epileptics with elevated serum alkaline phosphatase showed a rise in level of the bone isoenzyme. Apparently Mr. Rowe's opinions—or his methods—have undergone some change over the past three years.

It is correct that our photon absorptiometry method cannot tell whether a low B.M.C. is due to osteoporosis or osteomalacia; it is also correct that patients with osteoporosis do not respond to treatment with 2,000 IU of vitamin D_2 daily for three months. Our 116 epileptics on this treatment showed a highly significant increase in B.M.C., while the control group of 110 patients showed unchanged B.M.C. values. Mr. Rowe and Dr. Stamp will have a hard task in convincing the public—or us—that epileptics on anticonvulsants do not show signs of vitamin D deficiency. In trying to do this they seem to overlook some essential facts which may not fit their preconceived opinions but which nevertheless remain facts.

We have studied with interest the results of classical calcium balance studies in three patients reported by Mr. Rowe and Dr. Stamp (together with other authors) in two articles.[2 3] A common feature of these three patients was that calcium balance was studied in three *consecutive* periods: a control period, a period on vitamin D_2, and a period on vitamin D_3 (or 25-OH-D_3). If the effect of each vitamin had been studied for three months in these three patients it would have been relevant to compare the findings with our results in 116 patients.

Whether or not a dose of 2,000 IU of vitamin D daily can "heal anticonvulsant rickets or even . . . prevent its occurrence" is a question raised by Mr. Rowe and Dr. Stamp and certainly not by us. Our patients were between 21 and 70 years of age, a period of life where "anticonvulsant rickets" is seen rather infrequently, at least in Denmark.

We wonder why Mr. Rowe and Dr. Stamp remained silent when, in 1972, an authoritative British journal stated editorially that "though [anticonvulsant osteomalacia] may be only at a biochemical level, sound medical practice is to offer prophylactic vitamin therapy before frank bone disease develops."[4] This statement challenged us, but we should like to stress once more, as we did in our article, that it was not possible from our results to tell whether epileptics should be treated prophylactically with viamin D.

Our article supports a number of previous publications and demonstrates a definite effect of vitamin D. We are therefore somewhat bewildered that Mr. Rowe and Dr. Stamp do not see the point of a *possible* benefit of prophylactic vitamin D treatment in such patients, as also proposed by other authors.[4 5]—We are, etc.,

PAUL RØDBRO

Department of Clinical Physiology,
Aalborg Sygehus,
Aalborg

CLAUS CHRISTIANSEN

Department of Clinical Chemistry,
Glostrup Hospital,
Glostrup, Denmark

1 Richens, A., and Rowe, D. J. F., *British Medical Journal*, 1970, 4, 73.
2 Dent, C. E., *et al.*, *British Medical Journal*, 1970, 4, 69.
3 Stamp, T. C. B., *et al.*, *British Medical Journal*, 1972, 4, 9.
4 *Lancet*, 1972, 2, 805.
5 Hahn, T. J., *et al.*, *New England Journal of Medicine*, 1972, 287, 900.

Metastatic Processes

SIR,—Your reviewer of *Chemotherapy of Cancer Dissemination and Metastasis* (4 May, p. 286) asks, "Why does primary melanoma of the eye metastasize to the liver, breast cancer to the ovary, and Hodgkin's disease to the spleen?" I suggest that malignant cells metastasize to particular sites because they are able to obtain in those situations elements (such as amino-acids or hormones) on which they are dependent for their continued growth and survival. The process appears to be analogous to chemotropism, "an orienting response to a chemical stimulus, as in a plant root."

