Intermediate Coronary Syndrome

By Rustom Jal Vakil, M.D.

Severe or intractable chest pain, associated with sweating, vomiting, precipitate fall of arterial blood pressure, fever, and evidence of shock or collapse, clearly indicates a diagnosis of acute myocardial infarction. In marked contrast is the entity of angina pectoris, with its paroxysms of chest pain after effort, typical radiation of pain into the arm, feeling of viselike constriction in the chest, and prompt response to rest and nitroglycerin.

Between these two major forms of coronary heart disease is a wide and ill-defined zone, made up of many heterogeneous groups, but with the common denominator of pain, usually intermediate in severity and duration between that of angina pectoris and acute myocardial infarction. Characterized typically by one or more bouts of prolonged chest pain, each lasting from 15 minutes to several hours, an equivocal or poor response to rest and nitrites, usually unrelated to physical effort, and, as a rule, unassociated with peripheral vascular collapse, congestive cardiac failure, pulmonary edema, sustained fever or auscultatory abnormalities, this intermediate form of coronary attack is seldom if ever accompanied by evidence of gross myocardial damage, such as high values of serum glutamic oxaloacetic transaminase and erythrocyte sedimentation rate, leukocytosis, and pathologic Q or QS patterns in the electrocardiogram.

In the past, an attack of this type was indiscriminately classified either with angina pectoris or with acute myocardial infarction and designated by various terms including the following: atypical or anomalous angina; severe angina; angina of rest; angina decubitus; angina major; false angina;1 forme fruste or spasmodic angina; the prodromal, precursor, premonitory,2–6 impending,7–8 preliminary,9 ischemic or formative phase of myocardial infarction; "infarction without infarction," "slight coronary attack,"10 "subendocardial infarction," "premonitory period,"12 or "ambulatory form" of myocardial infarction.11

Despite the contention of Yater and associates12 that, since any given attack of angina on effort or rest may be the premonitor of a coronary attack, the "premonitory phase" of acute coronary occlusion is much too vague and intangible an entity to warrant attention, recent studies tend to confirm the existence and high incidence of a distinct entity, clinically intermediate between angina and acute infarction.13–15 Attention was first directed to this type of pain as a distinct entity in 1937 by Sampson and Elasier7 and Feil.9 Numerous small groups of cases of this type have been reported sporadically thereafter.

Since the terms coronary failure14,15 and coronary insufficiency16–22 are equally applicable on theoretical grounds to the syndromes of angina pectoris and myocardial infarction, these also being examples of failure or insufficiency of the coronary circulation, and since the term "coronary insufficiency" has been used indiscriminately in the past to include a variety of different entities, there is obvious need for a more suitable designation. The term "intermediate coronary syndrome," recommended independently in 1951 by Graybiel23 in the United States, and by Vakil24–26 in India, has proved acceptable to many, emphasizing as it does the "intermediate" character of the syndrome.

Because of the great tendency for these attacks to turn into classical episodes of myocardial infarction, and with a view to encourage attempts at prophylaxis, the alternative designation of "prethrombotic syndrome"
Figure 1

Figure 2
Types of S-T depression not encountered, as a rule in myocardial ischemia. A. Curvilinear depression with upward bowing and symmetrically inverted T wave (common as reciprocal depression in infarction cases). B and C. Downward sloping or curvilinear S-T with upward bowing and asymmetrical T (in left ventricular hypertrophy or strain and intraventricular conduction defects). D. Straight RS-T directed obliquely downwards and merged with an asymmetrically inverted T (as in digitalis effect).

was recommended, in 1951, and has been accepted rather widely in the Eastern countries. However, since the intermediate coronary syndrome probably follows episodes of further coronary artery narrowing or occlusion, but precedes myocardial infarction, the term "preinfarction syndrome" may prove more acceptable to many.

