Adaptation to Exercise in Angina Pectoris

The Electrocardiogram during Treadmill Walking and Coronary Angiographic Findings

By Rex N. MacAlpin, M.D., and Albert A. Kattus, M.D.

PATIENTS with angina pectoris due to coronary artery disease may have great variability in exercise tolerance. In some this variability fits a pattern wherein increased exercise tolerance is dependent on a preceding episode of exercise-induced angina pectoris. The most complete expression of this phenomenon may be in the patient who is able to overcome an attack of angina pectoris by persisting in the precipitating effort until the pain disappears, with subsequent continuation of exercise without distress. An unknown patient described just such an occurrence in a letter to William Heberden.

"I have frequently, when in company, borne the pain, and continued my pace without indulging it; at which times it has lasted from five to perhaps ten minutes, and then gone off."1

This has been compared to the occurrence of a "second wind" in athletes and described as "walking through one's angina."

A less impressive, but more common manifestation of the same phenomenon occurs when a patient, after being brought to a halt one or more times by his angina pectoris, is subsequently able to resume the same effort and continue it indefinitely without discomfort. This often occurs in the morning with the first exertion of the day, subsequent activity being carried on without discomfort. It has been likened to the improved performance of an athlete after he is thoroughly warmed up. This has been termed "angina of first effort," and has been called "first hole angina pec-

toris" when occurring during a round of golf.

In 1897, Osler described a patient who walked through his angina pectoris.2 Wenckebach likewise described this phenomenon briefly in 1924,3 and then again in more detail in 1928,4 when he introduced the term "toter Punkt" to describe that point during effort when the subject feels like dying, before getting his "second wind." Gallavardin found that it was not at all uncommon to discover this phenomenon in patients if they were specifically asked about it.5

Wayne and LaPlace were unable to find any patients who could walk through their angina.6 Moreover, they objectively tested some subjects who claimed to be able to do more effort after a first attack of angina pectoris, and found that this was not true if the rate of exercise was the same for both attempts. However, Wayne and Graybiel were able to document that this phenomenon did indeed exist in four subjects.7 They found that there was a period between about 2 minutes and 30 minutes after the first attack of angina when increased tolerance existed; however, there was decreased exercise tolerance if the subject was re-exercised earlier than this, and the increased exercise tolerance was lost if they were re-exercised after resting more than 15 to 60 minutes. Nitroglycerin increased the exercise capacity considerably in all cases showing this phase of increased exercise tolerance, and it was postulated that a prior attack of angina acted similarly to nitroglycerin, although in each case a greater effect was produced with the drug.

Patterson et al.,8 during evaluation of the anoxemia test in subjects with angina pectoris, found an occasional patient in whom ST segment deviation increased to a maximum and then decreased during continued hypoxia.

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They felt that this type of adaptation was related to the clinical phenomenon of "first effort angina" or walking through an attack of angina which several of their patients had described.

In 1951, Price\(^9\) reviewed the literature on this subject and reported 20 cases of his own who manifested this phenomenon, but he did not have confirmatory objective tests. He commented on the strong determination in the patients who would endure the pain in order to walk it off, and noted that in some cases the difficulty getting started could be prevented by a prophylactic dose of nitroglycerin; these observations had also been made by Wenckebach.\(^8,4\) Price estimated that this phenomenon could be found in one of every five cases of angina if the possibility were kept in mind during history taking.

Two case reports were added in 1953, by Leftwich\(^10\) but again objective confirmation was not given. The subject was discussed briefly by Burns in 1961,\(^11\) and by Pruitt\(^12\) and Hurst\(^13\) in 1963, but no new data were presented.

The subject is not mentioned at all in many recent textbooks of medicine or cardiology, those of Levine,\(^14\) Scherf and Boyd,\(^15\) and Bedford\(^16\) being exceptions. Many others have commented on this phenomenon very briefly and most of these have been mentioned in Price's paper.

Most of those who have studied this phenomenon have held that the adaptation which makes it possible must be dilatation of coronary vessels in response to the stimulus of myocardial ischemia, but there is little direct evidence to support this theory. Except for the observations of Wayne and Graybiel,\(^7\) and possibly those of Patterson et al.,\(^8\) objective studies of this subject are absent from the literature. Moreover, electrocardiographic and blood pressure monitoring during actual occurrence of this phenomenon have not to our knowledge been reported.

The present report describes the observations that were made on 12 patients with angina pectoris due to coronary arteriosclerosis who manifested the capacity to achieve a form of adaptation to their coronary insufficiency while walking on a treadmill as their electrocardiograms were monitored. The majority of these patients also had selective coronary cineangiography. The findings suggest that the ability to adapt is associated with certain distinct distributions of coronary obstructive lesions and that therapeutic implications may be inferred.

**Methods**

All 12 subjects were seen in consultation by members of the Division of Cardiology at the UCLA Center for the Health Sciences in the 2-year period, 1962-1964. All were males and had exertional chest pain consistent with angina pectoris with transient ischemic ST-segment depression on the exercise electrocardiogram during pain. The diagnosis of significant obstructive coronary artery disease was confirmed in eight of these subjects with selective coronary cineangiography.

A systematic search for patients exhibiting the "walk-through" phenomenon or "angina of first effort" was not made. Instead most subjects showing this phenomenon were discovered at routine treadmill testing during work up for angina pectoris. Therefore, its frequency in our patient population is not possible to estimate.

