DIFFERENTIAL DIAGNOSIS OF ANGINA PECTORIS

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In most instances, the diagnosis of angina pectoris can be made with comparative ease and assurance; however, in a small percentage of cases diagnosis is very difficult. Because of the far reaching prognostic and therapeutic implications of the diagnosis, these latter cases assume an importance far out of proportion to their actual frequency.

The difficulties in diagnosis occur because, up to the present time, objective tests are not available to determine whether attacks of pain are of cardiac origin. Now, as in Heberden's time, the diagnosis rests on the patient's ability to describe his symptoms and the physician's ability to evaluate the patient's description. In practice, difficulties in diagnosis arise from inability to obtain a clear-cut, dependable history, and lack of general agreement or lack of knowledge as to what should be included in the term angina pectoris. It is therefore advisable first to define the terms that are currently used, and to discuss the relationship of angina pectoris to other manifestations of coronary heart disease.

NOMENCLATURE AND INTERRELATIONSHIPS

Angina pectoris is a term applied by Heberden in 1768 to a group of symptoms consisting of short attacks of anterior chest discomfort, usually precipitated by exertion. According to present concepts, these attacks are due to temporary anoxia or ischemia of the myocardium which results when the coronary circulation is inadequate for the needs of the myocardium at that moment. The inadequacy of the circulation generally is due to abnormality of the coronary arteries, usually arteriosclerosis.

Angina pectoris is not a specific disease, but rather a symptom complex that constitutes a clinical entity with a characteristic clinical course. Incapacity for heavy exertion is a universal finding, and sudden death or myocardial infarction are the most common complications.

The terms "angina of effort," "angina decubitus," and "status anginosus" are used frequently but are often more confusing than helpful. They do not imply different types of angina pectoris, but rather different clinical conditions under which attacks may occur.

The frequency with which angina pectoris is associated with coronary artery sclerosis has resulted, unfortunately, in the interchangeable use of the terms "angina pectoris," "coronary artery disease," "arteriosclerotic heart disease," "coronary heart disease," and "coronary insufficiency." These terms are not synonymous; to prevent confusion they should be limited to their original or basic meaning.

Coronary artery disease indicates pathology of the coronary arteries. Arteriosclerosis is most frequently responsible, but other conditions, such as encroachment on coronary arteries by tumors and syphilis, distortion of the aortic valves, certain rare forms of arterial disease such as Buerger's or Raynaud's disease, embolism, and even prolonged hypotension due to shock, may result in poor coronary circulation (fig. 1).

Coronary artery disease does not always result in symptoms or signs of cardiac involvement (fig. 2). For example, the onset of angina pectoris, myocardial infarction, or unexpected cardiac death usually occurs on the basis of pre-existent coronary artery pathology, even though previous examination by electrocardiogram or any other clinical tests may have been normal. Postmortem studies show that unsuspected coronary artery disease is not uncommon.

Arteriosclerotic heart disease means cardiac...
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**Fig. 1.** Causes of coronary artery disease or poor coronary blood flow.

**Fig. 2.** Clinical manifestations of coronary artery disease.

damage or disturbance of function due to arteriosclerosis of the coronary arteries, aorta, endocardium, or pericardium (fig. 1).

**Coronary heart disease** means cardiac damage by impaired nutrition from coronary artery disease (fig. 2). The disturbance of function may be evidenced by pain, congestive failure, arrhythmias, etc. Anatomic damage may be demonstrated by abnormalities of the electrocardiogram or heart shadow but such findings are not necessarily accompanied by cardiac symptoms.

**Coronary insufficiency** is, basically, a physiologic term implying insufficient coronary circulation for the needs of the myocardium. This discrepancy between supply and demand may follow effort, coronary spasm (if it occurs), fall in blood pressure, abnormal rhythms, and coronary occlusion. Unfortunately, the term coronary insufficiency has been used to indicate not only the physiologic discrepancy between supply and demand, but also the many clinical results of this mechanism, namely, angina pectoris, coronary failure, myocardial infarction, cardiac asthma, pulmonary edema, arrhythmias, and both temporary and permanent electrocardiographic abnormalities. It would seem advisable to limit the use of the term coronary insufficiency to its physiologic meaning.

If the myocardial anoxia or ischemia resulting from coronary insufficiency is prolonged and severe, permanent anatomic changes may occur, i.e., myocardial infarction. If coronary insufficiency is short in duration, pain, dyspnea, or electrocardiographic changes may result; however, with readjustment of the balance between supply and demand, the abnormal symptoms and signs disappear and no permanent myocardial damage results. The short episodes of chest pain are *angina pectoris*.

The term *coronary failure* denotes a syndrome intermediate between angina pectoris and myocardial infarction. Physiologically it is due to anoxia or ischemia that is prolonged but does not result in irreversible changes in the myocardium. Clinically it is characterized by chest pain more prolonged than angina pectoris and often accompanied or replaced by disturbed cardiac function (such as cardiac asthma or arrhythmias) but not resulting in evidence of permanent myocardial damage, i.e., without fever, leukocytosis, or progressive electrocardiographic changes.

