3 h after the dose either before or after 10 days of drug administration. Isolated increases in plasma GH levels were noticed during the 10 days of treatment with BS 100-141 but were probably not drug-induced. No side effects were recorded. Blood pressure fell by a mean of 20/30 mm Hg.

Similar findings have been reported with levodopa.[5] Moreover, in subjects over 40 years of age a *decrease* of GH release has been reported after other stimuli (insulin, arginine, levodopa, exercise).[6] Weitzman[7] also found in an older adult group (aged 47-62 years) a marked reduction in GH secretory episodes, some subjects showing no GH peak at all during the 24-h study period. From the inability of BS 100-141 to increase GH secretion in patients aged 44-60 years, we may assume that with aging an important decrease in the number of α-adrenoceptors takes place.

Although a noxious effect of high plasma GH levels on the vascular system has been mentioned only in acromegaly and diabetes we think that these data may be of some interest since those subjects requiring antihypertensive therapy with clonidine or BS 100-141 are most frequently in the older age group.

IOANA LANCRANJAN
P MARBACH

Biological and Medical
Research Division,
Sandoz Ltd,
Basle, Switzerland

[1] Lal, S, *et al*, *Clinical Endocrinology*, 1975, **4**, 277.
[2] Lancranjan, I, and Marbach, P, *Metabolism*. In press.
[3] Scholtysik, G, *et al*, *Arzneimittel-Forschung*, 1975, **25**, 1483.
[4] del Pozo, E, *et al*, *Clinical Endocrinology*, 1977, **6**, suppl, p 49.
[5] Gomez-Sacher, C, and Kaplan, N M, *Journal of Clinical Endocrinology and Metabolism*, 1972, **34**, 1105.
[6] Bazzarre, T L, *et al*, in *Proceedings of the IIIrd International Symposium, Milan, 1975*, ed A Pecile and E E Müller. Amsterdam, Excerpta Medica, 1976.
[7] Weitzman, M D, *Annual Review of Medicine*, 1976, **27**, 225.

Benign mucous-membrane pemphigoid associated with penicillamine treatment

SIR,—There have been many recent reports of patients on penicillamine therapy who have developed pemphigus foliaceus[1 2] and other conditions in which autoimmune processes are believed to be important. We have recently seen a case in which benign mucous-membrane pemphigoid has appeared in a man taking penicillamine.

A man of 45 had suffered from rheumatoid arthritis for at least 12 years and had been treated with penicillamine 250 mg twice daily for two years as well as aspirin, indomethacin, prednisolone, and diazepam. In June 1976 he developed ulcers in the mouth and three months later soreness and bleeding of the nose and conjunctivitis. Penicillamine was stopped, but he continued to suffer the same symptoms and went on to develop blisters on the skin and hoarseness. At this stage (October 1976) he was seen by us at this hospital. He had a sparse crop of blisters on the skin, mainly on the hands and feet. There was extensive blistering and ulceration of the whole buccal cavity except the tongue and of the anterior nares. The voice was hoarse. There was bilateral conjunctivitis.

Biopsy of the skin and mouth showed blister formation at the level of the basement membranes. Conjunctival biopsy showed granulation tissue only. Direct immunofluorescence on the oral biopsy specimen showed linear binding of IgA to the whole of the basement membrane. Immunofluorescence elsewhere was negative.

He was treated with prednisolone and azathioprine as well as topical steroids. The eye lesions healed with conjunctival scarring and symblepharon formation. The skin lesions healed rapidly without scarring. By March 1977, when he was shown to the dermatological section of the Royal Society of Medicine, he still had soreness in the nose and one small blister on the palate.

The question remains whether this disease developed as a result of penicillamine treatment. Certainly it failed to respond to stopping the drug, but this is also seen in many cases of penicillamine-induced pemphigus foliaceus.[1 2] Benign mucous-membrane pemphigoid is an uncommon disease and is rare under the age of 60. This patient has also shown an unusually good response to steroids. Oral ulceration, the original symptom in this case, is a well-recognised side effect of penicillamine treatment and may arise in several different ways.[3] It is possible that some cases of penicillamine-induced mouth ulcers are formes frustes of this condition.

J S PEGUM
A C PEMBROKE

The London Hospital (Whitechapel),
London E1

[1] Hewitt, J, Benveniste, M, and Lessana-Leibowitch, M, *British Medical Journal*, 1975, **3**, 371.
[2] Marsden, R A, *et al*, *British Medical Journal*, 1976, **2**, 1423.
[3] Kuffer, R, and Noble, J P, *Revue de Stomatologie*, 1973, **74**, 309.

