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Trial of Clofibrate

SIR,—There has been very little comment on the two major trials on the use of clofibrate in the treatment of ischaemic heart disease (25 December 1971, p. 767 and p. 775). There must be hundreds of bewildered doctors wondering whether they should prescribe clofibrate; and certainly many thousands of patients demanding prescriptions because of the publicity that the trials received. I am sure that the lack of comment results from the mind-boggling effect of two very long papers on the same subject with many major and minor differences in design and conduct and with different conclusions placed side by side. Both papers are full of statistical prestidigitation: groups of patients were defined before the trial, and then combined, and recombined during the analysis; anticoagulants were discouraged, then accepted, and then included and excluded to help the figures; end-points and events were defined, and then added, subtracted, and mixed in a most confusing way.

The Scottish trial suffered a shattering blow when randomization produced groups of patients biologically different in two factors (serum cholesterol and blood pressure) known to be of prognostic importance in the disease being treated. A purist would say that no further statistical comparison of the prognosis of the two groups is valid. Even an easy-going critic would doubt the validity of combining a double-blind group with a non-double-blind (anticoagulant) group. Just as dubious is the combination of results from both trials in the joint summary (p. 784). The low annual death rate in the Scottish placebo group is used as an excuse for the failure of clofibrate

to benefit patients in one group, and for its apparent harmful effect in another group. This harmful effect is presumed to be "a chance finding," whereas apparent beneficial effects of the same statistical order are considered significant.

The most important criticism of the Newcastle trial, that non-cardiac deaths have not been reported, has already been made (8 January, p. 109) and apparently cannot now be answered (19 February, p. 506).

The wisdom of admitting patients to the trial on the basis of history alone is questionable. Presumably there is a subtle difference between "no statistical differences between" and "comparable," the latter meaning that statistical tests of difference have not been applied. In the comparable category are history of infarction and angina, smoking habits, past treatment with anticoagulants, and distribution of E.C.G. changes. If this presumption is correct there must be doubt whether the Newcastle groups were identical. More patients were withdrawn from the clofibrate than from the placebo group: their fate has not been reported.

It seems churlish to be critical of such an immense amount of hard work and careful thought. Nevertheless, I do not believe that conclusions about the value of clofibrate can be drawn from the Scottish trial because the groups were different. Until the Newcastle workers have answered the questions asked no conclusions can be drawn from their trial either. Until they do so doctors will continue to prescribe clofibrate for emotional reasons, not for rational ones.—I am, etc.,

General Infirmary, Salisbury

P. M. S. GILLAM

Yoga and the Vertebral Arteries

SIR,—If we are to believe that Yoga exercises were developed centuries before the circulation of the blood was discovered, it may be wise to point out that the extreme degrees of neck flexion and extension and rotation during some of these exercises (for example, "shoulder stand" or "cobra") must for some people be hazardous to the vertebral and anterior spinal artery circulation.

Varieties of the basilar artery syndrome appear to be precipitated by unnatural neck postures, such as may occur for example during anaesthesia, in a dentist's chair, at a ladies' hairdresser, while picking fruit from a tree, while painting a ceiling, driving a car, swimming breast stroke, or presiding over a meeting. The consequential cerebral lesion may be delayed perhaps to appear during the night following, and this delay of some hours distracts attention from the earlier precipitating factor, especially when there is a catastrophic stroke.—I am, etc.,

W. RITCHIE RUSSELL

Oxford

Ganglion Cysts of Bones

SIR,—Professor F. N. Ghadially might consider in his intriguing study of the pathogenesis of ganglion cysts (19 February, p. 508) a similar lesion which certainly does involve smooth muscle—namely, cystic degeneration of arteries. This also occurs in young subjects, especially males, and most commonly in the popliteal arteries or other vessels lying close to joints where they may be subjected to repeated trauma.¹ There are