

# Exposure of family members to antineoplastic drugs via excreta of treated cancer patients

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## Abstract

**Purposes:** (a) To measure the urinary excretion of antineoplastic drugs of three patients during 48 h after the administration of cyclophosphamide (two patients) and 5-fluorouracil (one patient). (b) To evaluate environmental contamination with antineoplastic drugs via excreta of patients in the home setting. (c) To evaluate exposure of family members to antineoplastic drugs by measuring the drugs in their urine during the 48 h after completion of the chemotherapy by the patients.

**Methods:** Two patients were administered cyclophosphamide by i.v. bolus injection. One patient was administered 5-fluorouracil by i.v. bolus injection and thereafter immediately administered the same drug by continuous infusion for 46 h. Urine samples from the patients administered cyclophosphamide and their family members, and wipe samples from their home environment, were analysed for the unchanged form of cyclophosphamide. For 5-fluorouracil, the urine samples from the patient and the family member were analysed for the 5-fluorouracil metabolite  $\alpha$ -fluoro- $\beta$ -alanine. Wipe samples were analysed for 5-fluorouracil. Drugs were detected and quantified with gas chromatography in tandem with mass spectrometry-mass spectrometry or by high-performance liquid chromatography with ultraviolet-light detection.

**Results:** A total of 35 and 16 urine samples were collected from the three patients and their family members, respectively. The drugs were detected in all samples.

Cyclophosphamide was detected at levels of 0.03–7.34 ng/cm<sup>2</sup> in 8 of the 12 wipe samples obtained from the homes of the patients administered cyclophosphamide. For the patient administered 5-fluorouracil, drug levels in his home environment were below the limit of detection.

**Conclusion:** We demonstrated contamination of the home setting and exposure of family members to cyclophosphamide via the excreta of outpatient receiving chemotherapy. Exposure of the family member of the patient administered 5-fluorouracil was also demonstrated. These findings indicate the importance of strict precautions by the members of treated cancer patients as well as healthcare workers, to reduce the risk of exposure to antineoplastic drugs.

## Keywords

Drug exposure, antineoplastic agents, drug contamination, cyclophosphamide, 5-fluorouracil

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## Introduction

With the development of antineoplastic drugs, the treatment of malignant tumours has been advancing rapidly. Antineoplastic drugs primarily exert cytotoxic effects on tumour cells, but often also affect normal cells. In other words, most antineoplastic drugs are harmful to all cells in cancer patients, causing both beneficial and toxic effects. These drugs not only exert therapeutic effects in cancer patients but also have the potential to harm healthcare workers who prepare and administer antineoplastic drugs, such as pharmacists and nurses, as a result of occupational exposure to these drugs. To date, numerous studies have demonstrated the occurrence of adverse effects due to occupational exposure to antineoplastic drugs, including acute allergic reactions, carcinogenicity, genotoxicity, fetal abortion and congenital anomalies.<sup>1-13</sup>

Antineoplastic drugs are classified as hazardous drugs that exhibit cytotoxicity. Various guidelines have been issued to ensure their safe use (National Institute for Occupational Safety and Health;<sup>14</sup> Occupational Safety and Health Administration;<sup>15</sup> American Society of Health System Pharmacists;<sup>16</sup> Oncology Nursing Society;<sup>17</sup> Health, & Safety Executive<sup>18</sup>). The guidelines recommend adopting preventive measures for 48 h after drug administration, because the unchanged form of an administered cytotoxic antineoplastic drug (or its active metabolites) may be part of the substances excreted by the patient. The guidelines also stress that drug-specific durations are desirable, as the duration of excretion of hazardous drugs varies. These guidelines also recommend that one should wear protective clothing/equipment (gloves, gown, goggles and a face shield if any scattering of bodily fluids is likely) while handling urine, faeces, blood or vomitus. Furthermore, these guidelines state that caution should be exercised during flushing the toilet (performed twice) after appropriately placing the toilet seat cover following disposal of the excreta of the patients administered cytotoxic drugs within the previous 48 h. However, no studies have provided evidence supporting the efficacy of flushing the toilet twice.

