*Papers and Originals***LATENT CORONARY HEART DISEASE DETECTED BY ELECTROCARDIOGRAM BEFORE AND AFTER EXERCISE**

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In 1954 we began a study to find out whether coronary heart disease could be detected by means of the electrocardiogram (E.C.G.) before the onset of symptoms. Details of the technique and criteria used have already been published (Acheson, 1957a; Rumball and Acheson, 1960). From 682 R.A.F. volunteers, 660 men (aged 19 to 55 years) were selected who had no clinical or radiological evidence of heart disease and a diastolic blood-pressure below 100 mm. Hg. After a standard 12-lead E.C.G. the men ran down and up 66 steps each 10 in. (25 cm.) high under medical supervision. Tracings from leads I, II, III, V₄, V₅, and V₆ were then repeatedly recorded, beginning one minute, three minutes, and six minutes after completion of the exercise. The E.C.G.s were classified into "normal" and "anomalous" groups. This paper reports the results of a follow-up study completed in 1961, four to seven years after the original survey. This was in two parts: (a) a postal follow-up of the whole series, and (b) re-examination of a sample of 176 men.

Anomalies in E.C.G. at Rest

In the 1954-7 survey the frequency of minor anomalies at rest was as follows:

	No.	%
Wolff-Parkinson-White syndrome	1	0.1
Complete right bundle-branch block	2	0.3
Incomplete right bundle-branch block	33	5.0
P-R interval of 0.2 second or more	11	1.7
Left axis deviation	10	1.5
Slurring of R in lead I	5	0.7
Minor anomalies in RS-T and T	25	3.7
	87	13.0

As these changes were unaccompanied by evidence of heart disease they did not disqualify a man from performing the exercise test. In four men more than one anomaly at rest was noted, and one of them also showed a fresh anomaly after exercise. In 24 other men with a single resting anomaly an additional electrocardiographic anomaly was noted after exercise.

Anomalies in E.C.G. After Exercise

These have been discussed in detail elsewhere (Rumball and Acheson, 1960). Their frequency and classification are summarized in Table I. RS-T depression* was found to become more frequent with advancing age, and in its pattern and temporal evolution bore a close resemblance to that seen in spontaneous attacks of angina pectoris, or after exercise in patients subject to angina. In no instance during the 1954-7 survey was the production of these changes accompanied by chest pain. RS-T depression of 1 mm. or more or negative T waves could always be repro-

duced by a similar exercise test performed after an interval of weeks or months. The mean blood cholesterol was significantly higher in a sample of the men in Group B2 than in a sample of Group A men matched for age.

TABLE I.—Classification of E.C.G.s After Exercise in 660 Apparently Healthy Men (1954-7 Survey)

Group	Definition	No.	%
A	No depression of the RS-T segment; no iso-electric or negative T waves	570	86.4
B	1. Iso-electric or negative T waves without RS-T depression	14	2.1
C	2. RS-T segment depression of 1 mm. or more, or of 0.5 mm. with iso-electric or negative T waves	31	4.7
D	RS-T segment depression of 0.5 mm. without iso-electric or negative T waves* on at least one occasion	33	5.0
	Unclassifiable	12	1.8

* Included 7 subjects with RS-T depression limited to leads II and III.
† Five cases with unclassifiable RS-T depression; 7 cases with marked baseline variation, and a suspicion of RS-T depression.

When allowance is made for the men in whom an electrocardiographic anomaly was noted both at rest and after exercise there were 149 (22.6%) men in whom, using the strictest criteria, the E.C.G. either at rest or after exercise departed from the usual response. This figure includes 33 men in whom the only anomaly was a minor degree of right bundle-branch block and 12 men (group D) in whom, because of variation in the baseline of the tracing after exercise, exact classification was impossible. If these 45 men were excluded a total of 104 (15.7%) were "placed under suspicion" by the test. In 511 men the tracings seemed entirely normal.

Postal Follow-up, 1958-61

In the case of men still serving in the R.A.F. an annual letter was sent to the station medical officer from 1958 onwards asking for details of any cardiac illness or symptoms reported in the previous year. Men who had retired were sent a personal letter inquiring about their health, which if doubtful or positive was corroborated by an inquiry to the relevant doctor or hospital.

