Electrocardiographic Changes During Selective Coronary Cineangiography

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Selective coronary angiography is being used with increasing frequency for clinical diagnosis in several forms of heart disease. Except for the works of Ross,1 Hale and Jefferson,2 and Lehman and associates,3 there have been no detailed reports in the literature about the electrocardiographic changes accompanying the injection of radiopaque media selectively into the coronary arteries of man. The purpose of this paper is to report the electrocardiographic changes observed in our series of selective coronary angiograms.

Methods

Between July 1, 1963, and December 31, 1964, selective coronary cineangiograms were made in 145 cases at the Center for the Health Sciences of the University of California at Los Angeles. In 107 of this series of 145 cases, technically satisfactory electrocardiographic recordings were obtained during the angiographic examination. These 107 records form the basis of this study. In the great majority of cases the indication for coronary angiography was evaluation of clinical or suspected coronary artery disease. There were, however, a significant number of cases of other types of heart disease such as valvular disease (principally aortic stenosis) and idiopathic myocardial infarction.

The percutaneous technique employed for selective coronary angiography has been reported in detail.1 Briefly, the right axillary artery was punctured percutaneously and a Sones catheter was introduced by a modified Seldinger technique. In all of the examinations, Hypaque-M 75% (sodium diatrizoate 25%, methylglucamine diatrizoate 50%) was used as the contrast agent employed. The usual injection was 3 to 4 cc of this contrast material, and it was introduced directly into the orifice of each main coronary artery. Repeated injections were made until satisfactory visualization of each coronary artery was obtained on the image intensifier and recorded on 35-mm motion picture film at 60 frames per second, or until it was decided that further attempts at coronary visualization would not be fruitful. Occasionally, when it was not possible to catheterize the coronary artery selectively, aortic valve cusp injections with 10 to 15 cc of contrast material were made in an attempt to visualize the coronary arteries.

In 91 patients contrast medium was injected selectively into each main coronary artery, and these records were used to determine the changes in QRS complexes and T waves. The coronary cineangiograms in 89 of these patients were reviewed to determine the anatomic state of the coronary arteries. The angiograms of two subjects were not available for review. In the first 50 cineangiograms reviewed, a careful evaluation was made of the degree of dilution of the contrast material with blood. The degree of opacification was arbitrarily classified as poor, fair, good, or excellent in ascending order of the radiographic density achieved.

All 107 records were included in the evaluation of arrhythmias; this included 16 cases in which there was selective injection of only one coronary artery.

Standard lead III was the sole electrocardiographic lead recorded in each case. This was continuously displayed for the angiographer on a large oscilloscope and was transcribed on one channel of an ink-writing recorder at a paper speed of 25 mm per second during each selective injection of contrast material. The gain of the electrocardiographic amplifier was adjusted so that satisfactorily large QRS and T wave complexes were obtained; however, there was no standardization of this gain. These electrocardiographic tracings were analyzed for changes in heart rate and rhythm, QRS and T wave alterations, and disturbances of impulse conduction.

Results

Normal Coronary Arteries

When the coronary arteries were normal and appeared to be perfusing roughly equal

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This study was supported in part by the Alfred Reschke-John Binnay Research Memorial Fund and by Grant HE-08470 from the U. S. Public Health Service.

Circulation, Volume XXXIV, October 1966
amounts of myocardium (34 cases), injection of the left coronary artery caused a decrease in height of the R wave (or an increase in depth of the S wave or both) and a positive increase in magnitude of the T wave. Injection of the right coronary artery caused an increase in the height of the R wave or a decrease in depth of the S wave or both and inversion of the T wave (or deeper inversion of a previously inverted T wave). An example of these changes is shown in figure 1.

Since only one lead was recorded, it is impossible to tell whether these changes reflect a change only in the direction of the mean QRS and T wave vectors or a combination of a change in both direction and magnitude. It appears clear, however, that at least a change in direction of these vectors is involved because the mean amplitude of their projection on lead III very frequently changed from a positive to a negative value or vice versa.

With left coronary artery injection, therefore, in the frontal plane it would appear that the mean QRS vector shifted counterclockwise to the left and the T wave vector shifted clockwise to the right. With right coronary artery injection the frontal plane mean QRS vector shifted in a clockwise manner to the right and the T wave vector shifted in a counterclockwise manner to the left. Thus with selective right and left coronary artery injections the mean frontal plane QRS vector shifted toward the side of the injection and the mean T wave vector shifted in the opposite direction, with a marked widening of the angle between the mean QRS and T wave vectors. With failure to deliver a high enough concentration of contrast medium for good or excellent opacification of the injected artery, these electrocardiographic changes were minimal or absent.

