Laboratories, Dr. Brian Scales), the usual therapeutic level being about 1.5 µg/ml.¹ To our knowledge these are the highest values reported in man so far.

Possibly any beta-blocker may cause heart failure in a patient whose myocardial performance depends critically on sympathetic drive. However, practolol seems to be less dangerous than others in this respect, and in normal therapeutic doses causes only modest reduction of cardiac output.² Practolol has been shown to possess some sympathomimetic activity. Its positive chronotropic activity may explain why the pulse rate fell relatively little and definite bradycardia did not occur in the case presented here. This may explain, partly at least, why the patient's heart condition did not deteriorate. Another possible explanation could be the less pronounced effect of practolol on myocardial contractility.

This case illustrates the low toxicity of practolol and its modest cardiodepressive effect which has proved valuable in the treatment of patients with supraventricular arrhythmias and rapid ventricular rates after myocardial infarction and cardiac surgery.—We are, etc.,

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¹ Fitzgerald, J. D. F., and Scales, B., *International Journal of Clinical Pharmacology*, 1968, 1, 467.
² Sowton, E., Balcon, R., Cross, D., and Frick, H., *British Medical Journal*, 1968, 1, 215.

Intestinal Motility and Absorption

SIR,—I was interested in the study by Dr. J. Nimmo and others (10 March, p. 587) demonstrating impaired absorption of paracetamol after the administration of propantheline and enhanced absorption after metoclopramide, especially as this apparently conflicts with a recent report from Helsinki¹ that the absorption of digoxin is decreased by metoclopramide and increased by propantheline. Unfortunately the techniques of the two studies are dissimilar and it is difficult to make valid comparisons.

I am beginning to suspect that absorption from the gut of a normal person is decreased by drugs which either increase or decrease motility and that the individual's normal gut motility gives optimal absorption. In Dr. Nimmo's study the highest plasma levels of paracetamol were in the convalescent volunteers. When they were given propantheline absorption of paracetamol decreased. The second group of subjects was chosen because they were known to have abnormal and slow gastric emptying. When given metoclopramide intravenously absorption of paracetamol increased—I suspect because motility was returned towards normal.

In a study of the absorption of xylose in patients with normal gastrointestinal function² I found that 20 mg of metoclopramide reduced absorption in eight out of 10 subjects, the mean decrease in xylose excretion in the urine being 15.9% ($P < 0.0125$). After an intravenous injection of 0.6 mg of atropine nine of 12 subjects had a decreased absorption, the mean decrease in xylose excreted in the urine being 18.7% ($P < 0.001$). These studies, though crude and simple, tend to confirm that normal motility gives optimal absorption. Other results suggest, however,

that in disease states these drugs, if they alter motility towards normal, enhance absorption. In five of a group of 11 myxodematous patients the absorption of xylose was increased by metoclopramide, and in one patient with carcinoid syndrome 15 mg of propantheline given intramuscularly increased the xylose excretion in the urine from 0.86 to 1.35 g.—I am etc.,

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¹ Manninen, V., Apajalahti, A., Melin, J., and Karesoja, M., *Lancet*, 1973, 1, 398.
² Kendall, M. J., M.D. Thesis, University of Birmingham, 1971.

Early Diagnosis of Nephroblastoma

SIR,—In your leading article on this topic (10 March, p. 567) you state that it is important to identify the group of neonatal renal tumours which have been called fibrosarcoma or congenital mesonephric nephroma, and you continue: "The importance of identifying this group is to prevent the infant from receiving radiotherapy and chemotherapy." The implication is that if a true nephroblastoma (Wilms's tumour) is diagnosed in early infancy it is reasonable to include radiotherapy and chemotherapy as part of the management.

It would be a pity if this impression were not corrected, for now there must be few teams dealing with embryonal tumours who would recommend in infants under one year of age any treatment other than surgery. The exception must be made of those unusual cases in which there is undoubted spread, local or distant, at the time of operation.—I am, etc.,

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Ultrasonic Detection of Deep Vein Thrombosis

SIR,—As experienced users of the ultrasonic Doppler technique for the detection of deep vein thrombosis, who have performed tests on over 650 patients in the past 2½ years, we should like to make two comments on the paper by Mr. O. B. Williams and others (3 March, p. 517).