Correcting the calcium

SIR,—Your leading article (5 March, p 598) approves of correction of the serum total calcium concentration when the serum albumin concentration is abnormal. Published mean "correction factors" range from 0·018 to 0·025, expressed as mmol/l change in serum total calcium concentration for each 1 g/l change in serum albumin concentration, and you suggest that a factor of 0·020 be used to correct to a serum albumin concentration of 40 g/l. However, the "correction factors" quoted are *mean* values and we have found a wide scatter of *individual* "correction factors" ranging from 0·013 to 0·052 with a mean of 0·025.[1] In a further, as yet unpublished, study of 17 normal subjects individual "correction factors" derived from a tourniquet test range from 0·015 to 0·040. These differences are both statistically (at the 0·05 level) and clinically significant. Routine "correction" of the serum total calcium concentration using a mean factor may not be misleading in the majority of cases, but where there is a clinical suspicion of a disorder of calcium metabolism this "correction" is inadequate. In these cases direct measurement of the serum ionised or ultrafiltrable calcium concentration should be performed.

PAT PHILLIPS
ROY PAIN

Institute of Medical and
Veterinary Science,
Adelaide, S Australia

[1] Pain, R W, *et al*, *British Medical Journal*, 1975, **4**, 617.

**Drs Phillips and Pain feel that the data in their original paper can be interpreted only as evidence that individuals vary greatly in the avidity of the plasma proteins for binding calcium. These conclusions are based in part on a study of regression coefficients of calcium on albumin in 25 hospital inpatients who had multiple estimations; such patients were almost certainly ill and it seems unlikely that changes in plasma albumin were the only factors affecting the plasma calcium. Their conclusions were also based on two other studies in which plasma albumin and calcium levels were measured in normal subjects before and after a change in posture or the application of a tourniquet. The accuracy of the measurement of a change in plasma level is very limited because the difference is small compared with the total amount and its error is large because the errors of both measurements are compounded. For these reasons we hesitate to accept their view that individuals have characteristic and reproducible "correction factors" with such a wide scatter. If their new study provides good evidence of the reproducibility of the factor it will be of great interest. In the meantime there seems no justification for not using mean values from the literature.

Drs Phillips and Pain suggest that in difficult cases the plasma levels of ionised or ultrafitrable calcium should be measured. In centres with a special interest in calcium metabolism and a large volume of samples from suitable patients these assays may certainly be useful. Sadly, however, even at their best, the methods currently available have a greater analytical error than have methods for total calcium or albumin.—ED, *BMJ*.

Medical hazards of air travel

SIR,—Two recent experiences on an intercontinental international air carrier prompt me to write this letter.

About one hour after departure for London a male passenger was found slumped in his seat, unresponsive to command, sweating profusely, and with a weak, thready pulse. Search of his baggage disclosed that he was on antihypertensive medication. At this point I was requested to see him. Without any equipment (not even a sphygmomanometer) a period of observation led me to a diagnosis of hyperventilation syndrome in an overworked, exhausted business executive. He completed the journey uneventfully.

On my return flight I was asked to see a 74-year-old woman who was travelling non-stop from Scotland to New Zealand. She was afflicted with most of the infirmities that accompany old age and, in addition, had an acute anxiety state triggered off by aerial claustrophobia (this was her first major airline trip).

My first comment, based on several prior incidents similar to the above, is that there is a need for far more careful medical clearance of older passengers travelling six hours or more at a time. The present requirement is carried out casually and cursorily and sometimes is ignored altogether. Who should be responsible for implementation is a moot point. Perhaps the travel agent should have a medical questionnaire completed by all intending passengers over the ago of 50 who plan to leave their own country. Secondly, inquiry reveals that there is no uniformity among IATA carriers about what should be included in first-aid kits on their aircraft. It seems to vary from carrying it all to next to nothing. So if anyone on board, including crew members, were to suffer a myocardial infarct nothing but oxygen would be available.

The objection has been raised that treatment depends on diagnosis and diagnosis can only be made by a physician. Nowadays physicians travelling on aircraft are advised not to identify themselves and generally refrain from doing so. I happen to be an exception. Is it not a sad commentary of our times that fear of possible malpractice litigation prevents a doctor from being a Good Samaritan? Perhaps a medical advisory ground-to-air service on all major routes could be developed similar to the sea-to-shore medical radio services in existence for