*Angina pectoris* is only one of the manifestations of coronary artery disease. Angina pectoris is usually caused by coronary arteriosclerosis; however, there are other causes (fig. 3).

There is a small but important group of patients in whom angina pectoris is precipitated by thyrotoxicosis, polycythemia vera, anemia, or abnormal rhythms. It is probable that these patients have underlying coronary arteriosclerosis. The impaired coronary circulation in these patients appears adequate under usual conditions but becomes inadequate for the needs of the heart when the demands are increased by thyrotoxicosis, the supply is decreased by arrhythmias, or the delivery of oxygen is impaired by anemia or polycythemia.

Another small group with coronary artery disease and angina pectoris, but without coronary arteriosclerosis, includes patients with metastatic tumors surrounding the coronary arteries, congenital malformations of the coronary vessels, and Raynaud's disease or...
thromboangiitis obliterans involving the coronary tree.

On the other hand, angina pectoris may occur in the absence of coronary artery disease. For example, a few patients with severe arterial hypertension have angina pectoris, yet show little coronary arteriosclerosis post mortem.

Similarly, congestive failure or aortic valvular disease may result in poor coronary blood flow, myocardial anoxia, and angina pectoris.

Finally, there is an important group of patients with symptoms suggesting angina pectoris in whom it is difficult to establish the diagnosis with certainty. In such instances, the terms “pseudo angina” or “atypical angina” are frequently used, and both the patient and the doctor may worry for years about the possibility of coronary artery disease. In most instances, however, a careful history and examination will separate these cases of “atypical angina” into those with typical angina and those who definitely do not have angina pectoris. A small but important group remains, however, in whom the diagnosis remains in doubt, even after careful study.

The Diagnosis

Heberden’s original (1768) 1-sentence description has not been improved upon for simplicity and clarity. “They who are afflicted with it are seized while they are walking, (more especially if it be up hill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or continue; but the moment they stand still, all this uneasiness vanishes.”

One hundred and forty years later (1910) Osler2 pointed out that little had been added to this description. Both of these master clinicians, however, included under angina pectoris other related or somewhat similar conditions such as myocardial infarction, “spasmodic disorders,” and cardiac neuroses. A more recent analysis (1937) of the histories of 100 patients whose angina pectoris was confirmed by observation during typical attacks showed 5 characteristics in common.3 These 5 diagnostic criteria, which are implied in Heberden’s original description, serve as a valuable yardstick for the diagnosis of angina pectoris: Sudden onset, Anterior chest, Vague discomfort, Exertion precipitates, Short duration = SAVES.

The diagnosis of angina pectoris depends on adequate history taking. The examiner should record the specific description given by the patient, not what he thinks the patient is trying to say (except in summary). A few well directed questions will usually fill in the gaps and clarify the picture, but leading questions should be avoided. At first the patient may not notice details such as the exact location or the duration of the pain; however, such questioning leads to more careful observation so that a much more detailed and accurate account can subsequently be obtained.

1. Angina is sudden in onset, the attack develops within a few seconds and, as has often been pointed out, between attacks the patient is perfectly comfortable. The patient who states, “I felt it coming on all morning,” or “it gradually increased in intensity over hours,” is not talking about angina.

2. The discomfort is in the anterior part of the chest. This area lies between the anterior axillary lines on the sides, the epigastrium below, and the suprasternal notch above. “Retrosternal” is a term that is used more often by physicians than by patients. Unfortunately this term is used too loosely to be of diagnostic value. The pain is most commonly located under the upper
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or mid portion of the breastbone but not always. It is least commonly felt at the cardiac apex; discomfort limited to the region under the left breast should be viewed with suspicion. Similarly, pain in the region of the mid or posterior axillary line is probably not angina. Patients may have pain in the upper thoracic back, but this is usually overshadowed by the discomfort in the anterior aspect of the chest.

Radiation is important, but occurs in only about 60 per cent of cases, most commonly to the inner aspect of the arm, especially the left arm. Pain in the outer aspect of the arm is likely to be due to disease of the cervical spine.

3. The discomfort is vague and difficult to describe exactly. It is painful but not necessarily described as pain. "Pressing," "squeezing," "choking" are terms commonly used. Often it will be described in relation to the patient's work or experience. For example, a real estate dealer described his attacks as "the Woolworth Building sitting on my chest," while a cowboy described a "branding iron in my chest and a lariat around my throat." The discomfort is different from pins and needles, and it is not shortness of breath, although this may also be present.

4. The attacks are precipitated by exertion. The relation to exertion is one of the most helpful points in diagnosis. Patients may also have angina on emotion, it may be more frequent in the cold, it may occur while at rest, after meals, or during sleep, but if the patient is asked "what brings on an attack," the usual answer is that he gets it "when walking out of doors." The patient who has angina after meals is more likely to have it on walking after meals than while sitting quietly at the table.

