Direct Arterial Pressure and the Electrocardiogram in Unrestricted Patients with Angina Pectoris

Peter Sleight, M.D., F.R.C.P., and Frank D. Stott, M.A., D. Phil.

SUMMARY
Direct arterial pressure and electrocardiogram have been recorded over a 24 hr period in 8 males with angina pectoris who were completely unrestricted throughout the study. Twenty-five separate episodes of angina occurred, precipitated by exertion, eating, smoking, and anxiety, in addition to 2 spontaneous attacks and 2 episodes of nocturnal angina. All but 2 angina episodes were accompanied by a rise in both arterial pressure and heart rate. In the cases of spontaneous and nocturnal angina these pressure and rate changes began 10-15 min before the pain. In exertional angina these changes were related to the degree of activity involved, while in other instances there was a brief surge of pressure and rate occurring at the time of onset of pain. In each patient pain tended to occur at approximately the same level of pressure-rate product. ST-segment changes in the electrocardiogram showed no consistent pattern, occurring before or after the onset of pain, while in some episodes there was no significant change. A limited number of observations were made on the effect of glyceryl trinitrate and β-adrenergic receptor blocking drugs.

Additional Indexing Words:
Sympathetic discharge Pulsus alternans Prinzmetal

ANGINA PECTORIS is a well described clinical entity, the physiology of which is still incompletely understood. Most of the recent literature has dealt with the hemodynamic changes during angina, but nearly all the information has been obtained from laboratory studies by conventional cardiac catheter techniques. Angina has usually been induced by exercise and/or drugs, observations during spontaneous angina being rare. While such information is extremely valuable, it is necessarily incomplete. The present study was undertaken to investigate the changes in arterial pressure and the electrocardiogram which accompanied attacks of angina pectoris in unrestricted patients going about their normal daily lives.

Methods
Eight male patients with a typical history of angina pectoris gave informed consent for this study. Their clinical details are summarized in Table 1.

The methods used for measuring direct arterial pressure and the electrocardiogram in unrestricted patients have been fully described in previous publications. Briefly, a Teflon catheter (length 10 cm, I.D. 0.9 mm, O.D. 1.04 mm) was inserted into the left brachial artery using the Seldinger technique. This catheter was connected to a capacitance manometer and perfusion pump by a 1 m length of teflon tubing, I.D. 0.35 mm, and was perfused with fluid at a rate of approximately 1.5 ml/hr. There was no complication of arterial catheterization in any of these 8 patients; in general there has been an occasional hematoma at the site of puncture, but we have seen no major occlusion of vessels, splinter hematomata or infection. The recording system was a miniature analogue tape recorder using standard compact cassettes. The transducer, perfusion pump and tape recorder were carried in a padded harness at heart level, the reference point for pressure was therefore constant irrespective of the position of the arm or body. The frequency response of the whole system was flat to 10 Hz. The electrocardiogram lead system consisted of bipolar electrodes placed over the V5R-V5L positions. Leads were held in place by electrode discs and secured by surgical tape to minimize movement artefact.

From the Departments of Cardiology and the Regius Professor of Medicine, Radcliffe Infirmary, Oxford, England.
Supported by a grant from the British Heart Foundation.
Address for reprints: Dr. William A. Littler, Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford OX2 6HE, England.
Received December 6, 1972; revision accepted for publication February 27, 1973.
Although the ST-segment level was lower than that ordinarily used on diagnostic electrocardiographs, and caused some slope of the ST-segment, it was long enough to allow measurement of changes of ST-segment level with sufficient accuracy for the requirements of this study. A longer time constant in practice leads sometimes to excessive baseline wander due to electrode movement artefacts, which are always a problem when recording from active subjects.

The tape cassettes were replayed on a separate playback deck at 25 times the recording speed. The output from the playback deck was fed into an ultraviolet recorder (Consolidated Electrodynamics) so that compressed or expanded records, for beat-to-beat analysis, could be obtained.

