Observations on the Carotid Sinus Reflex and Angina Pectoris

By A. Stone Freedberg M.D., and Joseph E. F. Riseeman, M.D.

The effect of carotid sinus pressure on the duration and character of attacks of angina pectoris induced by exercise under controlled conditions has been studied in 13 patients. Observations are presented which are consistent with the hypothesis that stimulation of the carotid sinus induces relief of cardiac pain by interruption of sympathetic reflex arcs or sensory pathways. The usefulness of carotid sinus pressure as a diagnostic test and a therapeutic measure in angina pectoris is discussed.

In previous studies\(^1\) data were presented in support of the concept that coronary artery vasomotor changes, reflex in origin, exerted a contributory influence in the precipitation of attacks of angina pectoris. The influence of reflexes mediated through the vagus nerve in precipitating attacks of angina pectoris has been the subject of few studies. It has been observed\(^2\)–\(^10\) that stimulation of the carotid sinus relieves the pain of angina pectoris. We have not been able to find any studies on the mechanism of relief of cardiac pain by carotid sinus stimulation. The purpose of this communication is to report our studies on the mechanism of the relief of cardiac pain induced by carotid sinus stimulation. The effect of carotid sinus pressure on the exercise tolerance of patients with angina pectoris is also reported.

**Materials and Methods of Study**

In most of the published reports of the beneficial effect of carotid sinus pressure in angina pectoris, the anginal attacks were spontaneous and the usual duration of pain unknown. In the studies of Wayne and Laplace,\(^8\) although anginal attacks were induced by exertion, the amount of exercise necessary to produce pain was variable from experiment to experiment. The importance of carefully standardized conditions, especially cold, in studying the precipitation and the duration of attacks of angina pectoris in the laboratory has been previously demonstrated.\(^11, 12\) Accordingly for the present study subjects were selected who had been observed at weekly intervals for many months to years in a special clinic for the study of angina pectoris. Thus their clinical course was well known, the response to exercise and to various therapies was repeatedly observed and the actual duration of attacks induced by exercise had been repeatedly measured and found to be reproducible.

In our previous studies\(^11\), \(^13a\), \(^13b\) the response to nitroglycerin was used to determine the likelihood of response to other forms of treatment and served to divide patients into three groups: Group I patients (tables 1, 2, 3 and 4) are "marked reactors" to nitroglycerin. Two minutes after the sublingual administration of 0.3 mg. of nitroglycerin these patients are able to perform approximately 100 per cent or more work than had been possible without medication. This increase in exercise tolerance in group I patients is accompanied by a marked decrease in the RS-T deviations consequent to exercise. Patients in group II, termed "moderate reactors," are able to do approximately 50 per cent more work two minutes after the sublingual administration of 0.3 mg. of nitroglycerin. Patients in group III, termed "nonreactors," show no response to the administration of nitroglycerin.

All tests were carried out at least one hour after a light breakfast and after the patient had rested a minimum of one-half hour after coming to the laboratory. Only one test was carried out on any one day. The patient received no medication during the carotid sinus experiments.

After the amount of exercise necessary to induce angina and the duration and characteristics of pain had been measured on numerous occasions (10 to 50) the effect of carotid sinus pressure on the duration of pain was measured in the following fashion. Immediately after the patient stopped exercise because of pain he seated himself on the two-step staircase; one observer, who was stationed behind the patient, then located as quickly as possible the right or left carotid sinus region and stimulated it by pressure and massage. The time necessary to locate the carotid sinus, the duration of stimulation and the duration as well as the character of

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pain was measured by another observer with the aid of a stop watch. In measuring the duration of anginal pain, all tests in which carotid sinus stimulation induced syncope were necessarily excluded. Uniform stimulation of the carotid sinus was attempted; involuntary stiffening of the sternocleidomastoid muscles (usually in later experiments) made accurate location and control of pressure of severity of pressure difficult to obtain.

As a control of the carotid sinus experiments, in other experiments with the onset of cardiac pain the patient was seated and pressure was exerted on the right or left sternocleidomastoid muscle. The latter procedure was without effect on the duration or character of the anginal attack.