Even the most obdurate and uncooperative patient, when forewarned of an impending attack of coronary thrombosis (by use of the prefix "prethrombotic" or "preinfarction"), is as a rule willing to accept any drastic restriction of activity or therapeutic regimen imposed by the physician. This term also alerts the physician in charge to the possibility of infarction in the near future. In a series of cases of coronary thrombosis, recently observed by the author, the incidence of the "premonitory" syndrome of pain was 39 per cent. The high incidence, in the case of acute myocardial infarction, of a preliminary phase of chest pain antedating the infarction by days, weeks, or months, is now accepted universally on the basis of a well-founded body of evidence. The importance of recognizing the entity lies in the prophylactic potentialities of early and appropriate therapy directed against imminent infarction. What is not sufficiently realized today is that the same syndrome of pain can arise in the course of any case of coronary atherosclerosis, with or without a history of angina or infarction, and may or may not develop into a classical attack of acute myocardial infarction. Studies by Blumgart and associates on the effects of temporary occlusion of coronary arteries in animals have shown that the duration and severity of hypoxia of the myocardium are both important in determining whether the effects on the heart muscle shall be transient and reversible, as in the intermediate coronary syndrome or irreversible and associated with necrosis as in acute myocardial infarction.

The terms "intermediate," "prethrombotic," or "preinfarction" coronary syndrome, as used here, imply prolonged chest pain of cardiac origin, usually intermediate in intensity, duration, and character between that of angina pectoris and acute myocardial infarction, with a duration of from 15 minutes to several hours, bilateral or unilateral in distribution, with or without radiation, usually arising at rest, somewhat refractory to nitrite therapy, hardly ever associated with signs of shock, congestive heart failure, pulmonary edema, or gross myocardial necrosis (such as leukocytosis, high erythrocyte sedimentation rate, and serum glutamic oxaloacetic transaminase values, and sustained pyrexia), almost invariably accompanied by electrocardiographic manifestations of myocardial ischemia, and terminating either in recovery or an attack of acute myocardial infarction. Since the electrocardiographic signs of my-
INTERMEDIATE CORONARY SYNDROME

Figure 3
Electrocardiograms of a 53-year-old man with hypertension and severe chest pain. Marked “horizontal sagging” or transverse depression of RS-T segments in leads I, II, V3, V4, V5, and V6. Anterolateral myocardial ischemia. High voltage of QRS in V leads suggest left ventricular hypertrophy. Another electrocardiogram 3 days later showed restoration of RS-T segments to isoelectric levels.

Figure 4
Electrocardiograms of a 43-year-old woman, with diabetes and obesity. Severe chest pain of 3 hours' duration at the time of record. Shallow transverse depression of RS-T segments in leads I, II, aVL, and V4, to V6 with left axis deviation and small T waves. Anterolateral myocardial ischemia. Complete clinical and electrocardiographic recovery within 12 hours.

Cardiac ischemia are usually observed best in the precordial leads, their recognition has been necessarily recent, after the routine introduction of Wilson's technic of extensive exploration of the anterior chest wall. The electrocardiographic signs of the syndrome, now fairly well defined, are usually of anterior wall myocardial ischemia. The present investigation is a correlation of clinical and electrocardiographic data in 251 personally observed cases of the "intermediate coronary syndrome." It attempts to investigate the incidence, clinical features, electrocardiographic manifestations, laboratory findings and clinical course in a fairly large and representative series of cases of the syndrome.

Material and Method
The subjects of this study were 251 cases of intermediate coronary syndrome selected over a 10-year period from the author's consultative practice. Certain rigid criteria were carefully observed in their selection: (1) prolonged and characteristic chest pain of more than 15 minutes' duration; (2) absence of clinical, laboratory, and electrocardiographic evidence of gross myocardial necrosis (e.g., high or sustained pyrexia, leukocytosis, high serum glutamic oxaloacetic transaminase, high values of C-reactive protein or erythrocyte sedimentation rate, and Q or QS patterns in the electrocardiogram); (3) evidence of electrocardiographic signs of myocardial ischemia at some time during the course of illness; (4) availability of two or more 12- to 16-lead electrocardiograms during the period of observation; (5) a personal follow-up of each case of at least 3 months. Approximately 980 electrocardiographic tracings were examined in the study, and the period of follow-up ranged from 3 months to 10 years.

