THE DIAGNOSIS of coronary stenosis can be made easily from the history alone if typical symptoms of angina pectoris are present. When these symptoms are atypical, however, the diagnosis is more difficult. For instance, pleural or pericardial irritation, intercostal neuralgia or sternal or humeral bursitis may be aggravated by exercise, and spastic pain from the gastrointestinal tract may be also partly relieved by nitroglycerin.\textsuperscript{1-4} If the patient happens to know the typical subjective complaints of angina, he may consciously or unconsciously shape his own symptoms to resemble them. On the other hand, true angina may sometimes be characterized by a completely atypical localization of the pain.

We know now that true angina is caused by insufficient blood supply to the heart, and this insufficiency should also affect the heart muscle and be reflected in the electrocardiogram. If the resting electrocardiogram shows definite signs of acute coronary insufficiency, no further tests are needed to confirm the clinical diagnosis. If the electrocardiogram is within normal limits, however, or shows changes that can be explained by other factors than coronary stenosis, it becomes necessary to wait for a spontaneous anginal attack, or to submit the patient to the conditions that usually provoke his anginal complaints to see whether a deficiency of the coronary circulation then becomes apparent. These conditions act usually by increasing the work of the heart and its oxygen consumption until the coronary circulation, which can only increase to a limited degree because of the existing coronary stenosis, can no longer keep up with the metabolic needs of the heart muscle. A test of this kind becomes necessary also in persons with diabetes, myxedema, or other types of hypercholesterolemia, and in applicants for insurance or for positions of unusual responsibility or physical endurance, who may have no symptoms or dissipilate them.

Among the most common factors that can provoke coronary insufficiency are physical exercise, sympathetic stimulation, and epinephrine discharge caused by emotional factors or by cold. The epinephrine test in angina pectoris has been found too unreliable and dangerous,\textsuperscript{5} since the individual response to injected epinephrine varies, and it is impossible to neutralize the effect of epinephrine rapidly.

The most easily controlled test is the electrocardiographic exercise test; this was first used in 1931 by Wood and associates,\textsuperscript{6} who, however, did not recommend it for clinical use. The test first applied widely by Scherf and Goldhammer in 1932\textsuperscript{7} consists of sitting up, doing knee bends, or climbing 1 to 3 flights of stairs, according to the severity of the patient’s complaints; in this test, however, the amount of exercise cannot be controlled exactly, and an electrocardiogram cannot be taken at any time if serious symptoms should develop. These objections are eliminated in the “2-step test” designed by Master,\textsuperscript{8-10} in which the patient walks up and down a short flight of stairs consisting of a central step 18 inches high and 2 side steps 9 inches high, while still attached to the electrocardiograph, so that a tracing can be registered immediately if angina pain should develop. The advantage of this test compared to the bicycle ergometer, leg exercise,\textsuperscript{11} step-up tests,\textsuperscript{12} or the treadmill\textsuperscript{13} is that it requires minimum equipment and involves a type of work to which everyone is accustomed, thus minimizing the effect of training.
Another type of test (the hypoxia test) depends on a reduction of oxygen concentration in the inspired air (usually to 8 to 10 per cent) to provoke coronary insufficiency. The advantages of this test over the exercise test are that it can be given to persons who are unable to climb stairs or follow instructions. Furthermore, since the electrocardiogram can be registered continuously, the test can be interrupted as soon as abnormalities appear even before pain develops; this can also be done, however, in the 2-step exercise test if special thoracic leads are used to register the electrocardiogram during as well as after exercise. Aside from the need for complicated and expensive special equipment, an important disadvantage of the test is that any normal person will develop anoxic changes in the electrocardiogram if the blood oxygen saturation becomes low enough. Because of the individual variations in pulmonary ventilation, dead space, and diffusion a given oxygen concentration in inspired air corresponds to a wide range of oxygen saturation in the blood. Accordingly, the test has been found less reliable in the diagnosis of coronary disease than the exercise test. Furthermore, unpleasant or dangerous side-effects such as extreme dyspnea, cyanosis, pulmonary edema, headache, and even loss of consciousness with clonic cramps occasionally occur during the hypoxia test, but not during the exercise test. Accordingly, the hypoxia test should probably be carried out only when the exercise test is not feasible, and in patients whose circulatory reaction to anoxia or low barometric pressure is to be studied (e.g., skin divers, pilots, and patients traveling in only partially pressurized aircraft or about to be submitted to gas anesthesia).