I. Effect of the Carotid Sinus Pressure on the Duration of the Pain of Angina Pectoris

The effect of carotid sinus pressure on the duration and characteristics of anginal pain was studied in 13 patients (table 1). In most instances three to seven seconds elapsed before the carotid sinus could be located. The usual duration of stimulation was approximately six seconds with extremes of 3 to 40 seconds. In all 13 patients some relief of pain was observed as a consequence of carotid sinus stimulation. In 11 of the 13 patients the onset of relief of pain occurred during or within a few seconds after carotid sinus stimulation. In four of five patients (cases 7, 10, 11, 12, and 13) with attacks of one to four minutes duration, carotid sinus pressure induced temporary relief of anginal pain, persisting for 22 to 64 seconds (table 1). In each of these four patients pain of unaltered intensity, compared with pre-carotid sinus pressure, recurred and the total duration of the attack was not appreciably altered from that observed in control experiments. In the fifth patient (case 12) the usual duration of pain was 180 seconds; following carotid sinus stimulation intermittently for 40 seconds, pain disappeared and did not return. In one instance (case 4) anginal pain disappeared from the right side of the chest during right carotid sinus pressure while persisting on the left side, while in case 7 anginal pain disappeared from the chest during carotid sinus pressure while persisting in the shoulder.

In two patients (cases 2 and 10) relief of pain was not uniformly induced by carotid sinus stimulation from experiment to experiment. In one of these, case 2, and similarly in cases 3 and 6, carotid sinus stimulation of one side was effective while pressure on the other side had no, or less, effect on cardiac pain. In two other patients (cases 5 and 8) right or left sided stimulation was similarly effective in relieving cardiac pain. In no instance was prolongation of anginal pain induced by carotid sinus stimulation.

STUDIES ON THE MECHANISM OF RELIEF OF PAIN

A. Effect of Carotid Sinus Pressure in Patients with Angina Pectoris as Compared with Patients in the Same Age Group without Angina Pectoris

Fifteen patients with angina pectoris of arteriosclerotic etiology and 50 patients of the same age group without angina pectoris were studied. None of the patients in either group had ever suffered a spontaneous episode of syncope or had a history suggesting a hyperactive carotid sinus syndrome. The patients were seated and connected to an electrocardiograph machine. Using lead V1R, with the camera running continuously, right carotid sinus pressure was applied for six seconds. Calculations of the cardiac rate changes were made from the electrocardiographic tracings. The degree and severity of carotid sinus pressure was felt to be the same in both groups. The blood pressure was measured by the auscultatory method.

Results. In 25 of the 50 patients in the control group, right carotid sinus pressure for six seconds induced no discernible change in cardiac rate or blood pressure and was unattended by symptoms. A similar lack of response to carotid sinus pressure was observed in 3 of the 15 patients with angina pectoris (table 1, cases 1, 12 and 13). The incidence of asystole and auriculoventricular block was the same in both groups. The duration of the induced asystole in the patients with angina pectoris averaged six seconds as compared with three seconds in the control group. Syncope and convulsions were observed in 5 of the 15 angina pectoris patients and in 2 of the 50 control patients.

Further Evidence of the Increased Sensitivity of the Carotid Sinus Reflex in Angina Pectoris.
### Table 1. The Effect of Carotid Sinus Stimulation on the Duration of Attacks of Angina Pectoris

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Unusual Duration of Pains (seconds)</th>
<th>Carotid Sinus Stimulation</th>
<th>Time from End of Exercise to Start of C.S. Pressure (seconds)</th>
<th>Time from End of Exercise to End of C.S. Pressure (seconds)</th>
<th>Time of First Disappearance of Pain (seconds)</th>
<th>Time of End of Attack (seconds)</th>
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<tr>
<td>1. H. B.</td>
<td>18</td>
<td>Right 4</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>Attack shortened.</td>
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<tr>
<td>2. S. E.</td>
<td>27</td>
<td>Right 3.5</td>
<td>10.5</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>Attack shortened.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Left 3</td>
<td>11</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>No change.</td>
</tr>
<tr>
<td>3. S. L.</td>
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<td>Right 2</td>
<td>4</td>
<td>4</td>
<td>4-6</td>
<td>22</td>
<td>Attack shortened.</td>
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<tr>
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<td></td>
<td>Left ?</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>22</td>
<td>Pain disappeared during carotid sinus pressure; returned 15 seconds after exercise.</td>
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<td>4. N. S.</td>
<td>30</td>
<td>Right 3</td>
<td>18</td>
<td>15</td>
<td>30</td>
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<td>At 15 seconds pain disappeared on right side of chest; pain on left side persisted for 15 seconds.</td>
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<tr>
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<td>Left ?</td>
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<tr>
<td>6. R. S.</td>
<td>58</td>
<td>Right 5</td>
<td>13</td>
<td>55</td>
<td>55</td>
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<td>No change.</td>
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<tr>
<td>7. S. R.</td>
<td>250</td>
<td>Right 2.6</td>
<td>8.2</td>
<td>8.2</td>
<td>200</td>
<td>200</td>
<td>Pain disappeared from chest during carotid sinus pressure, but persisted unchanged in left shoulder. Pain returned in chest 28 seconds after exercise.</td>
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<td>Right 3</td>
<td>14</td>
<td>24</td>
<td>24</td>
<td>212</td>
<td>Pain disappeared from chest 7 seconds after carotid sinus stimulation ended; pain persisted in shoulder. Pain in chest returned 41 seconds after exercise.</td>
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<td>8. P. R.</td>
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<td>Pain disappeared during carotid sinus pressure.</td>
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<tr>
<td></td>
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<td>Left 3</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>Pain disappeared during carotid sinus pressure.</td>
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#### Group II