The subjects walked on a motor-driven treadmill at a 10 per cent upgrade at initial speeds between 1 and 3 miles per hour (mph) depending on the severity of symptoms. The speed was increased at 3- to 10-minute intervals in 0.25- to 0.5-mph increments until ST-segment depression or anginal pain appeared. The speed was then kept constant until exercise was stopped or until it was desired to overcome a steady state by altering the speed. Continuous electrocardiographic monitoring during exercise was possible by means of a bipolar, transthoracic lead (CB\(_5\) or CB\(_6\)) although short electrocardiographic strips were usually taken only every minute. Indirect arterial blood pressures were taken at intervals before and during exercise on some subjects by the cuff method.

Coronary cineangiography was carried out by Hanafee's percutaneous modification of the Sones method.\(^17\) Contrast injections were made directly into the orifices of the left and right coronary arteries and the intensified fluoroscopic image was photographed on 35-mm. film at 60 frames per second. After detailed study of each of the cine films, a sketch of the coronary arterial system was made to display the pattern of disease in a single figure.
EXERCISE IN ANGINA PECTORIS

E. C. 8-26-63 NO MEDICATION

CONTROL

START AT 2 MPH

3 MIN. ONSET ST CHANGE

6 MIN. ONSET PAIN

10 MIN. PAIN STABLE

TO 2.5 MPH

15 MIN. PAIN LESS

TO 3 MPH

20 MIN. PAIN WANING

TO 3.5 MPH

26 MIN. MINIMAL PAIN

STOP

27 MIN. PAIN GONE

31 MIN.

45 MIN.

Figure 1

Treadmill test on subject 1. The blood pressure and heart rate are inscribed below the electrocardiographic strips. Note that anginal pain was diminishing despite increasing rates of exercise and persisting ischemic ST depression. The pain began to lessen before there was any significant change in heart rate or blood pressure.

Results

Clinical Data

Clinical and angiographic data are presented in table 1. In most of the subjects angina pectoris was of relatively short duration; one subject had had it more than 4 years and in six subjects it had been present 1 year or less. Angina pectoris on exertion was of mild to moderate severity in all cases and only two subjects were bothered by angina when at rest. Only six of the subjects had noted the phenomenon of walking through an attack of angina or improving their exercise tolerance after warming up. In nine subjects angina pectoris was fairly stable in its severity, and in one subject it was worsening. Two subjects had had their angina for such a short time that no trend was discernible. The resting electrocardiogram was normal in nine subjects.

All eight subjects who had coronary angiography demonstrated significant obstructive coronary disease. They may be divided into two categories: those who had frank occlusions with clear evidence of collateral channels (4 cases) and those who had strategically placed stenotic lesions without frank occlusion and without evidence of collateral development (3 cases). In one case both types of lesions existed.

Case Reports

Case 1, E. C.

This man had hypertension and mild angina with exertion when he first walked on the treadmill at 2.0 mph on August 24, 1963. Ischemic ST-depression began at 3.5 minutes and angina at 4.5 minutes. Depression of ST segments and angina reached a stable plateau at 9 minutes and this persisted until exercise was stopped at 35

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### Clinical Data

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Duration of angina</th>
<th>Degree of angina</th>
<th>Myocardial infarction</th>
<th>Resting ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. E.C.</td>
<td>53</td>
<td>1 mo.</td>
<td>Mild</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>2. J.Ha.</td>
<td>49</td>
<td>7 yr.</td>
<td>Mild</td>
<td>No</td>
<td>2 yr. before Old inferior infarction</td>
</tr>
<tr>
<td>3. R.A.</td>
<td>44</td>
<td>1 yr.</td>
<td>Moderate</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4. R.Bw.</td>
<td>49</td>
<td>3 yr.</td>
<td>Moderate</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5. M.P.</td>
<td>49</td>
<td>3 yr.</td>
<td>Mild</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>6. J.V.</td>
<td>57</td>
<td>4 yr.</td>
<td>Moderate</td>
<td>Moderate</td>
<td>No</td>
</tr>
<tr>
<td>7. L.S.</td>
<td>49</td>
<td>7 mo.</td>
<td>Moderate</td>
<td>Moderate</td>
<td>No</td>
</tr>
<tr>
<td>8. M.G.</td>
<td>55</td>
<td>4 yr.</td>
<td>Moderate</td>
<td>No</td>
<td>1 yr. before Normal</td>
</tr>
<tr>
<td>9. C.B.</td>
<td>59</td>
<td>1 yr.</td>
<td>Moderate</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>10. R.Bx.</td>
<td>34</td>
<td>2 yr.</td>
<td>Moderate</td>
<td>Rare</td>
<td>No</td>
</tr>
<tr>
<td>11. J.He.</td>
<td>41</td>
<td>1 yr.</td>
<td>Moderate</td>
<td>No</td>
<td>6 mo. before Old inferior infarction</td>
</tr>
<tr>
<td>12. W.H.</td>
<td>43</td>
<td>3 mo.</td>
<td>Mild</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

On August 26, 1963 (fig. 1), a similar plateau of angina and ST depression was found at 2.0 mph and in an attempt to overcome this steady state the speed was raised to 2.5 mph at 10 minutes and to 3.0 mph at 15 minutes. Despite the increases in speed, the anginal pain was lessening in severity after 15 minutes, and although the ischemic ST-segment depression remained stable, angina was minimal by the time exercise was stopped at 26 minutes. Blood pressure and heart rate remained stable as the anginal pain began to lessen although there was a fall in blood pressure later on in exercise.