On this hypothesis primary melanoma of the eye metastasizes to the liver, "the greatest chemical factor of the body," to obtain the amino-acid tyrosine, the parent substance of melanin. It may be noted that in the case of melanotic carcinomas of the skin metastases also occur particularly in the liver. Some breast cancers appear to be ovarian hormone-dependent and thus metastasize to the ovaries. They have been known to regress after bilateral oophorectomy. In lymph nodes affected by Hodgkin's disease there is hyperplasia of the reticuloendothelial cells. These metastasize to the spleen, which has the largest aggregation in the body of cells of the recticuloendothelial system, possibly to obtain a hormone (reticulin M) produced by this system.—I am, etc.,

M. COWAN

London S.E.6

Serological Tests for Amoebiasis

SIR,—I was surprised to see the letter (6 April, p. 59) from Dr. F. Scott minimizing the value of serology in amoebiasis. It would be a pity if, as a result of his letter, the use of this valuable tool was restricted. The number of tests we in Durban have carried out now runs into several tens of thousands, and the enthusiasm of our clinicians is indicative of the confidence they have in the test.

Using the micro-gel-diffusion or the latex tests (which avoid the difficulty of interpretation of titre) we know that many cyst-passers, especially from temperate zones, show no antibodies. We interpret this as meaning that the commensal *Entamoeba histolytica* responsible for the cysts has not made the parenteral contact necessary for the stimulation of antibody. On the other hand when patients are passing haematophagous trophozoites the proportion showing antibodies at some time is well over 95%. In proved amoebic liver abscess the figure is over 99%. These are impressive figures for any serological test. In infants the results are more erratic—possibly the appropriate mechanisms have not been established. The test cannot be blamed for the negative result.

The persistence of antibodies might be regarded as a nuisance, particularly in endemic areas, limiting the tests to exclusion of invasive amoebiasis. However, sero-epidemiology based on this fact is proving most useful. When one appreciates the many pitfalls in the morphological identification of *E. histolytica* and the lack of laboratories able to appreciate these the value of serology in amoebiasis is self-evident.

The workers at Loon Lake are to be congratulated on their operation, which has high-lighted the association between invasive amoebiasis and density of human population in the absence of adequate hygiene.—I am, etc.,

R. ELSDON-DEW

Amoebiasis Research Unit,
Institute for Parasitology,
Durban, South Africa

Drugs for Gastric Ulceration

SIR,—Unlike Dr. A. B. S. Mitchell (1 June, p. 501) I thought your leading article (27 April, p. 186) gave an excellent survey and I entirely agreed with its conclusion that carbenoxolone seems still to be the drug of choice. It seems to work by improving the defence mechanisms of the stomach by stimulating mucus production and by lengthening the life cycle of the epithelial cells, both facilitating the repair process.

I was associated with the first studies on this drug in this country and have followed closely the world literature ever since. Its beneficial effects have been repeatedly confirmed in many countries. It is clear that this treatment enables gastric ulcers to be treated in the ambulatory patient—a very considerable economic advantage. Like other modern effective drugs such as corticosteroids, carbenoxolone has to be used with some care and discretion and a few simple precautions observed. Used in this way it is an effective and safe treatment.—I am, etc.,

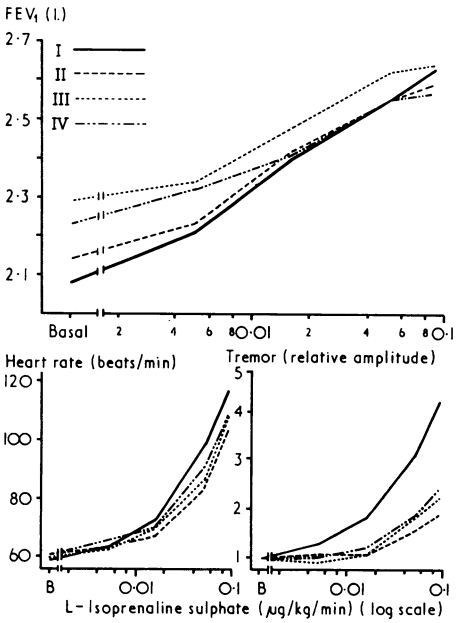
F. AVERY JONES

Central Middlesex Hospital,
London N.W.1

Studies of Resistance to Long-acting Adrenergic Beta-stimulators in Asthmatic Patients