The patients were all studied over a 24 hr period from 9 a.m. to 9 a.m. During this time, they attended the laboratory only once for 15 min after a 12 hr period in order to apply a calibration to the tape and to service the perfusion chamber. All went about their daily routine at both work and home; they were not encouraged to do anything exceptional, nor was their drug regime altered (table 1).

The subject carried a diary in which he recorded the timing of significant events such as the onset of anginal pain, and he indicated these simultaneously on the tape by an electrical pulse initiated by a microswitch.

When studying the data, each anginal episode was replayed for beat-to-beat analysis. Systolic and diastolic arterial pressure and heart rate were averaged over periods of one minute throughout the attack and for a similar period prior to the indication of pain. In tables 2 and 3 the figures given indicate the highest levels of these parameters as compared with pre-angina values.

### Table 1

*The Clinical Details of the Eight Patients*

<table>
<thead>
<tr>
<th>Case</th>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Occupation</th>
<th>Duration of symptoms</th>
<th>Treatment</th>
<th>Resting BP</th>
<th>Resting ECG</th>
<th>CXR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EC</td>
<td>67</td>
<td>M</td>
<td>Retired fitter</td>
<td>Angina pectoris 8 yr. Severe</td>
<td>GTN Propranolol 100mg tds</td>
<td>120/80</td>
<td>LAH</td>
<td>LV+</td>
</tr>
<tr>
<td>2</td>
<td>NB</td>
<td>55</td>
<td>M</td>
<td>Trimmer</td>
<td>Angina pectoris 18 mo. Severe</td>
<td>GTN Practolol 100mg tds</td>
<td>150/80</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>VS</td>
<td>56</td>
<td>M</td>
<td>Clerk</td>
<td>Angina pectoris 9 yr</td>
<td>Vineberg 1963 Endarterectomy 1963 GTN Propranolol 40mg tds Sustac</td>
<td>200/120</td>
<td>ST ↓ 2.3 aVF</td>
<td>V3-V6</td>
</tr>
<tr>
<td>4</td>
<td>RC</td>
<td>50</td>
<td>M</td>
<td>Bricklayer</td>
<td>Chest pain 3 mo</td>
<td>Valium 2mg tds</td>
<td>170/110</td>
<td>RBBB</td>
<td>LV+</td>
</tr>
<tr>
<td>5</td>
<td>FS</td>
<td>54</td>
<td>M</td>
<td>Concrete manufacturer</td>
<td>Angina pectoris 2 yr</td>
<td>GTN Practolol 100mg tds</td>
<td>135/80</td>
<td>ST ↓ aVL</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>GD</td>
<td>52</td>
<td>M</td>
<td>Master builder</td>
<td>Angina pectoris 3 mo</td>
<td>GTN</td>
<td>150/95</td>
<td>LAH</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>HC</td>
<td>62</td>
<td>M</td>
<td>Stonewoker</td>
<td>Angina pectoris 15 mo. Severe</td>
<td>GTN Furosemide 40mg daily</td>
<td>110/70</td>
<td>LBBB</td>
<td>LV+</td>
</tr>
<tr>
<td>8</td>
<td>GL</td>
<td>54</td>
<td>M</td>
<td>TV engineer</td>
<td>Angina pectoris 4 yr</td>
<td>GTN Propranolol 80mg tds</td>
<td>130/80</td>
<td>LAH Anterior</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Abbreviations: GTN = glyceryl trinitrate; LAH = left anterior hemiblock.

The differential input impedance of the ECG amplifier was 1 MΩ, and the time constant was 0.5 sec. Although the time constant was considerably shorter than that ordinarily used on diagnostic electrocardiographs, and caused some slope of the ST-segment, it was long enough to allow measurement of changes of ST-segment level with sufficient accuracy for the requirements of this study. A longer time constant in practice leads sometimes to excessive baseline wander due to electrode movement artefacts, which are always a problem when recording from active subjects.

The tape cassettes were replayed on a separate playback deck at 25 times the recording speed. The output from the playback deck was fed into an ultraviolet recorder (Consolidated Electrodynamics) so that compressed or expanded records, for beat-to-beat analysis, could be obtained.