**Figure 1**

Lead III of the electrocardiogram before and after selective injections of Hypaque into the left and right coronary arteries. Patient was a 46-year-old woman with normal coronary arteries. After injection of the left coronary artery the QRS complex changed to a Q-S complex and the T wave became very tall and peaked. After injection of the right coronary artery the R wave was markedly increased in height, the T wave became sharply inverted, and there was transient sinus bradycardia.
A few exceptions were noted. In one patient left coronary artery injection produced an increase in height of both R wave and T wave, and right coronary injection produced only slight T wave inversion without QRS changes. Unfortunately the cineangiogram in this case was not available for review, although the radiologist's official report stated that the coronary arteries were normal. Two patients had only minimal and barely discernible QRS and T wave changes despite excellent opacification of both coronary arteries.

In three additional cases the coronary arteries were normal but the right coronary arteries were unusually small. In each, the left coronary tree supplied areas of myocardium usually supplied by the distal ramifications of the right coronary artery, and the great majority of the myocardium appeared to be supplied from the left side. In these cases electrocardiographic changes produced by injection of either coronary artery were minimal. The cineangiographic findings in one of these cases is represented by a drawing in figure 2.

Abnormal Coronary Arteries

Thirty-nine patients had significant, occlusive coronary artery disease with sufficient patency of both main coronary arteries so that roughly equal amounts of myocardium appeared to be perfused from each side. The QRS and T wave changes produced by selective coronary injection of contrast medium in this group were qualitatively and quantitatively the same as in the group with normal coronary arteries.

The presence of complete occlusion of either the right main coronary artery (14 cases) or the left main coronary artery (one case) was associated with marked attenuation or absence of ECG changes during selective injection of both the occluded and the patent vessel.

One patient with multiple congenital cardiac defects had a single coronary artery. Injection of contrast medium into this single coronary artery produced no electrocardiographic changes.

Figure 3 illustrates the degree of these QRS and T wave changes in the first 44 cases reviewed in which both coronary arteries were adequately visualized. The mean QRS and T wave amplitudes (positive deflections minus negative deflections) of the control tracing were subtracted from those of the tracings after right and left coronary artery injections to give the change in mean QRS and T wave amplitudes. For example if the control tracing showed a 1 mm R wave, a 2 mm S wave, and a 1 mm upright T wave, the mean QRS amplitude was $1 - 2 = -1$ mm, and the mean T wave amplitude was $1 + 1 = 2$ mm. Then if the mean QRS and T amplitudes were $-7$ mm and $+9$ mm, respectively, after left coronary artery injection, the change in mean QRS amplitude, therefore, was $-7 - (-1) = -6$ mm, and the change in mean T amplitude was $+9 - (+1) = +8$ mm.

It is seen from figure 3 that, in general, selective injection of both the right and the left coronary arteries caused striking changes in the mean QRS and T wave amplitudes in
those subjects with patency of both main coronary arteries whether the rest of the coronary arterial tree was normal or diseased. On the other hand, patients with occlusion of the right or left main coronary artery showed little or no electrocardiographic changes with injection of either the occluded or the patent side.

The paucity of electrocardiographic changes in the group with right coronary artery occlusion may have been modified in those subjects marked with an asterisk in figure 3 because they had late, retrograde filling of the distal portion of the right coronary artery via collateral channels from the left coronary artery system with an associated biphasic electrocardiographic response. This biphasic electrocardiographic response with left coronary artery injection is shown in figure 4. The initial and expected decrease in R wave and increase

**Figure 3**

The magnitudes of the electrocardiographic changes in lead III after selective injections of the right and left coronary arteries are graphically illustrated. The mean QRS amplitude is derived by taking the height of the positive deflection (R wave) and subtracting from it the depth of the negative deflection (Q or S wave or both) with the result being expressed in millimeters. The mean T wave deflection is similarly derived. Illustrated here are the changes in mean QRS and T wave deflections associated with left and right coronary artery injections, and these are derived by subtracting the mean QRS and T wave amplitudes in the control tracing from the mean QRS and mean T wave amplitudes, respectively, after left and right coronary artery injections. Right coronary artery (RCA) injection caused a positive change in mean QRS amplitude and a negative change in mean T wave amplitude, while left coronary artery (LCA) injection caused changes in the opposite directions. Occlusion of one main coronary artery was associated with attenuation or absence of the expected ECG changes. An asterisk marks those patients with a biphasic ECG response to left coronary artery injection. See text for discussion.
in the T wave soon were reversed, and the T wave then became inverted. Such a biphasic electrocardiographic response to left coronary artery injection was always associated with right main coronary artery occlusion and late retrograde filling of the distal right coronary artery via collaterals from the left coronary system as is shown in figure 5. This biphasic response was present in seven of the 14 cases of right coronary artery occlusion; in the remaining seven cases in which it was absent, no collateral vessels were seen joining the left coronary system with the distal right coronary artery.