<table>
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<tr>
<th>Case No.</th>
<th>Unusual Duration of Pains (seconds)</th>
<th>Carotid Sinus Stimulation</th>
<th>Time from End of Exercise to Start of C.S. Pressure (seconds)</th>
<th>Time from End of Exercise to End of C.S. Pressure (seconds)</th>
<th>Time of First Disappearance of Pain (seconds)</th>
<th>Time of End of Attack (seconds)</th>
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</tr>
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<td>10. H. Y.</td>
<td>62</td>
<td>Right 2.5</td>
<td>8</td>
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<td>Pain disappeared during carotid sinus pressure; pain returned 22 seconds after exercise. Total duration of pain unchanged by carotid sinus pressure.</td>
</tr>
<tr>
<td>11. J. M.</td>
<td>125</td>
<td>Right 2</td>
<td>8</td>
<td>60</td>
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<td>No change.</td>
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<td></td>
<td></td>
<td>Right 7</td>
<td>12</td>
<td>12</td>
<td>116</td>
<td></td>
<td>Chest pain and wheezing disappeared during carotid sinus pressure. Chest pain returned 31 sec. after exercise. Total duration of pain unchanged by carotid sinus pressure.</td>
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<td>13. H. M.</td>
<td>250</td>
<td>Right 7</td>
<td>16</td>
<td>17</td>
<td>268</td>
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<td>Pain disappeared during carotid sinus pressure; pain returned 40 seconds after exercise. Total duration unchanged.</td>
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#### Group III

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<th>Case No.</th>
<th>Unusual Duration of Pains (seconds)</th>
<th>Carotid Sinus Stimulation</th>
<th>Time from End of Exercise to Start of C.S. Pressure (seconds)</th>
<th>Time from End of Exercise to End of C.S. Pressure (seconds)</th>
<th>Time of First Disappearance of Pain (seconds)</th>
<th>Time of End of Attack (seconds)</th>
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</tbody>
</table>

Comment:

1. H. B.
2. S. E.
3. S. L.
4. N. S.
5. M. L.
6. R. S.
7. S. R.
8. P. R.
9. B. K.
10. H. Y.
11. J. M.
12. N. B.
13. H. M.
The results presented above suggested that the carotid sinus reflex was more sensitive in patients with angina pectoris than in patients of the same age group who did not have angina pectoris. The opportunity arose to make studies of carotid sinus sensitivity in a patient with angina pectoris during a period when the patient was having many attacks of angina pectoris daily as well as during a prolonged period of remission from angina pectoris lasting many weeks.

In these studies the patient was seated and connected to the electrocardiographic machine. With the camera running continuously lead V4r was taken and right carotid sinus stimulated. The duration of stimulation was measured from electrocardiograms by marking the onset and offset of carotid sinus pressure. In varying the duration of stimulation from 1 to 10 seconds we attempted to keep the severity of pressure uniform in all experiments. Only one experiment was carried out on each day. The duration of the induced asystole was measured from the electrocardiographic tracings.

The effect of stimulation of the right carotid sinus was more marked when the patient was having many anginal attacks than during a remission from his angina (fig. 1). During the remission from angina, up to 10 seconds, right carotid sinus pressure produced a maximum asystole of 6.5 seconds. Faintness, syncope or convulsions were not observed. During the period when the patient was suffering two to three daily attacks of angina, pressure on the carotid sinus for two seconds induced an asystole of six and one-half seconds and pressure for five to six seconds produced an asystole of 8½ to 10 seconds and in both instances syncope and convulsions were observed (fig. 1). The patient was immediately laid down in each of these latter episodes. Recovery was prompt and sequelae were absent.