The patients were all studied over a 24 hr period from 9 a.m. to 9 a.m. During this time, they attended the laboratory only once for 15 min after a 12 hr period in order to apply a calibration to the tape and to service the perfusion chamber. All went about their daily routine at both work and home; they were not encouraged to do anything exceptional, nor was their drug regime altered (table 1).

The subject carried a diary in which he recorded the timing of significant events such as the onset of anginal pain, and he indicated these simultaneously on the tape by an electrical pulse initiated by a microswitch.

When studying the data, each anginal episode was replayed for beat-to-beat analysis. Systolic and diastolic arterial pressure and heart rate were averaged over periods of one minute throughout the attack and for a similar period prior to the indication of pain. In tables 2 and 3 the figures given indicate the highest levels of these parameters as compared with pre-angina values.

### Results

A total of 25 separate episodes occurred in the 8 patients; Case 3 had only one attack, while Case 5 had 6, Case 8 had 4, Case 1 had 2, and the remainder had 3 attacks each (table 2).

Angina was provoked by exertion, eating, driving, anxiety, and smoking. Case 7 had 2 spontaneous attacks during the day and one attack at night.

The anginal episodes lasted between 2 and 15 min.

### Arterial Pressure and Heart Rate

In 12 episodes the rise in blood pressure took place before the patients indicated pain; in 11 episodes the rise coincided with the onset of pain; in the remaining two episodes there was no change whatsoever. The greatest peak rise in systolic pressure was 80 mm Hg, and diastolic 25 mm Hg (Case 1), the smallest 14 mm Hg systolic and 4 mm Hg diastolic.

All patients except Case 8 developed a tachycardia during the angina attacks, the rate increase ranging from 10 to 30 beats/min (table 3). Case 8, who was taking propranolol, showed only a minimal increase in heart rate or none at all.
CIRCULATORY CHANGES IN ANGINA

Table 2

A Summary of the Changes Accompanying Each Individual Anginal Attack

<table>
<thead>
<tr>
<th>Case</th>
<th>No. of attacks</th>
<th>Precipitating factors</th>
<th>BP rise or fall</th>
<th>Duration (min)</th>
<th>BP change</th>
<th>Change in heart rate (beats/min)</th>
<th>ST-segments</th>
<th>Arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>Eating x 1</td>
<td>Rise*</td>
<td>10-15</td>
<td>80</td>
<td>25</td>
<td>20</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walking x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V. Ectopias</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walking x 2</td>
<td>Rise*</td>
<td>2-6</td>
<td>14-24</td>
<td>9-20</td>
<td>10-20</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anxiety x 1</td>
<td></td>
<td></td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>Walking</td>
<td>Rise*</td>
<td>3-4</td>
<td>40</td>
<td>22</td>
<td>20</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>Bus journey x 1</td>
<td>Rise 1*</td>
<td>2-3</td>
<td>16</td>
<td>16</td>
<td>20</td>
<td>Sag</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eating x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Driving x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>Walking x 2</td>
<td>Rise 2*</td>
<td>2-15</td>
<td>18-40</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stairs x 1</td>
<td>Rise 4†</td>
<td></td>
<td>18-20</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smoking x 1</td>
<td></td>
<td></td>
<td>23</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>Driving x 1</td>
<td>Rise†</td>
<td>5</td>
<td>14-24</td>
<td>12-24</td>
<td>10-20</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stairs x 1</td>
<td></td>
<td></td>
<td>14</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>Spontaneous x 2</td>
<td>Rise†</td>
<td>10-15</td>
<td>16-25</td>
<td>12-18</td>
<td>10-30</td>
<td>Sag 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sleep x 1</td>
<td></td>
<td></td>
<td>16</td>
<td>17.5</td>
<td></td>
<td>V. Ectopies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ectopic x 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>Carrying x 1</td>
<td>Rise 1†</td>
<td>10-20</td>
<td>34</td>
<td>15.5</td>
<td>6-12</td>
<td>Sag 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sleep x 1</td>
<td>Rise 2*</td>
<td></td>
<td>29</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Undressing x 1</td>
<td></td>
<td></td>
<td>34</td>
<td>15.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Walking x 1</td>
<td></td>
<td></td>
<td>22</td>
<td>14.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*BP rise occurred after the onset of chest pain.
†BP rise occurred before the onset of chest pain.

