Planning a professional curriculum

SIR,—Professor P Richards's book review gives a valuable insight into the mind of a medical school dean.¹ He likens redesigning the undergraduate curriculum to a confusing game of chess with an increasing number of pieces. This confusion is hardly surprising because he admits that the objectives of undergraduate medical education are not clear. He calls for each medical school to review and recast its philosophy of medical education.

While this stance is highly commendable, surely the task should be undertaken at a national level. The "opportunistic nature of clinical learning around the randomness and imperatives of disease,"² combine with the strengths and weaknesses of the individual medical school to provide an unpredictable experience for each student. It seems extremely unlikely that important changes in the balance of the curriculum will occur while powerful personalities at each medical school compete for their share of curriculum time.

The General Medical Council in supervising medical education displays much wisdom. Perhaps with its help medical schools in the United Kingdom might define the current objectives of undergraduate education. A national curriculum could then be defined with sufficient flexibility to allow the individual flavour of schools to persist. If we, as a profession, do not grasp this nettle, there may be others who wish to do it for us.

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1 Richards P. Classical variations? *Br Med J* 1990;300:1146. (28 April.)

Accuracy of weighed dietary records

SIR,—In their article on assessment of dietary intake Mr M B E Livingstone and colleagues quite rightly highlighted the potentially misleading conclusions that may be drawn from studies on diet and health when the measurement of food intake is liable to non-random errors.¹ They failed, however, to distinguish between non-random errors consistent for any given method of dietary measurement (causing systematic bias) and those errors introduced by measurement in a specific subject. Consideration of their analysis raises two points.

Firstly, the comparison of mean energy intakes for the subjects in the two studies in Northern Ireland were presented as a scatter plot with a correlation coefficient of 0.79 and a linear regression equation. Mr Livingstone and colleagues gave the slope for the regression of the second measurement on the first as 1.03, concluding that there was no regression to the mean and thus that low responders remain low. The correct regression coefficient, however, is 0.645, appreciably less than unity. This indicates substantial regression towards the mean.

Secondly, the comparison of energy expenditure and energy intake was not presented and explored in the same way as their comparison of repeated measures of energy intake. Information is lost by aggregating the data into thirds of the intake distribution. The published data were plotted in figure 1 to show the comparable relation ($r=0.55$, $n=31$). Although this value of 0.55 is not widely discrepant from the value of 0.79 when comparing the two measures of food intake, it suggests that some non-random interaction error is present. Is it possible to identify a subpopulation to which this non-random interaction is largely confined? After eliminating these subjects can the discrepancy between energy intake and expenditure be explained by systematic bias?

FIG 1—Comparison of mean energy intake with mean energy expenditure assessed by doubly labelled water method

In their discussion Mr Livingstone and colleagues raised the issue of minimum energy requirements in relation to basal metabolic rates and noted that a habitual mean intake of less than 1.35 times the basal metabolic rate is physiologically implausible, assuming long term energy balance. We reconsidered their data comparing mean energy intake 12 months apart, excluding subjects whose intake fell below this threshold in the more recent study. The excluded subjects had similar intakes in the two studies (fig 2), indicating a self consistent interaction with the method of dietary measurement. Without these subjects with low energy

FIG 2—Reproducibility of seven day weighed dietary records performed 12 months apart

intake the correlation between mean energy intakes in the two studies fell slightly to 0.72 ($n=21$). By contrast, the correlation between mean energy intake and measured expenditure increased substantially to 0.75 ($n=21$). So, for the restricted group, intake and expenditure are as strongly correlated as repeated measures of mean intake. Regression of mean energy intake on expenditure for this restricted group suggests a degree of underrecording of intake (slope=0.644, 95% confidence interval 0.373 to 0.913).

Systematic bias such as this may be accommodated in epidemiological studies, and if required, the observed scales of measurement may be related to true intake scales by performing calibration studies on a subgroup of the study population. The implication for epidemiological studies of diet and health is that valid interpretations may often be possible.

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1 Livingstone MBE, Prentice AM, Strain JJ, et al. Accuracy of weighed dietary records in studies of diet and health. *Br Med J* 1990;300:708-12. (17 March.)

Quality of hospital prescribing

SIR,—With reference to the study by Dr C J Hawkey and colleagues about the effect of pharmacists' interventions on the quality of prescribing,¹ we report the findings of a survey of prescriptions on discharge from a district general hospital with 530 mainly acute beds.

We surveyed interventions by pharmacists in a sample of 351 discharge prescriptions, the total received by the pharmacy over two weeks in December 1989. Interventions were necessary before 19% of discharge prescriptions could be dispensed because the prescribers' intentions were unclear. It seems unlikely that prescribing on discharge should be much worse than that for inpatients and outpatients; thus the 2.9% of prescriptions requiring interventions that Dr Hawkey and colleagues reported seems small—perhaps their data reflect the inclusion of a large number of long stay patients.