(1) The authors state that the high frequency (10 MHz) focused ultrasonic beam of the Parks Model 802 or 806 instrument has several advantages over "other models used in similar studies." Our experience of both the Park Model 806 and the Sonicaid Model D205 have led us to believe that the broad beam and lower frequency (2 MHz) of the Sonicaid is the more useful. Inclusion of the relevant vein in the broad beam is almost automatic if the Doppler signal from the adjacent artery is located. The test thus becomes much easier to perform for even the comparatively inexperienced user and false positive results arising from failure to include the vein in the beam are avoided. The greater penetration of the lower frequency of the ultrasound beam also enables the test to be performed routinely up to the level of the iliac veins.

(2) The results reported appear to contradict the author's own statement that "The experienced observer using the 806 direc-

tional machine can diagnose thrombotic lesions of the calf veins." It is our opinion that the existence of the plexus of veins in the calf results in transfer of blood through collateral pathways when individual veins in the calf are thrombosed. Consequently the flow at the level of the popliteal or femoral veins resulting from a calf squeeze will not usually be affected by a single occluded calf vein. Only widespread occlusion of the calf veins or occlusion at the level of the popliteal vein can be detected with any certainty.—We are, etc.,

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Cubital Tunnel External Compression Syndrome

SIR,—The paper by Messrs. T. G. Wadsworth and J. R. Williams (17 March, p. 662) prompts me to warn orthopaedic surgeons to be cautious before making this diagnosis on an immigrant from a country where leprosy is endemic. The ulnar nerve is the commonest peripheral nerve to suffer damage in leprosy. The patient may present with what may seem to be a typical entrapment neuropathy even in the absence of skin lesions, and the diagnosis will be missed if thickening of the nerve in the upper arm, immediately proximal to the cubital tunnel, is not noted.

As leprosy changes are within the nerve, surgical transposition is unlikely to prove of value. On the basis that repeated trauma will aggravate such changes, however, it has been suggested¹ that this operation will benefit a small minority, who can be selected on the following criteria: (1) presence of a small interval between the olecranon and the medial epicondyle of the humerus (25 mm or less with the elbow extended), and (2) increase of this interval by more than 50% with the elbow fully flexed.—I am, etc.,

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¹ Srinivasan, H., and Namasivayam, P. R., *Indian Journal of Medical Research*, 1971, 59, 1385.

Injury on the Football Field

SIR,—The present laws of rugby football permit the use of replacements in matches in which a national representative side is playing, "only when, in the opinion of a medical practitioner, the player is so injured that he should not continue playing in the match." Even at international level the emphasis seems to be whether the player can return, rather than whether it is advisable in the immediate and ultimate interest of the same player. In recent weeks, I have seen several match incidents in which players have returned to play and faced the likelihood of more grievous injury because substitutes are not yet permitted in county championship and other richly competitive games. The pressure is always on the injured player—self-applied, maybe, but inculcated by long tradition—to return to the field of play, given half a chance by medical

treatment. Naturally, because replacements are not allowed in a match below representative grade, the team doctor is expected to apply a hasty second-aid Elastoplast strapping and even a local anaesthetic to mask the agony. Admittedly, the player reappears of his own free will, but he knows well that if he does not, his team mates must battle on, with one position unfilled. His courage gets the better of his common sense, and the situation impedes the giving or accepting of sound medical judgement. Many doctors associated with clubs and teams throughout the whole rugby world must be familiar with cases of players who aggravate an injury by resuming exercise too soon and thus, ensure for themselves a long painful lay-off. It is well recognized that all this is further bedevilled by the all-round increase in fixtures and player engagement, which rarely leaves more than a couple of days to shake off the effects of even trivial trauma. Replacements will be more widely accepted in the future. Doctors and consultants, who are close to the problem, could hasten the day by using their influence in the corridors of rugby power.—I am, etc.,