Table 3

The Percentage Changes in BP and Heart Rate during Angina Attacks*

<table>
<thead>
<tr>
<th>Case</th>
<th>% Change SBP</th>
<th>% Change DBP</th>
<th>% Change HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+ 50</td>
<td>+ 50</td>
<td>+ 20</td>
</tr>
<tr>
<td>2</td>
<td>+ 9.5</td>
<td>+ 9</td>
<td>+ 19</td>
</tr>
<tr>
<td></td>
<td>+ 10</td>
<td>+ 11</td>
<td>+ 20</td>
</tr>
<tr>
<td></td>
<td>+ 16</td>
<td>+ 20</td>
<td>+ 20</td>
</tr>
<tr>
<td>3</td>
<td>+ 23</td>
<td>+ 22</td>
<td>+ 25</td>
</tr>
<tr>
<td>4</td>
<td>+ 11.5</td>
<td>+ 17</td>
<td>+ 25</td>
</tr>
<tr>
<td>5</td>
<td>+ 13</td>
<td>+ 4.5</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>+ 13</td>
<td>+ 0</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>+ 16</td>
<td>+ 11</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>+ 29</td>
<td>+ 6</td>
<td>+ 30</td>
</tr>
<tr>
<td></td>
<td>+ 14</td>
<td>+ 11</td>
<td>+ 40</td>
</tr>
<tr>
<td>6</td>
<td>+ 8</td>
<td>+ 34</td>
<td>+ 8.5</td>
</tr>
<tr>
<td></td>
<td>+ 14</td>
<td>+ 20</td>
<td>+ 30</td>
</tr>
<tr>
<td></td>
<td>+ 8</td>
<td>+ 12</td>
<td>+ 19</td>
</tr>
<tr>
<td>7</td>
<td>+ 14.5</td>
<td>+ 22</td>
<td>+ 10</td>
</tr>
<tr>
<td></td>
<td>+ 14.5</td>
<td>+ 22</td>
<td>+ 7</td>
</tr>
<tr>
<td></td>
<td>+ 20</td>
<td>+ 23</td>
<td>+ 22</td>
</tr>
<tr>
<td>8</td>
<td>+ 16</td>
<td>+ 12</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>+ 22</td>
<td>+ 11</td>
<td>+ 0</td>
</tr>
<tr>
<td></td>
<td>+ 26</td>
<td>+ 12</td>
<td>+ 15</td>
</tr>
<tr>
<td></td>
<td>+ 17</td>
<td>+ 22</td>
<td>+ 0</td>
</tr>
</tbody>
</table>

*Compared with the average value for each parameter determined over the 24 hr period.

Electrocardiogram

ST-segment changes were observed in only four patients, who between them had 14 attacks of angina. In Case 4 the ST-segment was depressed throughout the 24 hours. The most consistent change was a depression of the ST-segment which occurred in all attacks. In 12 of these the depression evolved with the appreciation of pain, but in one episode (fig. 1) it preceded this by 4 min.

Only one patient (Case 1) developed a significant arrhythmia during anginal pain. This patient produced ventricular ectopic beats at a rate of 5-6/min.

Drugs

Glyceryl trinitrate (GTN) was taken sublingually by 5 patients during the study (Cases 1, 5, 6, 7, 8). Cases 6 and 7 showed no obvious circulatory response to the drug (fig. 2), while in Cases 5 and 8 particularly there was a rapid and significant fall in arterial pressure with alleviation of angina (fig. 6). There was not a significant increase in heart rate at this time as compared with the rate at the onset of pain. Alleviation of pain occurred during the fall in pressure, though not necessarily at pre-pain levels.
Five patients were receiving beta blockers (table 1) (Cases 1, 2, 3, 5, 8). All but Case 8 showed a significant rise in arterial pressure and heart rate during their angina as compared with periods without pain; heart rate was very constant at other times. Case 8 also showed a fairly steady heart rate

Figure 1
A record from Case 5 obtained during an attack of angina pectoris induced by cigarette smoking (lower panel) compared with a control period during sleep. Note that there has been significant ST-segment depression in the electrocardiogram which preceded the subjective appreciation of chest pain.