**Comment.** In this patient there was a range of exercise levels in which some form of adaptation took place; angina was decreasing in intensity.
<table>
<thead>
<tr>
<th>Findings of coronary angiography</th>
<th>Manifestation of adaptation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete, proximal right occlusion. Distal right fills retrogradely via left circumflex collaterals</td>
<td>&quot;Walk-through&quot;</td>
<td>Mild hypertension. Not aware of adaptation</td>
</tr>
<tr>
<td>Complete, proximal right occlusion. Distal right fills retrogradely via left circumflex collaterals. Stenosis, branch of anterior descending</td>
<td>&quot;Walk-through&quot;</td>
<td>Right coronary endarterectomy 1 year before with subsequent re-thrombosis. Stable angina. Aware of adaptation</td>
</tr>
<tr>
<td>Complete, proximal occlusion of left circumflex with distal portion filling retrogradely from right. Distal stenosis of right</td>
<td>&quot;Walk-through&quot; with nethalide</td>
<td>Hypertension. Angina slowly worsening. Aware of adaptation</td>
</tr>
<tr>
<td>Distal occlusion of right with large collateral vessels arising proximal to occlusion. Occlusion of major trunk of anterior descending</td>
<td>&quot;Walk-through&quot; with nitroglycerin</td>
<td>Stable angina. Not aware of adaptation</td>
</tr>
<tr>
<td>Stenoses midportion and distal right and at origin of anterior descending</td>
<td>&quot;Warm-up&quot;</td>
<td>Stable angina. Aware of adaptation</td>
</tr>
<tr>
<td>Stenoses of left main and at origin of anterior descending</td>
<td>&quot;Walk-through&quot;</td>
<td>Stable angina. Not aware of adaptation</td>
</tr>
<tr>
<td>Stenosis of left main</td>
<td>&quot;Warm-up&quot;</td>
<td>Stable angina. Aware of adaptation</td>
</tr>
<tr>
<td>Occlusion, midportion of right with large collateral vessels arising proximal to occlusion and perfusing distal right retrogradely. Stenoses of anterior descending and circumflex. Collateral connections of right with circumflex</td>
<td>&quot;Walk-through&quot;</td>
<td>Stable angina. Aware of adaptation</td>
</tr>
<tr>
<td></td>
<td>&quot;Warm-up&quot;</td>
<td>Stable angina. Not aware of adaptation</td>
</tr>
<tr>
<td></td>
<td>&quot;Walk-through&quot;</td>
<td>Stable angina. Not aware of adaptation</td>
</tr>
<tr>
<td></td>
<td>&quot;Steady state&quot; after nitroglycerin Disappearance of angina 2 years later</td>
<td>Mild hypertension. Stable angina. Aware of adaptation</td>
</tr>
<tr>
<td></td>
<td>&quot;Walk-through&quot; Disappearance of angina 3 months later</td>
<td>Mild hypertension. Not aware of adaptation</td>
</tr>
</tbody>
</table>

during a period of increasing exercise. He was able to walk through his pain even though the persistent ST depression indicated continued myocardial ischemia.

The coronary arteriogram (fig. 2) disclosed complete occlusion of the right coronary artery with filling of its distal portions through collateral channels originating in the left circumflex artery.

**Case 2, J. Ha.**

This patient was completely relieved of incapacitating angina pectoris by endarterectomy of an occluded right coronary artery in April 1962. Negative treadmill tests were obtained in May and June, 1962. In December 1962, ischemic ST depression was noted during treadmill exercise. On April 30, 1963, the patient reported that he
Findings of coronary arteriography on subject 1. The arrow at (1) points to a complete proximal occlusion of the right coronary artery. The distal portions of this vessel (2) showed delayed filling in a retrograde manner via collateral channels from the left circumflex coronary artery (3). Dotted line indicates that portion of the distal right coronary filled by collateral channels from the left coronary injection.

J.H. 4-30-63
NO MEDICATION
1 YEAR POST ENDARTERECTOMY

CONTROL

START
2 MPH.

2 MIN.

6 MIN.

14 MIN.

25 MIN.

30 MIN. NO DISTRESS
STOP

35 MIN.

40 MIN.

45 MIN.

Figure 3

Treadmill test on subject 2. The subject had mild pain behind his left ear between 7 minutes and 10 minutes of exercise which disappeared as exercise continued. He walked through this variant of anginal pain despite the persistence of ischemic ST depression.

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Another treadmill test on subject 2 is shown in which he developed ischemic ST depression without anginal pain. Nevertheless, he did get a "second wind" and the ST depression diminished as exercise continued. The blood pressure (noted below the electrocardiographic strips) and heart rate remained fairly constant during the period where the "second wind" began.

Comment. This patient walked through pain on one occasion and through ST depression on another. A selective coronary cineangiogram on November 8, 1963, disclosed the pattern illustrated in figure 5. The previously endarterectomized right coronary artery had closed presumably by rethrombosis, but collateral filling of the distal branches of the right coronary from the circumflex branch of the left was clearly seen. The findings suggest that the capacity to adapt in this patient is related to the capacity of the collateral circulation to perfuse the bed of the right coronary artery. This patient's performance and his coronary circulation are strikingly similar to those of case 1.

Results of coronary arteriogram on subject 2. At (1) there was a complete proximal occlusion of the right coronary artery with a collateral vessel arising just proximal to the occlusion. The distal portions of the right coronary artery (2) filled late in a retrograde manner via collateral vessels from the left circumflex artery, which had a mild stenosis at its origin (3). A stenotic point was also present in a branch of the anterior descending coronary artery at (4).

