Menstrual problems in women starting or changing pill

Regimen	No of women	No (%) complaining of menstrual problems
Women first starting pill (on 1st day of cycle) . .	228	47 (21)
Women changing pill: Starting new pill on 1st day of cycle . .	125	23 (18)
Starting new pill immediately . .	214	31 (15)
Total	567	101 (18)

clinic for their three-monthly appointment and about whom, therefore, we have no information. The table summarises the results for the remaining 567 women, none of whom became pregnant.

Of the 101 women complaining of menstrual problems, 82 had spotting or breakthrough bleeding, 10 had amenorrhoea, and 9 had heavy periods. Although we did not include a control group in our study, the rate of reporting of menstrual problems (18%) is not abnormally high in comparison with the rates reported during the first cycle of use of low-dose contraceptives in other investigations.²⁻⁴

Seventeen doctors using the new regimens were asked their opinion of them; 15 thought they worked well, particularly the "immediate change-over" regimen. It was found to be easier to persuade patients to switch to lower-dose pills if extra precautions were not needed. Patients liked the new regimens and were not upset by spotting or breakthrough bleeding. Since an average supply of sheaths and pessaries for two weeks costs about £1, a saving of £645 was made during the course of the study.

Though the manufacturers of pills have expressed their opposition to the new regimens,⁵ we believe them to be effective, acceptable, and economical.

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¹ Family Planning Association, *Combined Oral Contraceptive—Amendment to Patient Instructions*. London, FPA Medical Research Department, 1977.

² Dionne, P, and Vickerson, F, *Current Therapeutic Research*, 1974, **16**, 281.

³ Allen, H H, *Current Medical Research and Opinion*, 1974, **2**, 101.

⁴ Pasquale, S A, and Yuliano, E, *Contraception*, 1975, **12**, 495.

⁵ Oral Contraceptive Manufacturers. Memorandum on starting the pill. Issued June 1978.

Patient package inserts

SIR,—With reference to your leading article (26 August, p 586) in which you state that critics of patient package inserts argue that, among other things, such inserts may "possibly diminish, rather than enhance, patients' compliance by making them afraid of adverse reactions" we would like to draw attention to our published work on this specific question.

In depressed patients treated with amitriptyline¹ and dothiepin² we found no statistically significant difference in the compliance rates between patients who were warned about side effects and those who were not warned. In a further study³ we found that

patients given written information about side effects of antidepressants had a significantly higher compliance rate than those given only verbal information or no information at all. We are currently investigating whether this is a cognitive effect or an "attention-placebo" effect.

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¹ Myers, E D, and Calvert, E J, *British Journal of Psychiatry*, 1973, **122**, 461.

² Myers, E D, and Calvert, E J, *Journal of International Medical Research*, 1976, **4**, 237.

³ Myers, E D, and Calvert, E J, *British Journal of Psychiatry*, 1978, **132**, 526.

Adverse reactions to intravenous induction agents

SIR,—Dr H L Thornton (23 September, p 897) suggests that the role of the polyoxyethylated castor oil (Cremophor EI) in which alpha-xalone/alphadolone (Althesin) is made up should be investigated in adverse reactions to this intravenous induction agent. It has been established that Cremophor may play a part in severe histamine-mediated reactions to Althesin.¹ However, it is not always the principal cause and in many cases is not implicated at all.² In a case I recently reported³ intradermal skin testing proved conclusively that the reaction had developed to the Althesin alone and that the Cremophor was completely innocent.

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¹ Kessel, J, and Assem, E S K, *British Journal of Anaesthesia*, 1974, **46**, 209.

² Fisher, M McD, *Anaesthesia and Intensive Care*, 1976, **4**, 33.

³ Jago, R H, and Restall, J, *Anaesthesia*, 1978, **33**, 644.

Effect of quinidine on plasma concentration of digoxin

SIR,—We would like to comment on the paper by Dr G Ejvansson (4 February, p 279) concerning an important drug interaction between quinidine and digoxin. In accordance with his results we also found that the serum digoxin concentration rose in three hospital inpatients when digoxin was administered in combination with quinidine (3 tablets Kinidine Durettes twice daily, each tablet containing 250 mg quinidine bisulphate).

A possible mechanism of this quinidine-digoxin interaction is a decrease of renal digoxin excretion during quinidine therapy. The influence of quinidine on the renal digoxin excretion was studied in these three patients by comparing the digoxin:creatinine renal clearance ratio on two days during and again on two days after quinidine therapy. The digoxin and creatinine clearances were

assessed by collecting a 24-h urine sample and a midpoint blood sample. Digoxin concentrations in serum and urine (after dilution with buffer) were determined by ¹²⁵I-digoxin radioimmunoassay (Schwarz-Mann kit). Quinidine or metabolites of quinidine did not influence the digoxin assay in serum and urine.

The results (see table below) indicate that quinidine inhibits renal digoxin clearance. The decrease of the renal digoxin clearance during quinidine therapy might explain the elevation of the serum digoxin concentration in these patients. Our data do not exclude the possibility that another mechanism may also be involved. Further study is required to investigate other mechanisms of this digoxin-quinidine interaction.

Nevertheless our findings confirm the phenomenon published by Ejvansson and we recommend careful observation of the serum digoxin concentration and the electrocardiogram when this combination of drugs is used.

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Health education in schools

SIR,—Mrs Rosalind Cole (2 September, p 703) seems to be letting national pride blur her judgment. Health education has been an important subject in American schools and colleges for many years. In Britain the Schools Council and the Health Education Council are still trying to investigate the nature of the subject, so I do not think we can afford to look down on the American way of doing things.

In 20 years of teaching and mixing with teachers I have never come across anything resembling the rosy picture she paints of health education in Britain. Most children, I fear, leave school without even knowing the series of facts which Rosalind Cole despises so much. This is in part due to the ignorance of their "educators." How many British teachers know enough about toxocara, rabies, toxoplasmosis, tetanus, "non-accidental injury to children," the probable causes of ischaemic heart disease, etc?

It would appear to me self-evident that the first stage in a health education programme is to inform the teachers of the facts. The second stage is more problematic. It is pertinent to ask, "Is it ethical to try and manipulate the behaviour of children?" The problems of health education bear some resemblance to ethical problems. Children are likely to think that what teachers tell them about health merely reflects the feelings of the teacher. To overcome this some teachers may resort to

Digoxin:creatinine clearance ratios on two occasions during and on two occasions after quinidine treatment

	Patient 1		Patient 2		Patient 3	
	During quinidine treatment	After quinidine treatment	During quinidine treatment	After quinidine treatment	During quinidine treatment	After quinidine treatment
Digoxin steady-state concentration (μg/l)	0.9; 1.0	0.5; 0.5	2.6; 2.6	1.0; 1.1	1.7; 1.6	1.0; 1.3
Digoxin dose (mg)	0.25	0.25	0.25	0.25	0.125	0.125
Digoxin clearance (ml/min/1.73 ² m)	74; 91	139; 143	43; 29	66; 68	42; 48	63; 54
Creatinine clearance (ml/min/1.73 ² m)	79; 78	98; 102	88; 62	71; 69	61; 64	60; 55
Digoxin:creatinine renal clearance ratio	0.94; 1.17	1.42; 1.40	0.49; 0.47	0.93; 0.98	0.69; 0.75	1.05; 0.98
	mean 1.05	mean 1.41	mean 0.48	mean 0.96	mean 0.72	mean 1.02