Figure 2
A record obtained during a truly spontaneous attack of angina (Case 7). The arterial pressure (art. press.) had risen at least 10 minutes before the subjective appreciation of pain. Note the lack of any marked hypotensive effect after glyceryl trinitrate (GTN). The heart rate and ST-segment drop also began at the same time as the pressure rise.
CIRCULATORY CHANGES IN ANGINA

Figure 3
A beat-to-beat analysis of figure 2 during the pain; pulsus
alternans is clearly present, indicating severe left ventricular
stress.

of 70-80 beats/min, which increased by only a few
beats during anginal episodes.

Spontaneous and Nocturnal Angina

Two episodes of spontaneous angina occurred during
the study of Case 7. In both instances the heart
rate and blood pressure had risen before the patient
indicated pain (fig. 2), the time intervals being 10
and 20 min, respectively. The magnitude of these
changes was approximately the same in both
instances. Pulsus alternans occurred at the height
of one attack and is clearly seen in figure 3.

One attack of nocturnal angina was observed in
Case 7. The blood pressure and heart rate had risen
some 15 min before the patient awoke with pain.
The electrocardiogram showed changes which were
thought to be compatible with the Prinzmetal type
of angina during this period (fig. 4), the ST-
segments initially sagging and then rising well
above the isoelectric line giving a typical infarct
pattern and finally returning to near the isoelectric
line.

Another episode of nocturnal angina occurred in
Case 8. The arterial pressure began to rise 15 min
before the patient awoke with pain; the extra surge
on awakening was genuine, as can be seen in the
beat-to-beat analysis (fig. 5). Heart rate did not
increase significantly in this patient (vide supra).
ST-segments showed some sagging occurring after
wakening.

Precipitating Factors

Thirteen episodes of angina were precipitated by
exertion; this included climbing stairs, walking,
undressing, and gardening.

Case 5 had two attacks of angina while hoeing
and digging (fig. 6). His pressure and heart rate
rose with exertion, but there is a further sharp rise
in systolic pressure at the time he indicates pain; his
pressure falls with a few minutes' rest, only to rise
steeply again on resuming digging.

Case 3 was pulled up with severe chest pain
while walking which forced him to stop and take
GTN. There was a sudden sharp rise in pressure
and rate coincident with his appreciation of pain.

Exertion itself may raise the arterial pressure and
heart rate but when angina occurs there is a further

Figure 4
A beat-to-beat analysis during an episode of nocturnal angina (Case 7). The interesting feature is the
evolution of the ST-segment change in the ECG. Note the initial depression of the ST-segment at the
onset of pain; this then evolves into a significant elevation during the height of pain reminiscent of
Prinzmetal's variant angina. When the pain has subsided, the ST-segment is almost isoelectric.
increase in these two parameters superimposed on the changes induced by exertion.

Four attacks of angina occurred during eating. With the appreciation of pain there was a rise in pressure and heart rate. Eating itself did not cause a significant rise in either arterial pressure or heart rate.

Angina was thought to have been precipitated by cigarette smoking in one instance (fig. 7). The onset of pain occurred 4 min after smoking and
there was a coincidental surge of pressure and heart rate at this time. On a beat-to-beat analysis (fig. 1) it can be seen that the ST-segments were already markedly depressed before the appreciation of pain, the change having apparently been initiated by smoking.

Two attacks of angina occurred while the patients were driving. In Case 4 the pain was described as mild and there were no significant associated circulatory changes. In Case 6, the patient was forced to stop the car in order to take GTN because of the severity of the pain. Pressure and heart rate only rose with the onset of pain. Our unpublished observations have shown that driving alone does not significantly affect arterial pressure or heart rate.

Discussion

The most striking observation of this study is that all but two attacks of angina, irrespective of how they were produced, were accompanied by an increase in arterial pressure and heart rate. These observations are unique only in the manner in which they have been obtained. We believe that for the first time accurate information has been obtained on the circulatory response to anginal pain in patients going about their normal lives in the absence of doctors and free from subjective stimuli.

