aspartate aminotransferase (SGOT) and alkaline phosphatase in 16 adults with serum salicylate greater than 35 mg/100 ml as a result of single-dose self-poisoning. In only one patient was the SGOT minimally increased to 44 units. This was an apparently healthy 24-year-old man with a serum salicylate of 80 mg/100 ml four and a half hours after taking aspirin tablets; his alkaline phosphatase was normal. A 60-year-old man with a serum salicylate of 131 mg/100 ml eight hours after ingestion was the only patient with a raised alkaline phosphatase (16 King-Armstrong units); his SGOT was normal.

These findings tend to support the implied conclusion of Dr. Russell and colleagues that, age apart, increases in these enzymes in serum are probably related to prolonged administration of salicylates.—I am, etc.,

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E.E.G. and Anticonvulsants

SIR,—While I must agree with Miss Coleen Darby and Dr. D. Fung (8 May, p. 341) that alteration of the state of awareness may influence the E.E.G., such marked slowing of the E.E.G. as I described (24 April, p. 207) is most unusual in normal states of diminished awareness (for example, drowsiness or mild confusion), and is seldom seen in cases of drug intoxication. In the case of anticonvulsant toxicity reported the patient was alert enough to open her eyes to command as shown (Fig. 1), and was also able to perform three minutes of hyperventilation with only a single encouragement. No specific response was seen to arousal stimuli ("K" complex), nor were sleep spindles seen as might be expected in such loss of awareness resulting in the widespread delta activity illustrated, if this were due to drowsiness or sleep. Thus the E.E.G. changes shown are presumably the result of the excessive drug therapy and are present as a complication, with the low serum folate, of the medications. At the time of the second E.E.G., eight days after the initial tracing, the patient was clinically much improved, up and about the ward, and was no longer confused or disorientated.

It is well known that very many factors may be associated with slowing and subsequent return to normal of cerebral rhythms. I reported this case to illustrate the association of a low serum folate in anticonvulsant intoxication with E.E.G. change, and to stress the value of the investigation in assessment and follow up of such cases.—I am, etc.,

W. I. M. Dow

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Diet and Diverticulosis

SIR,—Mr. N. S. Painter and Mr. D. P. Burkitt (22 May, p. 450) argue from clinical records that the increasing incidence of diverticulosis and diverticulitis in man is due to eating diets deficient in roughage.

Many years ago, when I was on the staff of the Rowett Institute in Aberdeen, I took part in a long-term experiment with rats

on a human dietary.¹ A large colony of rats was kept for several years on a diet which mimicked accurately the foods eaten by the people of Peterhead, a coast town in Aberdeenshire. One group of rats was kept on the "Peterhead" diet alone, another group had the "Peterhead" diet supplemented by the addition of milk and of green vegetables. The environment and treatment of both groups was otherwise identical. The rate of growth, the reproductive capacity, and the general health of the rats was followed generation after generation: each animal, when it died from illness or "old age," was examined.

Many of the old rats on the unsupplemented "Peterhead" diet had a condition of the gut which macroscopically closely resembled diverticulosis and diverticulitis in man. Microscopically, however, the condition differed from that in man. Some of the rats on the diets supplemented with milk and green vegetables also suffered but the incidence was not so great. These findings were reported in the *B.M.J.*²

We were commendably cautious and refused to jump to conclusions. Unfortunately, the intention to extend and elaborate the experiments on the rats with special reference to the condition of the gut could not be put into effect.—I am, etc.,

R. C. GARRY

Laich Dyke,
Dalginross,
Comrie,
Perthshire

¹ Orr, J. B., Thomson, W., and Garry, R. C., *Journal of Hygiene*, 1936, 35, 476.

² Lubbock, D. M., Thompson, W., and Garry, R. C., *British Medical Journal*, 1937, 1, 1252.

