advocate that ultrasound examination replaces these. The time factor prohibits the use of ultrasound for all patients with biliary symptoms.

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¹ Gravelle, I H, Jones, M, and Roberts, E S, *British Journal of Radiology*, 1973, **46**, 568.
² Hublitz, U F, Kahn, P C, and Sell, L A, *Radiology*, 1972, **103**, 645.

Management of childhood epilepsy

SIR,—I hope that Dr H Wykeham Balme (14 May, p 1284) does not imply that all children with epilepsy should live in a home with protected staircases, without bathroom locks, and with guards around the fires and radiators; that they should bath in less than three inches of water, go to school accompanied, and not climb trees or go swimming or camping.

The management of the patient with epilepsy consists in not only trying to prevent attacks using anticonvulsants—not so ineffective or poisonous when handled correctly—but also attempting to reduce the social and psychological complications by talking to his family. This latter aspect is frequently forgotten. If parents understand what epilepsy is and adopt a sensible attitude, so will the child, whereas if they are ashamed of him or become over-anxious he will react accordingly. Too often parents are given a long list of restrictions irrespective of the frequency of their child's attacks and without explanation.

The goal should be for children with epilepsy to live a normal life without restriction. Perhaps we have forgotten that taking risks is part of growing up and that a child must experience failure as well as success. The important point is that patients must be treated as individuals and with common sense. There will be some who will be unable to take part in certain activities, but most children with epilepsy can live in normal homes, take part in the usual school activities, and go swimming and camping provided they are adequately supervised. Over-protectiveness, either by parents or school, should be corrected early, as this will reinforce the stigma of epilepsy. Restrictions should be as few as possible. Surely it is better to err in favour of under-restriction than over-restriction.

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Acute renal failure associated with carbenoxolone treatment

SIR,—Following the report by Dr C Descamps and others on rhabdomyolysis and acute tubular necrosis associated with carbenoxolone and diuretic treatment (29 January, p 272) I wish to report another patient presenting with acute renal failure following administration of carbenoxolone.

The patient was a 38-year-old woman in whom gastric ulcer had been diagnosed five years previously. From this time onwards until her referral with renal failure she took carbenoxolone 200 mg daily. In addition, she was known to be hypertensive and had taken a proprietary compound analgesic preparation 2-3 times daily for 20 years.

Her present complaint to her own practitioner before referral was of progressive limb weakness for two weeks. She was found to have haematuria and proteinuria and was treated for pseudomonas urinary infection with nitrofurantoin. Over a period of days she became oliguric and was referred to this hospital for management of renal failure. She was hypertensive (blood pressure 190/110 mm Hg) and was found to be in renal failure despite adequate hydration (serum creatinine 640 μ mol/l (7.2 mg/100 ml), urea 21.5 mmol/l (130 mg/100 ml). Serum potassium was 1.6 mmol (mEq)/l, aspartate aminotransferase 1000 IU/l, and creatinine phosphokinase 2590 IU/l. Her renal failure progressed and she required peritoneal dialysis once and haemodialysis once. After a stormy clinical course marked by fever, severe hypertension, and pneumonia a diuresis ensued. Her treatment included ampicillin and gentamicin therapy. The serum creatinine ultimately fell to 150 μ mol/l (1.7 mg/100 ml), though she remained quite severely hypertensive and microscopic haematuria persisted after discharge from hospital. Attempts at intravenous pyelography were unsuccessful owing to a severe allergic reaction.

Multiple aetiology is presumed for this patient's renal disease. Pre-existing analgesic abuse, hypertension, urinary infection, and potentially nephrotoxic antibiotic therapy with gentamicin may have contributed to a greater or lesser degree. The striking feature of her presentation, however, was profound muscular weakness associated with severe hypokalaemia and oliguric renal failure. The high level of muscle enzymes approximates to those reported by Dr Descamps and his colleagues and it appears likely that carbenoxolone precipitated her acute renal decompensation.

