The note also states that "during 1970, 101 cases of malaria were reported by [Public Health] laboratories in the United Kingdom." This figure is a serious underestimate of the total number of cases of malaria notified in Britain.

Information provided by the Department of Health and Social Security indicates that the quarterly returns of the Registrar General for 1970 quote 137 confirmed notifications of malaria in England and Wales. In addition to that the Scottish Home and Health Department received in 1970 not less than 24 notifications of malaria of which 19 were confirmed. This brings the known number of malaria cases in England, Wales, and Scotland to at least 156. Carswell and Stevenson² reported recently that over the period 1965-9 the number of cases of malaria seen in Scotland averaged 20 per annum. Malaria is not notified in Northern Ireland but the cases confirmed by the Public Health Laboratories in 1970 were included in the figures reported in your note.

I wish to acknowledge with thanks the assistance obtained from the Department of Health and Social Security in providing me with the relevant data. I should also like to draw attention to the excellent *Notice to Travellers* of 1970 prepared by the D.H.S.S. and available on demand.

—I am, etc.,

L. J. BRUCE-CHWATT

London School of Hygiene and Tropical Medicine, London W.C.1

- ¹ Bruce-Chwatt, L. J., *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1970, **64**, 201.
² Carswell, J., and Stevenson, D. J. D., *Scottish Medical Journal*, 1971, **16**, 250.

Drugs and the Fetal Heart Rate

SIR,—We have read with interest the letter by Dr. J. C. Grimwade and others concerning the influence of morphine on the fetal heart rate pattern (7 August, p. 373). We have observed another effect on the fetal heart rate pattern of analgesics or central depressor drugs administered to the mother.

The normal fetal heart rate pattern shows both short term and long term irregularity.¹ These two types of irregularity can be distinguished and measured by automatic processing methods.² We have found that the short term irregularity decreases or even disappears, producing a "silent" fetal heart rate pattern, after administration to the mother of analgesics or central depressor drugs such as diazepam (10 mg i.v.), meperidine (75 mg i.m.), phenobarbitone (75 mg i.m.), mephobarbitone (75 mg i.m.), or the combination of meperidine (50 mg i.m.) with promazine hydrochloride (25 mg i.m.).^{3,4} We have seen cases of anencephaly with short term irregularity of the fetal heart, though others have had a "silent" fetal heart rate pattern.^{3,4}

Evidently short term irregularity can occur in the absence of the cerebral cortex, and this suggests that the central depressor drugs must be acting at a lower level of the central nervous system (possibly hypothalamus or medulla oblongata) when they abolish the short term irregularity. The short term irregularity appears to result from oscillating vagal activity.⁴—We are, etc.,

J. DE HAAN
L. A. M. STOLTE

Department of Obstetrics and Gynaecology, Academisch Ziekenhuis der Vrije Universiteit, Amsterdam, Holland

- ¹ Caldeyro-Barcia, R., in *The Heart and Circulation in the Newborn and Infant*. Ed. Donald E. Cassels. New York, Grune and Stratton, 1966, p. 7.
² Haan, J. de, et al., *European Journal of Obstetrics and Gynecology*, 1971, **1**, 95.
³ Haan, J. de, et al., *European Journal of Obstetrics and Gynecology*, 1971, **1**, 103.
⁴ Haan, J. de, *Short Term Irregularity in the Fetal Heart Rate Pattern*, M.D. thesis, Amsterdam, 1971.

Doctor in the Lab

SIR,—Your leading article (25 September, p. 719) draws an inference that pathologists who spend part of their time practising another specialty than their main one appear to tolerate a lower standard than is accepted in the bedside specialties, where you infer this does not happen. We all know it does happen, and often much to the benefit of patient and of doctor. A physician keeps his eyes, ears, and mind open to symptoms and signs outside his immediate specialized reference, and has the courage and modesty to accept the contribution of all the signs and symptoms he and others observe when forming his final opinion. The pathologist who neglects to consider every aspect of pathology he can turn his mind to when assessing the relevance of his laboratory's findings provides a lower standard of service than the one who keeps his mind open and refuses to dogmatize on the inadequate evidence of his own specialty.

