purpuric eruptions on the trunk and limbs. On the following day he developed bluish discoloration of several toes of both feet suggesting early gangrene. The skin overlying the area was warm and the peripheral pulses were palpable. The purpuric eruptions became more extensive and he had several bouts of haematemesis. At this stage, the possibility of disseminated intravascular coagulation was considered. No specific diagnostic laboratory test was then available. However, his platelet count was only 25,000 cu.mm. and thrombocytopenia is probably a constant feature in intravascular coagulation.

It was decided to treat the child with continuous intravenous heparin. The decision to anticoagulate the child was not an easy one as we were then faced with the paradoxical situation of gangrene on one hand and spontaneous bleeding on the other. After 48 hours of heparin therapy the child's condition improved remarkably, with rise in platelet count and cessation of spontaneous bleeding. The progress of gangrene was halted. During the course of several days the discoloration of the toes gradually disappeared, apart from small black necrotic areas at the tip of two toes. Heparin therapy was discontinued after seven days. Apart from loss of nail beds of his toes his feet are now perfectly normal.

The diagnosis of intravascular coagulation in this case was made mainly on clinical grounds and it does not fulfil the criteria of this syndrome as suggested by Corrigan and others[1]—namely, the combination of the thrombocytopenia, reduction of coagulation factors II, V, VIII and fibrinogen, and presence of fibrinolytic split products in the serum, but the dramatic response to heparin therapy was gratifying and possibly diagnostic. Disseminated intravascular coagulation or consumption coagulopathy, a relatively new terminology, is well documented in relation to virus diseases.[2]—We are, etc.,

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Temporary Cardiac Pacing Using the Subclavian Vein

SIR,—We were delighted to see the paper by Drs. M. B. Macaulay and J. S. Wright (24 October, p. 207). We hope that these authors' experience with supraclavicular percutaneous introduction of the pacing electrode into the subclavian vein will popularize this little-known technique. Wider appreciation of its enormous advantages over arm-vein routes in terms of electrode stability and comfort for the patient should do much to counter the nihilistic attitude towards the treatment of postinfarction heart block which now prevails in too many centres.

We adopted the subclavian technique some three years ago and can confirm its simplicity, safety, and patient-acceptability. Thanks to clear instructions from Dr. B. W. Lassers and the enthusiasm of Dr. J. H. N. Bett (now of Melbourne, Australia) the method proved easy to learn. The left subclavian vein is preferred here where temporary pacing is required in patients with chronic heart block so that later use of the right internal jugular vein (for insertion of a permanent electrode) is not prejudiced. Use of the left subclavian may also be more convenient for the right-handed operator and the natural curve of the temporary electrode favours correct placement of the tip in the right ventricular apex when introduced from the left side. There are unimportant differences in the equipment used and one potentially important difference—that is, we use only No. 5 F.G. bipolar electrodes, having known the stiffer No. 6 F.G. electrodes to perforate the heart in times gone by.

The Table shows the few complications we have encountered in 60 attempts to establish pacing with the subclavian technique and compares them with the complications of 19 temporary pacing procedures attempted during the same period using antecubital veins. No instances of pneumothorax, brachial plexus injury, or air embolism have been encountered. The latter complication might be anticipated in patients with low central venous pressure[1] unless tilted head down, and in those with obstructive airways disease and uncontrollable coughing; the subclavian technique is unsuitable for use in such cases.

TABLE.—*Comparison of Subclavian and Antecubital routes for Temporary Pacing*

	Subclavian Vein	Antecubital Vein
Technique Attempted ..	60	19
Pacing Established ..	54	16
Failed Procedure* ..	6	3
Subsequent Electrode Displacement ..	2	8
Phlebitis	0	2
Wound Infection ..	0	2
Patient Discomfort ..	±	+++

(*includes 2 subclavian artery punctures due to inexperience)

Failure to introduce the electrode into the subclavian vein is now rare (a foam plastic pad, 8 cm. thick, beneath the occiput appears important to success). In a recent case where difficulty was encountered, the patient suffering recurrent asystolic arrest throughout, satisfactory pacing was speedily established via the right internal jugular vein as described by Hoffman and Sokol.[3]—We are, etc.,

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Malaria in Britain

SIR,—There are still several deaths every year[1] in Britain from malaria. A man aged 55 was recently admitted who had been in Nigeria for two weeks, but was not offered or advised about prophylaxis for malaria. Ten days after his return he developed symptoms of a chest infection, and was treated with antibiotics. Five days later he collapsed and was admitted to hospital in coma and profound shock. Cerebral malaria was considered, and the blood film showed heavy infection with *Plasmodium falciparum*. Despite intensive treatment his condition slowly deteriorated, and he died a week later.

