

heparin in clearing veins of fresh thrombus." It is true that suggestive evidence from several small series of cases has been published, but demonstration of superiority requires large-scale controlled trials, which have not been reported. Failure to mention urokinase is to be regretted. This plasminogen activator is of human origin; it is non-antigenic and relatively non-toxic. It is probably much easier with urokinase to obtain the type of biochemical state found by Johnson and McCarty¹ to be most effective in producing thrombolysis in man.

Your leader's penultimate paragraph states: "Now that the dose, route, control, and efficacy of thrombolytic therapy are becoming firmly established, this form of treatment should be part of the therapeutic armamentarium of all physicians and surgeons." We believe this enthusiastic advocacy to be premature, uncritical, and unjustified on currently available evidence. We regret that you have lent the weight of your authority to this advice. Dosage and control of therapy are controversial, and claims for proof of efficacy rest on clinical trial of inadequate design or of small scale; hazards and complications are still numerous. We believe that thrombolytic therapy may have great promise, but it must be regarded as still in the clinical investigative phase. Despite the many difficulties as discussed above, it is hoped that large-scale controlled clinical trials may soon be executed on an international basis or on a national basis in this country, perhaps organized by a body such as the Medical Research Council.—We are, etc.,

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REFERENCE

- ¹ Johnson, A. J., and McCarty, W. R., *J. clin. Invest.*, 1959, **38**, 1627.

SIR,—I read with interest the leading article on thrombolytic therapy (21 December, p. 721) accompanying the report by Dr. J. Hirsh and others (p. 729). This once more raises the question of the value of heparin in the clinical application of thrombolytic therapy. The leading article appears to leave no doubt that "heparin has no thrombolytic effect at all." This is incorrect. It has been shown that heparin and heparin-like compounds do in fact induce thrombolysis both under experimental in-vivo conditions and in clinical practice.¹⁻⁶

This misunderstanding usually arises because of the assumption that traditional anticoagulant dose levels of heparin are assumed to be one and the same as those required for thrombolysis. To achieve satisfactory thrombolysis with heparin it should be given intravenously in doses of sufficient magnitude to produce a Lee-White coagulation time of between two and a half and three times the normal level *four hours after administration*.⁴ Intermittent intravenous therapy can be readily controlled in this way, whereas continuous infusion cannot. From the studies available so far it cannot be shown whether the maximum effect is produced by the high dose level obtained shortly after intravenous injection or at some level between that and the fall-off occurring in the subsequent four hours.⁶

The complications with this method are no greater than with any other currently

available thrombolytic agent in the hands of experienced workers.—I am, etc.,

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REFERENCES

- ¹ Halse, Th., *Sangre (Barcelona)*, 1964, **9**, 149.
² Lewis, J. H., Kerber, C. W., and Wilson, J. H., *Amer. J. Physiol.*, 1964, **207**, 1044.
³ Williams, R. D., and Karaffa, F., *Surg. Gynec. Obstet.*, 1965, **121**, 309.
⁴ Morris, L. E., and Balk, P., *Angiology*, 1965, **16**, 339.
⁵ Hellesen, W. O., *Acta chir. scand.*, 1942, **87**, Suppl. No. 73.
⁶ FitzGerald, D. E., Szeto, I. L. F., Spero, J., and Lewis, J. H., *Thrombos. Diathes. Haemorrh.*, 1967, **17**, 418.

Longer Space Voyages

SIR,—Your timely leading article (21 December, p. 719) points out several hazards to health—such as solar radiation and prolonged exposure to weightlessness—which may well pose serious problems as manned space missions become longer and more complex.

Of course, few would deny that, as manned space missions become longer, so it will be increasingly difficult to keep the crew members alive and in good health. Yet despite this there is one further relevant point which we may be in danger of overlooking at this stage—simply this: the major problems in space medicine—as opposed to the applied physiology of man in space—will occur not in deep space but in close earth orbit.¹ They will occur as soon as space flight ceases to be restricted to its present group of highly trained super-fit young adults. They will occur as soon as businessmen, diplomats, and others begin to make use of the sort of orbital transport vehicles already on the drawing-boards in advanced design offices.² They will concern not the applied physiology of man in space, but rather the interaction between space travel and the various diseases which affect man.

In this context, one cannot resist pointing out that the recent extraordinary hue and cry engendered in the Apollo 7 and 8 missions—by the sort of viral infection routinely seen and successfully treated several times per day by the average general practitioner—may well reflect in the Apollo programme a pre-occupation with space physiology to the detriment of true space medicine.—I am, etc.,

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REFERENCES

- ¹ de Dombal, F. T., *J. Brit. Interplanetary Soc.*, 1968, **21**, 385.
² Bone, P., *Spaceflight*, 1965, **7**, 38.

Operation for Obstructive Coronary Disease

SIR,—We have read with great interest the letter by Dr. H. David Friedberg and others (5 October, p. 57) concerning surgical myocardial revascularization. Their thoughtful, balanced, and aggressive approach to coronary artery disease is much to be commended. However, they are not alone in their "ultra-radical" belief that there is "a group of patients with little or no angina who may

well benefit from surgery." Experience has convinced us that severe coronary artery disease associated with electrocardiographic and haemodynamic evidence of myocardial ischaemia may be present in the complete absence of angina pectoris or other cardiac symptoms.

Over the past three years we have selected for the Vineberg operation 22 asymptomatic patients, the sole indication for operation having been the demonstration by selective cine-coronary angiography of obstructive coronary artery disease considered to pose a serious threat to the life or function of the patient.¹ Twenty-one subjects came to surgery, one having died of acute coronary occlusion in the interim and two having sustained three myocardial infarcts between them in the interval between angiography and operation. These accidents were not related to angiography. Most of the subjects, whose mean age was 44 years, had a history of some episode of acute coronary heart disease, but some presented with electrocardiographic abnormalities alone.

All subjects had at least one systemic vessel implanted in the left ventricular myocardium. Nine had a left internal mammary implant alone. The remainder had two or more vessels implanted, including the right internal mammary, the gastroepiploic, and the splenic arteries. Sites of implantation were selected on the basis of coronary angiographic findings. Most subjects also had a left upper dorsal and peri-aortic sympathectomy (for prevention of serious ventricular arrhythmias) together with epicardectomy and a free omental graft. Operative mortality has been nil and morbidity low.

No patient has died during follow-up. Two have sustained small myocardial infarcts. All are fully employed, many in senior, demanding, and responsible positions. Of patients subjected to implanted vessel angiography, 77% have at least one implant patent.

Whether these operations will increase life expectancy in this group of young men with great domestic and social responsibilities remains to be seen, but such is our hope and indeed our expectation.—We are, etc.,

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REFERENCE

- ¹ FitzGibbon, G. M., Hooper, G. D., Maciver, D. A., *The Vineberg Operation for the Patient Without Angina*, in preparation.

Management of Coronary Artery Disease

SIR,—The article "Management of Coronary Artery Disease" (4 January, p. 37) is distinguished for its complete disregard of surgery. If the article were designed to deal only with medical management, either this should have been stated in the title or the role of surgery alluded to in the text.

Surgery has much to offer: sympathectomy (of arguable value, maybe), myocardial revascularization, coronary endarterectomy, and a variety of grafting procedures on the coronary arteries. Not only do these operations improve the quality of life afterwards, they also may save life in otherwise hopeless cases.—I am, etc.,

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