undermine the whole basis of the doctor-patient relationship and shake the confidence of the public, especially the adolescent girl who so needs our help.—I am, etc.,

ERIC TOWNSEND

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Pathogenesis of Myasthenia Gravis

SIR,—Your most interesting leading article on myasthenia gravis (3 April, p. 1) prompts me to refer to earlier work indicating the presence of a hormone in the thymus influencing neuromuscular transmission. Torda and Wolff¹ showed plasma in myasthenia gravis inhibited acetylcholine synthesis, and in 1944 we² published a paper showing that normal thymus increases acetylcholine synthesis and thymus tumour in myasthenia gravis inhibits synthesis of acetylcholine. We concluded that the replacement of stores of acetylcholine in the neuromuscular junction was the deficiency in myasthenia gravis, and you indicate the same with the production of lower quanta of acetylcholine at the motor endplate.³ I also pointed out⁴ this correspondence in muscle weakness in thyrotoxicosis with "lymphorrhages" in muscle and myasthenia gravis, and suggested these lymphoid collections produced a similar substance.—I am, etc.,

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¹ Torda, C., and Wolff, H. G., *Science*, 1943, **98**, 224.

² Trethewie, E. R., and Wright, R. D., *Australian and New Zealand Journal of Surgery*, 1944, **13**, 244.

³ Thesleff, S., *Annals of the New York Academy of Sciences*, 1966, **135**, 195.

⁴ Trethewie, E. R., *Medical Journal of Australia*, 1956, **1**, 13.

Jejunal pH and Folic Acid

SIR,—In a recent report Dr. Ann Benn and others (16 January, p. 148) showed that the jejunal pH in epileptics on longterm anticonvulsant therapy was more alkaline than in controls, which might cause malabsorption of folic acid.

This explanation of anticonvulsant megaloblastic anaemia is fully in agreement with my results of in vivo perfusion experiments in rats.¹

These experiments showed that the absorption of folic acid depends on the intraluminal pH. Introduction into the jejunum of barbiturates in unbuffered solutions caused a rise of pH in the intestinal contents and consequently the absorption of folic acid was reduced by $\frac{1}{2}$ – $\frac{3}{4}$ of the total. In buffered solutions barbiturates caused neither alterations of pH nor decreased absorption of folic acid.

In one patient on treatment with phenytoin 150 mg twice daily for epilepsy the absorption of folic acid was reduced by approximately half by phenytoin (Fig.). As betaine hydrochloride, which in the stomach splits off hydrochloride, had an antagonistic effect on phenytoin it is assumed that in the gastrointestinal tract phenytoin causes a disturbance of the pH regulation, resulting in malabsorption of folic acid. I have also found malabsorption of folic acid in five out of six patients with anticonvulsant megaloblastic anaemia.²

Dr. Ann Benn and her colleagues claim that increasing alkalinity above pH 5.0 would cause a fall in the concentration of folic acid in the neutral form, in which condition folic acid crosses the intestinal wall. In my experiments it was found that the maximum of absorption for folic acid was about pH 6.0. Higher as well as lower pH decreased the absorption rate of folic acid. However, 100 mg barbitone (or phenytoin) taken by mouth might cause a concentration of barbitone of approximately 5 mmol/l, in the proximal jejunum. If P_{CO_2} is 40 mm Hg, intraluminal pH would be 6.8, which is well away from the maximum of absorption.—I am, etc.,

LARS ELSBORG

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¹ Elsborg, L., *Abstract of XIII International Congress of Haematology*, 1970, p. 378.

² Elsborg, L., in press.

Screened Fibrinogen for Prophylaxis of Venous Thrombosis

SIR,—Your recent leading article (6 February, p. 305) on the "Prophylaxis of Venous Thrombosis" stresses the usefulness of the ¹²⁵I labelled fibrinogen technique for the detection of thrombosis in the leg. Our own studies using this technique confirm its usefulness and that the findings correlate very well with those obtained by venography. The real value of the technique lies in the fact that it allows the investigator to observe the evolution of venous thrombosis in the legs of patients in whom there may be no clinical evidence of the complication, and to do so without disturbing the patient. Hence, the technique may be used to screen relatively large numbers of patients and as a tool for monitoring the effect of prophylactic measures it is unrivalled. Venography is expensive, uncomfortable, and not without risk and is therefore only warranted when there is no other evidence of thrombosis.

The fibrinogen used is from human donors and it is known that the blood fraction containing fibrinogen may transmit the infecting agent of serum hepatitis. This is a risk that has been known to be associated with blood transfusion and the giving of most blood

products for many years. Such risks may be acceptable in therapeutic and diagnostic situations but may not be in clinical trials. The recent advent of techniques which permit the recognition of the hepatitis associated antigen has made it possible to screen selected donors and donations in depth and to reduce considerably the risk of transmitting this infection. This being so, we have reluctantly decided that it would be unethical for us to continue to use fibrinogen for a clinical trial unless we could be sure that it came from donors and donations that had been adequately screened. To date, we have been unable to find any source of such material and have felt obliged to discontinue our clinical trials.

We feel that there is an urgent need to provide screened fibrinogen for this very valuable test and hope that suitable material will be available in the very near future.—We are, etc.,

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Nocturia during Steroid Therapy

SIR,—Three cases of nocturia associated with hypertrophic osteoarthropathy were recorded in the correspondence columns (12 December, p. 686). In Case 3 the patient is now well and symptom free. Serum sodium level 138 mEq/l. Serum potassium level 3.8 mEq/l. In conditions similar to those at preoperative assessment the urinary output of water, sodium, and potassium five months after lobectomy for carcinoma were:

Average over 5 days	7 am to 3 pm	3 pm to 11 pm	11 pm to 7 am
Urine Vol. (ml)	790 (340)	830 (520)	513 (900)
Total Sodium (mEq)	53 (16.5)	55 (35)	36 (65)
Total Potassium (mEq)	17 (10)	16 (15)	10.5 (17)

Figures in parentheses are the preoperative values.—I am, etc.,

LESLIE DOYLE

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Ulcerative Colitis

SIR,—The widely authoritative account of ulcerative colitis (20 March, p. 649) would be just that more complete if the very small section on psychological treatment had been amplified and a good reason for this had been given.

The reason is that, investigated in the way their cases were, the findings of the physicians who wrote on ulcerative colitis between 1930 and 1960¹ are still valid. Thus, in 44 cases seen in series in the Radcliffe Infirmary, Oxford, between 1962 and 1964 all were found to have temperamental or character abnormalities present before the onset of physical symptoms, as evidenced by careful history taking. Also the diarrhoea or