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Case 3, R. A.

This man had a moderate limitation of exercise capacity because of angina pectoris at the time of his first treadmill test on June 14, 1963 (fig. 6). He was able to walk only 2.5 minutes at 2.0 mph on the treadmill before the onset of pain and only 7 minutes before being stopped by anginal pain. On July 20, 1963 (fig. 6), while taking the beta-adrenergic blocker drug, nethalide, 100 mg. t.i.d., he walked at 2.0 mph and developed anginal pain and onset of ST changes at 3 minutes. The pain reached a stable state by about 10 minutes and thereafter declined in severity so that when exercise was discontinued at 30 minutes, only mild pain and slight junctional ST depression were present. He subsequently undertook a home program of walking 2 to 3 miles per day on at least 3 days of each week. On September 6, 1963 (fig. 6), he walked on the treadmill at 2.0 mph without medication and developed mild angina at 3.5 minutes, but this reached a plateau by 10 minutes. The speed was increased at 15 minutes to 2.5 mph, at 20 minutes to 3.0 mph, at 25 minutes to 3.5 mph with slight increase in degree of angina each time, yet each time a new plateau of stable pain was reached that did not progress. When exercise was stopped at 30 minutes his angina was still less than that requiring nitroglycerin for relief. ST changes during this test were minimal.

Comment. This patient first demonstrated "walk-through" adaptation under the influence of beta-adrenergic blockade by the drug, nethalide. Subsequently after a 2-month period of regular walking exercise he demonstrated a greatly improved exercise capacity with steady-state adap-

R.A.

<table>
<thead>
<tr>
<th>Date</th>
<th>Notes</th>
<th>Diagram</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-14-63</td>
<td>NO MEDICATION</td>
<td></td>
</tr>
<tr>
<td>CONTROL</td>
<td>START AT 2 MPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7 MIN. SEvere PAIN</td>
<td></td>
</tr>
<tr>
<td></td>
<td>STOP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.5 MIN. PAIN GONE</td>
<td></td>
</tr>
<tr>
<td>7-20-63</td>
<td>NETHALIDE</td>
<td></td>
</tr>
<tr>
<td>CONTROL</td>
<td>START AT 2 MPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 MIN. PAIN AT PLATEAU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>STOP</td>
<td></td>
</tr>
<tr>
<td>9-6-63</td>
<td>NO MEDICATION</td>
<td></td>
</tr>
<tr>
<td>CONTROL</td>
<td>START AT 2 MPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 MIN. PAIN AT PLATEAU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>STOP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5 MPH AT 15 MIN.</td>
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<tr>
<td></td>
<td>3 MPH AT 20 MIN.</td>
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</tr>
<tr>
<td></td>
<td>3.5 MPH AT 25 MIN.</td>
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</tr>
<tr>
<td></td>
<td>30 MIN. PAIN AT PLATEAU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>STOP</td>
<td></td>
</tr>
</tbody>
</table>

Figure 6

Serial treadmill tests on subject 3. Each column is a separate test. On June 14, 1963, he was stopped after only 7 minutes of walking by severe angina with ischemic ST depression. On July 20, 1963, he walked right through his ischemic ST depression and partially through his angina pain. On September 6, 1963, he was able to continue walking at increasing speeds after the onset of angina; with each increase in speed the anginal pain increased slightly but each time it leveled off at a tolerable magnitude. Only junctional ST depression was present.
Coronary arteriogram on subject 3 shows complete occlusion of the left circumflex coronary artery about 1½ cm. from its origin (1). The distal portions of this vessel (3) filled in a retrograde manner via collateral channels from the distal right coronary artery, which had a stenotic area (2) just proximal to the origin of these collateral vessels.

Identification being evident at several levels of progressively increasing exercise load.

His coronary arteriogram (fig. 7) showed complete occlusion of the proximal left circumflex coronary artery. Well-developed, visible, collateral channels filled the distal circumflex branch from the right coronary artery, which had a distal area of stenosis. The inference is drawn that adaptation was probably achieved through an increase in blood flow through the collateral connections.

Case 4, R. Bw.

This man was having mild exertional angina pectoris when his aortic coarctation was repaired on January 31, 1961. Postoperatively he continued to have exertional angina, which gradually increased in severity. On August 5, 1963 (fig. 8), while taking no medication he was able to walk only 3.5 minutes at 2.0 mph before he had to stop exercise because of severe anginal pain with ST depression. After resting 7 minutes he was given nitroglycerin and exercise was resumed. This time the onset of ST changes and angina was delayed; angina began at 14 minutes at which time there was ischemic ST depression. However, he was able to continue walking, and by 30 minutes he had walked through his angina, was having no more distress, and his ST depression had lessened. By 52 minutes mild angina had recurred and persisted along with ST depression until 60 minutes, when exercise was stopped. Each time this man was tested without medication his exercise capacity was drastically limited. Retesting after nitroglycerin resulted in a very marked increase in exercise capacity and even walking through the anginal pain.

Comment. This man appeared to achieve adaptation only with the aid of a pharmacologic agent. Nitroglycerin administration permitted him to extend his capacity from 3.5 minutes to 60 minutes of walking during which the "walk-through" phenomenon occurred. It is also possible that the prior exercise-induced episode of angina was playing a role in causing this improved performance. It does not seem likely that the nitroglycerin itself was active during this entire 1 hour of exercise. Coronary arteriograms (fig. 9) showed

Figure 7

Coronary arteriogram on subject 3 shows complete occlusion of the left circumflex coronary artery about 1½ cm. from its origin (1). The distal portions of this vessel (3) filled in a retrograde manner via collateral channels from the distal right coronary artery, which had a stenotic area (2) just proximal to the origin of these collateral vessels.