At necropsy there was very extensive cerebral involvement with numerous haemorrhagic foci having necrotic centres, surrounded by deposits of malaria pigment. In retrospect it is unlikely that he had any chance of survival after the onset of coma.

There is still, despite pressure from many quarters, no one body responsible for providing advice about malaria prophylaxis for travellers. The responsibility must surely lie with both general practitioners and travel agents to provide this much needed advice. This previously fit man was the fifth death due to malaria this year in England—he had no prophylaxis, and the diagnosis was not made until too late. In this age of air travel, it is vitally important to think of tropical disease in anyone who has recently returned from an endemic area.

Anyone who would like further information concerning malarial endemic areas, and recommended prophylactic schedules, should contact Professor P. C. C. Garnham, at the Malaria Reference Laboratory, Horton Hospital, Epsom, Surrey.—I am, etc.,

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1 Department of Health and Social Security. *On the State of the Public Health. Annual Report for the Year 1968*, p. 36. London, H.M.S.O., 1969.

Skin Disease and the Gut

SIR,—I have read with interest your leading article (1 August, p. 240) and the subsequent correspondence (29 August p. 521, and 5 September, p. 586) on skin disease and the gut and also the latest contribution of Dr. Janet Marks and Professor S. Shuster on dermatogenic enteropathy (12 September, p. 618). I am writing to draw attention to the similarities between dermatogenic enteropathy and the enteropathy associated with extraintestinal malignant tumors—which can be termed as "neoplastic enteropathy"—and to suggest that folic acid deficiency is mostly responsible for the small bowel dysfunction in both conditions.

Although jejunal mucosal abnormalities have been described in the past in patients with extraintestinal neoplasia[1 2] two recent investigations have shown that such changes are indeed very rare.[3 4] However, as in dermatogenic enteropathy, malabsorption does exist in the absence of morphological mucosal abnormalities. While the incidence and severity of malabsorption is proportional to the extent of rash in patients with skin disease, they appear to be related to the presence and extent of metastases in patients with carcinoma.[4]

Folic acid deficiency is quite common in patients with extensive skin disease,[5] as well as in patients with malignant neoplasia,[2 4 6] and it is generally believed to be due to an increased demand for the vitamin by the rapid turnover of cells in the skin and the tumor respectively. Folate coenzymes play a key role in cellular division through their action in nucleoprotein synthesis and an impaired synthesis of D.N.A. is a major defect in folate deficiency.[7] As the cell turnover in the intestinal epithelium is higher than in any other in vivo cell population,[8] interference with normal regeneration of villi, with resulting malabsorption, is only to

be expected in patients with folic acid deficiency (clinical or subclinical). The findings of Kaimis, Summerly, and Giles (personal communication to Marks and Shuster, 12 September, p. 618) and the demonstration of malabsorption in the proximal small bowel[4] which is the site of absorption of folic acid, would seem to indicate that, in addition to an increased demand, there may be malabsorption of folic acid in these patients which would further exacerbate folate deficiency.

As correctable malabsorption of vitamin B_{12} has been described in patients with folic acid deficiency,[9 10] it would seem likely that the malabsorption of vitamin B_{12} in patients with various skin diseases is also due to folic acid deficiency. I wonder whether the authors have repeated the study after a course of folic acid. It would also be interesting to see whether the small bowel dysfunction in dermatogenic enteropathy reverts to normal on folic acid therapy alone without local treatment of the rash. If it does (as I suspect) in addition to the local treatment of dermatosis early folic acid therapy would seem to be indicated in patients with enteropathy, even when there are no obvious haematological changes.

Similar explanation probably holds true in enteropathy associated with various chronic debilitating illnesses and also in conditions where increased cellular proliferation is a predominant feature.—I am, etc.,

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Myocardial Infarction and the G.P.

SIR,—The hospital doctor (14 November, p. 433) who can include without explanation a delay of two days in seeing a patient with a coronary thrombosis in a discussion of factors influencing early death clearly needs to spend some time as a general practitioner's receptionist.