At the end of 1961 14 men were known to be dead. 640 were known to be alive, and six were untraced. All 14 deaths were due to flying accidents or enemy action and in none was there any evidence to suggest that death had been preceded by a cardiac illness. Three deaths occurred in the 149 members of the anomalous group, a proportion of 2.0%, and 11 in the 511 men in the normal group (2.3%). Of the six untraced, one was in the anomalous group and five were in the normal group.

Ten definite episodes of clinical heart disease have been reported since the original study (Table II). Seven occurred in the 146 survivors of the men whose tracings had been classified as anomalous (4.8%) and 3 in the 500 survivors of those adjudged normal (0.6%).

*This term is used to mean flat or sagging depression of the whole RS-T segment of 0.5 mm. or more measured from the P-Q junction.

This difference is significant for the older age-group alone and for the whole of the material. Of the seven men with previous anomalies, two had suffered definite myocardial infarcts with classical clinical and electrocardiographic changes; two had developed angina pectoris; one had had a paroxysm of atrial fibrillation and later developed complete left bundle-branch block;

TABLE II.—*Clinical Heart Disease Elicited by the Postal Follow-up in 1961*

Age at Survey	Anomalies on Original Resting or Exercise E.C.G.			Normal Original Resting and Exercise E.C.G.			Probability
	Subsequently Developed Clinical Evidence of Heart Disease		Total Living, 1961	Subsequently Developed Clinical Evidence of Heart Disease		Total Living, 1961	
	No.	%		No.	%		
	19-39	1	1.7	60	1	0.3	
40-54	6	7.0	86	2	1.0	196	<0.05
Total	7	4.8	146	3	0.6	500	<0.02

another had atrial fibrillation with prolongation of the QRS interval and inversion of T in leads V_4 , V_5 , and V_6 ; and one had suffered an episode of complete heart block with attacks of syncope. Of the three men whose E.C.G.s in the 1954-7 series had been classified as normal, one had suffered a myocardial infarct (Case 8, Fig. 1), another developed angina pectoris, and the third had an episode of atrial fibrillation without other evidence of heart disease.

Case Reports from the Group Classified as Anomalous in 1954-7

Case 1.—Series No. 607/1. Born June 3, 1912; first examined on September 12, 1955. The resting E.C.G. showed slurring of the downstroke of R in lead I classified as a minor anomaly. The post-exercise tracing was normal. On August 18, 1956, he was admitted to hospital with a diagnosis of myocardial infarction. An E.C.G. taken soon afterwards showed classical acute anterior infarction.

Case 2.—Series No. 606/1. Born January 9, 1915; first examined on September 19, 1955. The resting E.C.G. showed slurring of the downstroke of R in lead I and left axis deviation, which were classified as minor anomalies. After exercise flat RS-T depression of 1 mm. developed in leads II and V_6 ; 0.5 mm. depression in V_5 . The T wave in lead I became inverted (group B2). A second exercise test performed on March 26, 1956, showed similar changes. On February 27, 1957, he developed severe central chest pain accompanied by shock. An E.C.G. showed the classical signs of posterior myocardial infarction.

The E.C.G.s in Cases 1 and 2 have already been published (Acheson, 1957b).

Case 3.—Series No. 637/1. Born October 31, 1909; first examined on March 28, 1956. Resting E.C.G. normal. After exercise negative T waves were noted in leads V_5 and V_6 , but there was no depression of the RS-T segment (group B1). A second test, performed on July 29, 1956, showed similar changes. In April, 1958, he began to notice central chest pain provoked by effort and relieved by rest. On May 15, 1958, a diagnosis of angina pectoris due to coronary heart disease was made. The resting E.C.G. was normal. A modified exercise test was now followed by RS-T depression of 1 mm. in leads II and V_5 .

Case 4.—Series No. 672. Born November 19, 1908; first examined on January 16, 1956. Resting E.C.G. normal. After exercise 0.5 mm. RS-T depression with deformity of the descending limb of T was noted in V_4 , V_5 , and V_6 (group C). He began to notice retrosternal discomfort while cycling in October, 1958. A diagnosis of angina pectoris due to coronary heart disease was made in hospital in November, 1958.

Case 5.—Series No. 84. Born May 16, 1921; first examined on November 2, 1954. The E.C.G. at rest showed complete right bundle-branch block. No additional abnormality was noted after exercise. On October 29, 1959, he lost consciousness while on duty. On recovery, a regular heart rate of 45 beats a minute was noted but no other physical signs were detected. E.C.G. showed complete heart block, atrial rate 135, ventricular rate 45, and complete right bundle-branch block. Subsequently his heart reverted to sinus rhythm and he has remained well. There is no definite evidence of coronary heart disease in this man.

