Lymphocyte Transformation and Myocardial Infarction

SIR,—It has been shown that the ability of the lymphocyte of a person to respond in vitro to phytohaemagglutinin decreases with the age of the donor.¹ Ischaemic heart disease may represent an age phenomenon not correlated with chronological age, but rather with the "biological age" of the individual.

Ten male patients aged 43 to 54 years were studied. They had all suffered from myocardial infarction six to 24 months previously, and had all been treated in a coronary care unit. At the time of the study they all appeared to be in good general health. Twelve healthy males living in the same geographic area and of approximately the same socio-economic background served as controls. Their ages were also between 43 and 54 years.

Great care was taken to ensure that neither patients nor controls took any drugs of any type permanently. For at least 48 hours before the blood samples were taken no medication whatever was allowed. All samples

were taken from fasting subjects on rising in the morning. Patients and controls were all studied on at least two separate occasions, a week or more apart.

Lymphocytes were separated from whole blood by sedimentation after the addition of gelatin.² The lymphocytes were washed and incubated in McCoy's medium supplemented with 30% fetal calf serum. Three parallel cultures were stimulated with phytohaemagglutinin (P.H.A.); one was unstimulated. Incubation was carried out for 43 hours and tritiated thymidine was added for the last 3 hours. The cells were washed, fixed, and dried on Millipore filters.³ The radioactivity was measured in a liquid scintillation system.⁴

The results were expressed as the average of all values from P.H.A.-stimulated cultures of a person. The mean coefficient of variation was 14%. The values were plotted (Fig. 1). A rank sum test (Mann-Whitney's test) showed values in patients to be significantly lower than in controls ($0.05 > p >$

0.02). The values from 53 normal men (Hagen and Frøland, unpublished) were used as a comparison (Fig. 2). It appears that the patients have values one would expect to find in much older, normal men.

This work was supported by a grant from the Danish State. Drs. P. Eskildsen and P. Fritz Hansen, Cardiology Dept., Copenhagen County Hospital, kindly put the records of their patients at our disposal.

—We are, etc.,

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1 Pisciotto, A. V., Westring, D. W., DePrey, C., and Walsh, B., *Nature*, 1967, 215, 193.

2 Coulson, A. S., and Chalmers, D. G., *Lancet*, 1964, 1, 468.

3 Mosedale, M. B., and Parke, J. A. C., *Proceeding of the Symposium: "The Biological Effects of Phytohaemagglutinin."* The Robert Jones and Agnes Hunt Orthopaedic Hospital, Management Committee, Oswestry, England, 1966, p. 97.

4 Sørensen, S. F., Andersen, V., and Giese, J., *Acta Pathologica et Microbiologica Scandinavica*, 1969, 78, 259.

FIG. 1.—³H-thymidine uptake in phytohaemagglutinin-stimulated lymphocytes from 10 males surviving myocardial infarction (M.I.) and 12 healthy controls (NORM.).

FIG. 2.—³H-thymidine uptake in phytohaemagglutinin-stimulated lymphocytes from 53 healthy males of various ages (●) and 10 males surviving myocardial infarction (X). A regression line is shown for normal men.

Stereophonic Auscultation

SIR,—May I recommend to those practitioners bored with routine auscultation an interesting method using two stethoscopes—preferably Littmann's, as they have fairly uniform sound conduction?

The left earpiece of one stethoscope is placed in the left ear in the usual way, and the right earpiece is passed beneath the chin and placed on the right sternomastoid muscle. The right earpiece of the other stethoscope is then placed in the right ear and the left earpiece placed on the left sternomastoid. If the righthand bell chestpiece is placed over the apex of the patient's heart and the lefthand bell chestpiece placed over the base it is possible in a patient with clear heart sounds to detect the "lub" in the right ear, and the "dup" in the left ear, thus giving a sort of stereophonic effect. It might possibly be easier to time a cardiac murmur in this way or even to detect the direction of a murmur. Similarly one can place the diaphragms one on each side of the patient's posterior thoracic cage and compare the air entry to both bases at the same time.

Bowel sounds are quite interesting if the bells of the stethoscopes are placed some distance apart on the abdomen, and occasionally one is entertained by the sound of gas thundering past and emulating an express train.—I am, etc.,

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Trial of Mefruside

SIR,—We have noted Professor D. N. S. Kerr's comments (15 January, p. 176) on our article. In our trial of mefruside, we were primarily concerned to show whether or not it was an effective diuretic and for that reason we compared it with frusemide as being a diuretic of proven potency. While we agree with Professor Kerr on the wide dose response property of frusemide, in practice it is commonly prescribed in the range of 40-80 mg per day for adults. Mefruside is dispensed in tablets of 25 mg and the suggested dose as a diuretic is 25-50 mg, increasing if necessary to 75-100 mg. We felt, therefore, that a comparison of 50-mg doses would be both

reasonable and informative. Although in these conditions mefruside gives a greater excretion of water and electrolyte than frusemide, no doubt in higher dosage frusemide with its different mode of action might prove relatively more advantageous, even, as Professor Kerr points out, in the presence of severe renal dysfunction. We have made no claim for mefruside therapy in this situation.—We are, etc.,

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Ampicillin and Mononucleosis

SIR,—Dr. G. D. W. McKendrick's letter (8 January, p. 114) does not answer my chief criticism (11 December 1971, p. 685), which was that to challenge with a standard dose of oral ampicillin a patient who has previously exhibited hypersensitivity to the drug is so hazardous as to outweigh all possible benefits. I would agree that ampicillin is a valuable antibiotic, but it is not unique and