The aforementioned guidelines<sup>14-18</sup> provide an outline for procedures, which healthcare professionals, janitorial staff and the family members of patients should conform to, in the hospital and at home.

The administration of chemotherapy in the hospital setting is different from that of an outpatient setting. Administration methods for outpatient chemotherapy (such as FOLFOX and FOLFIRI) include bolus i.v. administration of an antineoplastic and also continuous infusion of 5-fluorouracil (5-FU) for approximately 46 h. In the latter case, the antineoplastic drug is continuously administered over a long period of time

including while the patient is at home. This further increases the risk of exposure of the patient's family members and associates to the antineoplastic drug via the patient's excreta. Following outpatient chemotherapy administration, cancer patients spend most of their time at home or in the workplace. The exposure of the associates of a cancer patient to an antineoplastic drug via the patient's excreta can negatively affect their health, similarly as in the case of occupational exposure to these hazardous drugs. Thus, it is necessary to consider that the people at risk of exposure to antineoplastic drugs not only include healthcare workers but also the family members and associates of the patient. As far as we know, no papers have published the antineoplastic drug contamination of the homes of cancer patients via their excreta, and at present, it remains unclear whether the family members of these patients are exposed to these drugs.

The present study was conducted with the following three objectives: (a) to measure the urinary excretion of antineoplastic drugs of three treated patients during 48 h after the administration of cyclophosphamide (CPM; two patients) and 5-fluorouracil (5-FU; one patient); (b) to evaluate environmental contamination with antineoplastic drugs via excreta of patients in the home setting and (c) to evaluate exposure of family members to antineoplastic drugs by measuring the drugs in their urine during the 48 h after completion of the chemotherapy by the patients.

The antineoplastic drugs used in the current study have been extensively and frequently used in therapy. CPM has been used for adjuvant chemotherapy after breast cancer surgery. During chemotherapy, patients receive a bolus i.v. dose of CPM once every 3 to 4 weeks for several cycles at an outpatient facility. CPM is an alkylating agent, which is converted to its active metabolite, phosphoramidate mustard, and has been classified as a genotoxic carcinogen in humans by the International Agency for Research on Cancer.<sup>19</sup> 5-FU is used to treat colon cancer. For FOLFOX and FOLFIRI therapies using 5-FU, patients are first administered a bolus i.v. dose of 5-FU at an outpatient facility, followed by continuous i.v. infusion for 46 h. This procedure is repeated every 2 weeks. 5-FU is administered by continuous i.v. infusion, making it necessary to manage long-term administration of the drug in a patient's home, which increases the risk of exposure of the family members and associates of the patient.

## Patients and methods

Three cancer patients who were receiving chemotherapy at the Outpatient Chemotherapy Center of

University Hospital A in Japan were enrolled in this study. Each patient and their family members provided informed written consent to participate in the study. The antineoplastic drug administered in Patients 1 and 2 was CPM and in Patient 3 was 5-FU.

### Case 1

Patient 1 was a 58-year-old female diagnosed with breast cancer. This was her third course of chemotherapy, and she was administered CPM 700 mg ( $500 \text{ mg m}^{-2}$ ) via an i.v. bolus on an outpatient basis. Her husband (Family Member 1), who was in his 60s, underwent biological monitoring to measure CPM in his urine. Her husband was mandatorily retired and was often away from home pursuing his hobbies. Hence, his urine samples were collected only when he was at home during the 48-h post-administration period.

### Case 2

Patient 2 was a 44-year-old female diagnosed with breast cancer. This was her fifth course of chemotherapy, and she was administered CPM 712 mg ( $500 \text{ mg m}^{-2}$ ) via an i.v. bolus on an outpatient basis. CPM was measured in the urine of her husband (Family Member 2), who was in his 40s. The husband was away from home, at work, during the day and therefore, his urine samples were collected only during the time when he was at home, from approximately 19:00 in the evening until about 7:00 in the morning when he left for work (on two consecutive days).