Case 6.—Series No. 652. Born March 9, 1903; first examined on October 10, 1955. Resting E.C.G. normal. After exercise RS-T depression amounting to 0.5 mm. was noted in leads II, V_5 , and V_6 (group C). On October 8, 1957, he suddenly developed severe palpitation while sitting in a chair. His pulse rate was 112 and irregular. Half an hour later the palpitation stopped as suddenly as it had begun. Clinical examination and the E.C.G. the next day were normal, but a provisional diagnosis of paroxysmal atrial fibrillation was made. In 1961 a further E.C.G., performed because he complained of breathlessness on exertion, showed complete left bundle-branch block. It seems reasonable to assume that this man is suffering from coronary heart disease.

Case 7.—Series No. 868. April 2, 1911; first examined on March 11, 1957. The E.C.G. at rest showed a P-R interval of 0.24 second and low-voltage T waves (<1 mm.) in leads I and II. The post-exercise tracing was normal. In March, 1960, he complained of palpitation and was found to have atrial fibrillation. There was no evidence of thyrotoxicosis or rheumatic heart disease. Quinidine was given and his heart reverted to sinus rhythm. A P-R interval of 0.24 second was again noted. Atrial fibrillation had again supervened when an E.C.G. was taken on April 8. On February 24, 1961, a further E.C.G. showed atrial fibrillation, a QRS interval of 0.11 second, and T-wave inversion in leads V_4 , V_5 , and V_6 (the patient was not on digitalis). In the absence of any other evident cause this man's arrhythmia and other electrocardiographic anomalies are probably due to coronary heart disease.

Case Reports from the Group Classified as Normal in 1954-7

Case 8.—Series No. 701. Born July 31, 1904; first examined on January 30, 1956. Resting E.C.G. normal. The post-exercise tracing was reported as normal and has been classified as such in Table II. In retrospect, however, it shows a depression of the whole RS-T segment of 0.5 mm. in lead V_6 (Fig. 1). On November 12, 1959, he was admitted to hospital with pain behind the lower sternum radiating to the wrists. An E.C.G. taken on December 29, 1959, showed evidence of posterior myocardial infarction.

Case 9.—Series No. 161. Born January 15, 1925; first examined on December 15, 1954. E.C.G.s at rest and after exercise were normal. On February 28, 1961, he experienced the sudden onset of palpitation while flying. His medical officer found an apex rate of 130 with marked irregularity, but an E.C.G. taken later in the day was normal. A clinical diagnosis of paroxysmal atrial fibrillation was made. There had been no further symptoms, and on March 30, 1961, he was found to be clinically well and E.C.G.s taken before and after exercises were normal. He was returned to full flying duties with a diagnosis of paroxysmal atrial fibrillation due to a functional disorder of the myocardium. It was felt that there was no evidence of coronary heart disease.

Case 10.—Series No. 653/1. Born March 12, 1915; first examined on October 10, 1955, when he had no symptoms and E.C.G.s before and after exercise were entirely normal. On February 19, 1960, he was invalided from the Service with angina pectoris due to coronary heart disease. An E.C.G. taken then at rest showed inversion of T in leads I, AVL, and V_6 .

Although the results of the postal follow-up showed that the number of episodes of subsequent heart disease was higher in the anomalous group than in the remainder, the number was too small to determine which subgroups were at particular risk. It was therefore decided to call for further examination the remainder of the anomalous group, together with a sample of the normal group as controls.

FIG. 1.—Series No. 701. (Case 8.) Tracings before and after exercise on January 30, 1956: the post-exercise tracing shows 0.5 mm. flat RS-T depression in lead V₄. E.C.G. taken on December 29, 1959, showed posterior myocardial infarction.

