cause of apparent resistance to treatment. True resistance cannot be accepted without evidence that the patient was ingesting and absorbing a pharmaceutically satisfactory preparation of vitamin D. Such evidence has not been given for any of the numerous published cases of "resistance" to vitamin D therapy, but adequate assurance on all three counts would be provided by showing that the plasma concentration of 25-hydroxycalciferol had been raised to a level consistent with the dose.¹ I suggest that no further cases of supposed resistance to vitamin D therapy should be reported without this crucial piece of information.

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¹ Himsworth, H P, and Maizels, M, *Lancet*, 1940, **1**, 959.

² Dent, C E, et al, *Pharmaceutical Journal*, 1953, **170**, 126.

³ Parfitt, A M, *Australasian Annals of Medicine*, 1968, **17**, 56.

⁴ Stamp, T C B, et al, *Lancet*. In press.

Insurance companies' attitude to psychiatric illness

SIR,—Dr J T Hutchinson (19 March, p 775), says that insurance companies have made it difficult for patients to take out life insurance because they have a history of psychiatric treatment.

The insurance companies have a point in those cases in which the psychiatric condition is likely significantly to shorten life. Take, however, two patients, each of whom has suffered from some form of nervous anxiety. One of them has had psychotherapy as an outpatient and has thereby improved but the other has not and his condition has made less gainful progress. The insurance company in question will penalise the former but not the latter because they do not understand the situation. A third patient may have gone to his family doctor with similar symptoms and have been treated with tranquillisers. He will regard this as "medical" treatment and so will escape the net even if psychotherapy would have done him more good.

My personal view is that where the treatment has been confined to outpatient attendances for psychotherapy and perhaps for mild drug medication this should not be regarded as "psychiatric" treatment. I have on occasion said to a patient that he will have my backing in disregarding such circumstances while filling application forms. Alternatively I would write a certificate to this effect.

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Heparin and pulmonary embolism

SIR,—I should like to report the case of a fit 57-year-old man admitted for routine cholecystectomy three months after an episode of acute biliary colic. As prophylaxis against deep vein thrombosis he was given 5000 U of heparin with his premedication of pethidine 100 mg, promethazine 25 mg, and atropine 0.4 mg, then 5000 U thrice daily postoperatively. The operation was cholecystectomy with exploration of the common bile duct and

was uneventful. On the fourth postoperative day he developed massive bilateral pulmonary emboli, which produced a 60–70% loss on lung scan and arteriography and a pulmonary artery pressure of 85 mm Hg. Leg venograms and an inferior venaogram showed no evidence of thrombosis. Despite immediate heparinisation by constant infusion of 10 000 U four times daily and later 15 000 U four times daily, keeping the thrombin time prolonged by a factor of 3–4, his condition remained critical for several days, necessitating oxygen therapy and transfer to the intensive care unit for close monitoring of his blood gases. He eventually made a good recovery after treatment with streptokinase.

I wonder whether the use of prophylactic heparin transformed what would have been a deep vein thrombosis into early pulmonary embolisation and whether embolism which does occur in the presence of heparin prophylaxis tends to be early rather than late. Conversely, did the prophylactic heparin prevent an otherwise fatal episode?

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Misdiagnosis of urinary tract infection

SIR,—Professor A W Asscher (21 May, p 1332) is right to stress the importance of making an accurate initial diagnosis when a patient presents with symptoms suggesting a urinary tract infection. But I think he should have mentioned a very important cause for the persistence or reappearance of symptoms after treatment. This is that the symptoms may not be due to a pyogenic infection at all (and organisms cultured from a so-called midstream specimen of urine may be simply contaminants).

I frequently receive referral letters stating that a patient "has suffered from repeated urinary tract infections [*sic*] despite several courses of antibiotics, though the midstream specimens of urine are usually sterile." Each year I see on average two patients with advanced bladder tumour, one with genito-urinary tuberculosis, and one with bladder stones whose referral has been delayed by many months *only* because they were subjected to inappropriate and repeated courses of antibiotic therapy and the possibility of the true diagnosis never considered.

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Rise in antibodies to human papova virus BK and clinical disease

SIR,—Since the isolation of the human papova virus BK seroepidemiological studies have shown that infections with this virus are very common and often occur in children.¹ An accompanying clinical disease has not yet

been established, although a mild respiratory illness of children has been recorded at the time of appearance of antibodies against BK virus.²

We have investigated retrospectively serial serum samples from 77 patients which had been sent to our department for clinical virological examination. Three cases of primary BK virus infection, one in a child and two in adults, were found as indicated by the appearance of haemagglutination-inhibiting antibodies. The clinical findings and serological data on different days of the illness are shown in the table. Acute upper respiratory symptoms accompanied by neurological involvement occurred in all three patients.

Our findings suggest that primary infection by BK virus in older patients may be followed by acute inflammatory polyradiculoneuropathy (Guillain-Barré syndrome). It remains to be determined whether the BK virus is the aetiological factor. Seroconversions against other viruses (influenza A and B, adenovirus, respiratory syncytial virus, herpes simplex virus, echovirus 9, and measles virus) could not be detected. In one patient (the third in the table) a slight rise (<8 to 32) of complement-fixing antibodies against psittacosis was found.

A causal relationship between upper respiratory tract infections and inflammatory polyradiculoneuropathy has been extensively documented³ for a number of viruses and our findings suggest that BK virus may also be implicated.

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¹ Padgett, B L, and Walker, D L, *Progress in Medical Virology*, 1976, **22**, 1.

² Mantyjarvi, R A, et al, *Annals of Clinical Research*, 1973, **5**, 283.

³ Arnason, B G W, in *Peripheral Neuropathy*, ed P J Dych, P K Thomas, and E H Lambert, vol 2. Philadelphia, Saunders, 1975.

Further assessment of the normal cholecystogram

SIR,—Mr M H Gough (9 April, p 960) does not mention ultrasound in his excellent review of cholecystography. The value of ultrasound B scanning to assess the presence of calculi in the non-functioning gall bladder has been established.^{1 2}

It has become our practice to scan patients with a normal cholecystogram when the clinical symptoms are strongly suggestive of gall stones. Out of a large group of patients we have found gall stones in three when the cholecystogram appeared normal. At laparotomy two of these patients had gall stones but the third has not been explored. We have also detected calculi in the common bile duct in a patient with transient jaundice when a follow-up intravenous cholangiogram appeared normal. This patient had calculi in the duct when operative cholangiography was performed. The presence of pancreatitis in association with cholecystitis may also be demonstrated.

The majority of calculi are rapidly detected by conventional techniques and we do not

Clinical features and rise in BK virus antibody titre in three patients

Patient No	Clinical features	Age (years)	Rise in antibody titre
1	Upper respiratory tract infection, convulsions	3	<16 (day 3)→64 (day 13)
2	Respiratory infection, Guillain-Barré syndrome	45	<16 (day 9)→128 (day 24)
3	Respiratory infection, Guillain-Barré syndrome	33	<16 (day 13)→128 (day 28)

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