Information provided by pharmaceutical companies in respect of handling and disposal of cytotoxic drugs

Drug	Preparation suggestions	Laminar flow cabinet	Waste disposal	Incineration data
Daunorubicin (Cerubidin)	No	No	No	No
Dacarbazine (DTIC)	Yes	No	No	No
Vindesine (Eldisine)	Yes	No	No	No
5-Fluorouracil (Fluoro-uracil)	No	No	No	No
Mithramycin (Mithracin)	No	No	No	No
Mitomycin (mitomycin C, Kyowa)	No	No	No	No
Mustine hydrochloride (Mustine)	Yes	No	No	No
Cyclophosphamide (Endoxan-Asta)	No	No	No	No
Doxorubicin (Adriamycin)	Yes	No	Yes	Yes
Cytarabine (Cytosar-U)	No	No	No	No
Actinomycin D (Cosmegen)	No	No	No	No
Etoposide (Vepesid)	Yes	No	Yes	Yes
Teniposide (Vumon)	No	No	No	No
Vinblastine (Velbe)	Yes	No	No	No
Vincristine (Oncovin)	No	No	No	No
Thiotepa (Lederle)	No	No	No	No
Cisplatin (DBL)	No	No	No	No
Cisplatin (Platinol)	Yes	No	No	No
Cisplatin (Platamine)	No	No	No	No
Bleomycin (Blenoxane)	No	No	No	No
Methotrexate (Lederle)	No	No	No	No
Methotrexate (DBL)	No	No	No	No
Carbustine (Bicnu)	Yes	No	No	No
Amsacrine (Amsidyl)	Yes	No	No	No

Comment

It is certainly true that the clinical responsibilities associated with the use of cytotoxic agents lie with the prescribers—the oncologists. This is accepted. But would it not be appropriate for those who manufacture these agents to assume some responsibility? Should not the pharmaceutical companies who provide these agents offer practical advice on preparation and disposal problems? These companies presumably have access to the requisite scientific data and probably utilise them in the manufacturing and packaging processes. Might they not disseminate this information so that the pharmacists, nurses, and doctors at risk could make appropriate adjustments in their clinical practice? The drug packaging inserts would be an obvious place for this advice.

- 1 Harris CC. The carcinogenicity of anticancer drugs: a hazard in man. *Cancer* 1976;37:1014-23.
- 2 Reich SD. Antineoplastic agents as potential carcinogens: are nurses and pharmacists at risk? *Cancer Nursing* 1981; December: 500-2.
- 3 Knowles RS, Virden JE. Handling of injectable antineoplastic agents. *Br Med J* 1980;281:589-91.
- 4 Hillcoat BL, Levi J, Snyder R. Preparation and administration of antineoplastic agents. *Med J Aust* 1983;i:424-8.
- 5 Society of Hospital Pharmacists of Australia. Guidelines for safe handling of cytotoxic drugs in pharmacy departments and hospital wards. *Australian Nurses Journal* 1981;11(2):12-8.

(Accepted 24 July 1985)

University Department of Medicine and Department of Clinical Oncology, Christchurch Hospital, Christchurch, New Zealand

B M COLLS, FRACP, FRCP, associate professor in medicine and medical oncologist

Correspondence to: University Department of Medicine, Christchurch Hospital, PO Box 4345, Christchurch, New Zealand.

Renal disease and digoxin immunoassays

Nanji and Greenway have shown that patients with liver disease have a digoxin like immunoreactive substance in their plasma capable of interfering with certain immunoassay procedures for digoxin.¹ In an earlier study Graves *et al* reported that more than 60% of patients with renal impairment also had substances in their serum capable of cross reacting with the antibodies used in a range of immunoassay techniques. A further study showed similar interference in premature and full term infants,^{3,4} while a case report from Sweden described the measurement of false positive digoxin concentrations in a patient with an abnormal serum protein profile.⁵ With the exception of the Swedish case all the data to date are from North America. The aim of the present joint project was to investigate whether renal impairment gives rise to interference with principal assay techniques used for digoxin analysis in Britain and the Netherlands.