Most of the interventions in our study concerned either unintentional differences between drugs prescribed for patients in hospital and on discharge or unintentional changes in dosage regimens of medication administered. Very few interventions concerned illegible prescriptions or incorrectly written prescriptions for controlled drugs. Pharmacists' interventions led to alterations in 78% of the prescriptions.

We conclude that the interventions made by pharmacists probably benefited patients because so many were accepted by the prescribing doctors. Some of the interventions concerned potentially serious problems, and we are worried that so many patients would have received medication that was not intended for them if the pharmacists had not intervened.

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1 Hawkey CJ, Hodgson S, Norman A, Daneshmend TK, Garner ST. Effect of reactive pharmacy intervention on quality of hospital prescribing. *Br Med J* 1990;300:986-90. (14 April.)

Psoriasis and bone marrow transplantation

SIR,—Dr D J Eedy and colleagues described a case of severe intractable psoriasis which cleared completely after allogeneic bone marrow transplantation.¹ We would like to describe a similar case.

A 35 year old man had suffered from moderately severe psoriasis complicated by psoriatic arthropathy for over 10 years. The skin lesions had been treated with combinations of cold tar preparations, topical corticosteroids, and dithranol cream with only partial response. Non-steroidal anti-inflammatory drugs had been used to treat the active arthropathy. In 1986 Philadelphia chromosome positive chronic granulocytic leukaemia was diagnosed and the patient was treated initially with busulphan. In early 1987 he received a bone marrow graft (without depletion of T cells) from his histocompatible sister. Cyclosporin A (5 mg/kg) was given for 12 months after transplantation. Since transplantation the cutaneous psoriasis has cleared completely and the arthropathy has remained inactive. The chronic granulocytic leukaemia is still in remission.

Our case supports the observation that long-standing remission of psoriasis can be achieved by changing the patient's cellular immunity through allogeneic bone marrow transplantation. This is not totally surprising because experimental work

in animals has shown that allogeneic bone marrow transplantation can alter the course of immune mediated disorders such as lupus nephritis and diabetes mellitus.^{2,3}

It is interesting to speculate that allogeneic bone marrow transplantation may have a therapeutic role in the management of serious intractable autoimmune disorders.

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- 1 Eedy DJ, Burrows D, Bridges JM, Jones FGC. Clearance of severe psoriasis after allogeneic bone marrow transplantation. *Br Med J* 1990;300:908. (7 April.)
- 2 Ikehara S, Nakamura T, Sekita K, et al. Treatment of systemic and organ-specific autoimmune disease in mice by allogeneic bone marrow transplantation. *Prog Clin Biol Res* 1987;229:131-46.
- 3 Shiraki M, Fujiwara M, Kano K. Rectification of immunological abnormalities and lupus nephritis by transfer of bone marrow cells. *Ann NY Acad Sci* 1983;420:309-14.

Enalapril and metoprolol in diabetic nephropathy

SIR,—Dr S Björck and colleagues conclude that enalapril reduces proteinuria in patients with diabetic nephropathy by a specific action that is independent of its effect on systemic blood pressure, and they assume that the observed antiproteinuric effect of enalapril may be beneficial to the kidneys.¹ This promising finding appears to strengthen previous suggestions for using angiotensin converting enzyme inhibitors as the treatment of choice in diabetic hypertension. Nevertheless, their results should be interpreted with some caution.

Firstly, the reductions in blood pressure achieved by enalapril and metoprolol at the doses applied (with or without frusemide or hydralazine, or both) were not equal in the study. For example, the supine systolic blood pressure decreased from the baseline value by a mean of 22 mmHg after treatment with enalapril for eight weeks and by only 13 mmHg with metoprolol. The possibility cannot be excluded that the greater reduction in systemic blood pressure observed in the patients treated with enalapril partly caused the greater antiproteinuric effect of the drug.

Secondly, the treatment with enalapril over eight weeks caused a non-significant, but obvious and continuous, increase in serum creatinine concentration by 7.5%, whereas the concentration remained unchanged in the patients treated with metoprolol. Elevated serum creatinine concentration was a sign of worsening kidney function in these patients, even though the authors did not evaluate the glomerular filtration rate after treatment. Deterioration of renal function has been reported in some patients after the use of angiotensin converting enzyme inhibitors.² Enalapril may contribute to decline in renal function in certain vulnerable patients,² especially those receiving high doses of loop diuretics.³

Thirdly, the finding that treatment with enalapril over only eight weeks increased serum potassium concentration by 9% seems clinically important because such an increase could be life threatening. Regular monitoring of serum potassium concentration might be necessary during the use of angiotensin converting enzyme inhibitors.

