part.” Thirdly, he asks the question, “Or is there some congenital factor operating, giving rise to what may be termed an ‘organ inferiority’ in respect of the Polynesian lung?”

One finding, the relevance of which to the present study cannot be denied, is the degree of malnutrition among Polynesian babies compared with Europeans. Here is something tangible to which we believe great attention should be paid in similar future studies. Neither a genetic nor a nutritional factor for severe respiratory illness excludes the other. Further work will be required to elucidate the part played by either or both.

What of the adenovirus? Macfarlane and Sommerville (1957) wrote of a “non-tuberculous juvenile bronchiectasis; a virus disease?” van der Veen (1963) stated: “Further studies are needed to elucidate the role of adenoviruses in the development of persistent bronchial lesions.” Finally, Rytel *et al.* (1964) reported a very suggestive correlation between adenovirus infection and the subsequent development of bronchiectasis in naval recruits.

The present series suggests that adenovirus type 21 can produce lethal pneumonia or result in lung fibrosis or bronchiectasis in survivors. The question remains, could adenoviruses be of major importance in the as yet unknown aetiology of many cases of bronchiectasis?

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Significance of Electrocardiographic Changes in Hypertension

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Summary : Studies in 17 hypertensive patients showed that the electrocardiographic features of T-wave inversion and S-T segment depression distinguish those patients with higher systolic blood pressures. They do not indicate impaired cardiac function.

Introduction

The electrocardiographic pattern of depression of the S-T segments and inversion of the T waves in left-sided leads in a patient with systemic hypertension is generally accepted as evidence of severe left ventricular hypertrophy. The term “left ventricular strain” that is sometimes given to this electrocardiographic finding implies that left ventricular function may be impaired under these circumstances.

Our previous work (Hamer *et al.*, 1967) has indicated that the cardiac output on exercise is lower than normal in patients with hypertension. In this study we have attempted to correlate the electrocardiographic changes with the degree of disturbance in left ventricular function as assessed from the response of the cardiac output to exercise.

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Patients and Methods

Seventeen hypertensive patients aged from 22 to 64 were investigated. All had a diastolic pressure of 100 mm. Hg or over as outpatients. The clinical findings are summarized in Table I. On the basis of the electrocardiogram they were divided into two groups (Table II). Nine (group I) had a

TABLE I.—Clinical Features

Case No.	Sex	Age	Casual B.P.	Fundal Changes (Graded 0 to 4)	Chest X-ray	
					CTR %	Congestion
Group I						
1	M	40	180/120	3	42	0
2	M	46	220/120	1	47	0
3	M	62	215/140	2	48	0
4	M	45	190/115	1	43	0
5	M	59	220/150	0	56	+
6	M	36	210/110	1	43	0
7	M	39	145/100	1	48	0
8	M	24	145/100	0	48	0
9	M	50	160/100	0	42	0
Group II						
10	M	54	215/130	1	50	0
11	M	48	255/145	4	48	+
12	M	52	200/110	2	56	+
13	F	64	245/140	2	58	+
14	F	49	220/140	1	48	0
15	M	55	240/140	3	54	+
16	F	22	250/150	3	35	0
17	F	34	205/125	3	45	0

normal tracing or voltage changes of left ventricular hypertrophy with normal T wave and S-T segments (Fig. 1). The remaining eight subjects (group II) had S-T depression (Fig. 2) or T-wave inversion (Fig. 3) in the left chest leads. Patients with angina pectoris or previous myocardial infarction, as evidenced by abnormal Q waves in the electrocardiogram, were excluded from the study, and no patients were being treated with digitalis.

TABLE II.—E.C.G. Findings

Case No.	Mean Frontal QRS Axis	QRS Voltage			S-T Depressed	T Negative
		RV5	SV1	Sum		
Group I						
1	-10°	21	14	35	0	0
2	50°	14	14	28	0	0
3	40°	19	10	29	0	0
4	40°	18	11	29	0	0
5	-20°	15	15	30	0	0
6	70°	17	14	31	0	0
7	40°	15	10	25	0	0
8	65°	23	22	45	0	0
9	70°	12	9	21	0	0
Group II						
10	60°	24	20	44	+	+
11	-30°	29	17	46	0	+
12	-10°	21	15	36	+	+
13	0	27	22	49	+	+
14	30°	16	24	40	+	+
15	-20°	26	15	41	+	0
16	60°	14	14	28	+	0
17	-30°	6	7	13	+	0

The experimental technique was as reported previously (Hamer et al., 1967). Under local anaesthesia polyethylene cannulae were passed percutaneously into the left basilic vein and right brachial artery. Direct intra-arterial pressures were recorded by means of a P 23 Gb strain gauge (Statham Laboratories) and cardiac output was measured by indicator dilution

FIG. 1.—Electrocardiogram from group I—that is those with normal patterns or increased QRS voltage only.