All doubtful cases, cases free of pain (even though associated with so-called "pain equivalents," such as dyspnea, vomiting, or exhaustion), patients with inadequate investigation or follow-up, and cases that failed to fulfill the aforementioned criteria, were excluded from the investigation. Thus, of 364 possible cases of the syndrome, only 251 were selected for study; the others proved to be cases of transmural infarction, acute pericarditis, rheumatic pancreatitis, heart strain, pulmonary embolism, tobacco angina, hiatus hernia, gastrocardiac syndrome, psychoneurosis, and pheochromocytoma.

Clinical Data
Clinical Masquerades
Over 90 per cent of cases of the intermediate coronary syndrome had been incor-
Table 1

Occupational Classification of 216 Male Cases of Intermediate Coronary Syndrome

<table>
<thead>
<tr>
<th>Occupational class</th>
<th>Case numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>I  Executive or managerial</td>
<td>49</td>
</tr>
<tr>
<td>II Professional (e.g., doctors)</td>
<td>57</td>
</tr>
<tr>
<td>III Semi-professional (e.g., technicians)</td>
<td>20</td>
</tr>
<tr>
<td>IV Skilled workers (e.g., armed forces)</td>
<td>41</td>
</tr>
<tr>
<td>V  Semi-skilled workers (e.g., mechanics)</td>
<td>30</td>
</tr>
<tr>
<td>VI Unskilled workers (e.g., mill-hands)</td>
<td>16</td>
</tr>
<tr>
<td>VII Unemployed</td>
<td>3</td>
</tr>
</tbody>
</table>

216

Table 2

Incidence of Important Pre-existing Diseases in 251 cases of Intermediate Coronary Syndrome

<table>
<thead>
<tr>
<th>Etiologic factors</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>36.8</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>50.4</td>
</tr>
<tr>
<td>Obesity</td>
<td>28.4</td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>5.2</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>4.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13.6</td>
</tr>
</tbody>
</table>

Family History

Dependable information about parental health was obtainable in 182 cases, a history of coronary heart disease in one or both parents was present in 22 per cent. In a comparative series of 200 normal subjects free of coronary disease, the parental incidence of coronary disease was 6 per cent.

Racial Incidence

In view of the gross inequality of representation of various racial groups in the author's consultative practice, a correct appraisal of this factor was considered not possible and was abandoned.

Occupational Factors

The relatively higher incidence of coronary disease in executive and professional classes, as noted previously, was confirmed in this series (table 1).

Pre-existing Conditions

Evidence of past hypertension, previous attacks of myocardial infarction, angina pectoris, and noncardiac ailments was frequent (table 2).

Precipitating factors were frequent, though less frequent and less well defined than in the case of acute myocardial infarction. Of the numerous factors incriminated, the most important were excessive or unusual physical or mental activity, overeating, long journeys, acute hemorrhages, and drugs (particularly insulin and ganglion-blocking agents).

Clinical Analysis of Pain

Of the numerous symptoms reported, the most constant by far was that of pain, which was noted in every case. Although attacks of preinfarction syndrome free of pain are theo-
subjectively possible, an analytical study of the pain is pro-verbially difficult because of the great effect of drugs given by the attending physician.

**Site of Pain**

In over 65 per cent of cases, the pain was located in the center of the chest, either retrosternally or just to the left or right of the sternum. In 9 per cent, it was reported as diffuse and bilateral, and in 5 per cent as precordial or left mammary. In the remaining 24 per cent, the pain was located anomalously, either in the back, epigastrium, shoulder, arm, elbow, or wrist (usually left) or both arms, lower jaw, neck, tongue, or ear. In one case the pain was confined to the back of the tongue, throughout successive episodes of angina pectoris, intermediate coronary syndrome, and myocardial infarction.

**Radiation of Pain**

The intermediate coronary syndrome showed radiation of pain in 45 per cent of cases, which was less frequent and less diffuse than in myocardial infarction. Radiation to both arms or shoulders was observed in 24 per cent, to the left arm in 13 per cent, right

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**Figure 5**

Electrocardiogram of a 34-year-old man with chronic cholecystitis and obesity. Severe aching of left arm on and off for 3 days before examination. Top. Deep T-wave inversions in leads V₁, V₂, and V₃ as isolated abnormalities. Septal localization of myocardial ischemia. Bottom. Electrocardiogram, 3 days later, shows return to normal patterns.
arm in 4 per cent, epigastrium in 7 per cent, back in 9 per cent, and lower jaw or throat in 4 per cent.

