Drugs for Angina Pectoris

SIR,—A casual reading of the article by Dr. Brian Livesley and others (17 February, p. 375) might leave one with the impression that their results demonstrate the superiority of verapamil and propranolol over isosorbide dinitrate on a number of criteria. Such an assertion is not made in the paper, nor is it supported by the statistical data provided.

Dr Livesley's table I gives comparative figures on trinitrin consumption, number of attacks, systolic and diastolic blood pressure, and work done for 16 subjects on each of five treatments—placebo, verapamil 120 mg thrice daily, verapamil 80 mg thrice daily, propranolol 100 mg thrice daily, and isosorbide 20 mg thrice daily.

We have carried out a reanalysis of these data. The first four treatments were compared with isosorbide by means of the Wilcoxon matched pairs signed rank test. Our reanalysis demonstrates a significant superiority of isosorbide over placebo on the criteria of trinitrin consumption ($P < 0.05$) and number of attacks ($P = 0.02$). The remaining differences are not statistically significant at the 5% level, and so the conclusion follows that the data do not indicate superiority of verapamil or propranolol over isosorbide.

There appears to be a logical discrepancy between the results of the original analysis and our reanalysis, but this is at least partially due to the effect of different sample sizes. In the original study 32 observations were available for the comparison of verapamil and propranolol with placebo, as against only 18 for the comparison of isosorbide and placebo. As is well known, larger sample sizes enable smaller effects to be detected by statistical analysis, and give higher significance for the same effects. Our reanalysis thus suggests that this effect is at least partially responsible for the fact that in the original analysis significant differences were found between verapamil and propranolol and placebo, but not between isosorbide and placebo.—We are, etc.,

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Hypocholesterolaemia in Hyperadrenal States

SIR,—Two years ago Tipton *et al.*¹ reported abnormally low serum cholesterol levels in a woman with an androgen-secreting adrenal tumour. The purpose of this letter is to report a very similar case to the one described by Tipton *et al.* and to comment briefly on this problem.

We have recently seen a woman with an androgen-producing adrenal tumour secreting large quantities of corticosteroids (urinary 17-oxosteroids ranging from 328 to 590 mg/24 hr). She had relatively low serum cholesterol levels (136–142 mg/100 ml in three preoperative samples) which promptly increased after removal of the tumour (164–175 mg/100 ml in three samples taken between the fifth and the ninth postoperative days).

Other authors have recently reported on the relationship between adrenal function and serum cholesterol levels. Dingman² reported the lowering of serum cholesterol by prolonged metyrapone administration. In

congenital adrenal hyperplasia Okuno and Nakayama³ found low cholesterol levels which increased after inhibition of the adrenal function by glucocorticoid administration. Nosedá and Schlumpf⁴ reported similar findings in idiopathic hirsutism.

Two different explanations of these phenomena have been suggested. Tipton *et al.* ascribed the low cholesterol levels seen in their patient to the high androsterone secretion by the tumour. This explanation was based on the finding that the intramuscular administration of androsterone is followed by a marked decrease in the serum cholesterol level.⁵ The other authors mentioned above interpreted their findings as being due to the excessive utilization of cholesterol for steroid biosynthesis. In our opinion the explanation suggested by Tipton *et al.* is more convincing. In fact, metyrapone administration, congenital adrenal hyperplasia, and androgen-secreting adrenal tumours are conditions in which androsterone secretion is likely to be increased and this may also be true in some cases of "idiopathic" hirsutism. However, the two hypotheses are not mutually exclusive and the possibility that the excessive utilization of cholesterol for steroid biosynthesis may play a part as a cause of hypocholesterolaemia in hyperadrenal states ought also to be considered.—We are, etc.,

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Polyvinyl T-tubes in Biliary Surgery

SIR,—Polyvinyl chloride loses much of its flexibility after prolonged contact with bile. Despite a printed warning on Portex packets against the use of these T-tubes for prolonged biliary intubation, this is not common knowledge among general surgeons. The purpose of this letter is to publicize this warning.

A 34-year-old woman underwent cholecystectomy for cholelithiasis elsewhere on 26 October 1971. At operation the gall bladder was found adherent to the common hepatic duct, which was damaged during dissection. Two catgut stitches were inserted to close the hole in the duct. She developed a biliary fistula, was transferred to this hospital on 30 October, and was re-explored on 5 November 1971. A stricture was found at the junction of the common hepatic duct and common bile duct. Cholangiography demonstrated a complete blockage. The stricture was excised and, after mobilization of the duodenum, end-to-end anastomosis was performed over a Portex T-tube. The tube was brought out below the one-layer anastomosis made with 4/0 silk.¹ An initial biliary leak ceased spontaneously and she was discharged on 4 December. It was intended to leave the T-tube in situ as a splint for six months at least.² Advice on further management was sought from Mr. Rodney Smith. He drew attention to the loss of flexibility of the Portex T-tube after prolonged contact with bile and advised its immediate removal. The tube was visualized radiologically, using 3 ml of 45% Hypaque (sodium diatrizoate), and removal moni-

tored under the image intensifier. Marked rigidity was noted and considerable force was needed to remove the tube. This force could have caused further damage to her biliary duct system. So far she is quite well, and 15 months after operation she is afebrile, has normal liver function tests, and an intravenous cholangiogram shows no evidence of stricture.

Damage to the biliary duct system should usually be avoidable if adequate exposure, good illumination, and careful dissection are ensured.^{3,4} If the ducts are damaged, the best results follow immediate excision of the damaged area with end-to-end anastomosis. Where possible, patients with established bile duct injuries should be sent to special centres.⁵ Financial and geographical considerations made this impossible for this patient. While opinions vary nowadays whether drainage of the bile ducts is necessary after simple exploration, most specialized centres agree on the need for prolonged splintage of the anastomosis after excision of a stricture.³ If T-tube splints made of polyvinyl chloride are used, they will so lose their flexibility during prolonged contact with bile that their removal is likely to cause further damage to an already injured duct, with increased risk of further stricture. In this patient, even after 12 weeks, great rigidity had developed. That she is still well is fortuitous. A stricture is still possible.

Portex Ltd. print a warning on the wrappers of their T-tubes stating they are unfit for prolonged intubation. Nevertheless, when this patient was demonstrated at the East Mediterranean Medical Congress in Cyprus in 1972 many British surgeons were unaware of this problem with polyvinyl chloride T-tubes. This supports the suggestion that such patients should be sent to special centres when possible. Obvious loss of flexibility is evident in these T-tubes after only 10 days and it is probably preferable to use latex or rubber every time.

I am indebted to Mr. Rodney Smith for his helpful written advice on this patient, also to the Director General of Medical Services (R.A.F.) for permission to publish this letter.

—I am, etc.,

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Lymphocyte-depletion Hodgkin's Disease

SIR,—The clinical and pathological picture of the cases of "lymphocyte-depletion Hodgkin's disease" described by Neiman *et al.*¹ and referred to in your leading article (16 June, p. 625) is very similar to the two cases described as reticular Hodgkin's disease in 1957 in my M.D. thesis.² Both patients were relatively young males (31 and 44 years old) and presented with fever, progressive weight loss, some involvement of hilar lymph nodes and massive enlargement of abdominal lymph nodes, enlargement of liver and spleen, severe anaemia, and leucopenia. The time of survival from the beginning of their illness was 6½ and 7 months respectively. The