The concentration of contrast medium delivered to the coronary arteries bore a direct relationship to the magnitude of the QRS and T wave changes. Table 1 illustrates this with left coronary artery injection in one subject and right coronary artery injection in another subject. As the concentration of dye delivered to the coronary artery increased (as determined by the radiographic density of the vessel), the magnitude of the associated electrocardiographic changes likewise increased. Poor opacification of the coronary artery was associated with little or no electrocardiographic change.

Transient shifts of the ST segment in the direction of the T wave changes were common. Marked ST segment shifts not disappearing within 30 to 60 seconds were not seen in this group of patients.

Circulation, Volume XXXIV, October 1966
main coronary arteries patent (group 2), and in those having occlusion of the right main coronary artery (group 3). The percentage of patients showing some sinus slowing was similar in each of these groups ranging from 53% to 64% with a value of 59% for the combined groups. The groups were also similar in the percentage of cases showing sinus slowing after both right and left coronary injections. The most striking difference between groups was found by studying the relative degree of sinus slowing after right and left coronary injection in the individual cases. In the groups with patency of both main coronary arteries (groups 1 and 2), when slowing occurred, it was greater after right coronary injection in the majority of cases. However, in the group with right coronary occlusion (group 3), sinus slowing was greater in the majority of cases after left coronary injection. In the three cases in this group in which slowing was apparent after both right and left coronary injections, the right coronary artery was occluded in its midportion so that the sinus node artery could arise proximal to the occlusion.

Patients showing greater sinus slowing after right coronary injection had about the same degree of slowing as those showing greater slowing after left coronary injection. The maximum increase in P-P interval was 0.5 second or less in 83% of those having left coronary artery injections and in 78% of those having right coronary artery injections. This increase in P-P interval ranged to 2.44 seconds, but only four patients showed an increase of more than 1.0 second, and in these, this degree of sinus slowing was very transient, lasting only 1 to 2 beats.

Table 1

The Relationship of Electrocardiographic Changes to the Quality of Coronary Artery Opacification

<table>
<thead>
<tr>
<th>Site of injection</th>
<th>Quality of visualization</th>
<th>Change in mean QRS amplitude (mm)</th>
<th>Change in T wave amplitude (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left coronary artery (Patient M.M.)</td>
<td>Fair</td>
<td>− 1.5</td>
<td>+ 3.5</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>− 3</td>
<td>+ 6</td>
</tr>
<tr>
<td></td>
<td>Excellent</td>
<td>− 5</td>
<td>+ 7.5</td>
</tr>
<tr>
<td>Right coronary artery (Patient E.D.)</td>
<td>Fair</td>
<td>+ 2.5</td>
<td>− 5</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>+ 7.5</td>
<td>− 7.5</td>
</tr>
<tr>
<td></td>
<td>Excellent</td>
<td>+16.5</td>
<td>−17.5</td>
</tr>
</tbody>
</table>

*See legend for figure 3 for explanation.
In the individual patients showing slowing of the sinus rate, there was a rough correlation between the degree of slowing and the concentration of dye delivered to the coronary artery. Poor injections, where there was a great deal of mixing of blood with the dye as it entered the coronary artery, were associated with no or slight slowing of the sinus rate as well as no or slight change in the QRS or T configuration. Good or excellent injections into coronary arteries which were carrying large amounts of blood to the myocardium were associated with maximum degrees of sinus slowing for that patient. In general, diminishing of the electrocardiographic changes or of sinus slowing was not seen after the two to five injections of each coronary artery usually employed. Thus the lessening of the electrocardiographic changes after repeated injections of contrast medium in dogs reported by Guzman and West was not observed in our human subjects.