Comparison of Drugs for Asthma

SIR,—Dr. K. N. V. Palmer and others (27 March, p. 727) have done a one-dose, non-blind test comparing 300 mg of proxyphylline (a theophylline compound) with two new β_2 -receptor stimulant drugs. They found no significant changes after this proxyphylline, and conclude that "proxyphylline . . . cannot be recommended for the relief of asthmatic airway obstruction at least when given by mouth." They seem to be unaware of the fact that such a dose will not give higher serum level than a maximum of 8 μ g/ml. Hauge and Gamst¹ found that a single oral dose of 400 mg of proxyphylline produced a maximal serum level of about 8 μ g/ml. Recent studies² in five healthy volunteers using proxyphylline 600 mg twice daily yielded a mean serum level of 10 μ g/ml during 1-3 hours after the first dose of 600 mg. After five days of therapy the serum levels at the corresponding times were around 18 μ g/ml.

We have done two double-blind studies comparing proxyphylline in two dosages and placebo in 17 patients with chronic obstructive airway disease. Reversion of bronchoconstriction was evident by a mean increase of FEV₁ of 30% after two inhalations of Isoprenaline Medihaler O. Proxyphylline 150 mg four times daily for 48 hours produced a mean serum level of 8.7 ± 0.9 μ g/ml but no significant changes in FEV₁, either after 24 or after 48 hours. With a dose of 300 mg four times daily, however, the serum level averaged 18.3 ± 1.1 μ g/ml after 48 hours. FEV₁ increased on the average 8.5% after 24 hours ($p < 0.05$) and

18.7% after 48 hours ($p < 0.01$). Placebo therapy produced no significant changes in FEV₁.

These data confirm that proxyphylline, given in a sufficient dose for a time long enough to produce adequate serum levels, produces a statistically significant and a clinically noticeable reversion of airways obstruction, as measured by the FEV₁. Thus, I cannot agree with the statement quoted above.—I am, etc.,

LENNART TIVENIUS

Örebro, Sweden

¹ Hauge, H. E., and Gamst, O. N., *Tidsskrift for den Norske Lægeforening*, 1967, 87, 535.

² Graffner, C., Personal communication.

Analgesics in Terminal Disease

SIR,—A patient of mine has recently returned from a teaching hospital with unhappy memories. She has extensive pelvic carcinomatosis needing narcotic analgesics, but because she was written up four-hourly she often underwent an hour or more of agonising pain before she could be given the next dose.

She is now at home with a liberal supply of analgesics by her bedside and for the moment is more or less relaxed and free of pain. She has made it quite clear however that she will not consider returning, when the need arises, to the same hospital but only to her local cottage hospital. Here, although she knows that she will not receive the same degree of surgical skill, she is assured of relief at any time and that no one, and especially herself, will be watching the clock.

Is it not time that we adopt a more liberal attitude to prescribing and abandon the rigid time schedules?—I am, etc.,

P. B. SCHOFIELD

Walton on Thames

Levodopa and Anticholinergic Drugs in Parkinsonism

SIR,—Dr. R. C. Hughes and others (29 May, p. 487) described the effect of withdrawal of anticholinergic drugs on patients receiving levodopa for Parkinsonism. They found that only 11 out of 34 patients were able to tolerate withdrawal for more than eight weeks. They suggest that "the synergism which seems to exist between anticholinergic remedies and levodopa may be due to inhibition of dopamine inactivation by anticholinergic drugs."

The fact that patients suffering from Parkinsonism require anti-acetylcholine drugs may have a different explanation. We know that dopamine is released in the corpus striatum by impulses originating in the substantia nigra. Thus the nigra-striatal tract is composed of fibres closely resembling sympathetic postganglionic fibres except that the former release dopamine and the latter release noradrenaline. Recently the evidence that sympathetic fibres release noradrenaline through the prior release of acetylcholine has been greatly strengthened.¹ This release of acetylcholine becomes obvious when noradrenaline is removed, as by the injection of reserpine, for then stimulation of sympathetic fibres to the heart,² the spleen,³ and the blood vessels releases acetylcholine which is not used in releasing noradrenaline.

