alkalization of the upper small intestine by the drug with consequent malabsorption of folic acid (pteroylmonoglutamic acid). They present evidence that feeding either sodium bicarbonate or phenytoin to a normal subject depresses the rise in serum folate after an oral dose of 5 mg of folic acid. They also found that feeding 10 g of sodium bicarbonate to two normal subjects caused a rise in jejunal intraluminal pH from about pH 6·8 to pH 7·8 within five minutes. They emphasize that proprietary preparations of phenytoin are strongly alkaline in solution and infer that phenytoin depresses the folate absorption curve by raising the intraluminal pH in the upper small intestine and that this effect is mimicked by feeding sodium bicarbonate.

This seemed to us unlikely since, though both compounds are alkaline, their relative buffering capacities are very different. We have found that the amount of acid needed to bring a suspension of 100 mg of sodium phenytoin to pH 6·0 is 400 times less than that required to achieve the same pH with a 10-g suspension of sodium bicarbonate. As little as 0·3 ml of IN hydrochloric acid is needed to titrate 100 mg phenytoin in solution to pH 6·0. Dr. Benn and colleagues measured the intestinal pH of five epileptics who had received long-term phenytoin therapy with an in vivo pH electrode and found generally higher pH values than normal, both in the stomach and in the upper small intestine. However, these subjects had not received anticonvulsants on the day of investigation. Thus, they have no measure of the direct effect of phenytoin on intraluminal pH comparable to their measurements immediately after bicarbonate feeding.

We determined by the same method as Dr. Benn and colleagues the immediate effect of giving a suspension of 100 mg of phenytoin on the intraluminal pH of the third part of the duodenum in two fasting epileptics receiving long-term therapy with phenytoin, one of whom had been folate deficient. No alteration from the resting pH of 6·5 was observed over a 45-minute period. However, 10 g of sodium bicarbonate fed after this period caused the pH to rise to over 8·0 within five minutes.

We conclude that phenytoin has no immediate effect on the intraluminal pH of the third part of the duodenum in chronic epileptics. Whether or not the higher fasting intraluminal pHs observed by Dr. Benn and her colleagues in chronic epileptics are attributable to a secondary, delayed action of phenytoin or are unrelated to phenytoin therapy remains undecided.—We are, etc.,

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Trimethoprim-sulphamethoxazole in Typhoid

SIR,—Your leading article (8 August, p. 297) on trimethoprim-sulphamethoxazole in typhoid is interesting. I would, however, like to draw attention to an important omission of a drug, furazolidone, a nitrofuran derivative which has been widely and successfully tried in the treatment of enteric fevers in India,[1 2] Egypt,[3 4] and Pakistan.[5 6] All the studies published have equally confirmed the efficacy of furazolidone in the treatment of enteric fevers. The relapse rate has been extremely low, and no serious toxic reactions have been reported in patients with typhoid fever treated with furazolidone. Its success had earlier been reported in the salmonella carrier state.[7 8]

Typhoid fever is primarily a disease of developing countries. In general practice, as in the hospitals, treatment is normally instituted immediately upon clinical diagnosis of typhoid fever. Serological and blood culture facilities are not widely available in the countries where typhoid is most prevalent, and where available they are expensive and time-consuming. Under these circumstances, furazolidone, which is not only effective and relatively free from toxic reactions but at the same time is a highly economical drug, deserves mention.—I am, etc.,

M. A. BEG

Karachi, Pakistan — Medical Adviser and Head of the Department of Research and Development, Smith Kline and French of Pakistan Ltd.

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Restless Legs and Pulmonary Disease

SIR,—In your leading article "Restless Legs" (26 December, p. 758) you comment on Dr. J. D. Spillane's paper in the same issue (p. 796), on restless legs syndrome in chronic pulmonary disease, stating that the author gave reasons for preferring to consider restless legs a nervous manifestation of the patients' invalidism rather than a metabolic consequence of respiratory failure.

Certainly, in all of Dr. Spillane's 8 cases the respiratory disease had started years in advance of the symptoms of restless legs. In this connexion I would like to mention that I have myself been a sufferer from restless legs for about 10 years, during which time I have scarcely had a whole night's sound sleep. The last three years I have also been a victim of bronchial asthma, which has necessitated daily medication with corticosteroids for the last 2 years. Thus the symptoms of restless legs preceded the pulmonary disease by about seven years.

It does not necessarily follow, therefore, that the restless legs syndrome in a patient suffering from chronic pulmonary disease is a result of the pulmonary ailment. Perhaps there might yet be a causal relationship between some chronic pulmonary diseases and restless legs?

As to the difficulty of describing the discomfort of restless legs, I think that the nearest to what I experience was expressed by a patient who once told me "It feels as if my marrow bones are freezing."—I am, etc.,

KRISTIAN ØDEGAARD

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Naming the Compound

SIR,—There is still a tendency for papers to be published concerning oral contraceptives and their side effects without the authors stating the drugs involved.[1]

The various types and combinations of oral contraceptives available should be well enough known to make specific reference to the drugs involved possible. This information would be of value to those seeking rational definition of the side effects of oral contraceptives. If I were to submit a paper on, say, hypertensive drugs and their side effects, and omitted to mention even the types of drugs involved, I would hope that clarification would be requested.—I am, etc.,

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Northwick Park Hospital, Middx

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Treatment of Narcolepsy

SIR,—I would like to report a patient with narcolepsy with cataplexy, who is being successfully treated with imipramine.

My patient is a Barnardo boy, aged 25, of mixed race who knows nothing of his parentage. He works as a builder's labourer. Narcolepsy with cataplexy was first diagnosed at St. Catherine's Hospital, Birkenhead in 1965 when he was 19. He complained then that from his schooldays onward he would suddenly fall asleep—in class at school, driving a tractor, at dances, etc. Also, when excited, he would lose the muscular power in his limbs. He was a nervous young man, who suffered from nocturnal enuresis.

Clinical examination and E.E.G. were negative and no organic cause for the attacks was found. He was treated initially with ephedrine building up to a dose of 60 mg two or three times a day. This was successful in controlling his narcoleptic attacks; but, after moving to my practice area in 1966, he claimed that the tablets were losing their effect. He was then put on amphetamine sulphate. By the summer of 1970 he had worked up to a dose of 30 mg a day. He was getting side effects in the form of nervous twitches and neurotic excoriations on the forehead.

Since the beginning of last September he has been taking imipramine 25 mg three times a day. He says that the drug has been quite as effective as either of the others in controlling the narcolepsy, and it has also completely stopped the attacks of cataplexy, which neither the ephedrine nor the amphetamine touched ("I can now throw a double top at darts and still remain standing"). His nervous symptoms quickly cleared. The only fly in the ointment has been a weight gain of over a stone (6·5 kg.).—I am, etc.,

J. L. BOURDILLON

Dyserth, Flints