FIG. 2.—Electrocardiogram from group II showing depression of the S-T segments in left-sided leads.

with Gilford or Cambridge densitometers and indocyanine-green, the dynamic method of calibration (Shinebourne et al., 1967) being used. Measurements were made at rest, erect, and while walking on a treadmill at 2 m.p.h. and 3 m.p.h. on the flat and at 3 m.p.h. on 3° and 6° slopes. The systemic resistance was calculated by dividing the mean arterial pressure (mm. Hg) by the cardiac output (litres per minute), and the ejection rate from the stroke volume and ejection time, measured from the onset of the arterial pressure pulse to the dicrotic notch.

FIG. 3.—Electrocardiogram from group II showing inversion of the T waves in left-sided leads.

FIG. 4.—Blood pressure (mean and standard error at rest and on exercise) showing a significantly higher systolic blood pressure in group II (open circles) than in group I (closed circles).

FIG. 5.—Peripheral resistance at rest and on exercise, showing a tendency to a higher resistance in group II (open circles); these differences are not significant.

Results

The systolic blood pressure in group II, with S-T and T-wave changes in the electrocardiogram, is significantly higher than in group I at rest and at each work load (Fig. 4). Except for the resting supine measurements, no significant difference is shown between the diastolic pressures in the two groups. Peripheral resistance (Fig. 5) falls in both groups on exercise and is slightly but not significantly higher in group II patients.

FIG. 6.—Cardiac output at rest and on exercise is similar in the two groups.

FIG. 7.—Heart rate at rest and on exercise is similar in the two groups.

FIG. 8.—Ejection rate at rest and on exercise, showing a tendency to more rapid ejection in group II (open circles): differences are not significant.

No significant difference is found in the two groups with regard to cardiac output (Fig. 6), heart rate (Fig. 7), or ejection rate (Fig. 8).

Discussion

Assessment of cardiac function by measurements made during treadmill exercise has been discussed previously (Hamer *et al.*, 1967). The effect of nervous influences on peripheral arteriolar tone are abolished during exercise, and measurements made under these circumstances give a true estimate of the severity of hypertensive vascular changes. The treadmill provides a natural form of exercise to which patients easily adapt.

The depression of the S-T segments and inversion of the T waves in left-sided electrocardiographic leads in left ventricular hypertrophy is generally held to indicate a severe load on the left ventricle. The term "left ventricular strain" (Barnes and Whitten, 1929; Ackerman and Katz, 1933) is often used to describe the changes. The mechanism producing the alterations in repolarization is uncertain. It has been suggested that the changes are entirely secondary to the greater QRS voltages in these patients. Some delay in the spread of depolarization within the ventricular muscle would also lead to alterations in the S-T and T waves.

However, study of the relation between the changes in the activation and recovery phases indicates that the S-T and T-wave changes are usually greater than would be expected as a consequence of larger QRS voltages or delay in depolarization (Cuéllar Padilla *et al.*, 1945; LaDue and Ashman, 1946). The depression of the S-T segments and inversion of the T waves in patients with left ventricular hypertrophy are in most cases an indication of a primary disturbance in the recovery process in the left ventricular myocardium.

A delay in the spread of the action potential producing secondary S-T and T changes, or a primary alteration of the S-T segments and T waves, indicates an abnormality of myocardial function. It has been suggested that relative ischaemia in the hypertrophied left ventricle is responsible (Leishman, 1951), but this seems unlikely, as there is no undue incidence of angina in patients with S-T and T-wave changes (Simpson, 1960). It is not, of course, justifiable to postulate that changes in myocardial electrical activity will necessarily be associated with any abnormality in contraction. In fact, the persistence of the "left ventricular strain" pattern for many years in some hypertensive subjects suggests that the changes are not necessarily serious (Ranges, 1949), and for this reason the use of the term "left ventricular strain" has been thought undesirable (Wilson *et al.*, 1947).