It might therefore be expected that when

there was a deficiency of dopamine in the corpus striatum there would be a release of acetylcholine, which would produce symptoms of its own when it could not fulfil its usual function of releasing dopamine. This would account for the bradykinesia, increasing tremor, etc., which are controlled by giving benzotropine.—I am, etc.,

J. H. BURN

Oxford

- ¹ Burn, J. H., *Nature*, 1971, **231**, 237.
- ² Hukovic, S., *British Journal of Pharmacology and Chemotherapy*, 1959, **14**, 372.
- ³ Brandon, K. W., and Rand, M. J., *Journal of Physiology*, 1961, **157**, 18.

Registrar Cover for Obstetric Unit

SIR,—As an elected member of the various committees representing the consultants in this country I can confirm that the enforced registrar reduction implemented by the Department has never been agreed to by any of the committees (Mr. J. H. Hughes, 12 June, p. 656.)

This high-handed manner of changing hospital staff is an affront to the consultants in Britain, which would not be of moment were it not seriously to affect the care of the patients and the responsibility of the consultant to them.

The Department has been implementing these changes surreptitiously and it is only recently that its intention has been disclosed. Meanwhile, the standard of patient care has declined in these areas. It should be noted that this occurrence was used as a "lever" in the recent debates to put through national figures for staff ratios and to set up yet another controlling committee (Central Manpower Committee).

The profession is aware of the acute danger to the patients as a result of these irresponsible bureaucratically - motivated changes in staff. Major disasters may frequently occur if experienced doctors participating in the hour-to-hour care of the gravely ill patients are removed simply to keep the "books straight."—I am, etc.,

J. J. SHIPMAN

Letchworth,
Herts

False Economy

SIR,—Far from sharing the pious horror expressed by Dr. A. K. Clarke (29 May, p. 530) I applaud the Department of Health's action in circularizing the profession about the comparative costs of hypnotics.

Many insomniac patients are well suited by butobarbitone or amylobarbitone, and I object to my money being used to provide them with a drug costing seven times as much, except in cases of obvious irresponsibility.—I am, etc.,

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Bridge of Weir,
Renfrewshire

Treatment of Syringomyelia

SIR,—Your leading article on the treatment of syringomyelia (15 May, p. 355) draws attention to the good results obtainable in the communicating form of this condition. There is, however, an unthinking repetition of Gardner's attempts to explain the association with abnormalities at the foramen

magnum. There is no evidence that "stenosis of the foramen of Magendie" can ever be "of such a degree as to allow the flow of ventricular fluid at the rate it is being formed yet preclude sudden displacements of ventricular fluid during the cardiac systole." If there is impairment of the passage of fluid out of the fourth ventricle the result is hydrocephalus, not syringomyelia. His ideas that a pulse wave might be "funnelled" into the upper end of the central canal are without clinical, experimental, or theoretical basis. If a pulse wave engendered by arterial systole inside the ventricles were to destroy tissue it would produce damage within the head, not many inches away down the spinal cord.

A more rational explanation of the phenomenon is that it is secondary to fluid movements at the foramen magnum during straining. In the erect position an increase in abdominothoracic pressure may be accompanied by a movement of up to 8 ml of fluid through the foramen magnum. The cause of the upward movement is distension of the epidural veins.^{1,2} Under certain conditions cerebellar ectopia or arachnoiditis may cause fluid to move downwards into the communication. The sites of initial destruction of the spinal cord are determined by the relation of grey matter to white matter.³

Gardner's explanation is unable to account for syringobulbia. On this account the venous mechanism appears to be obviously the more correct one, but there is additional evidence. The forces and volumes involved in coughing are over 10 times greater than those produced by the "arterial" ventricular pulse wave. Syringomyelia may occur in cases where the aqueduct is blocked. The foramen of Magendie is not blocked in all cases. The venous mechanism can be demonstrated on a fluid analogue model. The "arterial" mechanism has not been successfully demonstrated. The pulsations of arterial origin within the head are highest in children. The pulsations of venous origin are higher in adults. Symptomatic syringomyelia most commonly has its origins in early adult life.