We have confirmed the findings of many other investigators that there is no one specific arterial pressure level or heart rate at which patients predictably have pain. Like Robinson, we found the pressure-rate index (which we did not correct for ejection time) was approximately in the same range at the onset of anginal pain within the same patient, indicating that pain was occurring at the same level of cardiac work.

One can only speculate on the mechanisms and relationships among arterial pressure, heart rate and pain which we have observed. In general, we have found that pain produced by effort is usually accompanied by an increase in work of the heart as indicated by the product of pressure and rate. However, in some instances there is a further increase in arterial pressure (and rate) coincidental with the onset of pain (fig. 6). This may be the result of a sympathetic discharge produced either by pain or possibly by reflexes from the heart. Although most cardiac ventricular receptors when stimulated result in reflex bradycardia, Malliani et al. have recently described a reflex sympathetic discharge resulting from stimulation of ventricular afferent receptors whose afferent fibres travel in sympathetic nerves in the same way as cardiac pain fibres have been shown to travel, and by which also vasoconstrictor nerves were thought to reach the heart. In several instances (fig. 7) we observed a sudden rise in pressure and rate coinciding with the onset of pain and not preceded by any gradual
increase in these parameters. These short sharp rises at the time of pain may represent a generalised sympathetic nervous discharge involving vasoconstriction, acute hypertension, tachycardia and augmented vigor of contraction which raise the cardiac need for oxygen. In one instance (fig. 8) we noted a severe bradycardia accompanying a rise in arterial pressure. It is not possible to say whether this is due to an active baroreceptor reflex or to a combination of reflex sympathetic stimulation to ventricular muscle and peripheral vessels as described above, in addition to reflex vagal effects on the sinus node here overcoming the sympathetic.12

The observations in Case 5 (fig. 7) were interesting in that the pain followed quickly after smoking a cigarette. The mechanisms of tobacco angina are not clear13 but it appeared in our case that the ST-segments were depressed before the onset of pain while the circulatory responses were coincidental. Hence smoking cigarettes may have increased myocardial MVO2, which in turn stimulated a sympathetic discharge, or the sympathetic discharge may be triggered by smoking.

In their review of the literature, Roughgarden and Newman14 found adequate data obtained in 30 attacks of spontaneous angina indicating that such attacks were uniformly associated with relative systolic and diastolic hypertension, averaging a 29 percent increase in pressure over control levels, and an increase of 30 percent in pulse rate. In 10 instances the hypertension preceded the onset of subjective pain, while in the remainder this relationship was not specifically observed. In her own series of cases, Roughgarden8 observed 21 attacks of spontaneous angina; in 86 percent of these the hypertension preceded the onset of pain.

We observed only two episodes of angina which were truly "spontaneous" (Case 7). Our findings confirm those of Roughgarden: the pressure and heart rate rose 10 to 15 min before the subjective appreciation of pain. In these instances the elevation of arterial pressure and heart rate seem to be more related to the cause rather than the effect of the pain. It is possible that a gradual accumulation of catecholamines has raised MVO2 to a critical level; perhaps there was no extra surge at the onset of pain because the vascular bed and myocardium were already saturated with vasopressor substances. An interesting feature of these spontaneous attacks is the occurrence of pulsat alternans at the height of the pain, indicating left ventricular failure and confirming findings observed at cardiac catheterization.15

The same patient (Case 7) had one attack of nocturnal angina. Once again, the arterial pressure and heart rate began to rise 15 min before he awoke with pain, while in Case 8 the arterial pressure alone began to rise 15 min before awakening. In this laboratory we have previously made recordings of intra-arterial pressure and electrocardiogram during sleep.16 We found the highest and lowest pressures of the night during dreaming or rapid eye movement (REM) sleep. Surges of pressure also

---

**Figure 8**

A portion of a record obtained from Case 6 during an attack of angina; this illustrates reflex slowing of the heart induced by hypertension; this reflex slowing in turn lowers the arterial pressure.
CIRCULATORY CHANGES IN ANGINA

occur associated with so-called "K" complexes characteristic of Stage II sleep, and these have been shown to be associated with tachycardia and increased sweat gland activity—all probably due to sympathetic discharge. It seems likely that the increased cardiac work which occurs at this time could be responsible for at least some episodes of nocturnal angina.