Cases with angina on emotion but not on exertion exist, but they are very rare. In such cases it is advisable to find out how much the patient walks, for it may be discovered that he walks slowly and as little as possible. If the patient states that he never gets attacks except when excited, ask "what would happen if you ran after a street car?" The answer probably will be, "I wouldn't dare do that for I'm sure I would have an attack."

5. The attacks are short in duration. Attacks measured with a stop watch, are practically always less than 3 minutes in duration. Few patients, however, except doctors with angina, measure their attacks. Most patients will state that the attacks are "short," "not long," "a few minutes," "5 minutes," or "less than 15 minutes" in duration. Doctors with angina frequently state that their attacks last "1 minute by my watch." Occasional attacks may last longer but be suspicious if the attacks always last an hour or more.

The patient with angina pectoris usually has all 5 of these characteristics. If 1 of these criteria is definitely absent, the patient probably does not have angina and another cause for the symptoms must be sought. A sixth important characteristic is the uniform pattern of the attacks in any given patient; although some variations may occur, they are usually slight.

The response to nitroglycerin may be helpful in diagnosis, but is often misleading. Many patients with angina pectoris are not benefited by nitroglycerin while patients with gallbladder disease or psychoneurosis may obtain relief.

Physical and Laboratory Methods. Physical examination and laboratory studies are of little value in the diagnosis of angina pectoris. At best they indicate a condition which may result in cardiac symptoms. About one half of the patients have cardiac enlargement. About one-third have blood pressures lower than 140/90; another third have pressures of 150 to 160 over 90 to 100; and the remaining one-third have blood pressures of 165/100 or higher. About one half to three fourths of patients with angina pectoris have abnormal electrocardiograms. It is important to realize that in about one fifth of all patients with definite angina pectoris, the heart size, blood pressure and 12-lead electrocardiograms are normal. In brief, the absence of objective signs of heart damage does not exclude angina pectoris, while the presence of such signs is not diagnostic.

Angina pectoris is infrequent in women under 45 without hypertension or diabetes, but it does occur.
DIFFICULTIES IN ESTABLISHING THE DIAGNOSIS

Problems of Nomenclature. Some of the confusion about angina is due to indiscriminate use of terms that are not interchangeable. Coronary arteriosclerosis, coronary artery disease, arteriosclerotic heart disease or coronary insufficiency does not mean that the patient necessarily has angina pectoris.

Problems in Obtaining an Adequate History. Inadequate history taking is a common cause of difficulty in diagnosis. This is illustrated by group of 108 patients, diagnosed as having angina pectoris, who were recently re-evaluated in preparation for therapeutic studies.5, 6

In 73 of these patients (67 per cent), the history showed the typical 5 characteristics discussed above. In 63 of these 73, typical attacks were induced and observed during Standardized Exercise Tolerance Tests (described below under Objective Tests). The remaining 10 were apparently in a period of remission of symptoms for, although they had had typical angina in the past, no attacks had been experienced for months.

In the remaining 35 patients (33 per cent) the history was variable and distinctly different from that described above; furthermore, in none of these was it possible to induce angina by exercise under the standardized conditions. In 5 of these patients the pain was gradual in onset; these patients could feel it coming on or developing for hours before the attack developed. In 6 patients the pain was not in the anterior chest but in the abdomen, or in the extremities or in the head. In 23 it was not vague, but very definite in character; 8 described it as “shortness of breath” or “difficulty in breathing;” 7 as “pins and needles,” 5 as “sharp” or “knifelike,” and 3 as “heartburn” or “throbbing.” In 21 it was not precipitated by exertion, but was either constant, or was brought on by deep breathing or occurred only on resting after exercise, or came only after meals or on damp days. In 11 patients the attack was not short in duration, but continued for hours or all day, while in 3 patients the discomfort was momentary only.

The sameness of the history in 73 of these cases and the marked variation of the histories

| Table 1.—Clinical Conditions Often Confused with Angina Pectoris |
|----------------|----------------|
| System          | Disease                  |
| Gastrointestinal | Abdominal angina         |
|                 | Pancreatitis             |
|                 | Esophageal disease       |
|                 | Peptic ulcer*            |
|                 | Hiatus hernia*           |
|                 | Gallbladder disease†     |
| Thoracic        | Pleuritis                |
|                 | Pulmonary infarction     |
|                 | Spontaneous pneumothorax |
|                 | Herpes zoster            |
|                 | Pulmonary or mediastinal |
|                 | tumors                   |
| Cardiac         | Acute myocardial infarction |
|                 | Coronary failure*        |
|                 | Arrhythmias              |
|                 | Valvular heart disease*  |
|                 | Congestive failure       |
|                 | Dyspnea                  |
|                 | Pericarditis             |
| Skeletal        | Lower cervical or upper dorsal |
|                 | lesions                  |
|                 | Bursitis or “shoulder arm syndrome” |
| Nervous         | Neuritis                 |
|                 | Psychoneurosis†          |
| Miscellaneous   | Thyrotoxicosis           |
|                 | Anemia                   |

* These conditions are confused frequently with angina pectoris.
† These conditions are confused very frequently with angina pectoris and their differentiation may prove especially difficult.

in the other 35 is quite striking. If the histories were taken more carefully and more completely in the latter 35 patients it is questionable if a diagnosis of angina pectoris would have been made.