The present attempt to appoint at least one specialist in each of the four current (and already outdated and technically illogical) subdivisions of pathology leads to quite ludicrous situations when these specialists have been trained in centres where the responsibility for whole groups of tests can be quite differently allocated. The same test may even be performed, with variations according to technical taste, in three or even four different divisions of the same laboratory.

The function of the clinical pathologist is to collaborate and consult with his clinical colleagues; to go back in fact to the beginnings of modern clinical pathology again.

F.D.P. in Glomerulonephritis

SIR,—We read with interest the paper by Dr. A. R. Clarkson and his colleagues (21 August, p. 447) and would like to add our own observations and comments.

We measured serum and urinary F.D.P. content on specimens taken from 20 consecutive patients attending two renal outpatient clinics. The tanned red cell haemagglutination inhibition immunoassay was used for all determinations. In our laboratory the normal range for serum F.D.P. is 1.25-20 µg/ml. Of 40 normal subjects 38 had no detectable F.D.P. in their urine, while the

His training must provide a wide clinical experience and a practised scepticism. The latter is most readily acquired in a laboratory with correlation and follow-up systems; and in the postmortem room. He gives his time freely to discussion with the clinician in assessing the relevance of his laboratory findings to any suspected diagnostic entity, and, more important still, to consideration of what next is to be done—to treat or test again. He must be on terms of complete and honest appreciation of his own and of his colleagues' limitations if his opinion is to have full value and if a mutual confidence is to develop for the benefit of future patients. The more factual information his data-storage and computer-analysis systems provide in the future, the more important (and just possibly the easier) this will become.

A transition to Zuckerman¹ (slow for reasons of pride and humanity) will help the clinical pathologist to concentrate on his re-found role. There will be plenty of scope for the ultra-specialist in the large central non-urgent laboratories of the future, and the universities will supply (according to funds, development of methods, and the availability of men and enthusiasm) the laboratory space, equipment, and stimulus for him. In the teaching hospitals, however, there must be a department of clinical pathology with one general pathologist at its head. He will have the functions I describe above, and there will be no need for him to compete for divisional chairmanship (or whatever) with his fellow pathologists on any other than equal terms, deriving his satisfactions from the knowledge that his functions are unique and not competitive with those of his fellow pathologists at one or more removes in their specialized laboratories.—I am, etc.,

G. A. C. SUMMERS

Group Pathology Laboratory, County Hospital, York

- ¹ *Hospital, Scientific, and Technical Services*. London, H.M.S.O., 1968.

remaining two had concentrations of 1.25 µg/ml.

Without recourse to the F.D.P. results, the patients were divided into three groups: (1) those with normal renal function; (2) those with impaired but static renal function; and (3) those with progressive impairment of renal function.

The criteria for the continued activity of the disease process were essentially the same as those offered by Dr. Clarkson and his colleagues.

Normal Renal Function		Static Impairment of Renal Function		Progressive Impairment of Renal Function	
Serum F.D.P. (µg/ml)	Urine F.D.P. (µg/ml)	Serum F.D.P. (µg/ml)	Urine F.D.P. (µg/ml)	Serum F.D.P. (µg/ml)	Urine F.D.P. (µg/ml)
10	0	10	5.0	20	20 (a)
5	0	10	1.25	10	10
5	0	20	2.5	20	10
10	1.25	20	2.5	80	>20 (b)
		20	1.25	5	5
		5	1.25	10	5
				<1.25	5
				20	>20 (c)
				40	20 (d)
				20	40 (e)

(a) Lupus Nephritis; (b) Hydronephrosis; (c) Polycystic Kidneys with Renal Failure; (d) Post-streptococcal Nephritis; (e) Proliferative Glomerulonephritis.

It is apparent from the results (Table) that there is a close relationship between the urinary F.D.P. concentration and the disease activity. Even in the apparently "static" group three patients were excreting increased concentrations of urinary F.D.P. Noteworthy is the observation that of 10 individuals judged to have progressive renal impairment only two had elevated serum F.D.P. while all had increased urinary excretion of these products. Highest urinary F.D.P. excretion concentrations were observed in polycystic disease with renal failure, hydronephrosis, lupus nephritis, post-streptococcal nephritis, and renal failure due to progressive proliferative glomerulonephritis. Serial urine studies in the patient with lupus nephritis, who was pregnant, showed close correlation with both her biochemical and clinical condition. Serum F.D.P. in this patient were less helpful and did not accurately reflect the marked fluctuations which occurred in the urinary F.D.P.