The original Master 2-step test was developed as a test of "circulatory efficiency," and prescribed a specific number of ascents to be carried out in 1½ minutes for each sex, age, and weight; this number corresponded to the greatest number of ascents that permitted the systolic blood pressure and the heart rate to return to within 10 "points" of the resting value within 2 minutes after termination of exercise, as determined empirically on a large number of normal persons. Ford and Hellerstein found that the increase in oxygen consumption during and after the Master test is approximately the same in all persons regardless of sex, weight, and age, and amounts to about 7 times the resting value. This corresponds to an approximately 100 per cent increase in cardiac output. Since the work of the heart during exercise is approximately parallel to the oxygen consumption, the Master test can be expected to cause the same relative increase in cardiac work regardless of age, weight, and sex, and is therefore better suited to comparisons among different persons than a fixed amount of exercise. It corresponds to approximately the maximum work encountered in everyday life, and is therefore not so strenuous as to endanger the patient or to cause the possibility of a physiologic coronary insufficiency, which has been seen in extreme exertion.

The external work performed during the Master test for a given sex and weight (table 1) decreases with age about 20 per cent from the early twenties to the late sixties. This is probably due to the fact that physical activity and the degree of training decrease with advancing age. Training has been found to result in a decreased oxygen cost and heart rate response for a given amount of external work. The lesser work prescribed in Master's table for children and teenagers than for adults, and for women than for men, is partly also due to a greater degree of training in adult men, but probably largely to the fact that a child or a woman of the same weight and age as a man is likely to be overweight. Since fatty tissue has a low metabolic rate, the resting oxygen consumption and cardiac output of such a person would be close to his original or normal weight, and the same amount of work would be expected to cause a greater increase of cardiac output, expressed as a percentage of the resting value, than in a tall, lean person of the same weight. This is also the reason why the external work in the table, expressed as a percentage of the body weight, decreases with increasing weight.
### Table 1

**Standard Master Two-Step Test**

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Number of ascents in 1½ minutes (values for women are in parentheses). Age is expressed in years, weight in pounds. Condensed from Master et al.3
EXERCISE TESTS IN CORONARY HEART DISEASE

Circulation, Volume XXII, November 1969

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This decrease is about 45 per cent between the weights of 85 and 225 pounds. In the original tables 16 Master used a correction for height, but later dropped it for the sake of simplicity. It is possible that by introducing a similar correction the tables would correspond better to the individual case. A correction for the degree of training and for the emotional response of the patient would be highly desirable, but these factors do not lend themselves readily to quantitation.

When the duration of exercise in the Master 2-step test was doubled (that is, double the prescribed number of ascents was carried out in 3 minutes), the percentage of abnormal electrocardiographic responses in typical angina was considerably increased while the response in normal persons was not appreciably changed. 3 This is probably because with the rate of exercise prescribed in the Master test a steady state of oxygen consumption is not reached until 2 or 3 minutes after beginning the exercise, and even later in persons with beginning heart failure; 17, 18 extending the duration of exercise to 3 minutes therefore results in a more accurate and predictable increase of cardiac work. Master therefore recommends that if the single test is within normal limits, a double test should be repeated on the next day or at least 1 hour after the single test. In many laboratories this procedure is followed only in patients with borderline resting electrocardiograms, or severe anginal complaints, while the double test is given from the beginning in patients whose resting electrocardiogram is completely normal and whose anginal complaints are slight or absent. 14, 20 At any rate, the patient is instructed to stop exercise and lie down immediately as soon as he feels any distress, unusual fatigue, dyspnea, or his usual anginal pain; the test can also be interrupted by the operator as soon as serious electrocardiographic changes appear, if a thoracic electrocardiogram is registered during exercise. In some patients anginal complaints are precipitated by emotional upsets, meals, or exposure to cold more readily than by exercise alone. If the double Master exercise test does not produce pain or significant electrocardiographic changes in such patients, it would be of value to repeat the test under these conditions, e.g., while a piece of ice wrapped in gauze is held in each hand, 21, 22 or after a meal. 4, 23 If these methods do not produce significant electrocardiographic changes or symptoms, it may be necessary to repeat the double test on successive days, increasing the rate of exercise 10 per cent each day up to 30 per cent until either of these signs appears.