Language difficulty may present an insurmountable barrier. Interpretation by a member of the patient’s family or a close friend rarely results in obtaining a clear description of the symptoms.

Phlegmatic or nonobservant patients may be unable to describe symptoms accurately. Fortunately such cases are not frequent.

Patients who are too observant may present a difficult diagnostic problem. In this category are those “neurotic patients” who are unable to overlook symptoms in other parts of the
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body, and at other times of their life. Such cases are among the most difficult; they require all the care and judgment of the observer and often leave the diagnosis in doubt.

Angina Pectoris Simulating Other Disease. Angina pectoris may simulate "neuritis" if the discomfort in the arm is more prominent than the thoracic component. Similarly, angina may simulate gastric or gallbladder disease if the symptoms characteristically appear after meals. In such instances the repeated precipitation of discomfort in the arm or epigastrium with exercise of the legs, and also the short duration of the symptoms, may be helpful in diagnosis.

Noncardiac Conditions that Simulate Angina Pectoris. The list of conditions that may simulate angina pectoris is long and involves many organs (table 1), constituting the most frequently encountered problem in differential diagnosis.

Angina Pectoris Plus Some Other Disease. These patients often cannot separate one group of symptoms from the other. Careful review of such a history may differentiate 2 types of attacks, for example 1 type of pain that comes on exertion, and another type that comes after meals.

Specific Problems in Differential Diagnosis

For convenience, the many specific clinical conditions that may be confused with angina pectoris can be divided anatomically, as in table 1.

Gastrointestinal Complaints

Abdominal angina, if it exists, must be extremely rare. While arteriosclerosis of the mesenteric vessels undoubtedly exists and at times results in thrombosis, the clinical manifestations usually are those of acute abdominal disease, are not repeatedly induced by walking, and are likely to be prolonged.

Pancreatitis similarly may result in pain that is usually more than a few minutes in duration and is not characteristically, repeatedly brought on by normal exertion.

Esophageal disease such as spasm, ulceration, or diverticulum may result in vague substernal discomfort, but this distress is usually related to food or the act of swallowing rather than to walking. Roentgen studies should establish the diagnosis.

Peptic ulcer is frequently confused with angina pectoris, especially in patients whose symptoms begin after 50 years of age, or in patients who describe their substernal discomfort as "heartburn." Careful history and x-ray studies differentiate the 2 conditions in most instances. There are, however, patients who suffer attacks of angina after eating; in such cases, a history of identical attacks brought on by exertion should establish the diagnosis.

Diaphragmatic hernia, presumably because the same nerve pathways are involved, may have the same localization and the same vague character as angina pectoris. Furthermore, both conditions may be episodic, with complete freedom from symptoms between attacks. The symptoms of diaphragmatic hernia, however, are likely to be precipitated by eating or assuming the recumbent position (rather than by exertion), and are more likely to be associated with other digestive disturbances such as vomiting or hematemesis. X-ray studies usually establish the presence or absence of diaphragmatic hernia, but angina pectoris may coexist.

Gallbladder disease is often confused with angina pectoris. In fact, it has been suggested that the 2 conditions are related and that gallbladder disease may lead to coronary artery disease or myocardial degeneration.

The frequent coexistence of gallbladder disease and angina pectoris can be explained by the fact that both occur in the same age group. Even though the patient may have definite evidence of gallbladder disease, any attacks of vague discomfort in the anterior chest precipitated by exertion and of short duration must be considered to be angina pectoris due to coronary artery disease.

Thoracic Disease

Noncardiac thoracic disease usually can be differentiated readily from angina pectoris. The pain of pleurisy or pleurodynia is usually lancinating and related to respiration. The pain of pulmonary infarction, spontaneous
pneumothorax, herpes zoster, or tumors of the chest wall or lungs is usually prolonged and does not occur in repeated identical attacks precipitated by walking.

**Cardiac Conditions**

*Myocardial infarction* can be differentiated by its prolonged duration, infrequency, signs of tissue damage, and characteristic electrocardiographic changes.

*Coronary failure*, may be difficult to differentiate except by careful observation over several days. Actually such episodes may be considered to be prolonged, severe attacks of angina pectoris. In most patients with angina, such episodes are sporadic rather than frequent.

*Arrhythmias* may be confused with angina pectoris. Premature beats may result in momentary episodes of vague anterior chest discomfort. If the extrasystoles are precipitated by exertion, the problem may be difficult. Careful history taking, however, should indicate that these episodes are less than a second, rather than minutes, in duration and may be described as “something turning over in the chest” or as “skipping.” In other instances, observation while the patient is actually experiencing the symptoms will reveal their true nature. Prolonged arrhythmias, especially when the ventricular rate is rapid, may be accompanied by chest pain typical of angina pectoris except that it may occur spontaneously and persist for as long as the rapid rate continues. Diagnosis in these instances is usually not difficult, especially if the patient is observed during a typical attack.