B. Relationship of Relief of Pain by Carotid Sinus Stimulation to Changes in Cardiac Rate

In previous studies3–9 the beneficial effects of carotid sinus stimulation in the relief of cardiac pain have been ascribed to cardiac slowing; the latter has been estimated by auscultation.

In our studies, the changes in pulse rate were calculated from electrocardiographic tracings. Standard electrodes were adjusted and affixed to both arms below the insertion of the deltoid muscle and also to the precordium over the cardiac apex. With the patient standing at rest, prepared to exercise, a 15 second tracing of lead V4r was obtained. The standard exercise test was performed as usual with the electrodes in place and the electrocardiographic machine (but not the camera) running continuously. The camera was started before the predicted cessation of exercise and tracings (at least 15 seconds in duration) were obtained at the onset of cardiac pain and the cessation of exercise and usually one, two, three and five minutes thereafter. The onset and offset of carotid sinus pressure was indicated on the tracing. The cardiac rate (beats per minute) was calculated for each cycle from the formula

\[ \frac{60}{R-R \text{ in seconds}} \]

I. Relief of Cardiac Pain by Carotid Sinus Stimulation Not Associated with Cardiac Slowing. In 10 of 13 patients studied (table 1) some degree of slowing was obtained by carotid sinus stimulation. In three patients (table 1, cases 1, 12 and 13) relief of cardiac pain by carotid sinus stimulation was obtained without slowing of the heart rate. In patient H. B.,
following pressure on the right carotid sinus for three seconds, the attack of pain ended; the attack was shortened from a usual duration of 18 seconds to 7 seconds. The heart rate was unchanged during the period of carotid sinus stimulation. In patient X. B. intermittent stimulation of the right carotid sinus was carried out for 40 seconds, at which time cardiac pain disappeared. The duration of the usual attack of angina pectoris in this patient was 180 seconds. In this patient, carotid sinus stimulation was without effect on the cardiac rate. Similarly in patient H. M., relief of cardiac pain for approximately one minute was obtained following stimulation of the right carotid sinus, although carotid sinus stimulation was not associated with any change in cardiac rate.

128 to 85, a more marked decrease in cardiac rate than was observed in the experiment illustrated in figure 2. Cardiac pain was unaffected.

**Fig. 2.** The effect of carotid sinus pressure on heart rate and anginal pain in H. Y. (See text for description.)

**II. The Lack of Relationship between the Degree of Cardiac Slowing and Relief of Cardiac Pain.** This is exemplified by the observations made in patient H. Y. (figs. 2 and 3). Pressure on the right carotid sinus (fig. 2) was begun two and seven-tenths seconds after the onset of cardiac pain and continued for five and one-tenth seconds. The cardiac rate fell from 105 to 80. During the period of carotid sinus stimulation cardiac pain disappeared and did not return for 16 seconds. The total duration of the attack was 55 seconds. In the same patient on a different day the onset of cardiac pain began after the same number of trips on the staircase (fig. 3). Stimulation of the right carotid sinus was begun three seconds after the onset of pain and continued for six and one-half seconds. The cardiac rate fell from

**Fig. 3.** The effect of carotid sinus pressure on heart rate in H. Y. showing marked cardiac slowing and no effect on anginal pain. The termination of cardiac pain after the second carotid sinus pressure was completed was coincidental with the decrease in cardiac rate. The usual duration of cardiac pain in this patient was 55 to 60 seconds. (See figure 3.)

**Fig. 4.** Marked cardiac slowing during right carotid sinus pressure in N. S. and no effect on the duration of the attack of angina pectoris induced by exercise. In other attacks in this patient temporary relief of cardiac pain occurred with carotid sinus pressure.

**III. Marked Slowing of Cardiac Rate during Carotid Sinus Stimulation without Effect on Cardiac Pain.** In patient N. S. cardiac pain began after 18 trips on the staircase (fig. 4). Stimulation of the right carotid sinus was begun five seconds after the end of exercise and continued for nine seconds. The cardiac rate fell from 115 to 56; the rate was below 80 for approximately half the duration of the attack of pain. The attack of angina pectoris continued unaltered and the total duration of pain was...
un ALTERED as compared with the duration of inducted but untreated attacks (fig. 5) during which the heart rate was over 100 beats per minute.