### Case 3

Patient 3 was a 78-year-old male diagnosed with rectal cancer who had undergone a colostomy. This was his eighth course of chemotherapy, and he was administered 5-FU 549 mg ( $400 \text{ mg m}^{-2}$ ) via an i.v. bolus on an outpatient basis. Immediately thereafter, a continuous i.v. infusion of 5-FU 3293 mg was initiated that lasted 46 h.

The patient's wife (Family Member 3) was in her 70s and her urine samples were analysed for  $\alpha$ -fluoro- $\beta$ -alanine (FBAL). The wife remained at her husband's side throughout his outpatient treatment. At home, both the patient and his wife spent most of their time at a small table in their living room, including sleeping at the same site each night in Japanese-style beds. Their toilet was Japanese style, having no toilet seat lid. The collection of the wife's urine samples was stopped at 32 h due to personal circumstances.

The performance status was Grade 0 for all patients according to the Eastern Cooperative Oncology Group criteria.<sup>20</sup>

This survey was conducted with the approval of the Ethics Committee of Fukushima Medical University.

### Urine sampling (biological monitoring) and wipe sampling (environmental monitoring)

After each patient completed outpatient chemotherapy in the hospital, the surveyor visited their homes and repeated the explanations of these tests and the urine sample collection method to the patients and their family members. A second visit was made to each patient's home 48 h after the completion of outpatient chemotherapy, during which time wipe sampling of the home environment was performed and the urine samples were collected.

Each patient and family member collected their own urine samples during the 48-h post-administration period. Each patient and family member was responsible for recording the frequency and time of voiding and measuring the urinary output at each urination. Ten millilitres of urine were collected (urine sample kit provided) and stored in a small freezer solely used for this purpose.

Wipe surveys were conducted in the homes of the three cancer patients to clarify the status of drug contamination during 48 h after administration. The surveyor visiting the patients' homes asked them how many times they had urinated and defecated after administration, and asked for information about vomiting, if occurred.

The surveyor identified possible areas of drug contamination based on the answers provided by each patient and conducted wipe surveys of these areas. The wipe samples were taken from 17 areas in the homes of the three patients. The areas from which wipe samples were taken included the toilet seat, toilet seat cover, flush handle, toilet door knob, floor around the toilet, toilet paper holder, toilet handrail and sink faucets. The wipe samples were collected in the following manner. After measuring the size of each target area, 17 mL of a 0.03 M NaOH solution were applied to each target area using a wipe kit to detect CPM and 5-FU. For target areas that were not flat, the solution was poured over the area and subsequently, the samples were collected using two pieces of nonwoven cloth, placed at a downhill location to soak up the solution.

All urine and wipe samples were immediately stored frozen at  $-20 \text{ C}$  after sampling and during transport until sample preparation and analysis by Exposure Control Sweden AB (Bohus-Björkö, Sweden). The urine and wipe samples were collected using Cyto Urine kits and Cyto Wipe kits with Exposure Control Sweden AB. The methods to collect, store and exact

urine sampling and wipe sampling were performed according to standard procedures.<sup>21-25</sup>

### Analyses of the samples

Analyses were performed to detect the unchanged form of CPM in the urine samples of the patients administered CPM and their family members, and in the wipe samples from their home environment. Analyses were performed to detect FBAL in the urine samples collected by the patient administered 5-FU and his family member. Wipe samples were analysed for 5-FU.

The wipe samples were prepared for analysis by adding a 0.03 M NaOH solution (total volume: 160 mL). After extraction, a portion of the extract was further purified according to the standard procedure.<sup>21-25</sup> The contamination per square centimetre was calculated by assuming 100% recovery and wipe efficiency. The limits of detection of CPM and 5-FU were 0.1 and 20 ng/mL NaOH, respectively.

The sample volume used for the determination of CPM and FBAL in urine was 5 mL. The limits of detection of CPM and FBAL were 0.01 and 5 ng/mL urine, respectively.<sup>21-25</sup>

CPM and FBAL were analysed with gas chromatography in tandem with mass spectroscopy-mass spectroscopy and 5-FU was analysed by high-performance liquid chromatography with ultraviolet-light detection.<sup>21-25</sup>

### Results

There were 35 and 16 urine samples collected for the three patients and their family members, respectively. Antineoplastic drugs were detected in all samples.