*Valvular heart disease*, especially aortic valvular disease, may interfere with adequate coronary artery filling and result in angina pectoris. Physical examination usually clarifies the situation. In patients over 50, the coexistence of coronary arteriosclerosis must be considered.

*Congestive failure* frequently brings about episodes of vague anterior chest discomfort on slight exertion, e.g., mitral stenosis. This is probably due to relative anoxia of the myocardium and is, therefore, similar to angina pectoris, both physiologically and clinically. However, in the absence of coronary arteriosclerosis, this syndrome does not progress to acute myocardial infarction; furthermore, these symptoms are usually overshadowed by other cardiac symptoms and signs of congestive failure.

*Dyspnea on exertion*, due to early congestive failure, emphysema, asthma, or lack of physical fitness, may be confused with angina pectoris. A careful detailed history clarifies the problem.

*Acute pericarditis* has been confused with angina pectoris, but the prolonged nature of the pain, fever, signs of inflammation, the characteristic clinical course, and electrocardiogram clarify the situation.

**Skeletal System**

*Spinal lesions*, especially arthritis or tumors of the lower cervical or upper thoracic spine, may result in sudden attacks of anterior chest and arm pain, short in duration, and difficult to differentiate from angina pectoris. The pain is usually sharp, and brought on by motion of the head or thorax. Forceful flexion and rotation of the head and neck should be included as part of the physical examination of every patient suspected of having angina pectoris. In some instances the fact that the pain is located in the outer rather than the inner aspect of the arm may be the first clue that the condition is radiculitis rather than angina pectoris.

*Bursitis or “shoulder arm syndrome” usually causes no diagnostic difficulty except in patients with recent myocardial infarction. In such cases both the patient and attending physician are likely to be sensitized to the occurrence of any pain in this region and confusion in diagnosis may result. Again the diagnosis is made by observing that the pain is induced by motion of the arm rather than exercise.

**Nervous System**

*Peripheral neuritis* is occasionally the diagnosis in patients with angina pectoris, when the twinges of discomfort in the arm overshadow the rest of the picture. Careful ques-
tioning will reveal that the arm pain is preceded or followed by pain in the anterior chest and that both are induced by exercise. Conversely, pain in the arm may be called angina pectoris unless a detailed history is obtained.

Psychoneurosis, used in its broadest sense, undoubtedly causes the greatest difficulty in diagnosis. Psychoneurosis is a poor term, for it includes not only patients with cardiac neuroses and patients with overawareness of all symptoms, but also many intelligent, emotionally stable persons who have been educated to the fact that heart disease is the greatest cause of death and incapacity. Such persons naturally want either to recognize the condition in its earliest stages or to be relieved of their justifiable anxiety.

In patients who are obviously neurotic, the question of additional organic illness arises. Although some complaints may be obviously functional, other symptoms may resemble angina pectoris. The problem is often complicated by disability compensation, a language problem, or coexistent gallbladder or gastrointestinal disease.

In this group, an objective test to differentiate between cardiac and noncardiac disease would be of greatest value. Observation of the patient during a typical attack usually helps to settle the diagnosis by enabling the examiner to determine accurately the location, the duration, and the precipitating cause of the symptoms. In clinical practice, however, such opportunities are rare.

In our experience, the diagnosis in this group of patients often is made only after prolonged observation. Repeated history taking, at widely separated intervals of time, may reveal a noncardiac cause for the symptoms, or may reveal a variability in symptoms inconsistent with angina pectoris, plus a persistently normal and unchanging electrocardiogram. Needless to say, the examiner must avoid indicating to the patient the difference between his symptoms and those typical of angina pectoris. Talking to other patients or reading popular or medical literature does not teach these patients to give a more typical history. This, however, might not be true of an intentional malingering.

Miscellaneous

Thyrotoxicosis may initiate angina pectoris, and it may be cured, at least temporarily, by adequate therapy of thyrotoxicosis. The clinical picture is usually sufficiently suggestive to indicate the advisability of metabolism tests. Anemia, like thyrotoxicosis, may precipitate angina, again, only in the older age group with coronary artery damage.

Objective Diagnostic Tests

An objective test of undoubted accuracy and direct clinical application would be helpful, especially in borderline cases. Such a test should have the following characteristics:

1. The results of the test must be directly applicable to the clinical diagnosis of angina pectoris.
2. The results must be reproducible.
3. The test should be positive in a high percentage of patients with angina pectoris, i.e., there must be few "false negative" responses.
4. The test must be negative in all or almost all patients who do not suffer attacks of angina pectoris, i.e., there must be few or no "false positive" tests.
5. The test must be without danger to the patient.