IV. The Occurrence of the Relief of the Pain of Angina Pectoris Following Carotid Sinus Pressure after the Cardiac Rate Has Returned to the Control Level. In patient P. R. during the stimulation of the right carotid sinus the heart rate slowed initially from 107 to 73, but promptly rose to 107, although stimulation was continued. Cardiac pain disappeared coincident with the end of carotid sinus pressure and at a time when the heart rate had returned to the precarotid sinus stimulation rate. The total duration of cardiac pain was 10 seconds, considerably shorter than the usual duration of control attacks (table 1).

A somewhat similar sequence was observed in patient S. R. (fig. 6); right carotid sinus pressure was begun approximately three seconds after the onset of chest pain and continued for 14 seconds. Eight seconds after stimulation was begun the cardiac rate abruptly fell from 115 to 73; chest pain continued undiminished. It is possible that actual stimulation of the sinus did not begin until seven to eight seconds after the onset of cardiac pain. Seven seconds after carotid sinus pressure was discontinued, chest pain disappeared for a period of 17 seconds (fig. 6). The cardiac rate at the onset of relief of pain was 115. It should be emphasized that although anginal pain dis-

appeared from the chest during this period of time, shoulder pain continued undiminished. The total duration of the attack of angina pectoris was 212 seconds (the usual duration was 250 seconds).

Fig. 6. The heart rate and effect of right carotid sinus pressure in S. R. The relief of cardiac pain occurred after the heart rate had returned to the same rate recorded before carotid sinus pressure. (See text for description.)

Fig. 7. Another experiment showing the lack of relationship between cardiac rate and relief of cardiac pain following carotid sinus pressure in S. R. (Compare with figure 6.)

In the same patient, S. R., on a different occasion, (fig. 7) right carotid sinus pressure was begun two and six-tenths seconds after the patient stopped exercise, and continued for five and six-tenths seconds. The cardiac rate momentarily slowed from 135 to 98, returning within one and five-tenths seconds to 120 at the end of carotid sinus stimulation, rising to 130 a few seconds later. Pain disappeared from the chest, while persisting in the shoulder, at the end of carotid sinus stimulation during a period when the cardiac rate was only slightly below the precarotid sinus pressure level. The
duration of relief of pain was approximately 22 seconds. The total duration of the attack of angina pectoris was 200 seconds (the usual duration 250 seconds, table 1).

C. The Effect of Carotid Sinus Stimulation on the Exercise Tolerance of Patients with Angina Pectoris: With a Comparison of the Effect of Nitroglycerin on the Exercise Tolerance of the Same Patients

The available evidence from animal experimentation concerning the influence of the vagus nerve on coronary blood flow is conflicting. Some observers, however, believe that the vagus nerve is vasodilator to the coronary arteries. It was hoped that some light might be cast on this subject by determining the effect of vagal stimulation on the exercise tolerance of patients with angina pectoris and comparing the results with those obtained after the use of a coronary vasodilator such as nitroglycerin. These studies seemed particularly appropriate since it was possible that the effect of carotid sinus stimulation in relieving the pain of angina pectoris might be due to coronary vasodilation.

The effect of carotid sinus pressure on the exercise tolerance was studied in 10 patients with angina pectoris (table 2). The exercise tolerance tests were performed under the usual standardized conditions except that immediately prior to exercise the right carotid sinus was stimulated for six seconds. The severity of pressure was, of necessity, mild since the stimulation was done with the patient erect. On another day, pressure of approximately the same severity and duration was exerted on the right sternocleidomastoid muscle immediately before exercise. The experiments in which the right carotid sinus was stimulated were performed on at least two occasions in each patient.

Results. After right carotid sinus stimulation five patients were able to perform at least 50 per cent more work before developing pain as compared with control exercise tolerance tests. The response to carotid sinus pressure was independent of the response of the patient to nitroglycerin; a marked increase in exercise tolerance was obtained following carotid sinus stimulation in some patients who did not respond to nitroglycerin, for example, patient H. M. (table 2), while little effect was observed after stimulation in some patients who showed a marked response to nitroglycerin, for example, patients M. L., and N. S. (table 2). In one, H. M., of the two patients in group III who did not respond to nitroglycerin, a 100 per cent increase in exercise tolerance was demonstrated after carotid sinus pressure. On the other hand, of the five patients in group I, carotid sinus pressure resulted in an increased exercise tolerance of 50 per cent in one patient, approximately 50 per cent in another and less than 25 per cent in the remaining three. In each of these five patients the prophylactic administration of nitroglycerin induced an increase in exercise tolerance of at least 100 per cent.