For Case 1, patient 1 urinated eight times (total volume: 1870 mL) and defecated twice during the 48-h post-administration period (Figure 1). The detected amount of CPM per urine sample ranged from 0.04 to 62.64 mg. The highest CPM excretion occurred at 3 h after drug administration. Thereafter, the amount excreted decreased gradually over time to 0.04 mg in the final urine sample. The total amount of CPM excreted in the urine during the 48-h post-administration period was 170.10 mg, representing 24.3% of the total administered dose.

Family Member 1 collected five urine samples (total volume: 1800 mL) during the 48-h post-administration period. CPM was detected in all samples. The detected amount of CPM per urine sample ranged from 24.0 to 35.0 ng, and the total detected amount was 152.0 ng.

For Case 2, patient 2 urinated 12 times (total volume: 1830 mL) and defecated twice during the 48-h post-administration period (Figure 2). The amount of CPM per urine sample ranged from 0.30 to 32.84 mg. The total amount of CPM during the 48-h post-administration period was 140.93 mg, representing 19.8% of the total administered dose.

Family Member 2 collected four urine samples (total volume: 900 mL) during the 48-h post-administration period. CPM was detected in all samples. Urine CPM levels ranged from 0.07 to 0.65 mg, and the total amount detected in the four samples was 1.81 mg.

For Case 3, patient 3 urinated 15 times (total volume: 1240 mL) during the 48-h post-administration period following outpatient 5-FU administration (including continuous infusion of 5-FU for 46 h) (Figure 3). This patient had a colostomy bag. The amount of FBAL per urine sample ranged from

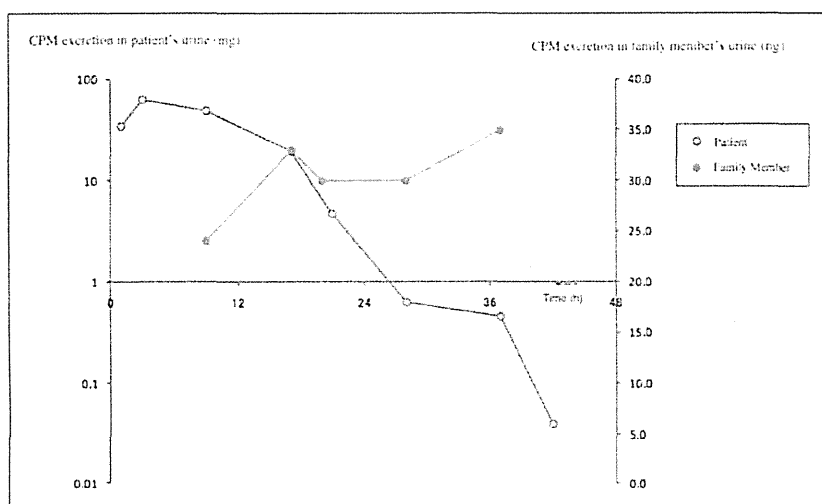


Figure 1. Time-course profiles of CPM excretion in urine samples of Patient 1 and Family Member 1. CPM: cyclophosphamide.

0.1 to 2.2 mg. The total amount of FBAL excreted in the urine was 16.9 mg, comprising 0.44% of the total administered dose.

Family Member 3 urinated eight times (total volume: 1120 mL) during the 32-h monitoring period. The amount of FBAL per urine sample ranged from 19.0 to 117.0  $\mu\text{g}$ ; the total amount in the urine was 421.0  $\mu\text{g}$ .

The results from the wipe samples are presented in Table 1. For Case 1, wipe samples from four out of six

positions were positive for CPM contamination. Of these areas, samples taken from the sink faucets and toilet seat exhibited the highest level of contamination of 3.02 and 0.57  $\text{ng}/\text{cm}^2$ , respectively. The level of contamination on the floor around the toilet and toilet door knob was 0.03 and 0.09  $\text{ng}/\text{cm}^2$ , respectively.