Figure 8

Treadmill tests on subject 4 are shown before and after nitroglycerin. The two tests were separated by a 9-minute resting period. Note that the second test, after nitroglycerin, demonstrated marked improvement in exercise capacity with the subject walking right through his anginal pain with a 22-minute angina-free period of continuous walking before his angina recurred.
Coronary arteriogram on subject 4 showed occlusion of the major trunk of the anterior descending artery with collateral development from other branches of the left coronary artery. There was also an occlusion of the distal right coronary artery which was bypassed by a collateral vessel arising proximal to the occlusion.

occlusion of the major trunk of the anterior descending artery in its midportion with collateral development from other branches of the left system; there was also a distal occlusion of the right coronary artery with collateralization from other neighboring branches of the right coronary.

Case 5, M. P.

This man with stable, mild angina pectoris had had two treadmill tests in 1962, in which the speed was increased at 5-minute intervals from 2 to 2.5, to 3, to 3.5, and finally to 4.0 mph. Each of these tests resulted in only mild junctional ST depression without anginal pain and were considered negative. On September 26, 1963 (fig. 10), walking was started at 2.0 mph with an increase in speed to 2.5 mph at 3 minutes and to 3.0 mph at 6 minutes. At 8 minutes he developed anginal pain with ischemic ST depression but by 15 minutes his angina had reached a steady state and at that time the speed was decreased to 2.5 mph, with disappearance of pain and ST changes. Subsequently the speed was increased in more gradual stages to greater than 3.0 mph before he again developed anginal pain while walking at 3.5 mph at 27 minutes. When exercise was stopped at 30 minutes, he had only mild angina and junctional ST depression. Thus he was able to walk at higher speeds without angina after warming up.

On November 4, 1963 (fig. 11), walking was started at 3.0 mph with the onset of anginal pain and dyspnea at 5 minutes. ST depression was maximal at 7 minutes. The angina worsened until 10 minutes and then was steady until 17 minutes when he noted "second wind" and the pain began to ease. The ST depression began to diminish after 10 minutes and had disappeared except for junctional depression, when the pain was completely gone at 25 minutes. Blood pressure and pulse rates rose while the angina was increasing early in the test but reached a relatively steady state and remained constant during the time the angina and dyspnea were waning. At the time exercise was stopped, the patient said that he was just "sailing along" and "feeling fine." In this test the patient literally walked through his angina.

On April 8, 1964 (fig. 12), walking was started at 3.0 mph with the onset of angina and ST depression at 3 minutes. By 7.25 minutes he had to stop walking because of increasing pain, at which time ischemic ST depression was present in the electrocardiogram. After a rest of 10 minutes, during which the angina and ST abnormalities disappeared, exercise at the same speed was restarted. This time the onset of mild angina began at 8 minutes; "second wind" appeared at 10 minutes and mild angina waxed and waned thereafter. Exercise was stopped at 25 minutes with only minimal pain present. It will be noted that on the second run his blood pressure did not rise as rapidly as on the first run, but it did eventually reach similar levels and was relatively stable during the period when the patient experienced his "second wind." In this test the patient was able to walk through his angina only on his second effort. During his first effort he failed to adapt and was stopped by symptoms of angina after only 7.25 minutes of walking.

Comment. This patient in multiple exercise tests, exhibited both the "warm-up" phenomenon and the "walk-through" phenomenon. In the first two tests, which were interpreted as negative, the walking speed was held constant for 5 minutes each time before increasing the speed. When the intervals were reduced to 3 minutes at each speed, then anginal pain and ST depression were induced. It would then appear that 5 minutes of warming up were enough to permit the patient to adapt to the next higher speed, whereas a warm-up of only 3 minutes was not time enough for adaptation to take place.

"Warm-up" was also evident in the test of April 8, 1964, when adaptation failed on the first effort but succeeded on the second effort. The "walk-through" phenomenon was the feature of the tests on September 26, 1963, November 4, 1963, and on the second effort of the April 8, 1964, test.
EXERCISE IN ANGINA PECTORIS

The observations that the heart rate and blood pressure were the same at the same time of maximal pain and ST depression, as they were after adaptation had been accomplished, suggest that the adaptation cannot be explained on the basis of a reduction of cardiac work load.

The coronary arteriogram was performed on November 4, 1963 (fig. 13). Local stenotic lesions were found at the origins of a major branch of the anterior descending artery and in the midportion and distal segments of the right coronary artery. The findings suggest that these stenotic areas may have the capacity to dilate slowly under the stimulus of the heart's need for an increased blood supply.

Case 6, J. V.

This patient was having severe exertional angina and moderate angina at rest when first tested on September 21, 1961. At 1.0 mph he walked only 3.5 minutes before having to stop with angina and ischemic ST depression. There was considerable variation in his exercise capacity, however, because when retested on September 27, 1961, he went 10 minutes at 1.0 mph and an additional 15 minutes at 1.5 mph before exercise was stopped at 25 minutes with mild angina and no significant ST changes. When retested 2 years later on October 2, 1963 (fig. 14), he was having less angina; walking was started at 1.0 mph with the onset of pain and ischemic ST changes with U-wave inversion at 3 minutes. By 10 minutes his angina was gone, however, despite continued exercise; his ST depression subsequently lessened. The rate was increased to 1.5 mph at 15 minutes and to 2.0 mph at 20 minutes with the re-onset of angina and ischemic ST depression at 23 minutes.