In hypertensive patients in general, however, the appearance of S-T segment depression and T-wave inversion on the electrocardiogram is associated with a poor prognosis (Sokolow and Perloff, 1961), and the present study was designed to determine whether the electrocardiographic changes were associated with any disturbance suggesting an impairment of left ventricular function. Though our patients with S-T segment and T-wave changes (group II) show a tendency to higher blood pressure and more pronounced fundal changes, as well as a higher incidence of pulmonary venous congestion on the chest x-ray films, there are no major differences in exercise performance between the two groups. The only haemodynamic factor distinguishing hypertensive patients with marked left ventricular hypertrophy on the electrocardiogram from those with less severe changes was the higher systolic blood pressure. This highly significant difference was present at rest and at all levels of exercise. The supine resting diastolic pressure was also significantly higher, but no differences were found with the patients standing or doing exercise.

The cardiac output in all patients fell on standing, but rose progressively with increasing work-loads. Though the values found were lower than expected in normal subjects (Strandell,

1964; Hanson *et al.*, 1966; Sannerstedt, 1966) the relative depression of cardiac output was similar in the two groups in spite of the electrocardiographic differences. The peripheral resistance rises on standing and then falls during exercise. In group II the resistance does show a tendency to be higher than in group I, as might be expected from the higher systolic pressures, but the changes were not significant. The finding that the mean heart rates as well as the mean cardiac outputs show no difference in the two groups of patients indicates that there is also no difference in stroke volume.

Provided there is no change in ventricular volume, the ejection rate reflects the velocity of shortening of the individual myocardial fibres. Patients in group II tend to have bigger hearts on the chest x-ray examination than those in group I. This finding suggests an increase in left ventricular volume in group II, though we have shown a poor correlation between heart size on chest x-ray examination and direct measurements of left ventricular volume in aortic stenosis (Fleming and Hamer, 1968). The slightly faster ejection rate of group II subjects could be accounted for on this basis, as an identical velocity of contraction in a larger ventricle will result in a faster rate of ejection. The relation of the velocity of fibre contraction to the force generated is a useful way of assessing the contractile state of the myocardium (Sonnenblick, 1962). As the force generated by the myocardium in group II patients is, because of both pressure and volume changes, if anything greater than in group I and the ejection rate is no lower, there is no evidence from our studies of impaired myocardial contractility in the patients with the more severe electrocardiographic changes. The higher systolic blood pressures in our patients in group II suggests that the myocardium has to generate greater force in those with S-T segment and T-wave changes. This finding is consistent with the hypothesis that a greater intraventricular systolic pressure leads to a primary change in the S-T segments and T waves by producing localized subendo-

cardial changes which may alter the direction of repolarization (Goldberger, 1947) or interfere with the spread of the activation process (Lepeschkin, 1951). However, the S-T and T-wave changes must represent more than a simple mechanical effect, as they do not resolve immediately when the left ventricular pressure is reduced.

Our finding that severe left ventricular hypertrophy on the electrocardiogram is particularly related to systolic blood pressure is in keeping with the suggestion (Ramirez and Garcia Pont, 1965) that cardiac size in hypertension is more closely related to systolic than to diastolic pressure. The evidence suggests, as did our previous work (Hamer *et al.*, 1967), that the systolic pressure is an important determinant of the pathological effect of hypertension on the heart.

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Intermittent Chemotherapy for Tuberculosis in an Urban Community

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Summary: A regimen designed for effective foolproof antituberculosis treatment, acceptable on a routine basis, was applied to all patients newly diagnosed at the Chest Clinic, Hammersmith Hospital, in 1963, 1964, and 1965. During the first three months of treatment patients received daily (six days a week) streptomycin 0.75 g. plus isoniazid 300 mg. plus sodium para-aminosalicylate (P.A.S.) 12 g. The P.A.S. was usually stopped when bacterial sensitivity reports made this possible. For a further 15 months streptomycin 1 g. plus isoniazid 600 mg. was given on three alternate days each week to complete a total of 18 months' treatment.

Of the total of 140 patients (66% sputum-positive) 112 (80%) completed the planned 18 months with intermittent streptomycin plus isoniazid and a further eight completed treatment on alternative regimens (a total of 85%). The

equivalent figures for one year are 88% and 94%. Excellent clinical and radiological results, together with sputum conversion, were achieved in 138 of the 140 patients (99%). Only two patients were lost from surveillance, because of failure to co-operate, before quiescence was obtained.

It is concluded that the total efficiency of supervised intermittent treatment is greater than that of unsupervised daily regimens. Since 100% arrest of tuberculosis is possible with co-operative patients, less should not be accepted in developed countries.

Introduction

The management of antituberculosis chemotherapy, even in developed countries, still poses problems, particularly in relation to drug-taking and the development of bacterial resistance (Simpson, 1956; Dixon *et al.*, 1957; Fox, 1958, 1962; Rigby, 1958; Wynn-Williams and Arris, 1958; Poole and Stradling,

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