Other Arrhythmias

Ectopic ventricular beats were infrequent unless the catheter slipped into the left ventricle. Ventricular fibrillation occurred during the second injection of the right coronary artery in a man with hypertrophic subaortic stenosis who was taking digitalis; resuscitation was unsuccessful, and the patient died.

A single short run of ventricular tachycardia lasting 6 beats occurred in two subjects; one of these occurred with right coronary artery injection in a patient with a normal heart, and the other occurred with left coronary artery injection in a digitalized patient with mitral stenosis and insufficiency. Subsequent injections into these coronary arteries were accomplished in both subjects without arrhythmias.

Short periods of frequent premature ventricular beats occurred in one undigitalized subject with clinical coronary artery disease during left coronary artery injection.

Three other patients had only occasional premature ventricular contractions; this was associated with right coronary artery injection in one subject and left coronary artery injection in the other two. One patient who had frequent premature ventricular beats before and during the procedure had no change in the electrocardiogram after injection of dye into the left coronary artery.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>With either right or left coronary injection</th>
<th>Greater after right coronary injection</th>
<th>Greater after left coronary injection</th>
<th>After both right and left coronary injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Normal coronary arteries</td>
<td>30</td>
<td>16 (53%)*</td>
<td>11 (37%)</td>
<td>5 (17%)</td>
<td>6 (20%)</td>
</tr>
<tr>
<td>2. Coronary arteries diseased but right and left main coronary arteries patent</td>
<td>39</td>
<td>24 (62%)</td>
<td>14 (36%)</td>
<td>10 (26%)</td>
<td>13 (33%)</td>
</tr>
<tr>
<td>3. Right main coronary artery occluded</td>
<td>14</td>
<td>9 (64%)</td>
<td>1 (7%)</td>
<td>8 (57%)</td>
<td>3 (21%)</td>
</tr>
<tr>
<td>All groups combined</td>
<td>83†</td>
<td>49 (59%)</td>
<td>26 (31%)</td>
<td>23 (28%)</td>
<td>22 (27%)</td>
</tr>
</tbody>
</table>

*Percentage values have been rounded off to the nearest whole number.
†The single case of left main coronary artery occlusion has been left out of this tabulation.
in their frequency with either right or left coronary artery injection.

Frequent premature atrial beats occurred transiently in one subject during left coronary injection. Single premature atrial beats occurred after right coronary injection in two other subjects.

During the period of marked sinus slowing attendant on right coronary artery injection, a 5-second run of nodal rhythm occurred in one patient. Single nodal escape beats were seen during sinus slowing in two other subjects, after left coronary artery injection in one, and after right coronary artery injection in the other.

Conduction Disturbances

A brief increase of PR interval from 0.14 to 0.28 second occurred in one patient without heart disease after left coronary artery injection. Very brief episodes of second degree A-V block, consisting in the failure of one sinus beat to be conducted to the ventricle, occurred after right coronary artery injection in two patients and after left coronary artery injection in one.

Widening of the QRS interval or the appearance of bundle-branch block was not seen in any case.

Discussion

The selective injection of concentrated radiopaque medium into a coronary artery in humans was associated with an apparent rotation of the T wave vector away from the portion of the myocardium being perfused by the medium. This has been reported by others.\(^1\)\(^-\)\(^3\) The concomitant shifts of the QRS vector in the opposite direction have not been mentioned previously although they are apparent in figure 3 of Ross' paper.\(^1\) Electrical repolarization of the heart as manifested by the T wave of the electrocardiogram can be altered by a wide variety of circumstances; it is a much more labile electrocardiographic process than the QRS complex (myocardial depolarization). It is therefore more difficult to explain the changes in the QRS vector produced by selective coronary injection than to explain the changes in the T wave vector. The work of Gensini and Di Giorgi\(^6\) on dogs suggests that the T wave changes at least are related to the high concentration of sodium in the radiopaque medium (the concentration of sodium in Hypaque-M 75% is approximately 400 mEq/L).