M.P. 9-26-63
NO MEDICATION

CONTROL

START
2 MPH
TO 2.5 MPH
AT 3 MIN.
TO 3 MPH
AT 6 MIN.

8 MIN. ONSET
DISCOMFORT

15 MIN. PAIN
AT PLATEAU

TO 2.5 MPH

18 MIN.
PAIN GONE

TO 2.75 MPH
AT 19 MIN.
3 MPH
AT 21 MIN.
3.25 MPH
AT 23 MIN.

25 MIN.

TO 3.5 MPH

27 MIN. ONSET
PAIN

30 MIN. - STOP
MILD ANGINA

Figure 10

Treadmill test on subject 5 demonstrated his ability to exercise without angina at greater speeds after being warmed up and after a slower build-up of the walking speed.
M.P. 11-4-63
NO MEDICATION

Figure 11
Another treadmill test on subject 5 demonstrated his ability to walk through both his angina and the associated ischemic ST depression during a steady state of heart rate and blood pressure.

M.P. 4-8-64 NO MEDICATION

Figure 12
This series of two treadmill tests on subject 5 demonstrated that after being warmed up by the first test, he was, on the second test, able to perform more exercise before the onset of pain, to walk through most of his pain with only minimal ST changes, and to perform much more total exercise. The blood pressures and heart rates are inscribed below the electrocardiographic strips on the left and right, respectively.
EXERCISE IN ANGINA PECTORIS

By 29 minutes his angina was worse and exercise was stopped.

Comment. This man was able to walk through an attack of angina pectoris at a speed of 1.0 mph but not at 2.0 mph. This finding suggests that it may be possible to find a work level at which adaptation can take place in many angina patients if careful titration of the work load is carried out.

A coronary arteriogram performed in September 1961 disclosed stenosis of the left main coronary artery extending into the proximal anterior descending branch.

Case 7, L. S.

This man had moderate exertional and nocturnal angina when tested on July 15, 1964 (fig. 15). Walking was started at 2.0 mph with the onset of ST changes at 2 minutes and pain at 3 minutes. The angina built up slowly, forcing cessation of walking at 8.5 minutes with 4-mm. ischemic ST depression. After 16 minutes of rest, walking was begun again at 2.0 mph with the onset of ST changes at 3 minutes. The speed was raised to 2.25 mph at 10 minutes, to 2.5 mph at 17 minutes, and to 3.0 mph at 22 minutes. Mild angina began at 25 minutes at which point exercise was stopped, with 2-mm. ischemic ST depression. Blood pressure and pulse rates did not rise as high during the second run as they did in the first during the episode of severe pain.

Comment. This man was able to increase his exercise capacity over 300 per cent after being warmed up by a preceding exercise test leading to a bout of angina. A coronary arteriogram (fig. 16) disclosed a single localized stenotic lesion in the left main coronary artery. The findings suggest that the "warm-up" may have dilated the stenotic lesion enough to permit a significant augmentation of blood flow through it.

Case 8, M. G.

This physician had effort angina of 4 years' duration and had often experienced pain on the first two holes when playing golf. He suffered a posterior myocardial infarction in January 1963, following which his angina became somewhat worse, causing him to ride in a cart while playing golf. He was having moderate angina of exertion when tested on November 27, 1963. At this time he walked at 2.0 mph for the first 3 minutes and at 2.5 mph for the remainder of the test. Anginal pain began at 4 minutes with 1 mm. of ST de-

Figure 13

Coronary arteriogram on subject 5 demonstrated stenotic areas (1 and 2) at the origins of the two main branches of the anterior descending artery as well as in the midportion (3) and distal segment (4) of the right coronary artery.

Figure 14

Treadmill test on subject 6 demonstrated his ability to walk through his anginal pain at 1 mph; but at a speed of 2 mph he developed a recurrence of his angina and electrocardiographic changes which forced him to stop exercising.
pression. Between 6 minutes and 20 minutes his pain and 1.5 mm.-ST depression remained stationary. Thereafter the pain began to wane, and it had almost disappeared when exercise was stopped at 25 minutes. At this time the ST segments were slanting upward but the J point was 1 mm. depressed. He thus almost walked through an attack of angina after reaching a steady state.

Comment. This patient was greatly surprised that he was able to walk through his angina. The performance resulted in a great boost to his morale. The coronary angiogram (fig. 17) disclosed essentially complete occlusion of the right coronary artery about 1 inch distal to its origin. This undoubtedly accounted for the posterior infarct. Proximal to the occlusion a large collateral branch arose from the right coronary and coursed over the posterior of the heart to connect directly with the distal branches of the left coronary artery, and also with the distal portions of the right coronary artery which filled in a retrograde manner. Severe local stenotic lesions were seen in the midportions of both anterior descending and circumflex branches of the left. His coronary tree contained both local stenoses and visible collateral channels bypassing an occlusion.

Case 9, C. B.