For Case 2, CPM contamination was detected on four out of the six positions. The levels of contamination were between 0.18 and 7.34  $\text{ng}/\text{cm}^2$ . The toilet seat was the most contaminated position.

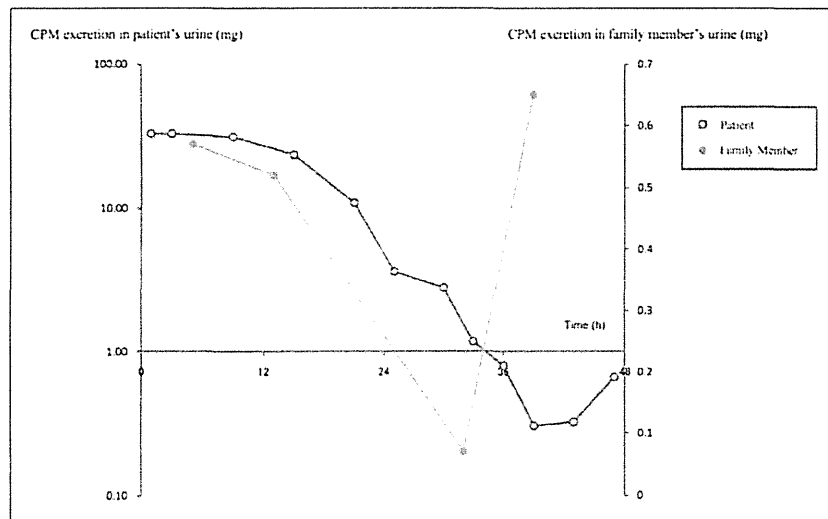


Figure 2. Time-course profiles of CPM excretion in urine samples of Patient 2 and Family Member 2. CPM: cyclophosphamide.

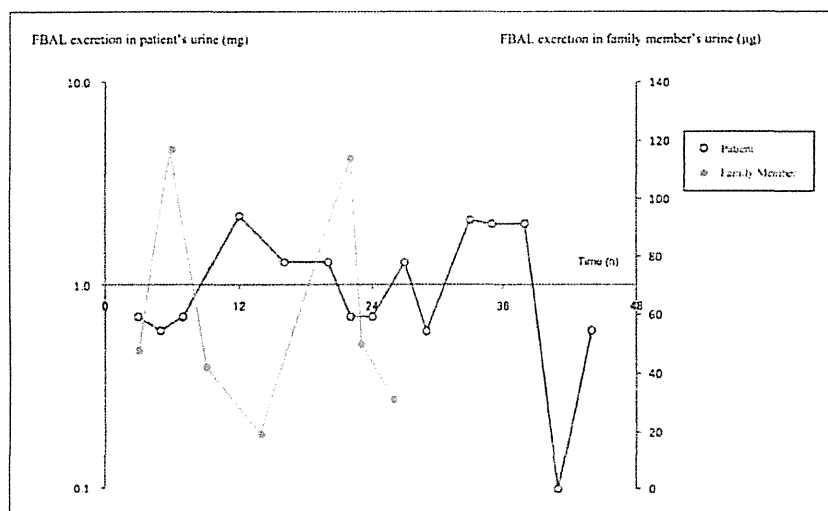


Figure 3. Time-course profiles of FBAL excretion in urine samples from Patient 3 and Family Member 3. FBAL:  $\alpha$ -fluoro- $\beta$ -alanine.