Subjects, methods, and results

We studied 26 patients receiving renal dialysis (16 from the Netherlands, 10 from Northern Ireland). Blood samples were taken before dialysis and the separated serum assayed for creatinine and digoxin concentrations using assays

routinely employed in the respective hospital laboratories. At the time of the study none of the patients was receiving digoxin. The table shows the age and sex of the patients and their serum creatinine concentrations. When analyses were complete at one centre the samples were exchanged and reassayed at the other centre. The methods used included two radioimmunoassay techniques (Amerlex, Amersham International, England; DPC, the Netherlands), a fluorometric enzyme immunoassay (Stratus, USA), and a fluorescence polarisation immunoassay (Abbott Diagnostics, USA). The samples from the Netherlands (cases 1-16) were also assayed using fluorescence energy transfer immunoassay (Syva, USA). With the exception of the fluorescence polarisation technique, which was used in the liver disease report,¹ none of the methods had been tested for cross reactivity with endogenous immunoreactive substances in serum. In all cases the assay techniques yielded negative digoxin values (detection limit 256 pmol/l (0.2 ng/ml)).

Data on patients whose serum was assayed for digoxin like immunoreactive substance using range of immunoassay techniques.

Case No	Age (years)	Sex	Serum creatinine (μmol/l; normal up to 150 μmol/l)
1	49	F	1325
2	67	M	1184
3	60	F	870
4	54	F	1057
5	67	F	1313
6	42	F	1455
7	25	M	973
8	61	M	1675
9	64	M	1002
10	24	M	1020
11	59	M	1139
12	65	M	1351
13	71	M	1276
14	68	M	988
15	67	F	524
16	54	F	789
17	57	M	1115
18	42	M	976
19	24	M	1104
20	61	M	907
21	33	F	804
22	45	M	969
23	21	M	1170
24	54	F	933
25	47	M	667
26	45	M	1150
Mean (SD)	51 (15.3)		1066 (248)

Conversion: SI to traditional units—Creatinine: 1 μmol/l ≈ 0.01 mg/100 ml.

Comment

We found no evidence of endogenous interference with the digoxin assays used. Since all the patients had severe renal impairment requiring dialysis the results suggest that the assay procedures tested do not cross react with digoxin like immunoreactive substances supposedly present in the serum of patients with renal disease and that the methods may be used with confidence in therapeutic drug monitoring in patients with renal disease receiving digoxin. Nevertheless, until further information is available serum digoxin concentrations measured by any immunoassay procedure should be viewed with caution in premature and full term infants, patients with hepatic failure, and patients with abnormal serum protein profiles.

We thank Dr M G McGeown, renal unit, Belfast City Hospital; Mr M McMaster, clinical chemistry laboratories, Belfast City Hospital; and Mr J Clissen, department of clinical pharmacy, Hospital Sittard, for their help.

- 1 Nanji AA, Greenway DC. Falsely raised plasma digoxin concentrations in liver disease. *Br Med J* 1985;290:432-3.
- 2 Graves SW, Brown B, Valdes R. An endogenous digoxin-like substance in patients with renal impairment. *Ann Intern Med* 1983;99:604-8.
- 3 Pudek MR, Seccombe DW, Jacobson BE, Whitfield MF. Seven different digoxin immunoassay kits compared with respect to interference by a digoxin-like immunoreactive substance in serum from premature and full-term infants. *Clin Chem* 1983;29:1972-4.
- 4 Valdes R, Graves SW, Brown BA, Landt M. Endogenous substance in newborn infants causing false positive digoxin measurements. *J Pediatr* 1983;102:947-50.
- 5 Vingé E, Nilsson L-G, Molin L, Ekman R. Spurious results of digoxin radioimmunoassay. *N Engl J Med* 1984;310:725.

(Accepted 22 July 1985)

Department of Pharmacy, Medical Biology Centre, The Queen's University of Belfast, Belfast BT9 7BL, Northern Ireland

JAMES C McELNAY, BSC, PHD, lecturer in biopharmacy

Department of Clinical Pharmacy, Hospital Sittard, 6131 BK Sittard, The Netherlands

PIET M HOOYMANS, BSC, PHD, clinical pharmacist

Correspondence to: Dr McElnay.