We agree with Dr. Clarkson and his co-workers that in certain groups of patients the urinary F.D.P. are derived from the renal glomeruli and do not represent filtration from the systemic circulation. In this context it is of interest that we have observed two patients with disseminated intravascular coagulation but with normal renal function. Both had serum F.D.P. greater than 1,000 $\mu\text{g/ml}$, but in neither patient were we able to detect F.D.P. in the urine. We note that the Edinburgh workers were unable to detect urinary F.D.P. in patients with uncomplicated polycystic disease. We also were unable to detect breakdown products in this type of patient, but in one patient with polycystic disease and progressive impairment of renal function urinary F.D.P. were greater than 20 $\mu\text{g/ml}$, and it may be that in this group also urinary fibrin/fibrinogen breakdown products may be of value in assessing the progression of the renal lesion.

Though an estimation of the 24-hour excretion of F.D.P. provides a more accurate assessment of renal involvement such collections are difficult to carry out on an out-patient basis, and it is of some value therefore to note that our results were obtained from random urine samples collected during an afternoon outpatient clinic.

We would like, therefore, to reiterate the views expressed by Dr. Clarkson and his colleagues that estimation of urinary F.D.P. may afford a simple but sensitive means of assessing the activity of the disease process in patients with certain types of renal disorder.—We are, etc.,

F. E. PRESTON

R. G. MALIA

E. K. BLACKBURN

University Department of Haematology,
Sheffield

M. PLATTS

Department of Medicine,
Royal Hospital,
Sheffield

Treatment of Myocardial Infarction

SIR,—Dr. G. R. Fearnley (21 August, p. 473) in commenting upon the findings of the European working party's statistically-controlled trial of streptokinase therapy in acute myocardial infarction (7 August, p. 325) expresses a personal view that thrombolytic therapy is unlikely to be useful in the treatment of this disease. Nevertheless, as with other such therapeutic problems, the role of

thrombolytic therapy in this disease will be defined on the basis of scientific evidence rather than by disputation.

While the evidence is still incomplete, it should be noted, particularly since this evidence is not fully cited by the European working party, that this study is one of seven therapeutic trials in which approximately similar streptokinase dosage schedules have been employed. Of these studies, three others show statistically-significant benefit in favour of streptokinase,¹⁻³ though in one study randomization was less than perfect.¹ Two studies show a trend in favour of streptokinase treatment,^{4,5} and in the last study, with very low total mortality, there was no treatment preference.⁶

Clearly, these clinical-trial data offer substantial encouragement to investigators developing such new approaches to the treatment of acute myocardial infarction.—I am, etc.,

ANTHONY P. FLETCHER

Department of Internal Medicine,
Washington University,
St. Louis, Mo., U.S.A.

¹ Schmutzler, R., et al., *German Medical Monthly*, 1966, 11, 308.

² Betts, N., et al., *International Society on Thrombosis and Hemostasis*, 1971, Proceedings in press.

³ Gebauer, D., et al., *International Society on Thrombosis and Hemostasis*, 1971, Proceedings, in press.

⁴ Fletcher, A., Sherry S., Alkjaerig, N., Smyrniotis, F., and Jick, S., *Journal of Clinical Investigation*, 1959, 38, 1111.

⁵ Gormsen, J., *Acta Medica Scandinavica*, 1971, in press.

⁶ Italian Cooperative Trial of Streptokinase Therapy in Acute Myocardial Infarction, *Journal of Clinical Pathology*, 1971, in press.

The Gut and Dermatitis Herpetiformis

SIR,—I consider your leading article on the gut and dermatitis herpetiformis (2 October, p. 5) exceptionally ill-informed and misleading. The article itself is contradictory; it starts with the sentence "enteropathy may be associated with dermatitis herpetiformis" (no references), but in the second paragraph reports a study¹ which shows that enteropathy is almost invariably present (21 out of 22 patients studied). However, your article should really be criticized for failing to refer to any of the original, and now already considerable, literature on the subject, which has answered many of the questions raised by you and is also at variance with a number of the statements in your article.