The ideal test of undoubted and universal clinical value has not yet been devised. The tests advocated to date have considerable value in the laboratory for studying angina pectoris, but they cannot be recommended for general office use. They can be divided into 2 general types: tests with direct clinical application including those that attempt to reproduce attacks of angina pectoris in patients suspected of having such symptoms; and tests with indirect clinical application.

Direct Tests

Adrenaline Test

The adrenalin test, which attempts to induce angina by the subcutaneous injection of epinephrine, is dangerous and therefore contraindicated.

Standardized Exercise Tolerance Test

The Standardized Exercise Tolerance Test
has been used successfully by the author and his associates in the Beth Israel Hospital since 1932. Attempts are made to induce attacks of angina pectoris by having the subject exercise by repeatedly mounting and descending a 2-step staircase either in a cold room, 45 to 55°F, or while holding an ice cube in one hand. The test is considered positive when the patient is forced to stop exercise because of the onset of discomfort that is typical of angina pectoris and is identical with what he experiences in daily life. The test is confirmed by repetition. The Standardized Exercise Tolerance Test differs from the "Master's test" in many respects, but especially in the fact that the former aims to induce typical attacks of angina pectoris in patients with such symptoms, while the latter aims to induce electrocardiographic changes that are not necessarily related to any cardiac symptoms.

Clinical Applicability. The test has direct clinical application because:

1. The conditions under which the attacks are induced are directly comparable to those responsible for the majority of attacks in daily life; a normal and familiar exercise, stair climbing, in the cold.

2. The attacks are identical with those experienced by the patient in daily life.

3. The characteristics of the attack can be more accurately evaluated by observation during such typical episodes. The examiner can observe the sudden onset (within 2 to 6 trips before being forced to stop). The location can be determined accurately by direct delineation on the patient's chest and arms while he is experiencing the discomfort. The short duration, usually less than 3 minutes, can be measured by a stop watch. The induction by exercise is self evident, and the character of the discomfort can be confirmed by direct questioning during the attack.

Reproducibility. Unless there has been a marked change in the patient's clinical condition, i.e., remission or exacerbation of attacks in daily life, typical attacks are invariably induced after comparable amounts of exercise when the conditions of the test are standardized by being performed: (a) in a cold environment, (b) at least 1 hour after a light meal, (c) on a day when the patient has experienced no recent attack, (d) when he has received no medication that might change the exercise tolerance, and (e) after the patient has become accustomed to the test. In fact, the reproducibility of attacks with comparable amounts of exercise under the standardized conditions not only serves to confirm the diagnostic value of the test, but also makes it possible to study the efficacy of treatment.

False Negative Tests. These are extremely rare. As discussed in the section on diagnosis, patients suspected of angina pectoris who failed to develop typical attacks under the standardized condition proved to have symptoms quite different from those characteristic of angina pectoris. No medical test is infallible, and undoubtedly false negative tests must occur, but unless the clinical history indicates a complete clinical remission of symptoms, these errors are very rare. During the past 23 years only 2 have been brought to our attention. One patient was a 40-year-old Polish refugee who had typical attacks whenever he heard of the German invasion of his homeland, but he did not develop attacks in the cold room or on walking through the snow. The other was a man approximately 50 years of age who had several attacks of peculiar discomfort every hour while lying in bed; he did not develop similar attacks on exercise in the cold room, but a typical myocardial infarction occurred within a few weeks after the test.

False Positive Tests. These are also rare, especially if the test is repeated in all doubtful cases, and clinical judgment is exercised. Some difficulty arises in patients with asthma or severe dyspnea, but examination and observation should serve to discover such patients. Undoubtedly a well informed deliberate malingerer could confuse the examiner but, to our knowledge, this has not occurred.

Safety. In view of the unpredictable course of patients with angina pectoris and the frequency of myocardial infarction, no studies in angina pectoris are completely safe. For this reason the Standardized Exercise Tolerance Test cannot be recommended as a routine office procedure. It has proven to be a useful
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Indirect Tests

These aim to induce electrocardiographic evidence of anoxia in patients whose tracings under normal conditions show no evidence of myocardial disease. Such tests are indirect, because a positive electrocardiographic result does not prove that the patient has cardiac symptoms or will develop cardiac symptoms in the future. Many different test conditions have been employed to induce electrocardiographic changes. The “Master’s test” currently used has the advantage of simplicity of technic and considerable accumulated experience. Several characteristics of the test limit its usefulness.

Master’s Test

The procedure consists of obtaining the 3 standard and 1 apical precordial leads while the patient is at rest. With the electrodes and cable still attached to the subject, but not to the machine, the patient then repeatedly mounts and descends a 2-step staircase 18 inches high. The duration of the exercise is 1½ minutes, the number of trips performed in this period of time is prescribed according to the sex, age, and weight of the subject. Immediately after exercise the cable is connected to the machine and short strips of the 4 leads are again obtained.