While exercise after a meal, after medication with atropine, or in hot or cold surroundings does not lead to definitely abnormal electrocardiographic changes in normal persons, the degree of the abnormality appearing in coronary disease may be influenced by these factors. 4, 5, 21-23 If the effect of certain therapeutic procedures is to be studied, it is therefore advisable to carry out the exercise test under as constant and as nearly basal conditions as possible; under these conditions and in patients showing definite electrocardiographic changes of coronary insufficiency after the Master exercise test, these changes can be reproduced quantitatively on the same or successive days. 24, 25 Over a period of several years, however, the response to the Master test was reproducible in only about 40 per cent of the patients. 26 If vasodilating drugs such as nitroglycerin, nitrites, or amino-phyline are taken a short time before exercise, the usual electrocardiographic changes on exercise may not appear. 4, 5, 24-27 Therefore, such medication should be avoided on the day of the test. Digitalis may cause an apparently abnormal electrocardiographic response to exercise, even if the resting electrocardiogram shows no trace of digitalis effect. 5, 26, 28, 29 It is therefore necessary to withhold digitalis medication for at least 2 weeks before the test. The test should also not be carried out within 1 week of a cold, since abnormal electrocardiographic changes on exercise have been observed in normal persons during convalescence from infections. 4, 5, 26

An exercise test should not be carried out if resting electrocardiogram shows definite
changes attributable to acute coronary insufficiency (i.e., true S-T segment displacement). It may be done in myocardial infarction more than 1 month old, when only QRS changes remain, or in the presence of the pattern of left ventricular hypertrophy or of bundle-branch block with only secondary T and S-T changes of borderline T and S-T changes (e.g., low T waves and a horizontal S-T without depression). In all these cases it is necessary to make certain that the patient does not have the symptoms of impending myocardial infarction; if anginal complaints appear at rest or without apparent cause, the electrocardiogram should be repeated after a few days and the test should be done only if there is no change. The exercise test may precipitate or aggravate myocardial infarction once coronary thrombosis has started. Although more than 50,000 exercise tests have been reported in the literature, the occurrence of myocardial infarction on the day following the test was reported in only 6 instances, and in none of these were the above precautions observed; in most cases the electrocardiogram had returned to normal following the test, so that the coincidence of the test and the myocardial infarction was probably fortuitous.

In the original Master test, the patient is asked to walk faster or slower, if it becomes apparent that he will not complete the required number of trips in 1 1/2 or 3 minutes; this may cause a variable rate of exercise during the last trips of the test, by which the subsequent electrocardiogram is influenced most. This difficulty can be remedied partly by controlling the number of trips completed at the end of each 30-second interval of the test. Another solution is to have the patient climb each step to the rhythm of a metronome, allowing 2 counts for the ascent, 2 for the descent, and 1 for turning around; the number of counts per minute can be determined from table 1 by multiplying the number of ascents by 10 and dividing by 3. In this case, it is well to have the patient practice walking in time to the metronome for 1 or 2 ascents before beginning the test proper.

A direct-writing electrocardiograph with an “instantaneous” switch is essential for the exercise test. Since small displacements of the S-T segment must be evaluated, it is important to obtain clear definition of the baseline by proper positioning and temperature of the stylus; the rectangular style give better definition than the V-shaped ones. The sensitivity should be adjusted accurately to 1 mv. per cm. Wandering of the baseline must be avoided by using an electrocardiograph with a built-in voltage stabilizer, vigorous application of electrode paste, and, if necessary, asking the patient to hold his breath during registration. The test should be carried out only in the presence of a physician well acquainted with electrocardiographic interpretation, and only after registration of a complete 12-lead resting electrocardiogram, which enables him to decide what type of test to give, if at all. The precordial electrodes are fastened in the V4, V5 and V6 positions by means of a special rubber strap provided with most electrocardiographs; slipping during exercise can be prevented by fastening the strap at the back of the patient, carrying the loose end over the left shoulder, and fastening it again at the V4 precordial electrode. To facilitate rapid switching among the precordial electrodes, the precordial lead cable can be provided with a spring clamp (battery clamp); during exercise this cable is left in the V4 position, since this is usually the most “sensitive” lead. The leg electrodes are best fastened just above the calf, and the cables inserted from above. The arm electrodes are fastened on the wrist with the cable inserted from above or just below the shoulder with the cable inserted from below; the latter method causes a considerable reduction of muscle tremor. When the patient walks, he holds the crook of the cable in his left hand and always turns toward the electrocardiograph after each descent of the 2-step stairs. If the patient keeps his right arm hanging loose at his side, it is possible to register CR4 during exercise at 30-second intervals; after exercise it can be switched to the V4 position. Leads I and II as well as 3 precordial leads.
are registered in rapid sequence, for 6 to 10 seconds each, immediately, and 2, 4, and 6 minutes after exercise. If the electrocardiogram has not returned to normal after this time, it should be repeated also at 8 and 10 minutes.

