alterations in the kidney with some specific sensitivity of the target organ.[4] Our findings suggest that it is the metabolic environment which determines the development and reversal of the renal lesion of diabetes rather than any sensitivity of the target organ. Nephropathy recurred in the patient who became diabetic but not in the patient who remained euglycaemic. Perhaps diabetic nephropathy can be prevented or early diabetic nephrosclerosis at least stabilised, if the abnormal milieu can be corrected by pancreatic transplantation. In two recipients of pancreatic allografts with early diabetic nephropathy in kidney grafts transplanted several years earlier the nephropathy regressed.[5] In another series, while most kidneys transplanted into diabetic recipients became nephrosclerotic, this did not happen in two patients given a pancreas graft at the same time.[6]

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TOPICAL PGE_2 ENHANCES HEALING OF CHEMOTHERAPY-ASSOCIATED MUCOSAL LESIONS

SIR,—Mucosal lesions are severe and painful complications of aggressive chemotherapy.[1] Few treatments are available. Sucralfate has been reported to yield encouraging results in chemotherapy-induced oral stomatitis[2,3] but this substance has primarily been introduced for treatment of duodenal and gastric ulcers. Similar beneficial results in the gastrointestinal tract were obtained with oral prostaglandin E_2 (PGE_2).[4] We have been investigating the value of topical PGE_2 in chemotherapy-associated mucosal lesions.

Six heavily pretreated patients with severe painful ulcerations were given topical PGE_2. Chewing of 0·25 mg PGE_2 three times daily was prescribed in five patients (table). For the sixth patient 1 mg PGE_2 was dissolved in 5 ml hydroxyethylcellulose and locally applied to vaginal lesions.

Significant pain relief was obtained in four out of six patients within 6 h of the start of treatment. In these patients a rapid reduction in the inflammatory reactions was seen and epithelialisation of lesions occurred after treatment for 2–3 days. In case 3 pain relief was only moderate and temporary.

Prophylactic topical PGE_2 was given to three patients and was entirely successful in two (7 and 8). One of them had a history of severe ulcerative lesions during previous chemotherapy, but was symptomless during PGE_2 prophylaxis. Oral lesions were also prevented in a patient during total body irradiation (1200 rad), which often is complicated by severe mucositis.[5] In the third prophylactically treated patient mucositis was not prevented during total body irradiation (1350 rad) but was not painful. After 4 days epithelialisation led to complete healing.

OUTCOME OF TOPICAL PGE_2 TREATMENT (CASES 1–6) AND PROPHYLAXIS (CASES 7–9) IN PATIENTS WITH OR AT RISK OF CHEMOTHERAPY-ASSOCIATED MUCOSAL LESIONS

Lesions	Site	Results	
		Pain relief	Epithelialisation
1. Multiple ulcerations	Oropharynx, tongue	No	10 days
2. Multiple ulcerations	Tongue	Yes	7 days
3. Multiple ulcerations	Oropharynx	Yes	3 days
4. Aphthous stomatitis	Oral cavity	Yes	3 days
5. Multiple ulcerations	Oropharynx	Yes	3 days
6. Multiple ulcerations	Vagina	Yes	<2 days
7. ..	..	Lesions prevented	
8. ..	..	Lesions prevented	
9. ..	..	Multiple oropharyngeal lesions developed; epithelialisation in 4 days	

No unifying concept explaining the cytoprotective effect of prostaglandins is available. Several mechanisms have been implicated in contributing to the protective effect of prostaglandins in the gastrointestinal tract. Among these, an increase of intracellular cAMP production mediated by prostaglandins with stabilisation of the mucosal cytomembrane seems to be of major importance. An increase in mucosal blood flow, maintenance of epithelial zone cells, and, probably, yet unknown factors seem to protect against disruption of the mucosal barrier.[6,7]

Our positive findings with topical PGE_2 in four out of six patients at grave risk of oropharyngeal mucositis warrant further investigations on the clinical value of this approach.

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DIGOXIN SERUM REQUESTS

SIR,—Mr Hallworth and Dr Brodie (Jan 11, p 95) have provided important evidence about the overuse of digoxin serum assays in hospital patients. Similar data reported by us in outpatients[1] suggest worldwide misuse of therapeutic drug monitoring (TDM). We need to know not only for which patients the drug assay is requested (correctly or not) and the use made of the result but also for which patients monitoring of drug levels might have been clinically useful, though not done.

From a preliminary analysis of data collected in a project assessing the quality of hospital TDM services, 1204 inpatients were identified in eighteen centres, all on long-term digoxin. The patient's age and clinical status, and details of renal and liver function, drug treatments, and drug monitoring[2] were recorded.[3] Of the 481 requests for serum digoxin measurements (in 289 patients, 24% of the total population), 67·8% fell within a wide "therapeutic range" (0·8–2·4 ng/ml). According to Hallworth and Brodie's data no increase in this proportion should be expected for patients with repeated measurements. 22 samples (3·5%) were drawn inappropriately (within 8 h of the dose), and should be considered misleading or even dangerous if used to adjust therapeutic schedules. Only 98 (20·6%) of the 475 elderly patients (75 years or more, 39·5% of the population) and only 14 (18%) of the 80 patients with mild and/or severe renal liver failure were monitored for digoxin.

The two drugs most probably leading to clinically appreciable interactions—namely, quinidine and spironolactone (serum concentrations of digoxin may increase several-fold when