The duration of carbenoxolone therapy (200 mg daily for five years) must surely be an all-time record. If she was taking her tablets as instructed it is remarkable that she did not present earlier with toxic effects from carbenoxolone.

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Transient hypotension following intravenous ethamsylate (Dicynene)

SIR,—I am concerned at the recent introduction by Delandale Laboratories of their "theatre pack" of ethamsylate, an agent for capillary haemostasis. The new pack consists of 1 g of ethamsylate in 2 ml in a disposable dental-type syringe. The suggested dose is 1.5 ml (750 mg) but I am sure there will be a tendency to give the extra 0.5 ml and empty the syringe.

Slight transitory hypotension has been reported following this drug, but in a series of eight consecutive patients given 500-750 mg over 30 to 40 s intravenously an immediate fall of blood pressure was seen in all cases, the minimum fall being 25 mm Hg and the maximum 85 mm Hg—not "slight" by any standard. Fortunately the effect was short-lived and in all but one case the blood pressure had returned to within 10 mm Hg of the preinjection level within five minutes.

The fall was more marked in the elderly, is almost certainly dose-related, and probably could be avoided by slow intravenous injection. This, however, is not facilitated in the "theatre pack." All eight patients were under general anaesthesia but none was judged to be hypovolaemic at the time of injection.

I therefore write to suggest care in using the

"theatre pack" or possibly its avoidance when intravenous administration of ethamsylate is required.

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Coronary artery spasm

SIR,—As emphasised in your leading article (7 May, p 1176) coronary artery disease is likely to have a variety of subtypes of which coronary artery spasm may be one. The onset of "variant angina" without provocation in patients with an arteriographically normal coronary arterial tree is quoted as a possible example of coronary artery spasm.

Is this not reminiscent of the time when "cerebral artery spasm" was thought to be responsible for transient ischaemic attacks now recognised to be due, in the main, to micro-embolisation from atheromatous plaques in the large extracranial vessels? It is recognised that these plaques may be quite small, producing neither stenosis nor bruit, and be demonstrable only by refined techniques such as "trickle angiography." I wonder whether information is available as to the presence (or absence) of ulcerated atheroma in the coronary arteries of patients with Prinzmetal's angina, plaques perhaps insufficient in extent to show on conventional arteriography?

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¹ Hugh, A E, *British Medical Journal*, 1970, **2**, 574.

Effect of antihypertensive drugs on growth hormone secretion

SIR,—Lal *et al*¹ reported that clonidine, an antihypertensive drug with central α -adrenoceptor agonist properties, increased growth hormone (GH) secretion in normal volunteers in an acute trial. We have found the same effect in a study with young (20-33 years) normal male subjects after a single oral administration of 2 and 4 mg of BS 100-141,² a new α -adrenoceptor agonist.³ On the other hand no increases in plasma GH levels were found in 10 young (30-40 years) hypertensive subjects who had been under BS 100-141 treatment (3-6 mg/day) for 3-12 months. The question which then arose was whether treatment with BS 100-141 is able to stimulate GH secretion in older hypertensive patients, who more frequently require antihypertensive therapy.

Six male patients aged 44-60 years with mild hypertension (range 160/100 to 180/100 mm Hg) volunteered for the study. After an overnight fast and 30 minutes' bed rest an indwelling venous catheter was inserted. Blood for GH determination was drawn before and 30, 120, 150, and 180 min after oral administration of 2 mg of BS 100-141. The subjects remained in a recumbent position and ate nothing during the test. They also abstained from smoking. This test was followed by treatment with BS 100-141 2 mg thrice daily for 10 days, during which time no other medication was given. Every second day at 0900—that is, 2 h after the first daily dose of BS 100-141—blood was collected for GH determination. After 10 days of treatment the test carried out on the first day was repeated, blood samples being taken before and at intervals after the final 2-mg dose of BS 100-141. GH was assayed by double-antibody radioimmunoassay as previously reported.⁴ No significant increase in plasma GH concentration was noticed during the

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 Weitzman⁷ 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.

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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.

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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.

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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 ultrafiltrable 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 age 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