Types of Pain

Although many types of chest pain were described by patients, they were grouped in three main types: "angina-like" pain, "infarction-like" pain, and "anomalous" or "ill-defined" pain. The angina-like pain, particularly common in those with a history of past angina, was similar to that of classical angina but showed longer duration (from 15 minutes to 2 hours), greater intensity, wider radiation, atypical character (aching, burning, or lancinating), greater frequency, tendency to arise during rest or sleep and little or no response to nitrites.

The infarction-like pain, was comparatively much more prolonged, less frequent, occurred during exercise or rest, was frequently referred to both arms, back, or epigastrium, displayed a "crescendo" character, and was usually described as "weight-like," "vice-like," "crushing," or "boring," in character. More than three bouts of this type of pain were not observed in any case. In some of the more severe cases, repetitive bouts of angina-like pain were associated with one or two bouts of more prolonged infarction-like pain.

The anomalous or ill-defined type of pain was readily recognized when it was associated with one of the more characteristic types of pain; when it occurred alone, it proved a source of great diagnostic confusion. It was described as a precordial ache or oppression (at times associated with local tenderness), a sharp and repetitive pricking pain in the left mammary or inframammary region, a persistent heart burn, an ache in the shoulder or wrist, or a high interscapular pain. For days, at times, the pain was dismissed as neurotic or osteoarthritic in origin. The crescendo character and aching or burning nature of the premonitory pain were confirmed in a fair percentage of cases.

Number of Attacks of Pain

The number of attacks of chest pains was extremely variable, ranging from one solitary bout of prolonged pain to over 250 paroxysms of angina-like pain. In some, angina-like pains of increasing severity, duration, and frequency were observed for days at a time, with a final, severe, and prolonged bout of infarction-like pain lasting from 4 to 40 hours.

Relieving Factors

Although the response to nitroglycerin or analgesic tablets was poor in most cases, a minor degree of relief was sometimes experienced after these measures. In the great majority, relief occurred either spontaneously or after the parental administration of an opiate.

Accompanying Symptoms

Associated with pain in the chest were many other symptoms, the most frequent being fatigue or exhaustion, dyspnea, palpita-
tion, aching of the arm, backache, epigastric discomfort, missing of beats, aerophagy or excessive flatulence, nausea, dizziness, "choking," peripheral sensory manifestations (such as tingling or "pins and needles"), vomiting, and sweating.

**Physical Findings**

Clinical examination of the heart, even at the height of pain, was surprisingly devoid of abnormal signs. Apart from frequent disturbances of cardiac rate and rhythm, occasional low-grade systolic murmurs at the base or apex, and rare instances of "bruit de gallop," there were no signs of heart disease. Initial rises of blood pressure, of from 10 to 90 mm. Hg systolic and 5 to 40 mm. diastolic, were observed during the bouts of pain in the majority of cases, later to be followed by normal or somewhat low levels. In some cases, paradoxical falls of blood pressure (systolic, diastolic, or both) of from 5 to 50 mm. systolic and 5 to 20 mm. diastolic were noted from the very outset of pain. The highest pressures recorded in the present series were 228 mm. systolic and 130 mm. diastolic. Mild rises of body temperature of 1 to 2 F. and lasting for 1 to 6 days were noted in about 12 per cent of cases. No examples of sustained or high pyrexia were encountered except for one case in which fever of over 103 F. for 2 or 3 days resulted from an upper respiratory virus infection.