Cases are on record in which a sudden onset of syringomyelic symptoms has occurred in response to a strain likely to give rise to venous distension.⁴ The cord cavity is usually flaccid. A flaccid cord can be subjected to stresses by movement of fluid within its cavities whereas the arterial hypothesis demands that the cord be tightly inflated.

Arachnoiditis is not a common finding in cases of late cervical syringomyelia following injuries to the dorsal and lumbar spinal cord. In these cases the explanation is similar to the mechanism which produces syringobulbia, that the inside of the cord contains fluid and the upward driving force imparted to the cerebrospinal fluid by the epidural veins during straining drives fluid upwards within the syrinx and thus cause further cavitation.⁵ The objective for operation is to make an artificial cisterna magna with free access both upwards and downwards.⁶

Lastly, your leading article does not make a clear distinction between the common, communicating form and cases in which there is an intraspinal tumour causing the syrinx. With tumours the syrinx is not in communication with the cerebrospinal fluid pathways. The investigation, treatment, and prognosis are entirely different.⁶ Such cases

should be clearly distinguished from cases of "communicating syringomyelia."—I am, etc.,

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- ¹ du Boulay, G., O'Connell, J. E. A., Currie, J., Bostick, T., and Verity, P., *Acta Radiologica*, in press.
- ² O'Connell, J. E. A., *Proceedings of the Royal Society of Medicine*, 1970, **63**, 507.
- ³ Ommaya, A. K., *Journal of Biomechanics*, 1968, **1**, 127.
- ⁴ Williams, B., and Turner, E. A., *Acta Neurochirurgica*, in press.
- ⁵ Williams, B., *Lancet*, 1970, **2**, 41.
- ⁶ Williams, B., *British Journal of Hospital Medicine*, 1970, **4**, 331.

Calcium Carbonate, Hypercalcaemia, and Peptic Ulcer

SIR,—I have only recently become aware of the case report "Acute Hypercalcaemia and Renal Failure after Antacid Therapy," by Dr. D. N. S. Malone and Dr. D. B. Horn (27 March, p. 709). While agreeing with their emphasis that ingestion of varying proprietary antacid preparations containing calcium may lead to renal failure and confusion with hyperparathyroidism in peptic ulcer patients, it is felt other points deserve emphasis. The pharmacologically effective dose of calcium carbonate is 4-5 g each hour if neutralization of gastric juice is to be maintained in male duodenal ulcer patients.^{1,2} The administration of this enormous dose of calcium carbonate fails to accelerate the healing of gastric ulcers,³ and the hypercalcaemia rate is approximately 30%.⁴

Consequently, it is strongly felt that intensive antacid therapy has no place in the treatment of peptic ulcer and calcium and sodium containing preparations should never be used. Calcium containing preparations carry the risk of hypercalcaemia, renal stones, and renal failure, as demonstrated by Drs. Malone and Horn, and sodium preparations the risk of heart failure in those whose cardiac reserves are limited. Any of the many sodium and calcium free antacid tablet preparations available appear to be adequate for pain relief.—I am, etc.,

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- ¹ Myhill, J. A., and Piper, D. W., *Gut*, 1964, **5**, 581.
- ² Piper, D. W., and Fenton, B. H., *Gut*, 1964, **5**, 585.
- ³ Baume, P. E., and Hunt, J. H., *Australian Annals of Medicine*, 1969, **18**, 113.
- ⁴ Stiel, J. N., Mitchell, C. A., Radcliff, F. J., and Piper, D. W., *Gastroenterology*, 1967, **53**, 900.

Care of Chronic Psychotics

SIR,—In your leading article (15 May, p. 351) you quote me as having shown that 30% of admissions to a particular mental hospital were of "no fixed abode". In my original paper which was read at a seminar at the Royal Medico-psychological Association meeting on 10 February, and later quoted in the *Lancet*¹ I made it clear that I was referring to male patients only. Destitution of this kind is of course far less common among women, so that the overall proportion of "no fixed abode" admissions is considerably less than 30%. Although I believe that this problem is a serious one I would not like to spoil my case by exaggerating it.