Since exercise is always accompanied by hyperventilation, which may produce considerable T-wave changes even in normal persons, it is advisable to ask the patient to breathe as deeply and rapidly as he can for 30 seconds and to register the same electrocardiographic leads immediately before the exercise test.

The electrocardiographic changes most important in the diagnosis of coronary insufficiency are those of the T wave and S-T segment, and it is important to know the normal behavior of these electrocardiographic components during and after exercise. The sympathetic stimulation that appears at this time leads to an increase in voltage of the P wave and of the atrial T wave (Tₐ or Tₚ wave) that follows it. This wave has a direction opposite to that of the main area of the P wave and a duration corresponding to that of the ventricular T wave. As long as the P-R interval remains within normal limits, the Tₚ wave is superimposed on the P-R interval, the QRS complex, and the initial portion of the S-T segment. Because of tachycardia the descending branch of the elevated U wave also becomes superimposed on these deflections. As a result, the P-R segment assumes a more or less steep downward course and causes the S-T junction to appear depressed when compared to the beginning of the P wave or to the beginning of the QRS complex (fig. 1). The upper edge of a thin transparent ruler or of a piece of cellophane tape folded upon itself can be used as a straight line for this purpose. However, even when the "false S-T depression" caused by the Tₚ and U waves was eliminated in this way, 30 (12 per cent) of 243 apparently normal persons still showed S-T depression exceeding 0.5 mm. after the double Master exercise test. On the other hand, if the normal limit of S-T depression is raised to 0.75, 1, or even 2 mm., the percentage of typical cases of angina pectoris showing such changes decreases from 60 to 98 per cent to 20 to 40 per cent and the percentage in apparently normal persons is still 2 to 5 per cent. The same is true if the duration of the electrocardiographic changes is taken to differentiate the normal from the abnormal response. None of our apparently normal persons had a true S-T depression of 2 mm. or more, lasting 4 or more minutes, but less than a third of patients with true angina showed such a response.

A possible means of differentiation between normal and abnormal S-T depression is that the normal S-T depression, which is caused by more rapid repolarization of the myocardial cell at rapid heart rates, would be expected to affect predominantly the portion of the S-T segment immediately following the

![Figure 1](image-url)
QRS complex, or the S-T junction, leading to an ascending course of S-T° (fig. 2). On the other hand, S-T depression caused by coronary insufficiency is due to development of an injury current (incomplete repolarization or depolarization) in the subendocardial muscle layers of the left ventricle; this injury current would be expected to persist throughout the entire systole, and therefore cause depression of the entire S-T segment. Robb, Marks, and Mattingly have differentiated the normal, junctional, or ascending type of S-T depression from the "ischemic," horizontal, or descending type, which also involves the middle portion of the S-T segment or its entire length. Of 920 persons subjected to the double Master exercise test and followed up to 10 years, the death rate from coronary disease per 1,000 person-years of observation was 24.1 in persons showing the typical "ischemic" type, 6.9 in those showing a borderline "ischemic" type, 3.8 in those showing the "junctional" type, and 3.1 in those showing no depression or one less than 0.5 mm., in any one of the recorded leads.

In order to quantitate the configuration of the depressed S-T segment, the author proposed to express the duration of the interval between the beginning of QRS and the point where the depressed S-T segment crosses the baseline (point X in figure 1; Q-X interval) as a percentage of the duration from beginning of QRS to the end of the T wave (Q-T interval). This percentage would be much less dependent on the heart rate than the absolute duration of the depressed S-T segment. It was found that the best differentiation between apparently normal persons and those with typical angina was S-T depression of 0.75 mm. or more beyond the continuation of the P-R segment into QRS, with Q-X exceeding 50 per cent of Q-T, persisting for at least 2 minutes after exercise; still this behavior was found in 3.6 per cent of apparently normal persons. It is possible that a higher degree of accuracy could be obtained if S-T displacement were expressed as a percentage of the QRS voltage in the same lead. Extracardiac factors such as the distance of the heart from the chest wall and the conductivity of the tissues surrounding the heart (e.g., emphysema or obesity) should influence the

*Figure 2*

Electrocardiographic response to a double Master exercise test of a normal 29-year-old man, showing false S-T depression in leads II and III and true junctional S-T depression (Q-X not exceeding 40 per cent of Q-T) in lead V4, immediately through 2 minutes after exercise.
voltage of QRS in the same way as that of S-T depression. This question will be the object of further study.