SIR,—Since the report of Conolly and others[1] the development of resistance to long-acting adrenergic beta-stimulators has been much discussed. We have begun a study to see whether resistance develops in the beta-receptors in the bronchi, heart, and skeletal muscle during oral terbutaline treatment of patients with chronic obstructive bronchitis who have not previously taken beta-stimulating drugs. We first observed the effect on forced expiratory volume, heart rate and blood pressure, and muscular tremor of increasing intravenous doses of isoprenaline. After this treatment was started with terbutaline 5 mg thrice daily orally. So far we have repeated the observations of the effect of intravenous isoprenaline in increasing dosage after one, two, and three months' terbutaline treatment. The figure shows the mean values in eight patients. The dosage of isoprenaline was so selected that the highest dose caused nearly maximum bronchodilation. All tests were performed in the morning after the patient had been without terbutaline for 10 hours.

The higher basal value in the morning during terbutaline treatment suggests that the patients did not develop resistance to their own adrenaline or noradrenaline. In addition the same maximum bronchodilatation was obtained with isoprenaline, suggesting that no resistance occurred during terbutaline treatment. All patients experienced powerful muscular tremor towards the



Effects of increasing intravenous doses of isoprenaline in eight patients with obstructive lung disease not previously treated with adrenergic beta-stimulating drugs (I) and effects after one, two, and three months' treatment with terbutaline (II, III, and IV).

end of the first isoprenaline infusion. This was much less pronounced after one, two, and three months' terbutaline treatment. The rise in pulse rate was also somewhat less during treatment.

From these preliminary findings it seems that resistance does not develop in the bronchial muscles after this dose of terbutaline, while there is an obvious development of resistance to isoprenaline-induced muscular tremor. This accords with clinical experience. We shall observe further isoprenaline dose-response curves after six, nine, and 12 months' treatment with terbutaline to avoid seasonal variations in bronchial obstruction and finally after giving terbutaline in very large doses for several days.

This work was supported by grants from the Swedish Medical Research Council, the Swedish National Association against Heart and Chest Diseases, and AB Draco, Lund.

—We are, etc.,

NILS SVEDMYR
SVEN LARSSON
GUNNAR THIRINGER

Clinical Pharmacology Laboratory,
Lung Clinic,
Renströmska Hospital,
Göteborg, Sweden

1 Conolly, M. E., *et al.*, *British Journal of Pharmacology*, 1971, **43**, 389.

Vein Stripping

SIR,—Dr. D. Freedman rightly asks (18 May, p. 387) whether, apart from the removal of small isolated segments of abnormal veins, stripping of the long saphenous vein should ever be done. I was never an enthusiastic vein-stripper and only regret that I was ever persuaded to undertake this procedure at all widely in the past. However, I agree that a stripper can be of value in removing short lengths of vein.

When varicose veins cause symptoms and operation is clearly indicated their eradication may necessitate (1) ligation of long and/or short saphenous veins flush with the deep vessels, (2) careful ligation of tributary veins and leaking perforators, and (3) meticulous excision of troublesome varices, or various combinations of these three basic procedures. It is essential that the examination and assessment of these cases should be done by an experienced surgeon. Huge numbers of patients are still far too casually selected for operation by inexperienced doctors, and many operations are ill-planned and badly executed. The use of a stripper is a poor substitute for better alternative procedures, and it is a pity to spoil an otherwise good operation by tearing out long lengths of straight and healthy vein.—I am, etc.,

REGINALD S. MURLEY

Radlett, Herts

SIR,—In the article by Mr. S. J. Cox and others (9 March, p. 415) the conclusion was reached that retrograde stripping of the long saphenous vein was preferable to orthograde stripping in order to prevent neurological damage to the long saphenous nerve. The problem with retrograde stripping is that the stripper does not always easily pass from the groin to the ankle. More often it is easier to pass it in orthograde fashion. In a series of 54 patients in which careful exposure of the nerve at the ankle was obtained, ensuring that the stripper passed clear underneath the bifurcation, only two patients showed very minor sensory disturbance. Thus I would suggest that orthograde stripping is easier, provided that a proper dissection is carried out to clear the bifurcation of the nerve from the saphenous vein above the ankle.—I am, etc.,

