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The efficiency of protective gloves used in the handling of cytotoxic drugs

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Summary. *A range of clinical and industrial gloves have been evaluated to determine their ability to exclude penetration by cytotoxic drugs.*

Radiolabelled cyclophosphamide, methotrexate, daunomycin, cytosine arabinoside, and vincristine sulphate were studied in an equilibrium dialysis system in which the glove material was used as the dialysis membrane.

The thicker gloves were the most effective, but very little drug crossed any of the gloves tested under laboratory conditions. Further studies to evaluate gloves in conditions of clinical use are now needed.

Introduction

The potential dangers associated with the handling of cytotoxic drugs are causing increasing concern [3]. Many antitumour agents demonstrate both mutagenic and carcinogenic activity [5]. Cytotoxic drugs, especially alkylating agents, have been associated with the development of second malignancies when given to patients in therapeutic doses [4].

Recent studies have shown that nurses handling cytotoxic drugs may develop evidence of mutagens in the urine, as detected by the Ames or the fluctuation test [1, 2]. While there is considerable controversy about the significance of these results, the possibility of personnel being exposed to significant, albeit small, quantities of these drugs is worrying. It has been suggested that the use of vertical laminar flow cabinets may provide protection against contamination with cytotoxic drugs [1]. Whether it is possible to administer cytotoxic drugs safely using only protective clothing and careful technique, but excluding vertical laminar flow, has yet to be established.

The commonest protective measure against contamination by cytotoxic drugs is the use of surgical gloves. However, the protection afforded by commonly used surgical gloves has been questioned [6].

The present study was conducted because of the considerable anxiety about the ability of gloves used in clinical practice to provide protection against contamination by cytotoxic drugs and the absence of any quantitative data to support or refute this concern. To assess the possible importance of glove material and thickness two types of industrial gloves were also included.

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Table 1. Concentrations of cytotoxic drugs

Radioactive drug	Specific activity of radioactive drug	Total drug concentration
1. [Ring-4-^{14}C] Cyclophosphamide	52.5 mCi/mmol	20 mg/ml
2. [5-^{3}H]Cytosine *B*-D-arabinoside	11.2 Ci/mmol	20 mg/ml
3. [G-^{3}H]Vincristine sulphate	4.3 Ci/mmol	0.1 mg/ml
4. [3′5′7-^{3}H]Methotrexate	19.0 Ci/mmol	10 mg/ml
5. [G-^{3}H]Daunomycin	4.34 Ci/mmol	2.4 mg/ml

Materials

Gloves. Six types of gloves were studied:
1) Polyvinyl chloride (PVC) (Triflex Gloves by Travenol); 2) Latex (Searle Medical Gloves by Franklin Medical); 3) Latex (Regent Dispo Surgeons' Gloves by LRC Products); 4) Solution rubber (Surgeons' Gloves by Purittee Medical); 5) Latex with neoprene (Marigold Industrial Featherweight Plus Gloves); 6) Nitrile synthetic rubber (Marigold Industrial Gloves).

Cytotoxic drugs. Five cytotoxic drugs were used (Table 1). It was not possible to obtain radiolabelled nitrogen mustard, but a range of commonly used cytotoxic drugs, including an alkylating agent, a vinca alkaloid, an anthracycline antibiotic, and two antimetabolites, was studied.

Labelled cyclophosphamide and daunomycin were obtained from New England Nuclear and all other drugs from Amersham International. Details of the radiolabelled and cold drugs used are given in Table 1. The total drug concentrations were those most commonly used in clinical practice.

Methods

Radiolabelled drug was dialysed against phosphate-buffered saline (pH 7.3), using a circular disc of single-thickness glove material as the dialysis membrane between acrylic dialysis cells. Radiolabelled drug was added to the reconstituted drug solution giving radioactivity of about 200 nCi/ml. The compartment facing the outside surface of the glove membrane was filled with 1 ml drug solution containing the corresponding labelled drug, while the other compartment was filled with 1 ml

phosphate-buffered saline. Four replicate assays were performed for each type of glove and each drug. The dialysis cells were allowed to equilibrate, with rotation to ensure constant mixing, at room temperature for 1 h. (The external surface of a surgical glove when worn is at approximately room temperature.) The disintegrations per minute (DPM) in the drug and the buffer dialysates were measured using a Packard PRIAS PLD liquid scintillation counter. The amount of penetration of the drug through the glove membrane into the buffer was expressed as the percentage of buffer DPM/drug DPM. No attempt was made to assess different degrees of stretching or to simulate the movement present in the clinical situation.

