care, who was taking 300 mg. per day of chlorpromazine, collapsed in a hypothermic state while swimming in a public swimmingbath. Rewarming and resuscitation produced complete recovery.

The possible hazard of hypothermia and respiratory distress due to swimming in patients taking phenothiazine drugs is not generally recognized, and would merit further laboratory and clinical investigation .--- I am, etc.,

JOHN JOHNSON.

REFERENCE

¹ Shepherd, M., Lader, M., and Rodnight, R., *Clinical Psychopharmacology*, 1968. English Universities Press Ltd., London.

Anticoagulants in Acute Myocardial Infarction

SIR,-It was good to see the complete short-term anticoagulant vindication of therapy after cardiac infarction provided by the findings of the M.R.C. Working Party (8 February, p. 335). However, the summary, if read in isolation, might tend to confirm the nihilist in his views. There seems to be undue emphasis on the minimal difference found between the overall mortality rates in the two groups. The statement that this difference "could have occurred by chance" is, of course, statistically true, but, on the evidence of the published findings, clinically misleading.

Reinfarction occurred more commonly in the low-dosage group (Table XIV). The difference between the two groups did not reach "technical levels of significance," but there is only a 6% likelihood (corresponding approximately to the χ^2 value of 3.575) that this observed difference was a chance finding. From the clinical standpoint these very substantial odds that such evidently safe therapy may avert some reinfarction episodes and their consequences surely justify its use from the outset. The differing pattern of reinfarction in relation to time in the two groups is mentioned in the text, though the highly significant degree of this difference is not pointed out $(\chi^2$ with correction factor = 7.7, p < 0.01), nor the fact that the trend reversal in favour of the low dosage group after the first week is confined to females.

The significant reduction in thrombo-embolic complications in the "high-dosage" group is recognized in the text. While in itself a justification of therapy, this finding and the above reinfarction differences make one wonder why the low-dosage group of patients did not show a clear-cut increase in mortality. The answer to this apparent paradox may lie in the subsequent clinical management of patients in this group who suffered such complications. In 67 cases "high-dosage" anticoagulant therapy was instituted following reinfarction or other thromboembolic incident (Table XIX), presumably because the physician considered it potentially beneficial. However, the final results in these cases were analysed with the remainder of the lowdosage group. This would have been justifi-able only if "high-dosage" therapy were known to have no influence on the results, and, of course, the trial was instituted to provide evidence on this very point. If "highdosage" therapy has indeed a beneficial effect the mortality rate in the low-dosage group will thus have been artificially lowered and any real difference between the two groups will have been masked.

The highly significant reduction in morbidity due to systemic artery occlusion, leg vein thrombosis, and pulmonary embolism will presumably make further trials of this nature ethically unjustifiable. It would therefore be interesting to know the times of occurrence of the thromboembolic complications and also the time of death in those found to have thromboembolism at necropsy. We found¹ that all the thromboembolic episodes in patients with heart failure and on phenindione occurred within the first 10 days of the drug's administration. By contrast, such episodes in the control group occurred between 7 and 44 days after zero time (day of admission). We concluded that this difference might have been due to some thrombogenic tendency of the oral anticoagulant during the early days of its administration-that is, before "therapeutic" prothrombin levels had been attained. There is some experimental evidence to support this concept.2 Intermittent heparin therapy during the first 36 hours, as given in the trial, is unlikely to provide adequate protection against any such effect .--- We are, etc.,

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REFERENCES

Domenet, J. G., Evans, D. W., and Stephenson, H., Brit. med. 7., 1966, 2, 866. Merskey, C., and Drapkin, A., Blood, 1965, 25,

SIR,-Dr. L. Poller (1 March, p. 572) has unerringly pinpointed the weakness in the M.R.C. report on anticoagulant treatment for acute myocardial infarction (8 February, p. 335), and this should do much towards redressing the balance that its "weighty" conclusions appear to tilt against this form of therapy. As in some former trials, once more it can fairly be said that the bad results of anticoagulant treatment in this condition are the results of bad anticoagulant treatment; and it can still be shown that this therapy is meat for humans with coronary artery disease, even if it is also (in the words of a world-famous cardiologist) poison for rats.-I am, etc.,

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Treatment of Hypertension with Propranolol

SIR,-The paper by Drs. B. N. C. Prichard and P. M. S. Gillam (4 January, p. 7) was of particular interest, containing as it did an extension to propranolol of the excellent comparative study of bethanidine, guanethidine, and methyldopa in hypertension,¹ as well as a general review of the place of propranolol in hypertensive therapy.

It is true that a number of papers in the last few years have not shown propranolol to have any consistent hypotensive effect. However, the value of much of the work done has in my view been reduced by three factors: (1) The comparatively small numbers involved; (2) the comparatively short duration of the trials; (3) the arbitrary (and not necessarily optimum) dosage of propranolol used. The situation might be clarified by a double blind trial in which the participants had already been taking a dose of propranolol known to be appropriate for their needs. Clearly this can only be done in a department where the drug has been studied for some time and where a prima facie case for its value in hypertension has been established.

I have been engaged on a detailed study of propranolol for nearly five years, involving 240 patients, with a smaller percentage of failures than with any other drug used in the past 15 years, and, having carefully studied the comments of Drs. Prichard and Gillam on the side-effects of propranolol and its general acceptability to patients, I feel bound to agree with them completely and to endorse their conclusions. Drs. G. S. Humphries and D. G. Delvin (15 February, p. 445) remain sceptical, but in my experience the doses which they used are by no means adequate for a large percentage of hypertensive patients. In my department we have been conducting for the past five months a double blind trial in which all participating patients have already been adequately controlled by propranolol, many of them for a year or more, and when completed this trial will have lasted eight months .--- I am, etc.,

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Reference

¹ Prichard B. N. C., Johnston, A. W., Hill, I. D., and Rosenheim, M. L., Brit. med. 7., 1968, 1, 135.

Progestogen is not Progesterone

SIR,-It is unfortunate and misleading that Dr. L. Poller and his colleagues (1 March, p. 554) should use the term progesterone in their valuable paper reporting studies on blood coagulation in women using continuous low dosage progestogen for oral contraception. Although this term occurs several times in the paper, not once does it refer to Δ_4 -pregnene-3,20-dione, the only compound properly called progesterone. The compound studied, chlormadinone (Δ_6 -6) chloro-17 α -acetoxyprogesterone) is, of course, not progesterone, and neither has any formulation hitherto used for contraceptive purposes ever contained progesterone.

It seems a pity that the important finding reported by the authors-that, within the limits of their trial, chlormadinone, unlike oestrogen-containing oral contraceptives, does not appear to cause increased coagulability or platelet aggregation-should be vitiated by terminological misuse producing such inaccurate and unwarranted statements as, for example, the one on which the article concludes: "... the investigation does suggest that the thrombogenic constituent of conventional oral contraception may have been eliminated by the use of progesterone alone." Of course, it does nothing of the kind. -I am, etc.,

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