A positive result is indicated by the development of electrocardiographic evidence of anoxia or ischemia in 1 or more leads; most commonly the changes consist of S-T depression with or without a tendency to T wave inversion. If the test is negative, it can be repeated with the patient performing twice as many trips in twice the time.

Clinical Applicability. This must be considered from several points of view.

1. Clinical significance of a positive test. A positive test does not imply that the patient experiences the symptoms that we call angina pectoris. Electrocardiograms taken continuously during exercise in patients with severe angina pectoris may show no change even when the patient is forced to stop exercise because of an attack. In other patients, electrocardiographic changes appear shortly after

laboratory technic of direct clinical value in the diagnosis and therapy of angina pectoris. Experience during the past 23 years with over 10,000 tests in many hundreds of patients has resulted in untoward effects on 5 occasions. Two of these occurred during the first 2 years of our experience, during studies of the characteristics, limitations, and criteria of the test. The first patient lost his attacks following total thyroidectomy and was given large amounts of thyroid extract. After return of the basal metabolism to normal, attacks of angina pectoris recurred in daily life, but they were more severe and more frequent than preoperatively. The Standardized Exercise Tolerance Test at this time was followed by a severe attack with death a few minutes later. The second patient complained of generalized weakness and faintness rather than chest pain on exertion. The test was followed by one of his typical attacks of weakness and faintness from which he recovered within a half hour. Since that time the following precautions have been taken: the test is not done in a patient whose history suggests myocardial infarction, either impending or within the preceding 6 months; the test is never performed in a patient who complains of marked weakness or faintness on exertion; the first test in each patient is used to allay apprehension and to accustom the subject to the procedure, i.e., the patient is rarely permitted to perform more than 20 trips. The comparative safety of the test during the past 20 years is undoubtedly due in great measure to these precautions and, considering the nature of the condition, undoubtedly due, in some measure, to good fortune. Two of the 3 untoward effects in the last 20 years were in patients who had been treated with hypotensive drugs (octyl nitrite and reserpine). These patients developed severe hypotension, faintness, and perspiration a few minutes after the completion of the test; recovery was complete in both subjects within a half hour. The third patient developed transient ventricular tachycardia and collapse after 1 of many tests; recovery was complete and prompt.
exercise begins, long before onset of pain, and do not coincide in duration with the attack.\textsuperscript{11}

A positive test does not necessarily indicate the patient has pathology that might result in cardiac symptoms. At this time it is pertinent to point out that the control studies have been performed for the most part on subjects under the age of 45, while the vast majority of patients with clinical coronary artery disease are over 50 years of age. A control study of active, working, apparently healthy subjects over 50 years of age is necessary, together with observation for a sufficiently long period of time to determine the clinical significance of the positive results.

Unfortunately, the specific symptoms that we call angina pectoris and the more general condition called coronary artery disease have not been carefully differentiated in the literature. In order to study subjects with coronary artery disease, patients with angina pectoris were selected, but in the interpretation of the results it is intimated that subjects with positive tests either have symptoms or are likely to develop symptoms.

2. Clinical significance of a negative test. It is generally agreed that a negative test does not prove that the patient is free from coronary artery disease. Many reports from several different clinics show that from 40 to 80 per cent of patients with undoubted angina pectoris may have negative single Master's tests.\textsuperscript{12-14} The negative results with the double Master's test in patients with angina pectoris are apparently less frequent\textsuperscript{15} but occurred in 61 per cent of patients with angina pectoris and normal electrocardiograms at rest.\textsuperscript{12} Negative double tests have also been obtained in patients with active or impending myocardial infarction.\textsuperscript{16}

3. Technical considerations. A positive or abnormal response may be evidenced by a change in the level of the S-T interval of as little as 0.5 mm. This is extremely difficult to measure accurately especially in a tracing with a shifting baseline. Study of continuous electrocardiograms shows considerable variation from complex to complex due to respiration, motion, and other factors. In our experience, it is necessary to average the measurements of at least 10 consecutive complexes in order to rely on the accuracy of the results. This requires a longer strip than taken by the usual technic.

The 3 standard and 1 apical precordial leads are not most suitable for observing the results. Although changes in rhythm or the duration of P-R or QRS should be evident in any lead, changes in S-T and T are most frequently evident and most striking in the unipolar right arm lead and the apical precordial lead. If a single lead were to be used, as would seem advisable, lead 4R, in which potentials in the right arm and in the apical lead are summated, would be more likely to demonstrate changes than any of the 4 leads currently employed.

4. Theoretic considerations. The tables describing the number of trips to be performed were originally used as a test of myocardial or circulatory efficiency and represent the amount of work that normal subjects could perform in 1½ minutes with a return of pulse and blood pressure to the resting level within 2 minutes after the cessation of exercise.\textsuperscript{17} It is questionable if the amount of work that has proved useful in measuring myocardial efficiency is the same as that necessary to measure coronary sufficiency. In fact, the frequent necessity of doubling the work suggests that the prescribed amount of work has no sound physiologic basis in coronary artery disease.