DOUGLAS MILLAR

Colchester

Assessing the Safety of Comatose and Postanaesthetic Patients

SIR,—We were very interested in the method of assessment of the degree of airway security described by Drs. A. W. Grogono and A. R. de C. Deacock in patients with impaired consciousness (20 April, p. 174). For the past eight years we have regularly used a three-stage test of airway security. The method was originally devised for patients recovering from 4-hydroxybutyrate narcosis, a condition in which there is a propensity to maintain a clear airway during unconsciousness. This contrasts with what happens following the administration of narcotic analgesics as part of an anaesthetic sequence, as Drs. Grogono and Deacock quite rightly indicate: here a potentially conscious patient tends to lose his airway when not being stimulated.

In our test stage I consists of pinching the nostrils to occlude the airway; stage II involves closing the nose as in stage I and simultaneously pressing the jaw backwards exactly as described by Drs. Grogono and Deacock; in stage III the nose is closed and the lips are held together. Graduated assessment of the degree of unconsciousness is possible according to whether the patient attempts to open his mouth (stage I) or turns his head to the side (stages II and III). If he responds satisfactorily he is classified as being reasonably safe.

Before the use of epidural anaesthesia in the management of toxaemia during labour pethidine was used for pain relief. Combined with the anticonvulsant chlormethiazole this sometimes resulted in excessive sedation of the patient and a tendency to airway obstruction in the absence of stimulation. To assess safety, the airway tests were used in the sleeping patient without simultaneously assessing the level of consciousness. If the patient was only lightly asleep the manoeuvre caused only transient arousal and he quickly dozed off again.

A word of warning is required. The test should be undertaken only by properly trained medical personnel as they can best decide whether it is reasonable to obstruct two or three attempts at inspiration in any given patient. Furthermore, we have by this test on one occasion provoked vomiting. —We are, etc.,

M. E. TUNSTALL
M. EDITH BEVERIDGE

Aberdeen Maternity Hospital and
Royal Aberdeen Children's Hospital,
Aberdeen

Musical Bumps

SIR,—The description by Mr. J. M. Thomas (1 June, p. 504) of the way in which a classical guitar is held by the player is, of course, accurate but it applies only to male players. The way in which a classical guitar is held by a female player is somewhat different: the right handed female player sits with her legs crossed and the instrument rests on her right knee. The top edge of the soundbox will then overlie the region of the right nipple. The three patients described by Dr. P. Curtis (27 April, p. 226) were all female.—I am, etc.,

NORMAN P. MELIA

Cardiff

SIR,—If the classical guitarist's left foot is supported by a footstool approximately 6 inches (15·2 cm) high, then the upper and lower bouts of the guitar rest on the anterior aspects of the player's left and right thighs respectively. This avoids compression of the left long saphenous vein described by Drs. R. Semple and J. Gillingham (1 June, p. 504). Elevation of the left thigh in this way also minimizes pressure on the sciatic nerve between chair and ischium, while avoidance of the alternative position in which the guitar's waist is supported on the left thigh crossed over the right obviates temporary paralysis of the left common peroneal nerve resulting from pressure against the head of the fibula. Since adopting the use of the footstool I have not suffered from "guitarist's foot-drop," previously the bane of practice.

Without inconveniencing the action of the right hand the back of the instrument can be made to clear the nipples by several inches provided the musician is not unreasonably convex.—I am, etc.,

D. G. ROSS

Aberdeen

T.V. Programme on Heart Disease

SIR,—The B.B.C. documentary on heart disease on 21 May was disappointing in its lack of specific detail for the viewer to