He would learn some of the forms in which coronary thrombosis can be presented when first brought to the notice of the medical services. He might then be in a better position to inform general practitioners what information is useful to them so as to avoid once again finding that only five out of 41 of their letters contain any useful information. Those of us who work in hospital can make everyone's work easier by explanation rather than by damning comment.—I am, etc.,

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Safety-pin Swallower

SIR,—We would like to draw the attention of surgeons to the habits of a man who has recently been admitted to Gulson and Walsgrave Hospitals in Coventry, and to St. Bartholomew's Hospital.

His initials vary between H.H. and E.H. and he gives his place of origin as Whiston, Manchester, where he has also been hospitalized on many occasions. On each of these numerous admissions he has claimed to have inadvertently swallowed a safety pin in the course of cleaning his teeth while travelling in a lorry. *X*-rays have shown the presence of two open safety pins in the stomach or small bowel. His abdomen has been opened a number of times, by his account for ulcer operations, but according to his previous hospital notes for the removal of open safety pins. On several recent occasions the pins have been successfully passed without any operative intervention.

We write to point out to any other surgeons under whose care he may come that despite the rather worrying appearance of the pins on *x*-ray, he seems to have the capacity to pass them through the gastro-intestinal track without coming to any harm.—We are, etc.,

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Nephrotic Syndrome in the Tropics

SIR,—Dr. J. S. Cameron's excellent review of the nephrotic syndrome (7 November, p. 350) summarizes experience of this disorder in non-tropical areas of the world.

The *British Medical Journal* is very widely read in tropical countries, and readers in these areas may be seriously misled about the causes of the nephrotic syndrome and its management by the account recently published. It has now been established beyond any reasonable doubt that there is a very high incidence of the nephrotic syndrome in West and East Africa, and that in the vast majority of patients an aetiological relationship with quartan malaria can be demonstrated. These patients, however, do not show a response to antimalarial therapy, and the majority also do not respond to steroid administration. Recent experience with immunosuppressive agents like cyclophosphamide and azothiaprine has also been disappointing.[1-5]

If one takes a "world" view of medicine, then quartan malaria must rank as one of the major causes of the nephrotic syndrome in childhood. The wide international circulation of the *B.M.J.* makes it imperative that future reviews of the nephrotic syndrome, or for that matter any well-recognized clinical entity, should indicate whether the author has taken a "local" or "global" approach to the subject.—We are, etc.,

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Allergy to Iprindole (Prondol) with Hepatotoxicity

SIR,—I must protest about the assumption that the hepatic damage attributable to iprindole administration is due to a hypersensitivity mechanism. The four letters published to date (7 February, p. 367; 25 April, p. 238; 7 November, p. 368; 21 November, p. 494) do not contain any evidence to suggest that the reported tissue damage is any more than a direct toxic effect of the drug. The finding which prompted Dr. P. J. W. Young's "feeling" (7 February, p. 367) is insufficient to incriminate an immunological mechanism. Thus to continue using the term allergy is both misleading and unjustified.

Consider for a moment what the word allergy implies. In the first instance the individual must come into contact with an antigen, which in the case of drugs is usually a macromolecular complex of drug and protein. Then, as Von Pirquet proposed,[1] a state of altered reactivity exists within the individual with respect to the antigen. This "allergic state" is not manifest as a clinical entity. Upon further contact with the antigen a hypersensitivity reaction might be produced which results in some degree of tissue damage detectable at a clinical level.

With iprindole, therefore, it is imperative to demonstrate that the liver damage is due to either the interaction of a normal antibody with antigen or between specifically allergized cells and antigen. This has not yet been reported and until it has the term "allergy to iprindole" should be discontinued.—I am, etc.,

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SIR,—The suggestion by Drs. D. F. Harrison and I. M. Stanley that the drug iprindole be withdrawn on the evidence presented of hepatotoxicity (7 November, p. 368) is very properly rejected by Drs. L. J. Clein and M. D. Cashman (21 November, p. 494). The drug has been in regular use in this hospital for seven years with no evidence of any serious side effects. In fact, continued clinical use has fully confirmed the findings of our clinical trial[1] that the drug has a particularly low incidence of side effects.

It is not disputed that the occasional hepatotoxic reaction can occur, but it should be borne in mind that this possibility exists for other tricyclic antidepressants as well, and has been recorded.[2] Nevertheless, the tricyclic antidepressants are regarded as a particularly safe group of drugs. Greater danger exists in the potentiality of some to