In his original studies Master considered inversion or isoelectric configuration of T in leads I, II, or V4 as an abnormal response; later he stated "minor T waves changes alone are less significant but definite T wave inversion is probably abnormal."19 Inversion of T in leads II, V4, or V6, without significant changes of S-T, after the exercise test was reported in about 1 per cent of nearly 1,500 tests in apparently normal persons,20 but may appear in left ventricular hypertrophy. Acheson12 found T-wave inversion without S-T changes after vigorous exercise in 2.3 per cent of 300 apparently normal men below the age of 40 and 1.7 per cent of 240 similar men above this age. He concluded that this type of T-wave inversion is probably independent of the development of coronary disease. In the combined series of Robb, Marks, and Mattingly,14 followed up to 10 years, deaths from coronary disease were 3.6 per cent in the 110 persons showing only T-wave changes and 2.0 per cent in the 1,126 persons showing a normal response, as contrasted to 17 per cent in the 215 persons showing "ischemic" S-T depression.

T-wave inversion in normal persons may be due to two mechanisms. Persons with QRS complexes of high voltage and duration and low resting T waves (this is especially common in tall, slender persons) may show T-wave inversion in leads showing positive QRS area when the heart rate becomes fast, simply because of the normal decrease of the ventricular gradient with the heart rate. The ventricular gradient in such persons usually does not show a significant decrease when it is corrected for heart rate26 (fig. 3). This gradient may allow differentiation between this normal variant and a borderline abnormal response. Ingestion of potassium was seen to prevent this response in some cases.42 The second type of T-wave inversion appears also in leads V2 to V6, where the main area of QRS is negative, usually when the heart rate has almost returned to resting values (fig. 4); it cannot be due, therefore, to decrease of the ventricular gradient. All persons showing this type of T-wave inversion were women; in some of them it also appeared after hyperventilation without exercise.20 The mechanism of this type of T-wave inversion is not clear, but it can also be prevented in some cases by ingestion of potassium.37 Perhaps the high incidence of women among persons showing this type of T-wave inversion is related to the longer persistence in women of the almost identical juvenile T-wave pattern, which can also be normalized by ingestion of potassium.5

In typical angina pectoris, T-wave inversion often follows significant S-T depression after the exercise test, and usually appears at a time when the heart rate has almost returned to normal values8,20 (fig. 5). It is probably caused by delayed repolarization in and around the regions of the left ventricle that showed the acute injury current immediately after exercise, possibly because of loss of potassium, calcium, or magnesium from the cell.5 There are no statistical studies available, but the general impression is that persons who show significant changes of both S-T and T tend to have more severe angina than those with S-T changes alone. In asymptomatic persons after exercise this pattern was much more common in persons over 40 (1.7 per cent) than those under 40 (0.3 per cent); it is therefore more likely to be caused by early coronary disease.12

It has been suggested20 that an excessive elevation of the T wave after exercise signifies a pathologic response. An elevated T wave of pointed configuration can be expected to appear as a late phase of the subendocardial injury pattern in leads that previously had shown depression of S-T, just as pointed, inverted T waves appear in subepicardial injury in leads showing S-T elevation.5 On the other hand, elevation of T is also part of the physiologic response to exercise, where it can be caused partly by elevation of serum potassium, and partly by an increase of intraventricular temperature gradients due to increased cardiac heat production.5 Elevation of T was present in over one half of all ap-
Figure 3

Electrocardiographic response of a normal 23-year-old man to leg exercise in the recumbent position for 2 minutes, at a rate of work corresponding to the Master test. Inversion of the T wave without significant S-T segment depression in leads II and III. The same changes could be reproduced by tachycardia due to injection of epinephrine ("epin"). F, heart rate; GII, ventricular gradient in lead II; GcII, same gradient corrected for the heart rate.3

Apparently normal persons, in whom it may reach 5 mm. or 3 times the resting value.20 In typical angina pectoris elevation of T may exceed these values, but this happened in only 10 per cent of the cases.20

Abnormal changes of T and S-T after exercise in coronary disease are caused largely by differences in repolarization of the heart muscle cells in different regions in the heart.5 If the entire ventricular muscle showed a repolarization delay, the form of the T wave would not be modified appreciably but the Q-T duration, corrected for the heart rate (Q-Te) would be abnormally prolonged. In normal persons Q-Te increases during exercise, as long as the heart rate is rising, since Q-T is slow to adapt to sudden changes of heart rate and remains relatively long. After exercise Q-Te is shortened as long as the heart rate is slowing down, but returns to resting values 5 to 10 minutes after exercise.5, 29, 43

