup>g</sup>	100 <sup>g</sup>	100 <sup>g</sup>	100 <sup>g</sup>

n, number of measurements per task.

<sup>a</sup>Total hands = handwash + gloves.

<sup>b</sup>Glove level of protection =  $[\text{CP}_{\text{gloves}} / (\text{CP}_{\text{gloves}} + \text{CP}_{\text{handwash}})] \times 100\%$ ; measurements with both gloves < LOD and handwash < LOD are not included in calculating the median.

<sup>c</sup>Two pairs of latex medical gloves used; only outer gloves collected.

<sup>d</sup>One pair of vinyl examination gloves used.

<sup>e</sup>One pair of powder-free latex examination gloves used.

<sup>f</sup>Based on n = 3.

<sup>g</sup>Since all handwash samples were non-detectable, the level of protection for gloves used for cleaning the patient's toilet is set to 100%.

Table 4. Median cyclophosphamide (CP) concentrations in bulk and surface contamination samples per task

Sample	<i>n</i>	Median	Range	Median volume (ml) or total surface area (cm <sup>2</sup> )
<b>Preparation</b>				
CP solution used during preparation <sup>a</sup> (ng/ml)	4	20 000 000		275 ml
Wipe sample safety cabinet (ng/cm <sup>2</sup> )	4	1.49	<0.009–18.0	1170 cm <sup>2</sup>
<b>Decanting urine</b>				
Urine (ng/ml)	4	16 675.0	13 350–22 550	175 ml
Wipe sample urinal or bedpan (ng/cm <sup>2</sup> )	2	1.21	0.20–2.23	1300 cm <sup>2</sup>
<b>Washing patient</b>				
Washing water (ng/ml)	4	54.7	49.8–114.0	2200 ml
Washing cloth (ng/cm <sup>2</sup> )	4	16.6	6.3–27.9	560 cm <sup>2</sup>
Towel (ng/cm <sup>2</sup> )	4	19.4	17.9–42.7	4416 cm <sup>2</sup>
<b>Removing sheets</b>				
Pillowcase (ng/cm <sup>2</sup> )	4	17.5	5.6–143.5	5082 cm <sup>2</sup>
<b>Sheet</b>				
Back of patient <sup>b</sup> (ng/cm <sup>2</sup> )	4	0.56	0.46–0.78	7200 cm <sup>2</sup>
Abdomen of patient <sup>b</sup> (ng/cm <sup>2</sup> )	4	0.50	<0.107–0.72	7200 cm <sup>2</sup>
<b>Vacuum samples</b>				
Pillowcase (ng/cm <sup>2</sup> )	4	0.23	0.04–1.02	5082 cm <sup>2</sup>
Sheet (ng/cm <sup>2</sup> )	4	0.24	0.16–0.42	28 800 cm <sup>2</sup>
<b>Cleaning toilet</b>				
Cleaning water (ng/ml)	2	<0.067		3750 ml
Cleaning cloth (ng/cm <sup>2</sup> )	4	4.80	0.69–8.52	1600 cm <sup>2</sup>

*n*, number of measurements per task.

<sup>a</sup>Cyclophosphamide concentrations in solution is based on the reported formulation by the pharmacy technician.

<sup>b</sup>Corresponds to one-quarter of the bed sheet.

during preparation in the hospital pharmacy and 150–500 times higher than the concentration in the washing water (Table 4). However, the median volume of the washing water handled (2200 ml) was higher than the median volume of the cyclophosphamide solution used during preparation (275 ml) and the volume of urine handled (175 ml). It is important to realize that direct contact with the cyclophosphamide solution during preparation and with urine during decanting urine is minimal, as both fluids are contained within semi-closed containers, while there is almost constant contact between the (covered) hands and the exposure sources (washing water, washing cloth, towel and the patient's skin) during washing of the patient. Similar amounts of cyclophosphamide per square centimetre were found in the washing cloth, towel and pillowcase, and those levels were more than 10 times higher than the levels of contamination per square centimetre found on the front edge of the safety cabinet and on the outer urinal or bedpan (Table 4). All cleaning cloths used for cleaning the patient toilet appeared to be heavily contaminated with cyclophosphamide. The water used to clean the toilet was not contaminated, because the cleaning cloth was not put back into the water after it had been used for cleaning (Table 4). The amount of cyclophosphamide per square centimetre found in the matrix of the pillowcase was

higher than in the accompanying sheet, however, in the vacuum samples from the pillowcase and sheet similar amounts of cyclophosphamide were found per square centimetre (Table 4). No obvious correlations were observed between a patient's sheets, pillowcases, washing water and his or her urine, however, due to the limited number of samples (*n* = 4) no formal statistical evaluations could be made.