Electrocardiographic Studies. We have previously shown (13) that the administration

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\begin{array}{|c|c|c|c|}
\hline
\text{Case} & \text{Control Exercise Tolerance Tests. No Medication. Pressure on Sternocleidomastoid Muscle} & \text{Pressure on Carotid Sinus Immediately before Exercise} \\
\hline
\text{Trips} & \text{Trips} & \text{Per cent Increase} \\
\hline
\text{Group I} & & \\
\text{HS} & 24 & 36 & +50 \\
\text{SR} & 40 & 58 & +45 \\
\text{HB} & 75 & 100* & +33* \\
\text{NS} & 24 & 30 & +25 \\
\text{ML} & 36 & 42 & +16 \\
\text{RS} & 20 & X & \\
\hline
\text{Group II} & & \\
\text{LW} & 40 & 74 & +85 \\
\text{PR} & 45 & 74* & +65* \\
\text{BK} & 30 & 23 & -23 \\
\hline
\text{Group III} & & \\
\text{HM} & 20 & 41 & +105 \\
\text{BA} & 40 & 40 & 0 \\
\hline
\end{array}
\]

* No attack. Stopped because of fatigue.
X Exercise not attempted because of faintness.
of nitroglycerin to patients with angina pectoris not only results in an increased ability to perform work before the development of pain, but also prevents the S-T segment and T wave changes which are consequent to exertion.

In two patients with angina pectoris (H. B. and P. R.) electrocardiograms were obtained in the manner described above after a fixed exertion insufficient to produce pain, namely 10 to 15 trips. The changes in the RS-T segment and T waves were measured in at least 10 consecutive complexes and the results averaged.

Pressure on the carotid sinus before exertion did not prevent the RS-T segment and T wave changes consequent to exertion.

The Effect on the Exercise Tolerance of a Group of Vagomimetic, Vagolytic and Antispasmodic Drugs. The increase in exercise tolerance consequent to carotid sinus stimulation in some patients suggested the possibility that vagomimetic substances such as physostigmine salicylate might have a beneficial effect in patients with angina pectoris. It also seemed appropriate to study these and vagolytic substances in the hope that some light might be thrown on the role of the vagus on the coronary circulation.

The administration of 1.3 mg. of physostigmine salicylate four times daily, the last dose being taken two hours before the performance of the exercise tolerance test, was followed by an increase in exercise tolerance in 2 (H. B. and H. St., table 3) of 11 patients with angina pectoris studied. It may be noted that an increase in exercise tolerance of similar magni-

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<th>After Physostigmine</th>
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<td>40</td>
<td>31</td>
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Table 3.—The Effect of the Oral Administration of Physostigmine Salicylate (1.3 mg. q.i.d.) on the Ability to Work

Table 4.—The Effect of the Oral Administration of Atropine Sulfate (0.5 mg. q.i.d.) on the Ability to Work

* No attack. Stopped because of fatigue.
The disappearance of pain occurs within a few seconds; the speed of the relief of pain is in favor of a neurogenic mechanism. The previously mentioned disappearance of pain in certain areas while persisting in others, indicates alteration in sensory pathways. This is similar to the disappearance of pain following thyroidectomy and nerve blocking procedures. The relief of cardiac pain by interruption of sympathetic nerves has been well established. Interruption of nerve pathways in the skin, cervical ganglionectomy, and injection of various sympathetic nerves in the cervical and thoracic region are also associated with relief of cardiac pain.

The relationship of the carotid sinus to the sympathetic nervous system has been clearly demonstrated by Heymans and associates. Together with stimulation of the vagus nerve, there is a simultaneous inhibition of the sympathetic nervous system. Bronk and his co-workers showed that during carotid sinus stimulation there was a decreased number and strength of action potentials as recorded from the cervical sympathetic fiber to the carotid sinus.

Ferris, Capp and Weiss postulated that the effect of carotid sinus pressure in inducing syncope was, in some instances, due to stimulation of a cerebral center. In our studies, the patients were able to perceive the pain of a needle while obtaining relief of cardiac pain during carotid sinus stimulation. Instances where a changed sensorium or syncope consequent to carotid sinus stimulation were observed have been excluded. We cannot, however, deny the possibility of an effect on some cerebral center.