This patient had a fairly stable pattern of moderate exertional angina pectoris. On multiple treadmill tests between March 1, 1963, and October 2, 1963, he exercised at 2.0 mph for 5 to 8 minutes before having to stop because of angina. At times there would be ischemic ST depression with the angina, at other times there would be only equivocal ST changes and U-wave inversion. On November 6, 1963, he was tested at 1.5 mph with the onset of angina at 5 minutes. Exercise was stopped at 12 minutes with severe angina but only borderline ST changes and U-wave inversion. After a rest of 18 minutes, walking was again started at 1.5 mph, again with onset of angina and borderline ST depression at 5 minutes; however, this time the rate was slowed to 1.0 mph at 6 minutes and by 9 minutes the angina had gone. At 10 minutes the rate was increased to 1.25 mph and at 16 minutes it was raised again to 1.5 mph. Angina began again at 22 minutes but was mild and did not increase even though exercise was continued until 37 minutes, at which time no ST- or T-wave abnormalities were present.

Comment. This man was forced to stop because
of angina at a rate of exercise that he subsequently was able to perform for an extended period of time after warming up and building up to the work load gradually. Systolic blood pressures during exercise were significantly higher at this same work load on the initial run than on the second run after he had warmed up (165/85 peak at end of first run and 140/68 peak during second run) although the heart rate was about the same each time. No coronary arteriogram was performed.

Case 10, R. Bx.

This man was having moderate and stable exertional angina when first tested with no medication on April 1, 1963 (fig. 18). He was able to walk only 8 minutes at 2.0 mph before having to stop with severe angina and ischemic ST depression. After a 10-minute rest he was given nitroglycerin and retested; this time he walked for 10 minutes at 2.5 mph before he developed slight angina, and an additional 4 minutes at 3.0 mph before stopping with mild angina and no ST depression. He was then placed on a program of daily exercise (walking 4 miles per day) with subsequent lessening of his angina and improvement in exercise tolerance. When retested on July 1, 1963 (fig. 18), with no medication he walked at 2.0 mph for 5 minutes and 2.5 mph for 5 more minutes before the onset of mild angina and ischemic ST depression. However, while continuing to walk, the angina disappeared at 13 minutes and ST depression was gone by 20 minutes when the speed was further increased to 3.0 mph. Angina recommenced at 29 minutes and exercise was stopped at 32 minutes with only mild angina and junctional ST depression.

Comment. The subjective impression that exercise capacity had increased during a program of daily exercise was confirmed by treadmill testing in which the subject walked through an episode of angina pectoris. Coronary arteriography was not carried out.
Coronary arteriogram on subject 8 showed two points of stenosis separated by a segment of poststenotic dilatation in the proximal anterior descending artery (1) and in the midportion of the left circumflex artery (2). There was a point of stenosis in the branch of the left circumflex artery (3) which was connected by collateral channels to the terminal portion of the right coronary artery system at (6). There was essentially complete occlusion of the right coronary artery about 2 cm. from its origin (4); the portion of this vessel distal to the occlusion (5) was perfused in a retrograde manner via a collateral vessel (7) arising proximal to the occlusion. This collateral vessel communicated with a branch of the left circumflex artery at (6) and there was filling of this area from both the left and right coronary arteries.

Case 11, J. He.

This man was having exertional angina when first tested on December 19, 1961, at 2.0 mph. There was onset of pain at 3.5 minutes but this reached a steady state despite an increase in speed to 2.5 mph at 10 minutes. Only mild angina and junctional ST depression were present when exercise was stopped at 18 minutes in order to adjust the electrode. Exercise was recommenced at 20 minutes, with the reappearance of mild angina and ischemic ST depression at 25 minutes, when exercise was stopped. A program of daily exercise was recommended. When retested on March 22, 1962, he felt that his angina was worse. He started walking at 2.0 mph with prompt appearance of discomfort in his throat, which grew worse and forced cessation of walking at 6 minutes when ischemic ST changes were present. He rested for 10 minutes, was given nitroglycerin, and was retested at 2.0 mph. This time his throat distress began at 5 minutes but soon reached a steady state with ischemic ST depression; this state of affairs persisted until exercise was stopped at 15 minutes. This man was able to reach a "plateau" of angina and ischemic ST depression after nitroglycerin. Unfortunately one cannot separate the possible effects of the prior exercise and the nitroglycerin in evaluating this result. He was advised to continue his exercise program and when retested on July 27, 1964, he was having no angina. At 2.0 mph there was no pain or ST changes and the speed was raised to 2.5 mph at 10 minutes and to 3.0 mph at 20 minutes. Exercise was stopped at 30 minutes with no symptoms or electrocardiographic changes. He was therefore free from the symptoms and electrocardiographic signs of angina pectoris at this time.

Comment. The evidence of steady-state adaptation found first in 1961 and then the adaptation induced in March 1962 by nitroglycerin prompted the recommendation of a therapeutic exercise program. Two years later the symptoms and electrocardiographic signs of angina could not be in-

Figure 17

Figure 18
EXERCISE IN ANGINA PECTORIS

duced by treadmill testing. The findings suggest that the adaptive mechanisms may be stimulated and augmented by regular muscular exercise.

Case 12, W. H.

This commercial airline pilot had been ground-ed because of the onset of mild exertional angina pectoris. When first tested on March 11, 1964 (fig. 19), he walked on the treadmill at 2.0 mph for 3 minutes and at 2.5 mph for the remainder of the test. ST depression began at 4 minutes with an ischemic configuration by 7 minutes. Mild angina began at 6 minutes but had diminished by 11 minutes as he continued walking. By 15 minutes the pain had gone and he said he had gotten his “second wind.” Thereafter the ischemic ST depression began to wane. Exercise was stopped at 33 minutes at which time no symptoms were present and only slight J-point depression was discernible in the electrocardiogram. He had walked through an attack of angina. He was placed on a program of exercise (18 holes of golf every day) and subsequently had no further attacks of angina. When retested on June 15, 1964, walking was started at 2.0 mph with increases of speed to 2.5 mph at 3 minutes, to 3.0 mph at 9 minutes to 3.5 mph at 13 minutes, and to 4.0 mph at 17 minutes. Exercise was stopped at 20 minutes; he had no symptoms or electrocardiographic changes during this test. A coronary angiogram was not performed.

