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For oral communications with more than one author, an asterisk(*) denotes the one who presented the work.

COMMUNICATIONS

Diminishing compliance with a hospital formulary in the absence of continuous feedback of information to prescribers

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Hospital Formularies are now widely accepted and there is evidence (Collier & Foster, 1985; Feely *et al.*, 1987) that a Formulary can both improve prescribing habits and reduce drug costs. Little information, however, is available on the long-term effects of a Formulary and the need for continuous input and feeback to prescribers. In a prospective study we observed prescribing habits and drug costs prior to the introduction of a Formulary, for 12 months following a Formulary during which a number of discreet feedback exercises were undertaken and in a subsequent year when no form of feedback or intervention took place.

St James's Hospital is an 800-bed general hospital whose annual drugs bill had been rising at about 20% per annum to approximately £1.7 million in 1985. A minority of prescriptions were written generically, approximately 50% on medical wards and 40% on surgical wards. Following the introduction of a Formulary, prescribers were given regular feedback with regard to their compliance to the agreed list including the use of generic names and adherence to the antibiotic policy by means of individual prescribing information, peer comparison and open discussion at the monthly Medical Committee meeting. During the course of the subsequent 12 months generic prescribing increased by 50% ($P < 0.01$) both in medical and surgical wards. Non-Formulary requisitions counted on a monthly basis initially constituted 5% of all prescriptions and remained static until subjected to intense feedback falling to 2% but when not the subject of any feedback they continued to run in the order of 4–5%. Similarly in the year during which no intervention took place the level of generic prescribing fell to pre-Formulary levels both on surgical and medical sides. The use of a third generation cephalosporin (cefotaxime) was the subject of intense feedback and the cost of the latter fell in the year following the introduction of the Formulary from £112,000 to £75,000. Of particular interest was its use in a series of samples of patients ($n = 35$) receiving cefotaxime. Pre-Formulary it was a drug of first choice in 68% of these patients and in only 42% had appropriate microbiological assessment been made. Following feedback including a Drug Information Note on the use of cefotaxime it was the antibiotic of first choice in only 37% of the sample and appropriate microbiological assessment had been undertaken in 84%. In the year in which there was no active intervention the overall usage of cefotaxime rose to pre-formulary levels and despite a price reduction the annual cost of cefotaxime rose to £94,000 and again its use in uncomplicated respiratory and urinary tract infections and often without appropriate microbiological assessment increased.

In the year following the introduction of the Formulary overall drug expenditure remained static. Drug costs per patient decreased marginally by £1 because of a small increase in patient turnover and bone marrow transplantation. In the subsequent year overall hospital activity showed a small fall and drug retail costs remained static. Nevertheless hospital expenditure on drugs rose by 6%.

While a Hospital Formulary can produce significant savings and improve drug usage, it appears that regular feedback of prescribing habits and continuous educational programmes should be undertaken if this is to be maintained.

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Feely, J. *et al.* (1987). *Irish med. J.*, **80**, 286.

Adverse drug reactions—incentives to enhance reporting

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The reporting of adverse drug reactions (ADR) through the yellow card system either to the Committee of Safety of Medicine or its Irish counterpart the National Drugs Advisory Board (NDAB) represents the major avenue of detecting the toxicity of drugs in widespread use. Only 30–35 ADR per annum are reported from St James's Hospital, with approximately 800 beds and 15,000 admissions per year. As this voluntary reporting system is obviously under-utilised we undertook a number of initiatives to enhance reporting from our Hospital.

Nifedipine dose titration in primary Raynaud's phenomenon

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POSTER COMMUNICATIONS

The interaction between neuropeptide Y and noradrenaline in reduction of forearm blood flow

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The vasoconstrictor neuropeptide Y (NPY) coexists with noradrenaline (NA) in mammalian perivascular sympathetic neurones including those of man (Wharton & Gulbenkian, 1987). *In vitro* it has direct pressor effects and may modulate both the release and the post-synaptic action of NA (Edvinsson *et al.*, 1987). We have previously shown this peptide to cause myocardial ischaemia when infused directly into coronary arteries in man (Clarke *et al.*, 1987) and reduce coronary blood flow by small vessel constriction after intracoronary infusion in the open chest greyhound (Larkin *et al.*, 1988).

In the present study we have examined the effects of locally infused NPY in forearm resistance vessels in man. Further, using low doses of NPY, we studied its influence on constriction resulting from simultaneously infused NA and reflex sympathetic forearm arteriolar constriction provoked by lower-body negative pressure (LBNP).