**Table 1.** Wipe test results: Surface levels of CPM and 5-FU.

	Surface description	Surface area (cm <sup>2</sup> )	CPM (ng/mL NaOH)	CPM (ng)	CPM (ng/cm <sup>2</sup> )
Case 1	Toilet seat	1960	7.03	1125	0.57
	Control panel	490	ND	–	–
	Flush handle	30	ND	–	–
	Toilet door knob	319	0.18	29	0.09
	Toilet floor	4000	0.63	101	0.03
	Sink faucets & surroundings	208	3.93	629	3.02
Case 2	Toilet seat	700	32.12	5139	7.34
	Toilet seat cover	1440	2.01	322	0.22
	Flush handle	100	ND	–	–
	Toilet door knob	260	0.30	48	0.18
	Toilet floor	1000	1.16	186	0.19
	Sink faucets & surroundings	100	ND	–	–
	Surface Description	Surface area (cm <sup>2</sup> )	5-FU (ng/mL NaOH)	5-FU (ng)	5-FU (ng/cm <sup>2</sup> )
Case 3	Toilet seat	3200	ND	–	–
	Toilet handrail	210	ND	–	–
	Toilet door knob	225	ND	–	–
	Portable pail	400	ND	–	–
	Paper holder	150	ND	–	–

CPM: cyclophosphamide; 5-FU: 5-fluorouracil; NaOH: sodium hydroxide; ND: not detected (CPM  $\geq$  0.10 ng/mL NaOH, 5-FU  $\leq$  20 ng/mL NaOH).

The level of contamination on the toilet seat cover, floor around the toilet and toilet door knob was 0.22, 0.19 and 0.18 ng/cm<sup>2</sup>, respectively.

For Case 3, wipe samples were taken from five positions and the level of 5-FU was below the limit of detection at each site.

None of the three patients vomited during the 48-h post-administration period.

## Discussion

The present study assessed the amount of cytotoxic drug excreted in the urine of patients and their cohabiting family members during 48 h after the patients have received chemotherapy in an outpatient setting. The study also demonstrated environmental contamination with antineoplastic drugs at patients' home via excreta of the treated patients.

The percentage of the dose unchanged CPM in the urine of patients 1 and 2 during the 48-h post-administration period was approximately 24 and 19, respectively. According to previous studies, the percentage of CPM excreted in the urine during the 24-h period after CPM administration ranged from approximately 14 to 20 of the administered dose.<sup>26,27</sup> Moreover, the present study demonstrated that CPM continued to be excreted at low levels in the urine of treated patients for at least 48 h after administration. Bagley et al.<sup>28</sup> injected radiolabelled CPM by i.v. and found that 62% of the

administered dose was excreted in the urine within 2 days, whereas 1.8% and 1.2% were excreted in the faeces and expired air within 4 days after dosing, respectively.

Another important finding of the present study is that the administered cytotoxic drugs were detected in all urine samples collected by each cohabiting family member. Although the family members did not receive chemotherapy, CPM was detected in their urine samples collected during the post-administration period, indicating exposure to CPM. All five urine samples collected by Family Member 1 tested positive for CPM (range: 24.0–35.0 ng). However, urine samples were collected by Family Member 1 only when he was at home and thus, the number of samples was approximately half of the expected number. Therefore, it can be surmised that the actual level of exposure to the drug was higher than measured. Similarly, Family Member 2 collected four urine samples during the time that he was at home, and CPM was detected in all samples. The present study is the first to demonstrate CPM exposure of a family member of a patient at home.

The time-course profiles of CPM excretion in the urine of the Family Members 1 and 2 was also an interesting observation. Although the amount of CPM excreted by Patients 1 and 2 decreased over time following patient treatment, the urinary drug excretion remained fairly constant in Family Member 1, whereas it gradually decreased in Family Member 2, only to

rebound to a higher excretion later. These time-course profiles of CPM excretion by the family members can be ascribed to their continued exposure to the drug in their homes. Previous studies found that urinary CPM excretion by patients peaked at approximately 6–10 h after administration,<sup>29,30</sup> whereas in patients 1 and 2, the peaks occurred at approximately 3 h following administration. On the other hand, the time-course profiles of CPM excretion in the urine of the family members exhibited no clear peaks during the 48 h of monitoring.

