

Screened at ten months	78	}	92
Moved away from the practice	13		
Declined	1		

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#### Reference

Fisher, J. and Keating, K. (1973). *Community Health*, 5, 153.

## HORMONE REPLACEMENT THERAPY

Sir,  
You have recently stressed (December *Journal*, p.745) the professional responsibility we should all exercise in warning patients about the hazards of drinking, driving, and taking certain drugs.

It is my opinion that this grave responsibility, which is both professional and moral, we owe to our patients in all circumstances. Not to acquaint any woman who is given hormone replacement therapy for the menopause with the increased hazard she incurs in respect of endometrial carcinoma, or at least hyperplasia, following therapy, borders on negligence.

At a recent series of seminars on therapeutics I put this point to the senior lecturer taking that particular session and it was his considered opinion that to give such information was totally unnecessary. When I pointed out that the Food and Drugs Administration in the USA (FDA) had now made it mandatory for each packet of such pills to carry a warning to that effect, his reaction was, "Thank God we do not yet permit such an infringement of our clinical freedom".

I submit, sir, that the "clinical freedom" he so describes and upholds is nothing less than a licence, and moreover, a licence to maim.

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## MONITORING THE DOSE OF DIGOXIN

Sir,  
I would like to comment on the recent article by Drs Manning and Brown (August *Journal*, p.470) which made a number of statements about digoxin

control that I think should be challenged both from the point of view of accuracy and methodology.

The authors stated that they had four aims for their research: to establish the prevalence of digoxin use; to determine whether patients on digoxin need regular electrolyte estimation; to establish the value of blood urea and serum creatinine measurements in determining renal function as a guide to digoxin dosage; and to determine whether periodic estimation of serum digoxin levels is needed. Apart from the first of these aims, which is a valuable exercise for most practitioners for many different aspects of medical care and is readily achieved, I have some fairly fundamental criticisms to make.

It is manifestly impossible to find out whether patients on digoxin are more in need of electrolyte measurements than patients not taking the drug, unless the results of estimates in digoxin takers are compared with equivalent estimates in very similar (or *matched*) patients who are not taking the drug. It is possible only for the authors to say that a certain percentage of their patients would have benefited from electrolyte estimation, as they did not match their cases. Unless it is known that this percentage is significantly larger than that in other patients it is scientifically improper to say that such evidence supports the view that additional precautions should be taken with digoxin takers. In any case, the authors do not present any analysis of this situation: they merely note that of those patients taking digoxin and a diuretic a proportion had evidence of hypokalaemia. Because these patients were all taking one specified diuretic the authors recommend special care in monitoring electrolyte levels. The fallacy here is that the numbers of patients involved in these analyses are very small, and statistical significance may not have been achieved by the data; or, to put it another way, it might have been an accident that all the patients found to have evidence of hypokalaemia happened to be taking one particular drug. Another survey might find a different situation.

The third aim is a composite which has not been achieved in part or as a whole by the authors. The first part, to establish the value of certain biochemical measurements in determining renal function, is a physiological issue which requires detailed laboratory investigations. Obviously a standard is required for the objective assessment of renal function before the value of any other test can be ascertained. The value of renal function as a guide to digoxin dosage is more a clinical matter.

Since digoxin is excreted through the kidneys it is axiomatic that serum

digoxin levels will depend on renal function in some way. A recent paper (Holt *et al.*, 1977) has demonstrated that the most important factors influencing the serum digoxin level are first, the daily dosage of the drug, secondly the patient's renal function, and thirdly, the time between taking the drug and drawing the blood for the assay. Unpublished data from the same study showed that there was no relationship between the daily dose and the patient's renal function. The implication is obvious: clinicians are not influenced by renal function estimates (or, probably more likely, they do not bother to undertake such estimations), a finding supported by Drs Manning and Brown. But is this acceptable? The mere fact that doctors do not let themselves be influenced by renal function might be an indication of the latter's clinical irrelevancy, but it might equally well be a manifestation of the clinician's ignorance. I would have been happier with the authors' implied conclusion, that the estimation of renal function is unnecessary, if they had supported this with scientific evidence.

Before leaving the subject of renal function I would like to comment on the authors' contention that "neither serum urea nor creatinine is adequate to assess renal function" and that "for digoxin we believe that creatinine clearance is the single most valid test". From what I have written earlier it is clear that these are not conclusions of the study because they were not aspects that were studied. It is not appropriate for authors to make *ex-cathedra* statements about related aspects in their discussion of a specific study; it is intellectually dishonest. In either case I wonder what the value of any of the authors' conclusions regarding the value of renal function can actually be when the correlation between blood urea and serum creatinine was so very low (0.49). I would have thought that most laboratories would have done better than this and in the paper by Holt and colleagues the equivalent correlation was noted to be 0.82. Incidentally, that paper uses the nomogram which Drs Manning and Brown dismiss on the basis of other people's experience without having attempted to use it themselves. In that study the correlation between the estimated renal function and the blood urea or creatinine measurements exceeded 0.6.

The fourth aim is, of course, a trend issue and even a two-sample study such as this one cannot establish beyond doubt the need for periodic digoxin estimates. The authors make recommendations which seem to be curiously at odds with their data. Of two patients with high digoxin levels only one