Our studies yield no evidence that carotid sinus stimulation induces coronary artery vasodilatation. No relationship was observed between the increase in exercise tolerance after stimulation, and that observed after the administration of vasodilators (table 2). An increased exercise tolerance was observed after stimulation in patients, in whom nitroglycerin was without effect, and vice versa. Furthermore, pressure upon the carotid sinus before exercise, while associated with an increased exercise tolerance, did not prevent the RS-T segment changes consequent to exertion. In
previous studies\textsuperscript{33} we have shown that the increased exercise tolerance following the administration of nitroglycerin is accompanied by a decrease or absence of the RS-T segment changes consequent to exercise.

An additional consideration against the occurrence of vasodilation as a causative factor in the relief of cardiac pain by carotid sinus pressure is the speed of the reaction. Previous studies\textsuperscript{12-16} using various vasodilators have shown that relief of cardiac pain occurs in 20 to 30 seconds. The relief of pain associated with carotid sinus pressure occurred in almost all instances during or shortly after pressure the average duration of which was about six seconds. It would be expected that if vasodilation occurred with pressure on a carotid sinus a period would elapse during which cardiac anoxia was relieved by increased blood flow (similar to that observed after amyl or octyl nitrite) before relief or cardiac pain occurred; recurrence of pain of unaltered intensity and an unaltered duration of prolonged attacks would not be expected if significant coronary vasodilatation occurred.

On the basis of auscultatory findings previous authors have pointed out the association of cardiac slowing with the relief of pain by carotid sinus stimulation. It was to be expected, as has been demonstrated by many others, that stimulation would induce cardiac slowing in most subjects with coronary artery disease and angina pectoris. Our studies, however, show no relationship between the changes in cardiac rate following pressure on a carotid sinus and the relief of pain. Thus, marked cardiac slowing was obtained without relief of pain and relief of pain occurred when cardiac slowing was absent or not significant. Furthermore, in the same patient (H. Y.) in several attacks similar degrees of cardiac slowing were obtained during carotid sinus stimulation with relief of pain in one attack, and not in others.

The Usefulness of Carotid Sinus Pressure as a Diagnostic Test

It has been suggested by Sigler and others\textsuperscript{6,7,26,27} that the demonstrated increased sensitivity of the carotid sinus reflex in patients with coronary artery disease may be used as a diagnostic test. The studies of Mandelstamm and Lipshtitz,\textsuperscript{28} Weiss\textsuperscript{29} and others indicate that the carotid sinus reflex is more active in the older age groups and particularly in the presence of coronary artery disease. Parry\textsuperscript{30} was presumably the first to observe this phenomenon. Others, including Hering\textsuperscript{21} and Prusick,\textsuperscript{22} also pointed out the increased sensitivity of the carotid sinus reflex in patients with angina pectoris. Sigler\textsuperscript{27} stated “the test may perhaps be considered to be a definite sign of coronary disease under the following condition; if it occurs as an independent phenomenon unassociated with other reflexes of the carotid sinus group such as a marked fall in blood pressure and cerebral manifestations including dizziness, sensory disturbances and syncope...and if it appears after comparatively slight pressure on the carotid sinus region and other vagal disturbances occur.” Our own studies show that the effects of a definite degree of carotid sinus stimulation are more marked in patients with angina pectoris of arteriosclerotic etiology, than in patients of a similar age group without this condition. It should, however, be pointed out that some patients with angina pectoris of arteriosclerotic etiology do not have a sensitive carotid sinus.

It has been well established that the effects of carotid sinus stimulation are more marked in the older age groups than in the younger age groups. It is, however, incorrect to assume that coronary arteriosclerosis need occur with aging, nor is coronary arteriosclerosis synonymous with angina pectoris. Many patients with coronary arteriosclerosis and old coronary occlusions never suffer from angina pectoris.\textsuperscript{33}