In six male volunteers NPY (50, 200 and 1000 pmol min^{-1}) was infused into the left brachial artery and forearm blood flow was measured using venous occlusion plethysmography and mercury in silastic strain-gauges (Whitney, 1953). Blood flow in the infused arm fell in a dose-dependent fashion from 3.8 ± 1.5 (mean ± s.d.) to 3.5 ± 1.4, 2.7 ± 0.8 and 1.8 ± 0.5 ml 100 ml^{-1} min^{-1} respectively (a reduction of 9, 31 and 53%, $P < 0.01$).

In a further study in six subjects we established a dose-response for infused NA (25, 50 and 100 ng min^{-1}) where forearm blood flow fell 48% at the highest dose. This response was unaltered (51% reduction) during co-infusion of NPY at 50 pmol min^{-1}.

In a further six subjects LBNP of 20 cm H_2O resulted in a reduction in forearm blood flow of 13% in the infused arm and 12% in the control arm during saline infusion. When NPY (50 pmol min^{-1}) was infused LBNP produced a 16% reduction in flow in the infused arm compared with a 20% reduction in the control arm. These small differences suggest that NPY does not alter the reflex sympathetic constriction.

While we have shown that NPY has a marked constrictor effect in forearm resistance vessels, we conclude that low doses of NPY do not influence constriction whether induced by exogenous NA or reflex sympathetic activity.

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Excretion of famotidine in breast milk

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Famotidine is a potent H_2-receptor antagonist that has recently been introduced for the treatment of gastric and duodenal ulceration. At therapeutic dose, 40 mg once daily, famotidine inhibits basal gastric acid secretion for 10–12 h but has a shorter plasma elimination half-life of approximately 2.8 h (Chremos, 1987). Although the pharmacokinetic profile of famotidine has been well documented, data on the excretion of this drug in human breast milk are lacking. Previous studies have shown that both cimetidine and ranitidine readily pass into breast milk and the concentration of drug in milk is generally greater than corresponding plasma concentrations. Reported milk:plasma concentration ratios range from approximately 3 to 12 with cimetidine (Somogyi & Gugler, 1979) and 1 to 7 with ranitidine (Riley *et al.*, 1981).

We have measured whole breast milk and plasma famotidine levels during three 'feeding' intervals following a single dose of 40 mg famotidine. Eight women aged 23–37 years, weight 52–120 kg, who had recently given birth but did not plan to breast feed gave informed consent to take part in the study. The women were given a 40 mg tablet of famotidine with 100 ml of water at 10.00 h on the day of testing. Blood samples were withdrawn 15 min pre-dose, and at 15, 30 min, 1, 2, 4, 6 and 24 h post dose. Following centrifugation plasma was separated and frozen at −20° C until analysis. Breast milk samples were extracted by standard breast pump at 2, 6 and 24 h post dose. At each sampling time three aliquots of milk each representing 5 min collection were taken initially from the right and then the left breast. pH was measured immediately and the milk samples were stored at −20° C. All samples were assayed for famotidine concentration by h.p.l.c. following solid phase extraction, using a modification of the method of Vincek *et al.* (1985).

The concentration of famotidine was similar in milk collected from the right and left breasts. The mean of the six milk aliquots was compared with the corresponding plasma concentration at the same time point, and the milk:plasma ratio was determined.

Time after dosing (h)	*Milk:plasma ratios* (mean s.d.)
2	0.41 (0.17)
6	1.78 (0.55)
24	1.33 (0.86)

Median pH of breast milk samples was 7.14 (range 6.77–7.64). The concentration of famotidine in breast milk appeared to lag behind that measured in plasma by 2–4 h. The observed peak breast milk concentration (mean 72 ± 21 ng ml^{-1}) 6 h after dosing was not significantly different from the peak concentration of famotidine in plasma (mean 75 + 22 ng ml^{-1}) measured 2 h post dose.

In conclusion, the present findings indicate that after oral dosing famotidine is detectable in human breast milk. However comparison with historical data suggests that famotidine is less extensively excreted in breast milk than either cimetidine or ranitidine. This should be taken into consideration when prescribing H_2-receptor antagonist therapy for nursing mothers.

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Riley, A. J. *et al.* (1981). In *The clinical use of ranitidine*, pp. 78–81. Medicine Publishing Foundation.

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