1961 Re-examinations

In 1961 the 138 men of the original anomalous group who were still living and could be traced, and who had not already reported symptoms, were called for re-examination together with an identical number of controls matched for age from the survivors of the normal group. Almost identical proportions of the two groups were able to attend: 73 (52.9%) of the anomalous group and 76 (55.1%) of the normal group. Of those who did not attend the vast majority were serving abroad, had retired to remote parts of the world, or were living in distant parts of the United Kingdom and could not reasonably be expected to attend for examination in London. Only 20 men who lived within 150 miles (240 km.) of London refused to come or did not answer our letter. Of these, 12 had been classified in the anomalous group and eight in the normal group. The proportions who attended in the various subgroups are shown in Table III. The proportion of those with anomalies at rest (including persons with incomplete right bundle-branch block or prolonged P-R interval)

TABLE III.—Attendance for Re-examination in the Various Subgroups

	Total Sampled	Reattended	
		No.	%
Normal { Matched controls ..	138	76	55.1
" Local ..	35	28	80.0
Total ..	173	104	60.1
Anomalies at rest only ..	54	20	37.0
B1 ..	13	8	61.5
B2 ..	29	20	69.0
" after exercise { C ..	30	18	60.0
D ..	12	7	58.3
	138	73	52.9

is low because these men were younger than average and an undue proportion were stationed overseas.

An additional control group was selected from other men known to be living close to London who had shown normal E.C.G.s at the original survey; 28 out of 35 of these attended. The median year of birth of this control group was 1913.

A careful history was taken from each man by one of us (C. A. R.), followed by a physical examination. At this point a decision was recorded whether or not the man had suffered from chest pain of cardiac origin. Bias was eliminated by arranging that the observer did not know into which category the subject had been classified at the previous survey. A resting E.C.G. was then performed followed by an exercise test using the technique previously employed (except that a Phillips three-channel direct writing instrument was now available, permitting leads I, II, and III and leads V₄, V₅, and V₆ to be recorded synchronously instead of in series). The E.C.G.s bearing an identifying number only were then posted to E.D.A., who classified them without knowledge of their previous classification or of C. A. R.'s clinical assessment. The results were collated and analysed.

In spite of the fact that all these men had recently stated that they were well in reply to the postal questionnaire, a diagnosis of cardiac chest pain was made on clinical grounds in 14 of the 177 men examined; 11 of these had shown an anomaly in the post-exercise E.C.G. at the time of the 1954-7 survey, but three had been electrocardiographically normal at that time (Table IV). One of these three men was obviously anaemic and was found to have a haemoglobin of 10.2 g./100 ml. Although it might be reasonable to exclude this man, he has been counted as a control suffering from coronary

TABLE IV.—Frequency of Symptoms in Subjects Re-examined in 1961

Symptoms Present in 1961	1954-7 E.C.G. Anomalous		1954-7 E.C.G. Normal					Probability
			Matched Controls		Other Controls	All Controls		
	No.	%	No.	%		No.	%	
Cardiac chest pain	11	15.1	3	3.9	0	3	2.9	<0.01
Non-cardiac chest pain	6	8.2	4	5.3	1	5	4.8	
Other non-cardiac symptoms ..	8	11.0	9	11.8	2	11	10.6	Not signifi- cant
Total examined ..	73	100.0	76	100.0	28	104	100.0	
								—

heart disease. The difference in the proportions with clinical coronary heart disease in the two groups is significant both when only the matched controls and when all controls are used in the comparison. All 14 men had central chest pain or oppression on exertion relieved by rest, and three had in addition suffered a more prolonged attack of chest pain or pain in the left shoulder at rest. In all, these symptoms had been attributed by the patient or his medical adviser to some other cause such as "indigestion," "wind," "fibrositis," etc.

The proportions of men suffering from non-cardiac chest pain (including "heartburn") and from all other symptoms combined were similar in the two groups. A curious and unexpected finding was that three men, all of whom had shown RS-T depression after exercise originally, now had gout.

The resting E.C.G. had deteriorated markedly since 1954-7 in five cases, all in the original "anomalous"

group. In three the resting tracing had previously been normal, but there had been RS-T depression after exercise. The tracings of two of them are shown in Fig. 2. They were felt to contraindicate a further exercise test. The third man, who was not exercised, has developed left bundle-branch block. These three men now all have classical angina pectoris. Another man who had slurring of R in lead I in 1954 now has a QRS interval of 0.11 second and a P-R interval of 0.20

In those of the sample who were 40 years of age or more at the time of the original survey the frequency of the subsequent development of angina pectoris was more than 10 times as great in those who previously showed RS-T depression after exercise ($29.7\% \pm 7.5\%$) as in those who did not ($2.5\% \pm 1.8\%$). This difference is highly significant ($P < 0.001$); the difference remains significant when the matched controls only are used in the comparison. Two examples of the electrocardiographic changes in these men before and after the development of symptoms are shown in Figs. 3 and 4.