**Laboratory Findings**

The total and differential white blood counts were normal in 72 per cent of cases. The remainder showed slight leukocytosis (usually less than 9,500 cells). The erythrocyte sedimentation rate, usually normal, was raised slightly (20 to 35 mm. at the end of 1 hour) in 23 per cent; and the C-reactive protein content was elevated (1 or 2 plus) in 20 per cent of cases. Of 52 cases, in which the serum glutamic oxaloacetic transaminase value\textsuperscript{32} was estimated, 33 showed values below 40; the remainder, values of from 40 to 79. The laboratory findings were of value in ruling out gross degrees of myocardial necrosis or damage.
Figure 8

Electrocardiogram of a 68-year-old man with hypertension (200/120), obesity, and anginal pains. Record, taken during a prolonged bout of anginal pain, shows coverying of RS-T segments with diphasic T waves in leads V2, V3, and V4, sharp and deep inversions of Tin aVL and V2, and shallow inversions of T in lead I and V6. Two months later, patient had a more severe bout of pain, resulting in an extensive anterior wall myocardial infarct.

vascular, embolic, and peripheral vascular complications were not observed in any cases. Peripheral failure or shock, with sudden drop of blood pressure, thready pulse, and cold and clammy extremities, were not observed in the entire series. Attacks of angina pectoris were experienced by 40 per cent of the patients, even after subsidence of acute episodes of premonitory pain.

Electrocardiographic Data

Despite a massive literature on the subject of electrocardiographic manifestations of coronary insufficiency, there is little unanimity of opinion regarding the incidence or nature of abnormalities. Electrocardiographic abnormalities, suggestive of myocardial ischemia were noted in every case of the present series, over 900 electrocardiograms having been recorded during the period of observation. It has been our experience that electrocardiographic signs of myocardial anoxia are always present in such cases, provided 12 to 16 leads are recorded during or just after the painful episodes. The absence of electrocardiographic abnormalities reported in earlier series may be due either to lack of serial electrocardiographic study or improper exploration of the anterior chest wall. Besides standard chest leads, high anterior and posterior leads were frequently necessary in doubtful cases. Electrocardiographic manifestations of myocardial ischemia may either antedate or form an integral part of the early phase of an acute myocardial infarction.

The electrocardiographic picture of intermediate coronary syndrome, although apparently similar to that of fresh myocardial infarction, is usually distinguishable by the following points: (1) the entire sequence of events or “temporal course of evolution” is far more rapid, being a matter of hours or days rather than weeks or months; (2) lack of involvement of the QRS complex; (3) lack of reciprocal changes in the ST-T segments, with most leads showing downward displacement.

Characteristic ST-T Patterns

Certain characteristic types of ST-T complex configuration were observed (either singly or in combination) in every case of the present series (figs. 1 to 12).

Type I

A horizontal trough-like depression or sagging of the RS-T segment, deep or shallow, was observed in over 92 per cent of all records (figs. 1A and B) and was frequently associated with an upright and symmetrical, short or tall, peaked T wave and a deep S

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Electrocardiograms of a 58-year-old man with chronic hypertension and obesity. Record taken during an attack of prolonged chest pain, shows in addition to a pattern of left bundle-branch block, marked horizontal "sagging" or depression of the RS-T segment, particularly in leads V₄ and II. After subsidence of pain, the RS-T segments returned to original levels.

Wave. At times, the S-T depression showed an obliquity upwards (fig. 1D) or a curvilinear or crescent shape with downward convexity (fig. 1C). Depression of S-T segments was particularly frequent in leads I, II, aVL, and V₄ through V₆ (fig. 3).

The S-T depression was seldom accompanied by reciprocal S-T elevation, as in the case of acute myocardial infarction, except when associated with left ventricular hypertrophy, left-sided heart strain, or bundle-branch block.

Type II

Isolated T wave negativity (fig. 1E and F). Inversion of the T wave in one or more leads, usually of the midprecordial series (V₂, V₃, and V₄), was encountered in 40 per cent of cases. Such changes have already been described as evidence of local myocardial ischemia. Transitory inversion of the T wave, whether deep or shallow, was usually confined to one to three leads but occasionally was diffuse enough to appear in most leads. Other noteworthy features of this type of tracing (fig. 7) were no displacement of the S-T segment and a symmetrical configuration of the T wave with a peaked apex and rounded shoulders. The degree of T-wave inversion often varied from time to time, even in the same case.

T-wave negativity does not necessarily imply myocardial ischemia unless it is transitory and associated with confirmatory symptoms and signs. Persistent or progressively increasing negativity of the T wave, besides being a rare physiologic variant, may be indicative of myocardial infarction.