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Bacteroides Infections

SIR,—In your epidemiological notes (17 March, p. 686) reference is made to reports gathered by the Public Health Laboratory Service of the isolation by blood culture of species of *Bacteroides* from 76 patients during the last 9½ months of 1972. This is the greatest concentration of such infections yet reported in the United Kingdom and the Irish Republic and it follows other recent accounts, such as that of six patients treated in Glasgow in 1972.¹

Between 1933 and 1944 I isolated organisms of the genus *Bacteroides* from 12 patients in hospitals in North London, and records of these were published in 1955,² with an analysis of 268 other cases in the literature from eight countries. From 1944 to 1965 no new example of the infection was found in the same hospitals, although looked for. The organisms are known to be common saprophytes of the human gastrointestinal tract and are relatively easily cultivated. From my own experience I think that the variation in the reported incidence of infection is more probably due to altered opportunities for the invasion of the tissues than to varying attention of bacteriologists to the possibility. The bacteraemia in 1972 "was most commonly reported in elderly patients, most of whom were known to have an underlying illness." In the records of 20 years ago² the patients were of all ages from childhood onwards and the infection was more often the primary and sole disease in the form of extensive and often multiple suppuration.

The bacteroides are the cause of many lesions in wild and domestic animals and reach human beings by contact and probably by consumption of infected animal tissues. Among the 280 cases which I analysed there were four main groups. One was of infection of the skin or subcutaneous tissues by way of civilian injuries or war wounds, or directly from live animals or their

tissues in the case of farm workers and butchers. A second group, the largest, was of infections which started in the throat, after tonsillectomy or with sore throat or otitis media as the first symptom. Thirdly, there were many infections by way of the female genital tract, mostly after abortion or in the puerperium, and fewer, in either sex, by the alimentary tract, sometimes after surgical operation, or by the urinary tract. The fourth group showed empyema, with or without lung abscess, as the first symptom. When lung abscess preceded empyema it was thought that inhalation from the mouth or throat might be the origin.—I am, etc.,

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- 1 Tracy, O., Gordon, A. M., Moran, F., Love, W. C., and McKenzie, P., *British Medical Journal*, 1972, 1, 280.
- 2 Alston, J. M., *British Medical Journal*, 1955, 2, 1524.

Zollinger-Ellison Syndrome Reclassified

SIR,—A number of recent papers in journals without correspondence columns have complicated the picture of the Zollinger-Ellison considerably and, despite your excellent leading article (6 January, p. 2), I find certain of my colleagues and most medical students thoroughly confused.

The syndrome to which Zollinger and Ellison gave their name¹ (though they were not the first to describe cases) had a diagnostic triad of (1) fulminating peptic ulceration (often multiple, recurrent, and atypically situated), (2) gigantic gastric acid secretion, and (3) non-insulin-secreting islet cell tumours of the pancreas. It was subsequently recognized that the tumours could occur in ectopic pancreatic tissue,² the substance they secreted was identified as gastrin,^{3,4} and eventually the secretory cells were shown to be D cells.⁵ The picture thus far is clear.

Unfortunately it was soon shown that the clinical features of the syndrome could be caused by mere hypertrophy of the pancreatic islets,² and more recently Polak and her colleagues showed that profound antral G cell (that is, gastrin-secreting cell⁶) hyperplasia could produce a similar picture.⁷ The latter divided patients into a group with hyperplasia or frank tumour in the pancreatic islets and a group with G cell hyperplasia and a normal pancreas. Last year, resection of a gastric tumour containing gastrin and appearing to arise from antral G cells from a case of "clinical" Zollinger-Ellison syndrome was reported.⁸