In persons with coronary disease Q-Te usually
shortens only slightly during exercise but becomes prolonged beyond resting values in the recovery phase, attaining maximal values 10 minutes after exercise; this prolongation is greater in patients showing an abnormal response of T and S-T.5, 20, 43 A significant prolongation (more than 0.012 or about 3 per cent of the resting value) was found in a much higher percentage of patients with angina pectoris than significant changes of S-T and T. 20, 43 The prolongation of Q-Tc was absent in persons in whom abnormal S-T and T-wave changes appear after exercise as a result of digitalis medication, and this could be a convenient point of differentiation. 20 These findings have yet to be confirmed in a larger series. One important source of error would be that persons without coronary disease who show only a slight increase of heart rate during exercise or a secondary acceleration during recovery would also tend to show prolongation.

Inversion or diphasic form of the U wave has never been seen to appear after exercise in persons without symptoms of coronary stenosis; it appeared in about one third of the latter cases and was usually accompanied or preceded by significant S-T depression. 20 A few cases have been observed, however, in which U-wave inversion was the only abnormal sign after exercise. 20, 26 Care must be taken not to confuse a notched U wave extending to the following QRS complex with a diphasic U wave. Inversion of U in angina
may be related to altered dynamics of ischemic cardiac muscle, as demonstrated in the precordial pulse curve.²

In his original work, Master considered the appearance of conduction disturbances, bundle-branch block, or premature beats as part of an abnormal response to his test, but recently he concluded³⁸, ⁴⁰ that they are of little diagnostic significance. Bundle-branch block is actually likely to appear whenever a critical heart rate is exceeded, regardless of the underlying cause.⁵ Single premature beats (not more than 1 in 6 seconds) were as common (13 per cent) in apparently normal persons with questionable changes of T and S-T as in anginal patients with significant changes, but in normal persons without changes they were less common (3.5 per cent).²⁰ The increased ventricular distention caused by increased stroke volume and blood pressure during and after exercise may facilitate the appearance of ectopic beats regardless of their cause. Multifocal ventricular premature beats or short runs of ventricular tachycardia have been seen sometimes during exercise or during spontaneous attacks of angina pectoris⁵, ²⁰, ³⁵ but not in normal persons; such changes should probably be regarded as indicating coronary stenosis. In many persons with premature beats after exercise but an otherwise normal electrocardiographic response the sensation of precordial pressure that they experienced after exercise was caused by the premature beats rather than by myocardial ischemia, as it disappeared when the ectopic beats were abolished by quinidine.²⁶

A difficult question is the evaluation of the electrocardiographic response to exercise in
the presence of left ventricular hypertrophy. Half of the apparently normal asymptomatic persons who showed significant S-T depression in our group had mild hypertension, and the percentage of persons with hypertensive or aortic valvular heart disease without anginal complaints who showed S-T depression exceeding 1 mm. after the Master test in other series varied from 13 to 90 per cent.17,30,44 In the pattern of left ventricular hypertrophy with a high positive QRS area and low T waves in left precordial leads, any acceleration of the heart may cause T to become diaphasic and S-T to become depressed due to a decrease of Q-T duration and the ventricular gradient.5 To be sure, increase in diameter of muscle fibers alone makes diffusion of oxygen into the interior of the fiber more difficult and, together with the increase in myocardial oxygen consumption resulting from increased cardiac work, may lead to coronary insufficiency.5,17 In case of aortic valvular disease additional factors that may lead to coronary insufficiency are a low mean arterial pressure and the possibility of syphilitic coronary stenosis. In all published and personal cases of left ventricular hypertrophy without anginal complaints, however, the abnormal S-T and T-wave changes after exercise were confined to leads with a large positive QRS area and were usually accompanied by inversion or more negative configuration of the T wave, as in the typical pattern of left ventricular "strain."26 If significant S-T depression appeared also in leads with negative mean area of QRS, or was accompanied by peaked and elevated upright T waves, typical symptoms of angina pectoris were usually present. This was also the case if the U wave became more inverted after exercise; in the pure ventricular "strain" pattern the U wave usually became more positive.26

We know that bundle-branch block in itself does not necessarily indicate heart disease, and an exercise test can be of value in making the diagnosis of coronary stenosis also in this condition.42 In right bundle-branch block the effect of tachycardia is to accentuate the slight elevation of S-T and tall T waves in leads with deep and wide S waves (lead I, II, and V4 to V6) and the depression of S-T and inversion of T in leads with wide R' waves (usually leads II, III, and V1 to V2). A slight but significant S-T depression in leads I, II, and V4 to V6 may therefore be masked, but marked changes will appear in spite of block and are therefore all the more significant. This applies, in lesser degree, also to all leads showing deep S waves in persons without definite bundle-branch block. In left bundle-branch block, on the contrary, accentuation of the secondary changes of T and S-T due to tachycardia leads to the same type of abnormality as coronary insufficiency, and this can accordingly be suspected only if S-T depression occurs in leads with negative or only slightly positive net area of QRS, or if it is accompanied by a change of the T wave in a positive direction. The same considerations apply also in cases of the Wolff-Parkinson-White syndrome, in which the delta wave is upright in leads I, II, and V4 to V6.