In several studies, exposure to CPM was investigated using the urinary excretion of CPM as a biomarker. The mean amounts of CPM detected in the urine of workers due to occupational exposure were 5.2  $\mu\text{g}/\text{day}$  in pharmacy personnels/nurses,<sup>31</sup> 1.36  $\mu\text{g}/\text{day}$  in pharmacy technicians,<sup>32</sup> 0.79  $\mu\text{g}/\text{day}$  in nurses, pharmacy technicians/cleaning women,<sup>33</sup> 0.47  $\mu\text{g}/\text{day}$  in nurses,<sup>34</sup> 0.39  $\mu\text{g}/\text{day}$  in hospital workers,<sup>35</sup> 0.18  $\mu\text{g}/\text{day}$  in pharmacy technicians<sup>36</sup> and 0.05  $\mu\text{g}/\text{day}$  in pharmacy technicians/nurses.<sup>22</sup> It can be assumed that the variation in these values reflects differences in the occupations and strict observance of precautions to prevent exposure to antineoplastic drugs. However, in our study, it is noteworthy that higher levels of CPM were detected in the urine samples of family members than in those of healthcare workers. Moreover, there is an important difference in the route of exposure to cytotoxic drugs between the previous reports and the present study. That is, in the case of healthcare workers, direct exposure via inhalation, skin contact, skin absorption and/or oral intake occurs during handling of the drugs. On the other hand, exposure of the family members at home occurred via contact with patient excreta containing the drug.

We estimated the areas in the patients' homes where CPM would likely be present. Our efforts at detecting the drug successfully confirmed the extent and level of CPM contamination in the home environment. Drug contamination was confirmed at four areas for both Patients 1 and 2. The areas with the highest levels of CPM contamination were the toilet seat, floor around the toilet, toilet door knob and sink faucets.

Yuki et al.<sup>37</sup> investigated CPM contamination in the homes of five female patients with breast cancer at 48 h after outpatient bolus i.v. administration of the drug. CPM was detected in 17 of 30 samples taken from the target areas. The toilet seat was contaminated by CPM in all the cases, and it also had the highest level of contamination ranging from 0.04 to 8.35  $\text{ng}/\text{cm}^2$ . CPM contamination was also confirmed for the floor around the toilet (0.19–1.53  $\text{ng}/\text{cm}^2$ ), toilet door knob (0.79  $\text{ng}/\text{cm}^2$ ) and toilet seat lid (0.22  $\text{ng}/\text{cm}^2$ ). The sites and levels of CPM contamination in "patients' homes" and the "dose of unchanged CPM" in this study are similar to those reported by Yuki et al.<sup>37</sup>

In the US and Europe, reports have documented the detection of antineoplastic drugs in surface wipe examination of the handling sites of antineoplastic drugs in hospitals.<sup>38–41</sup> The present survey data cannot be compared with those from previously reported studies since no previous study has investigated antineoplastic drug contamination in the home environment of cancer patients receiving outpatient chemotherapy. In Japan, the values obtained from two surveys conducted to assess the extent of environmental CPM contamination in hospitals via the same wipe test method used in the present study were used as reference values. In the study conducted by Tanimura et al. involving six target areas in the chemotherapy preparation room, CPM contamination was demonstrated at levels of 0.01–0.09  $\text{ng}/\text{cm}^2$  in all six target areas in the first wipe test.<sup>42</sup> Sugiura and colleagues performed a survey of environmental CPM contamination at six hospitals in Japan and reported low contamination levels of  $\leq 0.1 \text{ ng}/\text{cm}^2$  in the outpatient chemotherapy room, 0.01  $\text{ng}/\text{cm}^2$  on the table used for handling antineoplastic drugs and 0.04  $\text{ng}/\text{cm}^2$  on the floor under the drip in the fusion stand at half of the hospitals studied.<sup>43</sup> Compared with the results reported by these two studies, the CPM contamination levels detected in the present study were significantly greater, indicating a higher degree of environmental CPM contamination in the outpatient setting than in hospitals.

The high values of our findings for CPM contamination of the toilet seats, sink faucets, floor around the toilet and toilet door knobs at the patients' home indicate that urine and faeces of the patients containing CPM contaminated the toilet environment due to splattering, and that this was further spread via the patients' hands, which had been contaminated during the process of cleaning themselves after urination/defecation. Variable amounts of hazardous drugs and their metabolites are excreted in the urine, stool, sweat and other bodily excreta of patients receiving the drugs.<sup>17</sup> Bed sheets of patients who were treated with CPM appeared to be contaminated by the drug.<sup>44</sup> Thus, we can surmise that they were repeatedly exposed to the drug.