Type III

Coving of RS-T segment with diphasic or inverted T wave (fig. 1A). Somewhat similar to early ST-T configuration of classical myocardial infarction, this type of electrocardiographic pattern was encountered as a transitory event in 12 per cent of cases, the lead most frequently affected being the midprecordial lead V₃ (fig. 7). The complex usually displayed a high take-off with prominent coving or upward convexity of the RS-T segment and
Table 3

Localization of Myocardial Ischemia in 251 Cases of Intermediate Coronary Syndrome

<table>
<thead>
<tr>
<th>Localization</th>
<th>Leads involved</th>
<th>Case numbers</th>
<th>Percentage incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Anterolateral</td>
<td>V₄ to V₆, I, aV₄, and high V leads</td>
<td>65</td>
<td>26</td>
</tr>
<tr>
<td>2 Anteroseptal</td>
<td>V₁ to V₂ and V₆</td>
<td>24</td>
<td>9.6</td>
</tr>
<tr>
<td>3 Extensive anterior wall</td>
<td>V₁ to V₆, I, aV₆, VE, and high V leads</td>
<td>37</td>
<td>14.8</td>
</tr>
<tr>
<td>4 High anterolateral</td>
<td>I, aV₄, and high V leads</td>
<td>8</td>
<td>3.2</td>
</tr>
<tr>
<td>5 Localized anterior or anteroapical</td>
<td>V₂ and V₄</td>
<td>14</td>
<td>5.6</td>
</tr>
<tr>
<td>6 Posterior wall</td>
<td>II, III, aV₆, and Oe*</td>
<td>12</td>
<td>4.8</td>
</tr>
<tr>
<td>7 Posterolateral</td>
<td>II, III, aV₆, V₅, and Oe*</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>8 Posteroseptal or posteroinferior</td>
<td>II, III, aV₆, VE and Oe*</td>
<td>12</td>
<td>4.8</td>
</tr>
<tr>
<td>9 High posterolateral</td>
<td>I, aV₄, V''6 to V''9</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>10 Global or diffuse (anterior and posterior wall)</td>
<td>I, II, III, aV₆, aV₆, V₁ to V₆</td>
<td>23</td>
<td>9.2</td>
</tr>
<tr>
<td>11 Successive anterior and posterior or vice versa</td>
<td>——</td>
<td>11</td>
<td>4.4</td>
</tr>
<tr>
<td>12 Miscellaneous and indeterminate forms</td>
<td>——</td>
<td>28</td>
<td>11.2</td>
</tr>
</tbody>
</table>

*Esophageal leads.

Table 4

Frequency of Electrocardiographically Observed Arrhythmias in 251 cases of Intermediate Coronary Syndrome (980 Electrocardiographic Records)

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Number of cases</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus tachycardia</td>
<td>57</td>
<td>Atrial fibrillation 3</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td>9</td>
<td>Flutter fibrillation 1</td>
</tr>
<tr>
<td>A-V nodal rhythm</td>
<td>2</td>
<td>S-A block 1</td>
</tr>
<tr>
<td>A-V nodal escape</td>
<td>2</td>
<td>A-V block 10</td>
</tr>
<tr>
<td>Wandering pacemaker</td>
<td>1</td>
<td>First degree 8 cases</td>
</tr>
<tr>
<td>Premature systoles</td>
<td>44</td>
<td>Partial or complete 2 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intraventricular conduction defects 14</td>
</tr>
<tr>
<td>Atrial</td>
<td>5 cases</td>
<td>Right bundle-branch block 8 cases</td>
</tr>
<tr>
<td>Nodal</td>
<td>3 cases</td>
<td>Left bundle-branch block 2 cases</td>
</tr>
<tr>
<td>Ventricular</td>
<td>36 cases</td>
<td>Arborization block 4 cases</td>
</tr>
<tr>
<td>Paroxysmal tachycardia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Supraventricular</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Ventricular</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Associated Findings

Some of the records also showed abnormalities of the QRS complex, such as prominent S wave, small or absent R waves (particularly in the right precordial leads), and rarely pathologic Q waves in one or two of the anterior or posterior leads.¹⁰