One would expect the striking electrocardiographic changes produced by selective right and left coronary artery injections to cancel each other, at least partially, when both coronary arteries are injected simultaneously, as occurs with injections of large amounts of contrast medium into the root of the aorta. In our experience with the technique of aortic root flooding in attempts to visualize the coronary arteries electrocardiographic changes were not often marked. Others have had similar experience.\(^7\) On the other hand, this technique may not deliver as high a concentration of contrast medium to the myocardium as does the selective method, and the degree of the electrocardiographic changes are definitely and directly related to the concentration of contrast medium perfusing the coronary artery. In the single case observed in this study in which the entire myocardium was supplied by a single coronary artery, no electrocardiographic changes were observed during injection into this artery. This suggests that the striking electrocardiographic changes accompanying selective injections into one coronary artery are the result of differences in potential between areas of myocardium perfused with contrast material and areas containing no contrast material. The alterations in electrocardiographic response to selective coronary injection imposed by complete occlusion of one main coronary artery further support this thesis. When, for example, the right coronary artery is very small or is completely blocked and is supplying little or no myocardium, it is usual for injection of the left coronary artery which is supplying the great majority or virtually all of the electrically active myocardium to cause minimal or no electrocardiographic changes. In the much less common condition of complete left main coronary occlusion, injection of the right coronary which

\(^{Circulation, Volume XXXIV, October 1966}\)
is supplying all the myocardium is likewise associated with minimal or no electrocardiographic changes. There is the special case in which one main coronary artery is occluded but the distal branches of this vessel are perfused after a significant delay by collaterals from the patent side. Here, injection of the patent side causes first the expected electrocardiographic changes and, after a brief delay, a reversal of the QRS and T changes to the pattern associated with injection of the other coronary artery. This means that initially contrast medium is perfusing myocardium on the injected side while there is myocardium on the noninjected side not being perfused; later, the contrast medium reaches myocardium normally supplied by the occluded side at a time when contrast medium is no longer perfusing the myocardium on the nonoccluded side. Superimposition of these electrocardiographic changes in time would tend to cancel them.

It would be expected, therefore, that maximum electrocardiographic changes would follow selective injection of one main coronary artery when both coronary arteries are normal or at least when each coronary artery is supplying blood to roughly equal but distinct amounts of myocardium. This was the case in this study where the most striking electrocardiographic changes were produced in persons with normal coronary arteries and in those who, while sufficient disease was present in one or both sides to produce angina pectoris, had large and distinct areas of myocardium supplied through each main coronary artery system.

It can be seen that monitoring of the electrocardiogram during selective coronary angiography can be of assistance to the angiographer in interpreting the adequacy of his coronary injections. When a satisfactory injection of dye into one coronary artery causes striking electrocardiographic changes in the expected direction, this implies not only that the injected vessel is supplying a large amount of myocardium but also that there is a large and separate amount of myocardium supplied by the noninjected coronary artery, and hence that the latter vessel cannot be completely occluded proximally and its injection should produce striking electrocardiographic changes in the opposite direction. When a biphasic response occurs in the electrocardiogram after injection of one coronary artery, that is, when the expected electrocardiographic changes occur but are followed shortly by a reversal of these changes (fig. 4), the noninjected side must be severely diseased or completely occluded and its distal portions are filling late via collateral vessels from the injected side. These collaterals are usually easily demonstrated on the cineangiograms.

The presence of only minimal or no electrocardiographic changes after selective coronary injection can be due to several factors. Delivery of an insufficient concentration of dye into the coronary artery, as often occurs when the tip of the catheter is not properly positioned in the coronary orifice, is associated frequently with poor visualization of the coronary artery and only minimal or no electrocardiographic changes. Satisfactory injection of a completely or nearly completely occluded coronary artery, which is carrying only a small amount of blood to a small area of myocardium, produces minimal or no electrocardiographic changes. In this case injection of the opposite coronary artery causes minimal or no electrocardiographic change since the vessel is perfusing nearly all of the surviving myocardium.

Therefore, full interpretation of the significance of the pattern of electrocardiographic changes attendant on selective coronary angiography often requires a side-by-side review of the electrocardiogram with the angiograms. It is necessary to select the best injections of each coronary artery (preferably with injection directly into the coronary orifice) in order to compare the electrocardiographic changes from one side with those from the other side. Electrocardiographic changes from an injection of contrast medium directly into the orifice of one coronary artery cannot reasonably be compared with changes from a poor injection into the coronary cusp of the other side.

Even in the group with normal coronary
arteries, there was considerable variation between subjects in the degree of the electrocardiographic changes produced. This is not surprising since the gain of the electrocardiographic amplifier was not standardized, the concentration of contrast medium delivered to the coronary arteries was not the same in each case, and individual variations can be expected in the relative amounts of myocardium supplied from each coronary artery and in the responsiveness to the contrast medium.

It is suggested that the recording of multiple electrocardiographic leads or vectorcardiograms during selective coronary cineangiography would give more quantitative data about the changes in magnitude and direction of the electrical forces of the heart and in selected cases might allow some estimate of the relative location and amount of myocardium supplied by each main coronary artery.