Nowlin et al. observed rapid eye movements preceding 32 out of 39 attacks of angina and also preceded the electrocardiographic changes, suggesting that dreaming had resulted in angina. On wakening, patients recalled that their dreams had involved exertion and anxiety and some even remembered experiencing chest pain as part of their dream. Our two patients recalled no such dreams.

The electrocardiographic changes during the episode of nocturnal angina in Case 7 are interesting, in that there was elevation of the ST-segment. Roughgarden observed exactly the same phenomenon during two episodes of nocturnal angina. In addition, our patient had at least two other episodes where the ST-segment was significantly raised during the night; these were associated with tachycardia, but not with a notable pressure rise or with wakening the patient. The ST-segment changes are not dissimilar to those occurring in the variant form of angina described by Prinzmetal. Guazzi et al. studied four patients with Prinzmetal's variant angina and observed several episodes of ST-segment elevation unaccompanied by pain. In no anginal attack did hemodynamic changes precede the electrocardiographic ones; the former always began at the same time as the latter. During the electrocardiographic abnormalities there was a reduction in cardiac output, arterial hypotension, and evidence of impaired left ventricular function.

In those of our patients in whom ST-segment changes occurred during anginal attacks, the ST-depression usually occurred coincident with or after the onset of pain, although on at least one occasion it was several minutes beforehand (Case 5). We have already mentioned that we observed ST-segment changes without pain or hypertension while in three patients no significant change occurred. It is possible that our ECG lead system did not reflect the acute ischemia which occurred in a particular myocardial area. On the other hand, angina is known to occur in the absence of any electrocardiographic changes. Thus, like Roughgarden, we have not found any one consistent pattern in the time relationship between circulatory changes and ST-segment changes indicating myocardial ischemia.

All eight patients were allowed to continue their normal daily regime and although all of them had been prescribed glyceryl trinitrate (GTN), only five patients (Cases 1, 2, 5, 7 and 8) actually used the drug during the study. Cases 2 and 7 had no significant changes in arterial pressure or heart rate following administration of the drug (fig. 2). The possibility that patients taking large doses of nitrates for angina may develop tolerance to these drugs has been suggested repeatedly. However, one careful evaluation of the exercise capacity and circulatory response after prolonged therapy with isosorbide trinitrate failed to demonstrate such tolerance.

Three patients showed a rapid response with alleviation of their pain after sublingual GTN. There was an obvious decrease in blood pressure and pulse pressure (fig. 3) although there was not a significant increase in heart rate at this time as compared with the rate during anginal pain. Alleviation of pain usually coincided with a falling pressure, though not necessarily to pre-pain levels (fig. 6). Surprisingly, none of our patients took GTN prophylactically, an all too common failing in our experience.

Five of our patients were taking beta-receptor blocking drugs at the time of the study (table 1). Apart from Case 8, all showed exactly the same response (i.e., increased arterial pressure and heart rate) at the time of angina. In addition, the behavior of ST-segments at this time showed no outstanding difference between those taking beta-receptor blockers and those not. Case 8, however, showed very little change in his heart rate during anginal attacks, despite characteristic rises in arterial pressure. It seems likely that he was more adequately blocked than the other four patients.

References
8. Sleight P: Cardiovascular depressor reflex arising from the epicardium of the left ventricle of the dog. J Physiol (Lond) 173: 321, 1964
Direct Arterial Pressure and the Electrocardiogram in Unrestricted Patients with Angina Pectoris

WILLIAM A. LITTNER, A. JOHN HONOUR, PETER SLEIGHT and FRANK D. STOTT

Circulation. 1973;48:125-134
doi: 10.1161/01.CIR.48.1.125

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1973 American Heart Association, Inc. All rights reserved.
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:
http://circ.ahajournals.org/content/48/1/125

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/