## DISCUSSION

This pilot study has clearly shown that pharmacy technicians and oncology nurses are dermally exposed to cyclophosphamide during the performance of their tasks and that cleaning personnel only had detectable levels of cyclophosphamide on the gloves. Exposure occurred predominantly on the hands, sometimes on the forehead and forearms and sporadically on other body locations. A more efficient means of sample collection would therefore be to only collect hand samples (gloves and handwash) together with pads on the forearms and the forehead wipe sample. Using this sampling approach, 87% of the cyclophosphamide contamination on the body would have been detected according to the results from this pilot study. The suggested sampling strategy will reduce the number of samples required

(four instead of nine samples per measurement) and thereby substantially lowers the costs of the analyses.

Two pad samples measured on the back appeared to have detectable levels of cyclophosphamide contamination: one during preparation and one during decanting urine. These contamination levels were very low (0.02 ng/cm<sup>2</sup>/min) and just above the LOD. Since it is unlikely that this contamination was caused by splashing of the cyclophosphamide solution or urine, respectively, during performance of the task, the most likely explanation is that this exposure occurred accidentally from an exposure source that was not related to the task measured.

The level of protection given by protective gloves varied for the different tasks measured. Although the average task duration was almost 2 h, the median level of protection was highest (98.5%) for the preparation of cyclophosphamide, where two pairs of surgical latex gloves (on top of each other) were used and the gloves were very well connected to the apron. The average task duration for decanting urine was no more than 7 min, but the median level of protection was only 19.3%. This might be due to the fact that the forearms of nurses were not covered by clothing and therefore the hands might not have been fully protected by the gloves. Another possible explanation is that gloves were only worn during decanting urine and not during transportation of the urinal or bedpan from the patient's room to the 'washer room'. Therefore, bare hands might have been contaminated before the gloves were put on. The same nitrile rubber gloves were used for washing the patient. While performing this task the gloves were immersed in the washing water (contaminated with cyclophosphamide). The median level of protection for this task still seemed to be quite high (92.4%). A study on permeation of chemotherapeutic drugs through glove materials under static and flexed conditions reported earliest breakthrough times for cyclophosphamide of 10 min for examination gloves (Colligan and Horstman, 1990). This supports the possible penetration of cyclophosphamide during the tasks measured in this project. However, it still does not explain the lower level of protection for decanting the patient's urine.

Since contamination of body parts other than the hands was very low and not detectable more than half of the times the task was measured, uniform exposure of the specified body areas is highly unlikely. Therefore pads probably do not reflect exposure of the whole body surface. As a result, pad sample results were not extrapolated to total body contamination equivalents, because extrapolation of results from the pad samples with a surface area of 100 cm<sup>2</sup> (10 × 10 cm) to the body surface area would under non-uniform conditions lead to unrealistic levels of contamination. Therefore, exposure levels per body location were presented as contamination per square

centimetre per minute. Glove and handwash samples measured the whole surface area of both hands (820 cm<sup>2</sup>) and therefore reflect true exposure of the hands without extrapolation and without assumptions about the distribution of contamination of that body area.

Because most body locations other than the hands appeared to be contaminated once or twice during the preparation of cyclophosphamide, where the work was performed in a laminar down flow safety cabinet under strict conditions, it seems feasible that pad samples would also be contaminated during the nursing and cleaning tasks on the ward. However, because of the lower concentrations of cyclophosphamide in the source samples for these nursing and cleaning tasks, exposure levels might not have reached the LOD.

During removal of bed sheets on the oncology ward no cyclophosphamide was detected on any of the sampling locations, which is probably due to the fact that the cyclophosphamide found on the pillowcase and sheet is not readily available for dermal exposure and/or direct skin contact with highly contaminated areas is consciously avoided. However, cyclophosphamide was detected in all vacuum samples from both the pillowcase and bedsheets. It is therefore conceivable that textile fibres (or other particles) contaminated with cyclophosphamide could become airborne while removing the pillowcases and bedsheets from treated patients. This observation supports the findings in an earlier study, where airborne levels of cyclophosphamide were detected in a patient's room of a nursing clinic while administration of cyclophosphamide had taken place somewhere else (Kromhout *et al.*, 2000). This might indicate that exposure through inhalation for that specific task is more likely than the dermal exposure route.

In conclusion, hospital workers are being dermally exposed to cyclophosphamide during performance of their tasks. Exposure occurred mainly to the hands and sporadically to other body parts as well. Gloves used during preparation were more contaminated than gloves used for other oncology-related tasks in the hospital. Potential dermal exposure of the hands (glove samples) appeared to be correlated with actual exposure of the hands (handwash samples). The results for bulk (fluids) and surface contamination samples confirm that patients i.v. treated with cyclophosphamide excrete part of this drug unmetabolized via their excreta the morning after the drug had been administered. Contact with patient excreta (e.g. urine, faeces and sweat) could therefore lead to significant exposure. These results support the use of protective equipment in hospitals when working with patients treated with antineoplastic drugs, as has been standard procedure in The Netherlands since June 2001. The detection of cyclophosphamide in bed

linen, towels and washing cloths of treated patients and in material used during the cleaning of contaminated places (e.g. patient toilets) points in the direction of other workers either inside or outside hospitals (e.g. laundry workers and waste disposal workers) being potentially exposed to cyclophosphamide.

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