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a large, diphasic or inverted T wave. The transitory nature of the abnormality, absence of associated QRS involvement, and lack of reciprocal ST-T segment changes are usually sufficient to rule out acute myocardial infarction and to suggest myocardial ischemia instead.
Differential Diagnosis

Non-specific abnormalities of the ST-T complex, may be due to causes other than myocardial ischemia, such as ventricular strain, intraventricular block, digitalis effect, and thyrotoxicosis (fig. 2). The characteristic features of each type of ST depression, however, usually permit differentiation of the different varieties. In ventricular strain or intraventricular block, the ST-T complex is usually displaced opposite to the main QRS deflection, the RS-T segment is bowed or convex upwards whenever it is depressed, and the two limbs of the T wave are unequal or asymmetrical. In case of digitalis effect, the ST depression displays a downward slope and the T wave is grossly asymmetrical, with a long downstroke and a short upstroke. In thyrotoxicosis, besides horizontal sagging of the RS-T segment, there are present marked depression of the P-R segment, tall P waves and sinus tachycardia. In contrast, the ST depression of intermediate coronary syndrome is usually deeper, wider, more horizontal, and trough-like, and the T wave is peaked or pointed, symmetrical, and directed upwards, in a direction opposite to the S-T segment.

Localization of Myocardial Ischemia

Although infarction of the anterior wall is somewhat commoner than that of the posterior wall, the relative incidence of anterior wall ischemia (to posterior wall ischemia) is even higher. On the basis of distribution of ST-T abnormalities, the localization of myocardial ischemia was delineated (table 3): anterior wall ischemia (148 cases) was observed about 3.5 times as frequently as posterior wall ischemia (41 cases) in the present series.

Cardiac Arrhythmias

Besides the characteristic ST-T patterns of myocardial ischemia, transitory or persistent abnormalities of cardiac rate, rhythm, or conduction were also observed in some cases (table 4).

Stabilization of Electrocardiogram

A complete restoration of the electrocardiographic patterns to normal was observed in 98 cases, the restoration being effected in less than 24 hours in 18 cases, in 1 to 7 days in 38 cases, 1 to 4 weeks in 34 cases, and 1 to 3 months in eight cases, the average for the whole group being 7 days. In some of the cases, there were recurrences of myocardial ischemia with recurrent bouts of chest pain. In those cases in which acute myocardial infarction supervened, the electrocardiographic pattern of ischemia changed to one of infarction, either directly or more often after a normal phase.

Discussion

Recent work suggests that the syndrome is "at least half as common as acute transmural myocardial infarction" and represents the "third most important category of coronary heart disease," being next in importance only to coronary thrombosis and angina pectoris. The pathogenesis of the syndrome is also
Electrocardiogram of a 38-year-old man with typical intermediate coronary syndrome. The record, taken at the height of pain, shows paroxysmal supraventricular tachycardia with depression of RS-T segments in anterior and posterior wall leads. Eighteen days later, the patient had a typical attack of myocardial infarction with posterior wall myocardial damage.

Far from clear. According to Mounsey, the prodromal pain of myocardial infarction is due to the "gradually decreasing lumen of a coronary artery," irrespective of the nature of the occlusive process. Papp and Smith regarded "small intramural or patchy subepicardial infarctions" as likely causes of "slight coronary attacks." The average of two or more occlusions in the main branches of the coronary arteries, as demonstrated by Blumgart et al. in cases of angina pectoris, has revolutionized our concepts of coronary artery disease. On the basis of their work, it would be reasonable to assume the existence of similar, silent occlusions of the coronary vessels in cases of the intermediate coronary syndrome.

The entity of subendocardial infarction has assumed great importance in recent years, thanks to the widespread employment of unipolar chest leads. Recent studies confirm the existence of myocardial infarcts localized to the subendocardial layers of the myocardium (much less common than transmural infarcts) secondary to coronary occlusion or acute coronary insufficiency, and associated with persistent and characteristic depressions of the ST-T complex without involvement of QRS. Of the many cases of "myocardial infarction without acute coronary occlusion" or "nonocclusive acute coronary insufficiency with infarction," studied by Miller et al., 82 per cent were subendocardial. In another group of myocardial infarctions, the incidence of subendocardial infarctions was only 11 percent.