More recently Levine\textsuperscript{34} has suggested that the relief of pain after pressure on the carotid sinus may be used as a diagnostic test for angina pectoris. At the present time it has not been demonstrated that the relief of pain following carotid sinus stimulation is specific for cardiac pain; in some patients, carotid sinus pressure has no effect on cardiac pain.\textsuperscript{27,28} It should be emphasized, moreover, that the dangers of carotid sinus stimulation are real. Prusick and Herles\textsuperscript{22} concluded that the carotid sinus pressure test may be a dangerous diag-
nostic test. They reported four cases where carotid sinus pressure produced asystole, syncope and convulsions and in one instance a fatal result. Similarly, one third of a small group of patients studied by us showed syncope and convulsions following six seconds of carotid sinus stimulation. The degree of sensitivity in one patient was such that two seconds of carotid sinus pressure produced an asystole of over six seconds. Downes36 reported a series of surgical cases in which carotid sinus reflexes were implicated in the death of the patients. Askey36 has reported the appearance of hemiplegia in seven patients after carotid sinus stimulation; other observations are confirmatory.37,38 Ventricular fibrillation has also been reported after carotid sinus stimulation.

The considerations pointed out above militate against the usefulness of carotid sinus pressure as a therapeutic agent. Mandelstamm7 describes one patient, a female, aged 50, who obtained relief of angina pectoris by self pressure on the carotid sinus. Patients have, in instances of paroxysmal supraventricular tachycardia, been taught to stimulate their own carotid sinuses to abolish the attack.52 In contrast to the observations in angina pectoris, syncope and convulsions following carotid sinus pressure under these circumstances are rare.

SUMMARY AND CONCLUSIONS

1. The effect of carotid sinus pressure on the duration and character of attacks of angina pectoris induced by exercise under controlled laboratory conditions has been studied in 13 patients. In all 13 patients some relief of cardiac pain was observed consequent to right or left carotid sinus stimulation. In 11 of the 13 patients, the onset of relief of cardiac pain occurred during or shortly after approximately six seconds of carotid sinus stimulation. In patients whose attacks of angina pectoris ordinarily lasted less than one minute, carotid sinus pressure terminated the attack. In four of five patients with attacks of one to four minutes duration, carotid sinus stimulation induced temporary relief of anginal pain persisting for 22 to 64 seconds; in each instance anginal pain returned in complete intensity and the total duration of the attack was not significantly altered in comparison to induced attacks not treated by carotid sinus pressure. In one patient, pain disappeared from the right side of the chest during right carotid sinus pressure while persisting on the left side, while in a second patient, pain disappeared from the chest during carotid sinus pressure, while persisting in the shoulder. These observations are consistent with the hypothesis that stimulation of the carotid sinus induces relief of cardiac pain by interruption of sympathetic reflex arcs or sensory pathways.

2. Various studies yielded no evidence that carotid sinus pressure relieves cardiac pain by inducing coronary artery vasodilation or by altering the discrepancy between myocardial demand and blood supply observed in the attack of angina pectoris. Carotid sinus pressure before exercise resulted in an increase in exercise tolerance in 5 of 10 patients with angina pectoris. No relationship could be established between this increase in exercise tolerance and that observed in the same 10 patients when 0.3 mg. of nitroglycerin was administered before exercise. An increased exercise tolerance was seen after carotid sinus pressure in patients in whom nitroglycerin was without effect and vice versa. Carotid sinus pressure before exercise did not prevent, as does nitroglycerin, the R-ST segment changes consequent to exertion. The speed of relief of cardiac pain by carotid sinus pressure is also against the hypothesis that coronary vasodilation occurs with consequent improvement in the discrepancy between blood supply and myocardial demand. Continuous electrocardiographic studies were carried out before, during and after carotid sinus pressure in 13 patients during attacks of angina pectoris. No consistent relationship existed between the change in cardiac rate following carotid sinus pressure and the relief of cardiac pain. Marked cardiac slowing was obtained without relief of pain and relief of anginal pain occurred when cardiac slowing was absent or not significant.

3. The doubtful usefulness of carotid sinus pressure as a diagnostic test and a therapeutic measure in angina pectoris are discussed. The
dangers of carotid sinus pressure have been emphasized.

**SUMARIO ESPAÑOL**

El efecto de presión sobre el seno carotídeo en la duración y el carácter de ataques de angina de pecho inducidos por ejercicio bajo condiciones controladas ha sido estudiado en 13 sujetos. Observaciones son presentadas que son consistentes con la hipótesis de que la estimulación del seno carotídeo induce dolor cardíaco mediante la interrupción de arcos reflejos simpáticos o nervios sensoriales. El uso de presión sobre el seno carotídeo como una prueba diagnóstica y terapéutica en la angina de pecho se discute.

**REFERENCES**


