disease[12] and in Crohn's disease[13] should have some effect on absorption of these drugs. However, there are so many other factors involved in drug absorption and drug plasma levels that these other factors may obscure or alter effects that changes in the jejunal acid microclimate may produce.

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SIR,—We were interested in the comments by Dr R L Parsons and other (8 January, p 103) on our work on plasma propranolol levels in patients with coeliac disease (2 Ocotber, p 794). We cannot accept their claim to have shown a statistically significant rise in these levels at 1, 6, and 8 h after the oral administration of 40 mg of the drug. Using Student's *t* test, as they did, recalculation of the *t* values for the difference between the plasma propranolol levels in controls and coeliac patients from their own data[1] gave values of 1·8, 1·73, and 1·3 respectively. The corresponding P values were therefore on no occasion below or even near the 0·05 level of significance. It also seems strange that the difference between the areas under the curve for plasma propranolol levels in controls and coeliac patients should be significant when calculated according to one programme (Wagner and Nelson), but not significant when calculated according to another (Saunders and Natumen). In our patients the area under the curve in coeliacs was not significantly raised when using Simpson's rule.

The claim that the discrepancy between their and our results is due to the difference in the numbers of patients used in the two groups as well as to a difference in the duration of treatment on a gluten-free diet also is not acceptable. Although Dr Parsons and his colleagues[1] allegedly studied 14 patients compared with our eight, they gave data on only 13 and for their calculations indeed only use 11 of these. This reduces the difference between their and our series to only three patients instead of five as claimed in their letter. Although one can only guess which patients were included it does seem likely that the average duration of treatment in their series was shorter than in ours. This would suggest that duration of treatment does not significantly affect plasma levels of propranolol in coeliac disease as the data of Dr Parsons and his colleagues do not substantiate the claim of a significant difference at any sampling time. This situation is very different from that in Crohn's disease. Here the difference between the plasma propranolol levels in patients and controls is highly significant at all sampling times—apart from the ½-hour one—as are the C_{max} values as well as the areas under the curve.

We should like to emphasise once more that we do not necessarily equate this with enhanced absorption of the drug in Crohn's and other diseases.[2] Other factors are much more likely to be involved.

We should like to thank Dr J A H Waterhouse from Cancer Registry, Queen Elizabeth Medical Centre, for checking our statistical calculations.

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[1] Parsons, R L, *et al*, *Gut*, 1976, **17**, 139.
[2] Babb, J, *et al*, *Lancet*, 1976, **1**, 1413.

Allergy to diazepam

SIR,—I read with interest the report by Dr Louis Milner (15 January, p 144). The patient under review did give a history of being allergic to drugs including chlordiazepoxide and chlorazepate, both of which are members of the benzodiazepine family to which diazepam also belongs, implying that she had taken them in some form or fashion earlier in her life, when her allergy to those drugs was detected. May I point out the basic mechanism of this very rare anaphylactic reaction?

The active and common metabolite of all benzodiazepines (which include chlordiazepoxide, diazepam, nitrazepam, chlorazepate, oxazepam, chonazepam, and medazepam) is desmethyldiazepam,[1] which seems to be the real antigenic moiety and it is a case of cross-allergenicity between different members of the same chemical family. As the patient had taken chlordiazepoxide and chlorazepate earlier in her life tissue-fixed antibody to the common antigenic moiety was already present in the body; otherwise the very first administration of diazepam would not have led to the reported anaphylactic reactions (type I immune reaction). It would have been better not to give diazepam to a patient known to be allergic to other chemically allied members of the same family.

This reaction has thrown some light on the basic cause of this cross-allergenicity between different members of the benzodiazepine group of drugs which are prescribed so commonly today.

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[1] Lader, M, in *Advanced Medicine—Topics in Therapeutics—2*, ed P Turner, p 212. London, Pitman Medical, 1976.

SIR,—Dr Louis Milner (15 January, p 144) comments that "hypersensitivity reactions to the benzodiazepine derivatives have not been reported," but Dr R H Felix and I reported an allergic reaction to Valium (diazepam) in the *Lancet* in 1974 in a paper entitled "The value of patch and other skin tests in drug eruptions." Patch-testing with the injectable form of diazepam was positive on two separate occasions. I think there was little doubt of the diagnosis in that case. The case we described was an example of an epidermal (eczematous) reaction to a systemically administered drug.

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[1] Felix, R H, and Comaish, J S, *Lancet*, 1974, **1**, 1017.

Atrial fibrillation in the elderly

SIR,—In his answer (1 January, p 42) to the question "How should one treat atrial fibrillation in the elderly?" your expert has not included any mention of tachycardia. I am no cardiologist but have learned a little about this common problem in general practice. Gross tachycardia (110-150/min) with frank failure, or the threat of failure, is common at the onset of atrial fibrillation and may occur without obvious precipitating cause at any subsequent time. Adequate digoxin controls the pulse rate, usually cures the failure if present, and certainly lessens the risk of failure if it is not already present. Digoxin is less effective if thyrotoxicosis is present and there may be other, rarer, reasons for it to fail or be best avoided. I know of no adequate modern substitute. Incidentally, a return to normal rhythm within two or three days of digitalisation is fairly common too.

Having digitalised one of these patients, it has been my custom to maintain digitalisation indefinitely unless normal rhythm returns. I am aware that some, at least, relapse into tachycardia within a week or two of stopping their digoxin. I should much like to know—if anyone really knows—how many of them need life-time maintenance. Have we—the whole profession—or have we not a duty to go to some trouble to try to ensure long continuous treatment in every such case?

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**Our expert writes: "If a patient with atrial fibrillation has persistent tachycardia or goes into failure when digitalis is withdrawn, then clearly he or she should be digitalised permanently, thyrotoxicosis having first been excluded. This is not, however, the case with the majority of old people with atrial fibrillation and normal ventricular rates. Such patients often only go into heart failure when they have an intercurrent chest infection or an incident of cardiac infarction. In these cases permanent digitalisation is not necessary except during the incident of failure. Digitalis toxicity is now well documented and may provoke all kinds of dysrhythmia in the elderly, sometimes with fatal results. As with all powerful drugs it is better administered when it is needed rather than for long periods."—ED, *BMJ*.

Progestasert

SIR,—The recent widespread publicity in the national press and the active promotion of Progestasert (a new intrauterine contraceptive device which slowly releases progesterone over a period of one year) to general practitioners may have created the false impression that this item is prescribable on an FP10 prescription form.