Among the pathogenetic mechanisms suggested for the intermediate coronary syndrome are partial or complete occlusion of a coronary vessel by a thrombus, subintimal hemorrhage, atheromatous plaque, scar, or vasospasm.

In this era of scientific electrocardiography, when practically all electrocardiographic phenomena are explainable in terms of physical or physiochemical theory, the erratic or aberrant behavior of the ST-T complex continues to offer a challenge. Similar abnormalities of the S-T segment or T wave may be noted under widely dissimilar circumstances as in acute or chronic coronary insufficiency, subendocardial infarction, myocarditis, digitalis effect, ventricular strain, and intraventricular conduction defect. While one patient...
with marked RS-T depression or inverted T wave may be completely symptomless, another with an identical tracing may be moribund.

The causes of S-T depression are many. Depression of the segment may be either spontaneous or induced after exercise or anoxemia. The former may be evanescent as in angina pectoris, transitory as in acute coronary insufficiency, or persistent as in subendocardial or intramural infarction, early phase of transmural infarction, ventricular strain, or intraventricular conduction defect. Prolonged depression of RS-T segment without involvement of QRS, even when of coronary origin, may mean either an acute coronary insufficiency without infarction, a subendocardial or intramural infarct, or the early stage of evolution of a transmural infarct. The clinical picture in conjunction with the electrocardiographic tracing and a short-term follow-up frequently provides the desired clue for diagnosis.

Differential diagnosis of the intermediate coronary syndrome from angina pectoris or coronary thrombosis frequently requires a close observation of the patient for 7 to 10 days, with dependence on a careful history, serial electrocardiographic exploration, and repeated examinations of the blood. A correct diagnosis often depends on a correct appraisal of the various characteristics of the syndrome:13-15 (1) pain, usually intermediate between that of angina and myocardial infarction; (2) little or no alteration of blood pressure; (3) absence of clinical, laboratory, and electrocardiographic signs of myocardial necrosis; (4) absence of shock, embolization, and cardiac decompensation; (5) characteristic S-T depression or T-wave inversion without reciprocal elevation; (6) evidence of myocardial ischemia (usually) of the anterior heart wall; and (7) an uncomplicated recovery as a rule but with a subsequent tendency to infarction.

Regarding prognosis, most reports justify an outlook of optimism. In the present series, there were two deaths, one presumably from ventricular fibrillation and the other from acute pulmonary edema. Apart from an occasional fatality, therefore, the immediate outlook of cases of this syndrome can be regarded as good, provided acute myocardial infarction does not supervene sooner or later, as in 91 of the 251 cases of the present series, who developed infarction within 3 months of onset of preliminary pain. The role of rest and anticoagulant therapy as prophylactic agents against infarction, forms the subject of another study.

Summary and Conclusions

A clinical material of 251 cases of the "intermediate," "preinfarction," or "prethrombotic" "coronary syndrome" diagnosed on the basis of certain well-defined criteria and observed in consultative practice, forms the subject matter of this paper.

Each case was subjected to clinical, laboratory, and electrocardiographic investigation. Most of the cases had "infarction-like" or "angina-like" pains of moderate severity, in-
significant alterations of pulse rate and blood pressure, little or no rise of temperature, and no evidence of shock, congestive cardiac failure, or gross myocardial necrosis. Characteristic electrocardiographic patterns of myocardial ischemia were observed in all cases. Ninety-one of the cases developed acute myocardial infarction within 3 months of the initial attack of pain.

Of the 980 electrocardiograms, recorded during the course of the investigation, the great majority showed either markedly depressed, "trough-like" S-T segments, isolated deep or shallow inversions of T waves, or "coving" of S-T segments with diphasic or inverted T waves. Anterior wall involvement (particularly of anterolateral type) was encountered far more often than posterior. Electrocardiographic restoration to normal was prompt and complete in most instances.

On the basis of this study, the intermediate coronary syndrome appears to be a fairly common, recognizable clinical entity, usually self-limited but with a proclivity to develop acute myocardial infarction in the near future.

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INTERMEDIATE CORONARY SYNDROME


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Intermediate Coronary Syndrome
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