Post-exercise E.C.G.s in 1961

Table VI shows the results of the current series of exercise tests as compared with those carried out in 1954-7. Of the 123 men whose post-exercise tracings were normal in 1954-7, 9 now show RS-T segment depression, 1 has isolated T-wave changes, and 4 have unclassifiable changes. Three of the 9 men who now show RS-T depression have already been referred to as having angina pectoris. Conversely, a proportion of those with anomalies after exercise in 1954-7 now have normal post-exercise tracings. This proportion is lowest (20%) in the subgroup (B), which originally had the most marked anomalies, is higher (60%) in group C, and highest (90%) in the subgroup (D) regarded as unclassifiable. Some of these apparent recoveries may be spurious and may be due to misclassification of the

FIG. 2.—(a) Series No. 652. (Case 6.) No symptoms on October 10, 1955; resting E.C.G. normal but RS-T depression present after exercise. On October 4, 1961: angina pectoris; resting E.C.G. showed complete left bundle-branch block and he was not exercised. (b) Series No. 738. No symptoms on February 27, 1956; resting E.C.G. normal but RS-T depression present after exercise. July 6, 1961: angina pectoris; resting E.C.G. was grossly abnormal and he was not exercised.

second. His post-exercise E.C.G. shows no additional abnormality and he has no symptoms. A fifth man who had low-voltage T waves in 1954 now has complete right bundle-branch block, without symptoms.

When the cases of cardiac chest pain were analysed in terms of the type of electrocardiographic anomaly at the 1954-7 survey, it was found that all 11 of the subjects whose E.C.G.s had previously been anomalous had shown RS-T depression after exercise (Table V).

TABLE V.—Frequency of Cardiac Pain in 1961 in Those Who Had Shown RS-T Depression of 0.5 mm. or More After Exercise in 1954-7

Age at First Survey	1954-7 E.C.G.			1954-7 E.C.G.			Probability
	No RS-T Depression after Exercise			RS-T Depression Present after Exercise			
	Cardiac Pain, 1961		Total Examined	Cardiac Pain, 1961		Total Examined	
	No.	%		No.	%		
19-39	1	1.9	52	0	0.0	8	— <0.01 Not significant <0.001
40-49	0	0.0	60	8	29.6	27	
50-54	2	10.0	20	3	30.0	10	
All	3	2.3	132	11	24.4	45

FIG. 3.—Series No. 619/1. No symptoms on September 26, 1955; resting E.C.G. normal; after exercise RS-T depression of 1 mm. in leads II and V₄ and of 0.5 in V₅ and V₆. April 4, 1961: angina pectoris; resting E.C.G. again normal, but gross RS-T depression with T-wave inversion developed after exercise.

initial tracing as anomalous in the presence of baseline variation.

A further point of interest in Table VI is that all 14 subjects who now have cardiac pain have exhibited RS-T depression of 0.5 mm. or more after exercise on one occasion at least, and in 12 it has amounted to 1 mm. or more.

FIG. 4.—Series No. 774. No symptoms on September 8, 1954; resting E.C.G. normal; after exercise RS-T depression of 1 mm. in lead II, 2 mm. in lead V₄, and 1.5 mm. in V₅. June 4, 1961; angina pectoris; E.C.G. at rest shows 0.5 mm. RS-T depression in leads V₄ and V₅. After exercise gross RS-T depression with T-wave inversion.

TABLE VI.—Comparison of Results of 1954-7 Post-exercise E.C.G.s With Those Taken in 1961. Subjects Who Have Developed Cardiac Chest Pain in Parentheses

E.C.G. after Exercise, 1954-7	E.C.G. after Exercise (1961)						Total Examined
	Normal	Isolated T-wave Changes	Group B2	Group C	Group D	Not Exercised	
Normal	109*	1	4 (3)	5	4	0	123 (3)
Isolated T-wave changes	2	4	2	0	0	0	8
Group B2	4	4 (2)	9 (3)	1	0	2 (2)	20 (7)
" C	10	0	2 (2)	4 (1)	0	1 (1)	17 (4)
" D	7	0	0	0	1	0	8
Total examined 1961	132*	9 (2)	17 (8)	10 (1)	5	3 (3)	176 (14)

* 19 of these showed minor anomalies at rest on both occasions.