In the published reports, the criteria distinguishing normal from abnormal responses differ depending on whether one uses as the upper limit of normal the maximum changes observed in normal persons\textsuperscript{18} or if one uses the lower limit of abnormal, as changes commonly observed in patients with angina pectoris.\textsuperscript{10} If the former is used, a large number of patients with angina pectoris will have negative tests. If the latter is used, it is probable that abnormal results might be obtained in some normal subjects. It is not surprising that considerable overlapping occurs. Muscular contraction is an anaerobic phenomenon, oxygen being used for recovery; muscular contraction in all subjects results in some degree of anoxia or local oxygen debt.

Reproducibility. Electrocardiograms taken continuously during and following exercise that induces angina pectoris show rapidly progressive changes. Immediately after the
cessation of exercise, within 15 seconds, S-T depression is most common and most striking; later, progressive T wave changes become more evident. In publications that show 2 or more complexes in each of the 4 leads, the heart rate is considerably slower in the leads obtained toward the end of the test. This change indicates that an appreciable amount of time must have elapsed between obtaining the earlier and the later leads, and, therefore, the results are not comparable. Furthermore, it would be extremely difficult to repeat the test and obtain each of the 4 leads at identical times in the 2 tests.

In addition to the technical difficulties described above, even slight shifting of the precordial electrode in relation to the heart during the test may result in S-T and T changes unrelated to anoxia.

These technical considerations make it difficult to reproduce identical results in a given patient. In order to get results that are reliable and comparable, it is necessary to use either a multichannel electrocardiograph or take only 1 lead at a definite time (preferably within 15 seconds) after the cessation of exertion.

**False Negative Tests.** These are accepted as a necessary limitation of the general value of the test. The fact that the test does not give positive results in all patients with angina pectoris decreases the value of the test, but does not completely invalidate it. Unfortunately, when such tests were first described, before this limiting factor was appreciated, negative results had been accepted as proving the absence of heart disease. In at least 1 case where anoxia was used to induce electrocardiographic changes, the lack of change was made the basis for recommending discontinuance of insurance disability benefits.

**False Positive Tests.** Because of their clinical and emotional implications, false positive tests seriously limit the value of the test. While they have not been reported frequently, “Unfortunately, in a very emotionally unstable person, electrocardiographic abnormalities may appear even in such an objective examination as the ‘2-step’ exercise electrocardiogram or the 10 per cent oxygen test.” The recommendation that ergotamine derivatives be used to differentiate between the positive results seen in psychoneurosis from those observed in patients with coronary artery disease indicates that false positive tests occur in this important situation, where an accurate test is so urgently needed. As stated above, control studies in a series of normal adults over 50 years of age are in order.

**Safety.** If the test is not performed in patients with known coronary artery disease, such as those with previous myocardial infarction or those whose resting electrocardiograms are abnormal, it is undoubtedly as safe as any procedure carried out in patients with angina pectoris. However, if the test is limited to those cases where the diagnosis is in doubt, it will be of little value. A test that gives negative results in a high percentage of patients with undoubted angina pectoris and gives positive results in an unknown percentage of subjects without coronary artery disease cannot be relied on in the borderline cases where it is most needed.

**Summary**

The diagnosis and differential diagnosis of angina pectoris depend on obtaining an adequate history. Problems in diagnosis arise because of confusion of terminology, language difficulties, symptoms resembling noncardiac disease or vice versa, and the coexistence of angina pectoris with disease of other organs. Problems in differential diagnosis arise because symptoms resembling angina may result from disease or abnormal function of the brain, skeletal system, gastrointestinal system, or structures in the bony thorax or within the thoracic cage. The most difficult problems in differential diagnosis arise from psychoneurosis and gallbladder disease. Careful history taking will resolve the problem in most instances, prolonged observation will settle the question in others. To date, no objective tests have been adequate to determine whether or not the patient is subject to attacks of pain due to the physiologic effects of coronary artery pathology or dysfunction.

**Summario in Interlingua**

Le diagnose e le diagnose differential de angina de pectore depende del obtention de un
historia adequate. Problemas diagnostic se subleva a causa de confusion terminologic, difficulties linguistic, similitude de symptomas in angina de pectore e morbo non-cardiac, e le coexistencia de angina de pectore con morbos de altere organos. Problemas del diagnose differential se subleva proque symptomas de apparentia associabile con angina pote resultar de dysfunction o de morbo del cerebro, del sistema skeletal, del sistema gastrointestinal, e de structuras in le thorace osse e intra le cavia thoracie. Le plus difficile problemas del diagnose differential resulta ab psychoneurosis e morbo del vesica biliari. Grande attention prestate al historia del paciente individual va resolver le problema in le majoritate del casos; observationes pro- longate va resolver lo in alteres. Al tempore presente il non ha un test objective que es demonstramente adequate pro determinar si o non le paciente suffre de attaccos de dolor que resulta del efectos physiologic de pathologia del arteria coronari o de dysfunction.

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