Comment. In this patient the evidence of adaptive capacity manifested in the “walk-through” phenomenon on his first treadmill test prompted a therapeutic program of exercise which resulted in the disappearance of the clinical and electrocardiographic manifestations of angina pectoris within 3 months.

Discussion

The observations reported here indicate that some patients with angina pectoris have a capacity to adapt in a way that permits improvement in exercise tolerance. In some cases the adaptation is induced by drug therapy, e.g., nitroglycerin and nethalide, while in others exercise itself appears to evoke the adaptive response.

The mechanism underlying the phenomena of walking through an anginal attack or of getting warmed up by a previous anginal attack is not directly discernible. It is observed that the “walk-through” phenomenon usually occurs during a steady state of heart rate and blood pressure. It is therefore unlikely to be due to a decrease in cardiac work and oxygen need, since heart rate and blood pressure are major determinants of myocardial oxygen need.18, 19 The “warm-up” phenomenon appears to be a forme fruste of the “walk-through” phenomenon, since the former can sometimes be turned into the latter by a suitable adjustment of walking speed. Intermediate between these is a steady state of mild angina with accompanying ischemic ST changes which may be maintained during long periods of walking.

Adaptation to exercise has been observed in patients who have demonstrated two distinct pathologic patterns of coronary disease. Cases 1 through 4 had occlusion of major coronary vessels with good collateral channels circumventing the obstruction. Cases 5, 6, and 7 had no frank occlusions, but did have strategically placed stenotic lesions in major coronary vessels with no discernible collateral development. Case 8 had both local

Figure 19

Serial treadmill tests on subject 12. The first test demonstrated his ability to walk through his anginal pain and partially through the accompanying ischemic ST depression. Three months later neither angina nor ischemic ST depression could be produced by treadmill walking.

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stenoses and occlusion with good collateral vessels.

In each of these two types of lesions one might reason that there are coronary vessels which respond but slowly to the dilating stimulus of myocardial hypoxia. In one group it is postulated that the collateral coronary channels may dilate slowly, and in the other it may be the larger coronary vessels which maintain a reduced capability of dilatation at their stenotic points. A large increase in flow would result from only a small increase in diameter, since by Poiseuille's law the flow increases as the fourth power of the radius. A distinction between these two groups on clinical grounds seems important. Those with major occlusions and good collateral development might be expected to improve with further enlargement of collateral channels. In the absence of stenotic lesions, the prophylactic use of anticoagulant therapy would not seem necessary in such patients. On the other hand, those patients with proximal major vessel stenosis but no major occlusions may not have the same strong stimulus to collateral development. Such patients would appear to be in danger of a catastrophic thrombotic occlusion of a major coronary at a stenotic point and might be reasonable candidates for long-term anticoagulation prophylaxis.

The presence of some form of adaptation to exercise would seem to have other therapeutic and prognostic implications. Five of these subjects (cases 3, 5, 10, 11, and 12) showed striking improvement in anginal symptoms and exercise tolerance while on a program of regular walking exercise. The improvement could have resulted simply from the passage of time, but in two of these subjects (cases 3 and 5) subsequent worsening of exercise tolerance was observed when the exercise programs were allowed to lapse. It has been our experience that patients manifesting adaptation to exercise are the ones most likely to be benefited by a therapeutic exercise program. Patients with local stenosis are the best candidates for coronary endarterectomy if incapacitated by their symptoms.

From a psychologic point of view it has been helpful in attempting rehabilitation in some of these patients to prove to them that their exercise capacity is actually better than they had supposed.

Treadmill testing of the kind used in this study is time consuming and requires the constant supervision of a physician, but in our opinion the insights gained into the status of individual patients have proved to be useful. The information so obtained permits some prediction of the pathologic anatomy of coronary occlusive disease and on the basis of these predictions reasonable recommendations as to therapy may be made.

Summary

Twelve patients with angina pectoris manifested an ability to adapt to exercise during treadmill stress testing with electrocardiographic monitoring. Three patterns of adaptation were seen. Nine subjects had the ability to continue walking after the onset of angina with eventual disappearance or lessening of anginal pain and the associated ischemic ST-segment depression; anginal pain and ST depression began to diminish during a steady state of blood pressure and heart rate in those cases in which these factors were measured. Four subjects were able to continue walking for long periods of time during a state of angina and ischemic ST depression. Three subjects demonstrated an increase in exercise capacity after being warmed up by a preceding bout of exercise-induced angina; blood pressures and heart rates during the initial, "warming-up" effort tended to be higher than those during the early stages of the second effort. In three subjects more than one of these patterns of adaptation were demonstrated. Five of the subjects showed striking subjective and objective improvement in exercise tolerance while on a program of regular walking exercise.

Selective coronary cineangiography was performed in eight of these patients and two patterns of coronary disease were seen: (1) occlusion of a major coronary vessel with good collateral channels circumventing the obstruction; (2) strategically placed, proxi-
mal, stenotic lesions in major coronary vessels without frank occlusion and without discernible collateral development.

Some diagnostic and therapeutic implications of these findings are discussed.

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