In healed myocardial infarction, when only QRS or borderline T-wave changes remain, it may be of importance to determine how well healing has taken place and collateral circulation has developed, or how much coronary stenosis is present in other parts of the coronary arteries not affected by the occlusion that has led to the infarction. If even the double Master exercise test does not lead in significant displacement of S-T, the probability is that development of collateral circulation and the condition of the remaining coronary arteries are adequate for the average stresses occurring during daily life. In some cases the S-T displacement seen during the acute stage of the original infarction was seen to recur after exercise; this can mean only that collateral circulation became inadequate. In other cases typical S-T depression as in angina pectoris without infarction appeared.5,31 This indicates that there is diffuse coronary stenosis in addition to the myocardial scar. Sometimes both types of S-T displacement occur at the same time in different leads (fig. 5).

Many cases have been reported in which
abnormal T waves and S-T segments in angina or old myocardial infarction have become more normal after exercise.\textsuperscript{1, 5, 45} In 1 case this behavior was explained by a hypothetical secondary improvement of the coronary circulation caused by increased blood pressure or coronary dilatation due to liberation of vasodilator substances from the ischemic myocardium, since anginal complaints, which were present at the beginning, also disappeared toward the end of exercise ("second wind").\textsuperscript{46} This latter feature seems to be characteristic of the "variant form of angina" described by Prinzmetal and co-workers,\textsuperscript{10} which is attributed to spasm of a diseased coronary artery rather than organic stenosis. In the majority of the reported cases, however, the normalization was probably due to a secondary elevation of T and S-T caused by tachycardia in leads with a negative QRS area, to superposition of the normal elevation of T after exercise, or to the appearance of a beginning acute injury current in the region of an old myocardial infarction or localized coronary stenosis. In a small percentage of cases elevation of S-T as in acute myocardial infarction appears transiently after exercise or in the spontaneous attack of angina;\textsuperscript{5} in these cases the typical Q waves of myocardial infarction usually develop soon in leads previously showing S-T elevation.\textsuperscript{5, 10, 45} The S-T changes may be attributable in these cases to a severe stenosis of a smaller coronary artery branch rather than to a mild stenosis of a larger branch. When coronary stenosis is mild, most of the blood passing through it in systole is channeled into the more subepicardially situated arterioles, since intramyocardial systolic pressure decreases continuously from the subendocardial to the subepicardial muscle layers; this leads to greater myocardial ischemia in the subendocardial muscle layers, and the typical depression of S-T in unipolar leads facing the affected area.\textsuperscript{5} On the other hand, when coronary stenosis is severe, both subendocardial and subepicardial muscle layers suffer from ischemia sufficient to cause an injury current, and the result is a systolic potential difference between the entire region of the ventricular wall supplied by the stenotic artery and the remaining parts of the ventricle; this difference causes S-T elevation in unipolar leads facing the affected area.\textsuperscript{5}

A completely normal electrocardiographic response to the double Master exercise test indicates with great probability that no major coronary stenosis is present, or if it is present, it is well compensated by collateral circulation. This does not mean absence of coronary sclerosis. There is no complete certainty that a given patient may not develop a lethal acute coronary thrombosis with myocardial infarction a few hours after a normal exercise test; from a statistical point of view, however, his life expectancy is 8 times greater than if he had a definitely abnormal response. One theoretical possibility of a normal response in spite of major coronary stenosis is that the affected artery is so small that the muscle region supplied by it is completely surrounded by normal muscle; the injury currents at the boundary of this region could then completely neutralize each other. Another possibility is that the degree of coronary stenosis is intermediate between one leading to predominantly subendocardial and one leading to transmural localization, and that injury currents on the boundary between subendocardial and subepicardial muscle are partly neutralized by those between the latter and the normal muscle. A further possibility is that injury currents set up by 2 transmural lesions on opposite sides of the ventricle or by a subendocardial lesion and a neighboring transmural lesion may partly cancel each other. Such cancellation, however, cannot be expected to be complete. If a sufficient number of leads is recorded at small enough intervals after exercise, one of the localizations is bound to outweigh the other in some of these leads or at some time during development of ischemia and recovery from it.

