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.,

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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,
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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

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- 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.,

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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