Patient 3 was administered 5-FU via an i.v. bolus on an outpatient basis and then immediately started on a continuous i.v. infusion of 5-FU that lasted 46 h. The amount of FBAL per urine sample ranged from 0.1 to 2.0 mg. The total amount of FBAL excreted in the patient's urine during the 48-h post-administration period represented 0.44% of the total administered dose. FBAL was also detected in all urine samples collected by Family Member 3, demonstrating that she had been exposed to the 5-FU excreted by Patient 3. The concentration of FBAL excreted in the urine of Family Member 3 fluctuated greatly during the sampling period, and the total amount collected over a

32-h period was 421.0 µg. Several studies investigated the exposure of hospital workers and pharmacy technicians to 5-FU using the urinary excretion of FBAL as a biomarker. Two studies of pharmaceutical plant workers involved in the production of 5-FU found their levels of urinary FBAL excretion to be 12.5<sup>23</sup> and 56.3 µg/day.<sup>25</sup> The amount of FBAL excreted in the urine of Family Member 3 was higher than that reported previously and was even higher than the exposure of pharmaceutical plant workers dealing directly with 5-FU.

5-FU contamination of all wiped sites in the home of Patient 3 was below the limit of detection. Nevertheless, Family member 3 was exposed to the drug. Flushing the toilet has shown to produce aerosols of microbial agents. It is assumed that chemicals can also be spread in this manner, particularly in toilets without covers. A previous study indicated that splashing or aerosol generation during toilet flushing may spread infectious particles onto contact surfaces such as toilet seats or flush handles.<sup>45</sup> Therefore, aerosols produced by flushing of domestic toilets may be an important route of exposure to family members.

As described previously, our present study demonstrated that family members of cancer outpatients being administered CPM or 5-FU experienced exposure to these antineoplastic drugs in their homes and that the patients' homes were contaminated via their bodily excretions containing CPM. Several published guidelines directed at healthcare workers provide practical methods for handling excretory products of patients administered antineoplastic drugs. The guidelines were created mainly from the standpoint of occupational safety with regard to preventing the on-the-job exposure of healthcare workers who handle antineoplastic drugs and/or work with the patients who receive them. The guidelines stipulate procedures for healthcare workers in hospitals and institutions. Persons handling the excreta of patients receiving antineoplastics or equipment soiled by the excreta may be exposed to cytotoxic contamination. Instructions should be given on how to keep toilets in the patient's home free of antineoplastic material.<sup>46</sup> However, in Japan, patients at home rarely use disposable gloves and gowns when handling potentially contaminated urine, faeces, vomit or excreta. This reflects the inadequate education of patients and their families regarding preventive measures for exposure to antineoplastic drugs. Some patients will be treated several times with this treatment protocol and could repeatedly expose family members.

Furthermore, in patients' homes, only flushing the toilet twice is inadequate for preventing exposure to antineoplastic drugs. It will at least be necessary to apply measures to prevent drug contamination of the

toilet environment, including the toilet seat, floor around the toilet, toilet door knob and washbasin, as well as to take precautions when handling clothing and linen that have been in contact with the patient's urine and other body fluids. There is also a need to develop and adhere to appropriate measures for preventing exposure of the patients' family members and associates to antineoplastic drugs. The existing guidelines need to be modified to include the home environment while framing the guidelines to protect family and friends from exposure to antineoplastic drugs.

## Conclusions

Contamination of the home environment of two cancer patients administered CPM outpatient was demonstrated at 48 h after administration. Three family members of the patients administered CPM or 5-FU were exposed at home by contaminated excreta from the patients. Outpatient administration of antineoplastic drugs can be expected to become more pervasive in the future. The present findings show the need for additional measures to prevent healthcare workers and family members of patients from exposure to antineoplastic drugs.

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## Conflict of interest

Authors declare that there is no conflict of interest.

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