Discussion

The results show that by means of an electrocardiogram before and after exercise it is possible to divide a population of apparently healthy men into high- and low-risk groups in terms of their future liability to

clinical coronary heart disease well in advance of the onset of symptoms.

At the outset, in the absence of any previous similar studies, it was felt necessary to include persons with any type of electrocardiographic anomaly at rest (including minor degrees of right bundle-branch block) or with flat or sagging RS-T depression of 0.5 mm. or more, or isolated T-wave changes after exercise in the supposed "high-risk" group. Depression of the RS-T junction after exercise was at first also regarded with suspicion (Master, 1950), but was soon found to be so common (Rumball and Acheson, 1960) that it could reasonably be regarded as a physiological result of exercise (Robb and Marks, 1960).

Our experience up to the present (which is based on small numbers) suggests that flat or sagging RS-T depression after exercise stands out as the most important anomaly with regard to future clinical events. Thus of the 24 persons known to have developed clinical heart disease by 1961, 14 had been among the 64 men (Table 1; groups B2 and C) classified as having RS-T depression of at least 0.5 mm. in 1954-7; a further case (Fig. 1) should have been classified thus, but the RS-T depression was missed. Of the remaining nine cases of heart disease, three had anomalies at rest only (one slurring of R in lead I, one complete right bundle-branch block, one prolonged P-R interval), one had isolated T-wave changes after exercise, and five had entirely normal E.C.G.s at rest and after exercise. The degree of RS-T depression seems also to be of prognostic importance. Thus of three men who had RS-T depression of 1.5 mm. or more at the first survey, two are known to have developed clinical coronary heart disease; while 6 (27%) out of 22 with 1 mm. depression, and 6 (15.3%) out of 39 with 0.5 mm. depression have subsequently developed coronary heart disease. These proportions are probably underestimates, as about one-third of these men (Table III) have not yet been re-examined.

The cardinal importance of RS-T segment depression in prognosis in patients with symptoms has been pointed out by Robb, Marks, and Mattingley (1956) in a follow-up study of American Service personnel and insurance candidates with chest pain. They found that the subsequent death rate from coronary heart disease of persons who had shown depression of the whole RS-T segment of 0.5 mm. or more was 10 times that of persons who had no RS-T depression after exercise or of persons who showed isolated T-wave changes only. Robb and Marks (1960) confirm these findings and in addition show that persons with depression of the RS-T junction alone have an excellent prognosis identical to those without any form of depression.

Small numbers limit the value of further analysis in our material, but it is worth noting that of five men noted to have slurring of the downstroke of R in lead I in 1954-7 two have subsequently developed myocardial infarction, and a third, although symptom-free, now has a P-R interval of 0.20 second and QRS of 0.11. The development of gout in three men who showed RS-T depression in 1954-7 is of interest in view of the suspected connexion between hyperuricaemia and coronary heart disease (Gertler and White, 1954).

At this point it is important to emphasize the practical limitations of the method from the point of view of the management of individuals. Todd (1959) has drawn attention to the difficulties in interpreting routine E.C.G.s in symptomless people. He suggests that our ignorance

of the significance of minor abnormalities in the E.C.G.s of apparently healthy people makes it hazardous for us to acquaint the patient with their presence or to advise alterations in job or way of life. In this way much unwarranted cardiac invalidism might be engendered. Certainly none of our "high-risk" subjects were acquainted at any time with the nature of their E.C.G.s. Indeed, even in retrospect it is difficult to know what advice could usefully have been given them. Our present limitations in individual prognosis are underlined by the fact that of the 20 men re-examined in group B2 (who had the grossest changes in 1954-7), 13 are still absolutely free of cardiac symptoms (Table VI) and four of these now have no abnormality in the post-exercise E.C.G. Thus, although the risk of the subsequent development of clinical coronary heart disease is clearly high in persons with such changes, we must agree with Weitzman and Smith (1959) that in a patient with chest pain the presence of RS-T depression of even 1 mm. after exercise does not necessarily mean that the particular pain complained of is due to coronary heart disease, nor, we can add, does it mean that he will certainly develop symptoms over the next five years.