The infrequency of serious cardiac arrhythmias with the injection of the contrast medium directly into a coronary artery is reassuring. Only one patient developed ventricular fibrillation, and failure to resuscitate this man can be attributed to his severe hypertrophic subaortic stenosis. The two patients who had one very short run of ventricular tachycardia during injection of a coronary artery each had subsequent injections of the same vessel without arrhythmia.

Transient sinus bradycardia was a common result of the injection of contrast medium into either coronary artery. It is believed that this is a direct effect of the contrast medium on the sinus node, although a neurogenically mediated effect has not been excluded. If it is indeed a direct effect on the sinus node, our data suggest that the sinus node receives some blood from both the main coronary artery distributions in a much higher percentage of cases than suggested by James. James found this to be the case in only about 2% of his 106 cases examined after death while we found measurable sinus slowing after both right and left coronary injection in 22 of the 49 cases in which slowing occurred (45%).

The period of sinus bradycardia seems to be the point of greatest susceptibility to ventricular arrhythmias. Such an arrhythmia would be even more likely to occur if the injected artery perfused and the contrast medium depressed both the sinus and the A-V nodes simultaneously. In James’ series, both nodes were supplied solely by the right coronary artery in about 44% of the cases, and solely by the left coronary artery in about 4% of the cases. It would be suspected, therefore, that significant ventricular arrhythmias are more common after right coronary artery injection. The number of ventricular arrhythmias was too small in the present study to confirm this theory; about an equal number of right and left coronary injections caused ventricular ectopic activity. However, in the one case in this series in which ventricular fibrillation occurred, the arrhythmia was initiated during a period of sinus node slowing caused by right coronary artery injection. We have modified our technique of coronary angiography in light of these observations, and it is our current practice to inject the left coronary artery first and finish the examination with the right coronary artery injections. In addition, a direct current defibrillator is kept ready for use near the patient in the catheterization room so that immediate defibrillation can be carried out.

It is concluded from this preliminary study that the electrocardiogram recorded simultaneously with selective injections of contrast medium into the coronary arteries is an integral part of coronary angiography. It may supply supplemental information not readily apparent on the image intensifier at the time of injection and is of assistance in interpreting the angiogram when the latter is ready for viewing. These electrocardiographic changes with selective coronary angiography remain a fruitful field for further study.

Summary

Examination was made of standard lead III of the electrocardiogram recorded during selective right and left coronary artery injections of Hypaque-M 75% in 107 patients. Left coronary artery injection caused the mean frontal plane QRS vector to shift transiently to the left and T wave vector to shift toward
the right. Right coronary artery injection caused shifts of the QRS and T wave vectors in the opposite directions. Occlusion of one main coronary artery caused these ECG changes to be minimal or absent. Transient sinus bradycardia was common with injection of either coronary artery. Serious arrhythmias were rare. The electrocardiogram recorded during selective coronary arteriography can give information useful to the angiographer during the procedure itself as well as during the subsequent interpretation of the angiogram.

References

**Stereotyped Tragedy**

On Friday morning, March 11th [1955] he awoke in a very gay mood. . . . He got up, and went to have his bath. When he came back he looked very pale and complained of a feeling of nausea. . . . He asked for some hot water to drink, then for bicarbonate of soda. He got to his feet and began to walk about the room. His healthy, vigorous body was trying to shake off the unexpected malaise, refusing to accept it. But he had to give in and go back to bed. . . . Dr. Hunt, who had been alarmed at the anxiety in Lady Fleming's voice, rang her back. Fleming insisted on taking the call himself.

'Is it urgent? Shall I leave my other cases and come round at once?'

'No urgency whatsoever. . . . 'Look after your other patients first.' . . .

'She wanted to take his pulse. His arm was cold. 'Yes,' he said, 'I'm covered in cold sweat. And I don't know why I've got this pain in my chest.' This time, she felt panic-stricken: 'Are you absolutely sure it's not your heart?' 'It's not the heart,' he said, 'it's going down from the oesophagus to the stomach.' His voice was still strangely calm and serious. It was as though he were thinking deeply and trying to understand. Suddenly his head fell forward. Alexander Fleming was dead.—André Maurois: The Life of Sir Alexander Fleming. New York, E. P. Dutton & Co., 1959, p. 272. (By permission of the publishers.)
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Circulation. 1966;34:627-637
doi: 10.1161/01.CIR.34.4.627
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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