Diarrhoea was described early in certain cases of the Zollinger-Ellison syndrome¹ and has been variously attributed to hypersecretion by the small intestine, due to the direct action of excess acid;⁹ increased secretion of pancreatic enzymes;² and steatorrhoea, which undoubtedly occurs in many cases and is almost certainly due to irreversible inactivation of pancreatic lipase by the low jejunal pH, though dilution of bile acids and precipitation of glycine dihydroxyconjugated bile acids may play a part.¹⁰ A few cases have obvious causative anatomical lesions.² Two patients with intractable diarrhoea associated with non-β cell islet cell tumours of the pancreas were described in 1958 by Verner and Morrison¹¹ and further examples were discussed by

Telling and Smiddy,¹² who suggested that they were dealing with a situation different from classical Zollinger-Ellison syndrome. Howe² described more cases and even documented the lack of associated gastric hypersecretion (achlorhydria in many) and peptic ulceration, but merely classified them as a variant of the Zollinger-Ellison syndrome. I have found that certain of my colleagues still hold to this view. I, however, would agree with your leading article that these cases should be classified as a completely separate entity, since the only feature they have in common with "proper" cases of the Zollinger-Ellison syndrome is non-β cell tumours of the pancreas, which do not even secrete gastrin (it has been suggested that they produce gastric inhibitory polypeptide¹³), and some have been reported to respond to steroids,⁹ which are of no use in "proper" cases. The suggested name of W.D.H.W. syndrome⁹ seems to me as good as any, especially as the letters remind one of the cardinal features of the condition.

I should like to put forward a tentative classification of the spectrum of Zollinger-Ellison syndrome cases encountered. As the syndrome which Zollinger and Ellison actually documented included pancreatic lesions I suggest that cases of D cell hyperplasia be termed type I Z-E syndrome and those with tumours, whether in pancreas proper or ectopic pancreatic tissue, be termed type II. The cases with gastric lesions could conveniently be termed pseudo-Z-E syndrome type I (G cell hyperplasia) and type II (tumour of G cells). Cases with the clinical features of classical Zollinger-Ellison syndrome and undefined pathology would remain unclassifiable.

It is to my mind important to attempt some sort of classification in view of the different treatments applicable to the different types (for example, vagotomy and antrectomy for pseudo-Z-E syndrome type I¹³). I should be interested to see readers' comments.—I am, etc.,

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- 1 Zollinger, R. M., and Ellison, E. H., *Annals of Surgery*, 1955, 142, 709.
- 2 Howe, C. T., *Scottish Medical Journal*, 1965, 10, 307.
- 3 Gregory, R. A., Grossman, M. I., Tracy, H. J., and Bentley, P. H., *Lancet*, 1967, 2, 543.
- 4 McGuigan, J. E., and Trudeau, W. L., *New England Journal of Medicine*, 1968, 278, 1308.
- 5 Greider, M. H., and McGuigan, J. E., *Diabetes*, 1971, 20, 389.
- 6 Bussolati, G., and Pearse, A. G. E., *Histochemistry*, 1970, 21, 1.
- 7 Polak, J. M., Stagg, B., and Pearse, A. G. E., *Gut*, 1972, 13, 501.
- 8 Cowley, D. J., et al., *Gut*, 1973, 14, 25.
- 9 Marks, I. N., Bank, S., and Louw, J. H., *Gastroenterology*, 1967, 52, 695.
- 10 Go, V. L. W., Poley, J. R., Hofmann, A. F., and Summerskill, W. H. J., *Gastroenterology*, 1970, 58, 638.
- 11 Verner, J. V., and Morrison, A. B., *American Journal of Medicine*, 1958, 25, 374.
- 12 Telling, M., and Smiddy, F. G., *Gut*, 1961, 2, 12.
- 13 Pedersen, R. A., and Brown, J. C., *Gastroenterology*, 1972, 62, 393.

Results of Renal Transplantation

SIR,—We are grateful to Dr. S. C. Farrow and his colleagues (31 March, p. 800) for pointing out an error in our results. One of the patients who rejected was in fact omitted in error from the published actuarial survival curve. In addition, one of our patients rejected at the end of 12 months and Dr.