Results

The percentage transfer of each drug across each glove is shown in Table 2. In each case the amount of drug that crossed into the buffer was considerably less than 0.05%. The data is graphically presented in Fig. 1. There was a significant inverse relationship between glove thickness and the degree of penetration by the cytotoxic drugs (Spearman's rank correlation coefficient 0.857, $P < 0.01$). There was also a difference in the degree with which individual drugs penetrated the gloves. Methotrexate and daunomycin crossed the gloves to a greater extent than the other drugs tested ($P < 0.05$).

Table 2. Percentage penetration of drugs into buffer (in hundredths of 1%)

Drug[a]	Mean (SD)					
	PVC	Searle latex	Regent latex	Solution rubber	Latex with neoprene	Nitrile
Cyclo.	0.73 (0.30)	0.76 (0.17)	0.75 (0.25)	0.66 (0.28)	0.58 (0.23)	0.15 (0.10)
AraC.	1.20 (0.15)	1.09 (0.26)	0.79 (0.27)	0.88 (0.10)	0.57 (0.23)	0.94 (0.10)
Vinc.	1.33 (0.04)	1.52 (0.44)	0.84 (0.28)	0.48 (0.20)	0.40 (0.38)	0.54 (0.24)
Metho.	3.54 (1.28)	2.19 (0.57)	1.22 (0.51)	0.86 (0.62)	0.85 (0.21)	0.61 (0.21)
Daunomycin	2.51 (0.38)	1.80 (0.46)	2.30 (0.27)	2.83 (0.17)	0.96 (0.43)	1.41 (0.21)
Mean	1.86	1.47	1.18	1.14	0.67	0.73
SD	1.14	0.57	0.65	0.96	0.23	0.47

[a] Cyclo., cyclophosphamide; AraC., cytosine arabinoside; Vinc., vincristine; Metho., methotrexate

Discussion

The results of this study show little penetration by cytotoxic drugs through a wide variety of surgical gloves. This is in contrast to the data reported by Thomsen et al. [6], who tested drug penetration indirectly by assessing the degree of protection afforded by various gloves against a skin reaction in patients sensitised to nitrogen mustard. These studies suggested that gloves made of polyvinyl chloride gave better protection than rubber or polyethylene gloves. However, the amount of drug requires to cause an allergic reaction may be minute and it is impossible to quantitate the degree of drug penetration. It is also possible that the gloves themselves contributed to this reaction. This study is limited further by the inclusion of only four patients.

The data presented here show low levels of penetration with all the gloves tested, and do not support the suggestion that PVC gloves provide better protection than other commonly used clinical gloves. The conditions, though artificial, did allow the drug to be in constant contact with the gloves for 1 h, a duration of contact considerably greater than is likely to occur even in the event of massive spillage. On the other hand, it is possible that intermittent stretching and prolonged usage such as might occur in clinical practice would lead to increased penetration.

The extent to which cytotoxic drugs may be absorbed through the skin is unknown and there are no acceptable levels of contamination. Whether the protection afforded by gloves is sufficient must therefore be open to conjecture. However, clearly, personnel should be protected to the highest possible standard and the use of protective gloves considered essential.

Adequate quality control is essential in the manufacture of gloves to be used for the handling of cytotoxic drugs. It is suggested that more extensive studies be carried out to assess the within- and between-batch variation and to exclude the

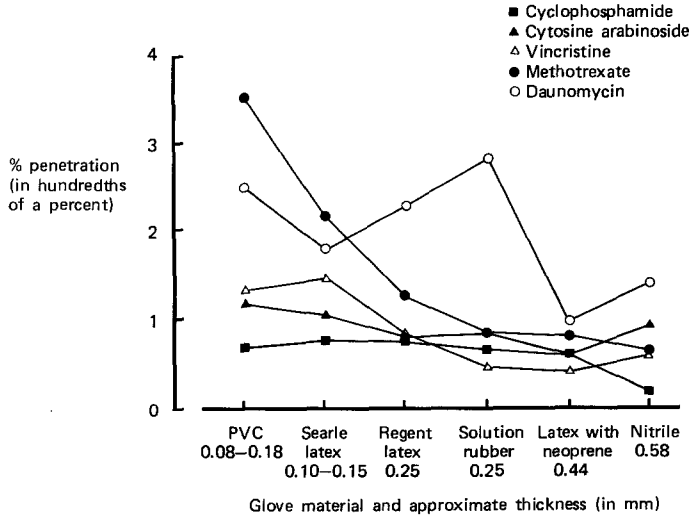

Fig. 1. Drug penetration through gloves

possibility that further glove penetration may occur under conditions of clinical use and with drugs not studied here. Such information should be available on product information sheets supplied with the gloves.

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