If the ultimate aim of antihypertensive treatment is to preserve kidney function in diabetic patients with advanced nephropathy rather than only reducing the amount of proteinuria, the comprehensive results by Björck and colleagues seem to reflect a potentially harmful effect of angiotensin converting enzyme inhibitors in these patients. The benefits of long term use of angiotensin converting enzyme inhibitors compared with other antihypertensive drugs in hypertensive diabetic

patients with reduced kidney function are still not clear.⁴

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- 1 Björck S, Mulec H, Johnsen SA, Nyberg G, Aurell M. Contrasting effects of enalapril and metoprolol on proteinuria in diabetic nephropathy. *Br Med J* 1990;300:904-7. (7 April.)
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SIR,—At the end of the study by Dr S Björck and colleagues patients receiving metoprolol and those receiving enalapril had similar mean arterial pressures (102 (SD 11) mmHg v 99 (SD 7) mmHg), but there was a considerable, albeit not significant, difference between the groups at the start of the study (109 (SD 10) mmHg v 114 (SD 8) mmHg, $p=0.09$). Consequently the reduction in mean arterial pressure in the enalapril group was more than twice that in the metoprolol group (15 mmHg v 7 mmHg).

If the decrement in blood pressure (as well as the final blood pressure) is important in reducing proteinuria then the greater antiproteinuric effects of enalapril can be explained in terms of its antihypertensive effect. Furthermore, metoprolol produced a significant reduction in systolic blood pressure only at eight weeks and did not significantly reduce diastolic pressure, unlike enalapril which significantly reduced systolic and diastolic blood pressure at both four and eight weeks. This suggests that metoprolol may not have been as effective an antihypertensive agent as enalapril, particularly during the first four weeks.

Finally, because of the significant effects on proteinuria of dietary protein restriction in diabetic nephropathy, it is important to establish that dietary protein intake did not change during the study.

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AUTHOR'S REPLY,—As both commentators point out, the baseline blood pressure was higher, although not significantly, in the patients given metoprolol. This is an effect of chance in the randomisation procedure. Our goal was to achieve similar blood pressure during treatment with both drug regimens and I believe we succeeded fairly well. Unfortunately, the wrong picture was printed as figure 1 but this error has now been corrected.¹

Using similar blood pressure control the degree of both albuminuria and proteinuria in the patients given enalapril was less than half of that in the patients given metoprolol. We concluded that this was caused by a pressure-independent antiproteinuric effect of enalapril. Many of the patients still show a reduction in proteinuria after up to 18 months' observation.

Dr Hardy asks about protein intake—there was no change in diet or in protein intake as measured by urinary excretion of nitrogen. Dr Baba and colleagues point out that the serum creatinine concentration rose in the patients given enalapril but not in those given metoprolol. This might reflect haemodynamic changes which led to the reduction in proteinuria. This is probably an early

adaptation to the angiotensin converting enzyme inhibitor because, during the next four months, the serum creatinine concentration increased by 11 (SE 9) $\mu\text{mol/l}$ in the patients given metoprolol and decreased 3 (SE 5) $\mu\text{mol/l}$ in those given enalapril.

It is too early to conclude whether enalapril treatment protects kidney function more than metoprolol treatment in the long term. Earlier uncontrolled data that remain to be proved show that angiotensin converting enzyme inhibitors might have a specific renal protective effect.² Hyperkalaemia is a complication of angiotensin converting enzyme inhibitor treatment in all patients with renal failure, thus frusemide is the logical first choice in these patients to reduce the risk of hyperkalaemia. The overall reported experience with angiotensin converting enzyme inhibitors in diabetic patients, now covering more than 450 patients, is that the treatment is effective, safe, and well tolerated.³ The lack of side effects on lipids and metabolic control and a lesser degree of orthostatic hypotension are advantages with these new drugs.

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- 1 Björck S, Mulec H, Johnsen SA, Nyberg G, Aurell M. Contrasting effects of enalapril and metoprolol on proteinuria in diabetic nephropathy [Correction]. *Br Med J* 1990;300:1170. (5 May.)
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Node negative breast cancer

SIR,—We accept the comment by Professor R W Blamey and colleagues that the Nottingham prognostic index can define subgroups of patients with operable breast cancer who have different prognoses and that these findings have been validated in Nottingham.¹ This index has, however, not achieved widespread acceptance. It is based on a combination of lymph node stage and size and histological grade of tumour. Lymph node stage in this instance is based on a triple node biopsy (that is, biopsy of a lower axillary node, an apical axillary node, and a node from the internal mammary chain) which is not a common procedure. In addition, while both the Guy's and Nottingham breast units are extremely fortunate to have histopathologists with special skills in classifying breast tumours, tumour grade can be highly observer dependent.²

Our review was confined to patients with node negative breast cancer.³ Knowledge of the state of the patients' axillary nodes clearly depends on adequate dissection. Dissection was routine practice when modified radical mastectomy was the treatment of choice for operable breast cancer. But as Drs Leslie and Maher have pointed out, since the advent of breast conservation techniques, many surgeons no longer dissect the axilla.⁴ We feel strongly that, particularly in younger women, knowledge of lymph node state is important to help determine whether adjuvant chemotherapy is indicated.⁵

For patients who have no affected nodes on full axillary dissection it is clearly possible to define prognostic subgroups. Using a combination of tumour size and either histological grade or S-phase fraction measured by flow cytometry three groups of patients with relapse-free survival rates of 95%, 78%, and 52% over five years can be identified.⁶ We are currently validating this in a larger group of patients. Both the Guy's and Nottingham prognostic indices can potentially