If the electrocardiogram remains normal after the double Master test and anginal complaints of the patient do not appear, the conclusion that no major coronary stenosis is present at the time is still justified. There is
still the possibility, however, that a functional stenosis may be precipitated by factors that are not present during the exercise test. If the correct diagnosis is important enough to justify the additional time and effort, the test can be repeated under conditions that are found to precipitate the complaints, or the rate of exercise can be gradually increased. If the electrocardiogram and subjective feelings are closely observed also during exercise, there is little danger of permanent damage to the myocardium. Also, if the double Master test is normal, there is reasonable probability that the coronary circulation would be adequate also in moderate hypoxia, but the hypoxia test should probably be made if a conclusion with a high degree of certainty is needed.

When criteria of the configuration and duration as well as the magnitude of S-T depression are used, a definitely abnormal response to exercise (e.g., true “ischemic” type S-T depression of 1 mm. or more) indicates coronary insufficiency with a high degree of probability. If, however, the electrocardiographic changes are less definite, involve only the T wave, or if marked tachycardia, ventricular hypertrophy, or pulmonary disease are present, the changes must be evaluated with great caution. The apparently abnormal responses reported in persons with neurocirculatory asthenia would probably no longer be considered abnormal with the new, stricter criteria. Appearance of similar changes after hyperventilation without exercise is strong presumptive evidence for their functional nature. It has been stated that if the response to the exercise test becomes normal after medication with certain ergot drugs, the response is purely functional, but many observations have been reported of the same response in persons with typical angina. Recently, it has been observed that an abnormal response due to coronary stenosis may become normal if the test is repeated with inhalation of oxygen, but functional abnormalities are not usually influenced; on the other hand, functional changes are more likely to become normal after ingestion of potassium than the former.

In this review the expression “positive” or “negative test” has been purposely avoided. Just as the degree of coronary stenosis and the many other factors that may aggravate or counteract its effects show a continuous gradation in different persons, so does the degree of electrocardiographic abnormalities. No test, and certainly not the exercise test, can be expected to furnish black and white information concerning the presence or absence of coronary disease. At any rate, the conclusions gained from the electrocardiographic exercise test must be based on careful consideration of the electrocardiographic and clinical peculiarities of each individual case, and even then they can be versed only in terms of probability, never of certainty. The electrocardiogram is still only an adjunct in the clinical diagnosis of angina pectoris, although its importance has increased considerably during the last 20 years.

**Summario in Interlingua**

Le diagnose de stenosis coronari es facile a facer super le base del anamnese sol in casos in que typie symptomas de angina de pectore es presente. Tamen, quando tal symptomas es absente, le diagnose deveni plus difficile.

Es disiutite le valor del electrocardiogramma post exercitio pro le diagnose de morbo cardiae coronari. Le conclusion es que iste test non differe de alteres in le facto que illo es incapace de fornir precise decisiones nigro-blanco concernente le presentia o le absenta de morbo coronari. Le conclusiones derivate ab le electrocardiogramma post exercitio debe prender in consideration omne le particularitates electrocardiographic e clinica del caso individual, e memmo alora tal conclusiones pote esser presentate solmente como probabilitates e nunquam como certitudes. Le electrocardiogramma es non ancora plus que un adjuncto in le diagnose clinica de angina de pectore, ben que il es ver que su importanita ha crescite considerablemente in le curso del passate 20 annos.

**References**

(This list contains only the most important and recent publications containing further references.)


36. Wasserburger, R. H., Siebecker, K. L., Jr., and Lewis, W. C.: The effect of hyperventila-
This is not the place for an extended discussion of the curriculum and the teaching methods and similar problems of medical education. But I would point out again that since there is too much factual knowledge and practical skill to impart in so short a period of time as four years, the part of wisdom seems to me to lie in training the student's capacities rather than stuffing his memory. What capacities? The capacity to observe, to reason, to compare his observations and reasoning with those of others, and the capacity to put himself in his patient's place—compassion. With such abilities trained, sharpened, and refined, the graduate of a medical school would find in his fifth, or intern year, and later as assistant resident and resident, the opportunities to use and refine those capacities to the immediate and the infinite advantage of his patients and himself.—ALAN GREGG, M.D. Challenges to Contemporary Medicine. New York, Columbia University Press, 1956, p. 112.