Our results raise some interesting theoretical points. The re-examination of a sample uncovered a surprisingly large proportion of persons suffering from undoubted but undiagnosed coronary heart disease. This emphasizes the deficiencies of the indirect postal follow-up technique. The results also suggest that a high proportion of cases of coronary heart disease can be found months or years before the clinical onset of the disease. A further study limited to men over 40 and including persons with asymptomatic hypertension could be expected to yield a large group with RS-T depression after exercise who would be suitable both for analysis of aetiological factors and for therapeutic trial.

Oliver (1962) has drawn attention to the fact that reduction of plasma cholesterol either by modification of diet or by drugs does not appear to alter the prognosis in persons who have suffered myocardial infarction. He favours the trial of such procedures in young men without symptoms, in the hope that irreversible changes will not already have been produced in their coronary arteries. It is unknown to what extent RS-T depression after exercise in symptomless men is a manifestation of an irreversible change. However, such men would seem to be a group in whom the trial of measures designed to increase collateral circulation or to reduce circulating cholesterol would be worth while.

Summary

Six hundred and sixty men in whom there was no clinical evidence of heart disease were examined by means of an electrocardiogram before and after exercise in 1954-7. The E.C.G.s were classified as "normal" or "anomalous." The subsequent fate of the men has been followed to the end of 1961 and news was obtained of all but six of them. In the interval a significantly higher proportion of the anomalous group than of the "normal" group had suffered a definite episode of clinical heart disease for which medical care had been required.

With precautions to avoid bias, 73 of the remaining men in the anomalous group and 104 controls from the normal group were re-examined in 1961. Fourteen additional cases of coronary heart disease were uncovered in this way—11 in the anomalous group and 3 in the

normal group. All 11 of the men whose E.C.G.s had been judged anomalous in the 1954-7 survey and had subsequently developed coronary heart disease had shown flat or sagging depression of the whole RS-T segment of 0.5 mm. or more after exercise.

The results show that it is possible, by means of an E.C.G. before and after exercise carried out in symptomless men, to identify a population with a higher-than-average risk of developing coronary heart disease in the next five years. The limitations of the method in individual prognosis are pointed out, and its theoretical and practical implications are discussed.

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REFERENCES

- Acheson, E. D. (1957a). *Lancet*, **1**, 26.
 — (1957b). D.M. Thesis, Oxford University.
 Gertler, M. M., and White, P. D. (1954). *Coronary Heart Disease in Young Adults*. Harvard Univ. Press, Cambridge, Mass.
 Master, A. M. (1950). *Ann. intern. Med.*, **32**, 842.
 Oliver, M. F. (1962). *Lancet*, **1**, 653.
 Robb, G. P., and Marks, H. H. (1960). *Proc. Soc. exp. Biol. (N.Y.)*, **103**, 450.
 — and Mattingley, T. W. (1956). *Trans. Ass. Life Insur. med. Dir. Amer.*, **40**, 52.
 Rumball, C. A., and Acheson, E. D. (1960). *Brit. Heart J.*, **22**, 415.
 Todd, J. W. (1959). *Lancet*, **1**, 845.
 Weitzman, D., and Smith, E. M. (1959). *Brit. med. J.*, **2**, 162.

A FOLLOW-UP STUDY OF LATE-ONSET EPILEPSY

I. NEUROLOGICAL FINDINGS

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An examination of the relevant literature on epilepsy of late onset reveals two important findings. The first is that the condition is not rare. Thus in a study of 245 patients investigated for seizures after the age of 12 years Martin and McDowell (1954) found an incidence of 43% starting after the age of 35; and Alajouanine *et al.* (1959), analysing 7,745 cases from the literature between 1901 and 1955, gives a figure of 32.7% in which epilepsy started after the age of 20. The second relates to the incidence of tumours. The incidence found may well reflect the source of reference, and it is not surprising to note that neoplasms and trauma are given as the commonest causes by Penfield and Jasper (1954). If unselected material is considered it has been shown repeatedly that tumours account for only a small proportion. Walker (1936), in a study of 100 cases with an age of onset after 20, found only 16 tumours and 4 head injuries. Sheehan (1958), in a study of 1,000 cases after the age of 20, could find a causal factor in 552 cases only, and 139 of these were tumours, giving an overall incidence of nearly 14%. A study reported by Du Saucy-Bayloye and Sorel (1959) of 265 patients over the age of 40 shows 20% of tumours. Raynor *et al.* (1959), reporting on 141 patients with a follow-up of 3 to 15 years, found only 16 certain tumours.