Your article looks for evidence as to whether the enteropathy in dermatitis herpetiformis is the same as that in coeliac disease. You rightly state the histological appearances of the small intestinal lesion are similar (first reported 1966²); that there is evidence of diminishing severity of the lesions in the distal small intestine (first reported 1967³ and 1968⁴) and there is evidence of gluten sensitivity (reported 1968^{4,5}). However, you then find it difficult to equate the syndrome (dermatitis herpetiformis enteropathy) with coeliac disease. As long ago as 1967³ when it was first suggested the enteropathy in dermatitis herpetiformis was due to gluten sensitivity further evidence was presented to show that the enteropathy in the two diseases had a similar aetiopathology. A high incidence of increased faecal fat excretion, of folate, iron, and M globulin deficiency, and of splenic atrophy was found in patients with dermatitis herpetiformis³ and is known to occur in coeliac disease. Further evidence that both diseases are similar has since been

forthcoming in that anticonnective tissue antibodies have been reported in both disorders.⁶

The next point where your article is incorrect is that though you state categorically that treatment of dermatitis herpetiformis with a gluten-free diet does not benefit the skin lesions (you give no references), you fail to mention the reports where a gluten-free diet has been shown to influence and in some instances control the eruption.^{5,7,8} This naturally leads to the following question (which you raised but could not answer) as to whether patients with dermatitis herpetiformis should be treated with a gluten-free diet.

In favour of treatment with a gluten-free diet it can be stated that in some patients the rash can be controlled by diet alone.^{5,7,8} Secondly, definite clinical (subjective and objective) improvement does occur in a number of patients with dermatitis herpetiformis.^{5,7} This is similar to patients with coeliac disease starting a gluten-free diet. Thirdly, as mentioned above, a large proportion of patients with dermatitis herpetiformis are iron and folate deficient and this deficiency has been shown to improve with a gluten-free diet.⁷ Finally, the question of reticulosis of the small bowel has to be considered. You say that dermatologists are not aware that their patients with dermatitis herpetiformis are specially liable to develop such neoplasms. However, you fail to mention that treatment with a gluten-free diet has already been suggested for this very reason by a dermatologist⁹ (and a patient under my care with dermatitis herpetiformis has developed a lymphoma of the small bowel—before starting a gluten-free diet).

The above are definite points (all but the last you fail to mention) in favour of treating patients with dermatitis herpetiformis with a gluten-free diet. However, in practice, because of the social and practical problems of adhering to a gluten-free diet, I find it is not possible to treat all patients with this diet, and it has been my policy to consider each patient individually, rather than lay down any definite rule.—I am, etc.,

LIONEL FRY

Department of Dermatology,
St. Mary's Hospital,
London W.2

¹ Brow, J. R., Parker, F., Weinstein, W. H., and Rubin, C. E., *Gastroenterology*, 1971, 60, 355.

² Marks, J., Shuster, S., and Watson, A. J., *Lancet*, 1966, 2, 1280.

³ Fry, L., Keir, P., McMinn, R. M. H., Cowan, J. D., and Hoffbrand, A. V., *Lancet*, 1967, 2, 729.

⁴ Shuster, S., Watson, A. J., and Marks, J., *Lancet*, 1968, 1, 1101.

⁵ Fry, L., McMinn, R. M. H., Cowan, J. D., and Hoffbrand, A. V., *Lancet*, 1968, 1, 557.

⁶ Seah, P. P., Fry, L., Hoffbrand, A. V., and Holborow, E. J., *Lancet*, 1971, 1, 834.

⁷ Fry, L., McMinn, R. M. H., Cowan, J. D., and Hoffbrand, A. V., *Archives of Dermatology*, 1969, 100, 129.

⁸ Van Tongeren, J. H. M., Van der Staak, W. J. B. M., and Schillings, P. H. M., *Lancet*, 1967, 1, 218.

⁹ Fry, L., *Postgraduate Medical Journal*, 1970, 46, 664.

Congenital Leukaemia and Mongolism

SIR,—Having failed to find a clinical report of congenital leukaemia in association with mongolism in the medical literature of this country, I should like to record the following case history.

A female mongol infant was born at Edgware General Hospital on 29 August 1970.