Effects of Autonomic Nerves and Their Mediators on the Coronary Circulation and Myocardial Contraction

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With the assistance of Earl B. Dawson, A.B. and Thomas W. Kitchen, B.S.

Mean and phasic coronary flows were recorded simultaneously by an electromagnetic meter, and peripheral coronary pressure was recorded distally from the temporarily occluded descending branch of the left coronary artery. From the results of these studies we conclude that: 1. The sympathetic cardiac nerves, as does levarterenol, increase myocardial contraction, (indicated by a shorter, more abrupt systole and more rapid isometric relaxation), and cause a slight degree of coronary arteriolar dilation. 2. Parasympathetic fibers exert no significant effect, although acetylcholine diminishes coronary arteriolar tone and may slightly diminish ventricular contraction. 3. That measurements of mean coronary flow and resistance are relatively satisfactory for indicating changes in coronary arteriolar tone, but are of relatively little value in evaluating myocardial contraction.

Conflicting reports have appeared in the literature regarding the sympathetic control of the coronary circulation; direct constrictor and dilator effects have been described as well as indirect dilator effects resulting from altered contraction. Very little information is available as to whether or not a true parasympathetic control exists. The available reports are conflicting but the general consensus in the published data is that vagal parasympathetic stimulation would, if it had any effect, cause constriction of the coronary arterioles. Most of the early investigators measured only mean flow. Heart rate, aortic pressure, and strength of contraction were usually not evaluated, nor was arteriolar resistance calculated. These various variables may have led to contradictory interpretations. It appeared that a clearer interpretation of these effects could be made if the various flow determining factors could be evaluated separately. This paper is a report of investigations designed to demonstrate whether or not either the vagal or the adrenergic nerve fibers have any direct effect on the coronary arterioles or on ventricular contraction.

Methods

General. The technique used in this study is similar to that described by Denison, Bardhanabadra and Green. The studies were done on open-chested mongrel dogs given morphine sulfate, 2 mg./Kg. subcutaneously, followed in one half hour by 0.25 ml./Kg. of a solution containing sodium pentobarbital, diallylbarbituric acid and urethane. This anesthetic kept the heart rate from increasing excessively as it often will with pentobarbital alone. Intermittent positive pressure artificial respiration was administered by means of a motor driven valve which alternately inflated the lungs with compressed air and allowed them to deflate at the rate of 30 to 60 times/min. This was supplemented by a continuous flow of oxygen into the tracheal catheter at the rate of 3 L./min. Clotting was prevented by mepesulfate, 40 mg./Kg. initially plus 15 mg./Kg. per half hour.

Registration of Flow. Blood from the left carotid artery passed through a cannulating type of electromagnetic flowmeter and into a cannula inserted into the descending ramus of the left coronary artery 1 to 2 cm. from the bifurcation of the common artery. The output of the flowmeter and flow analyzer was divided. One part went directly to a recorded and provided a moment to moment phasic flow record. Mean flow was recorded by putting the other part of the output into a resistance-capacitance circuit which damped out the...
two small filaments could be found going from the first thoracic ganglion and lying close to the vertebral bodies. The vagosympathetic chain could be identified going caudal to the vertebral column. The ansa subclavia (the branches of the sympathetic fibers which surround the subclavian artery) was exposed by teasing away the loose, fatty tissue overlying the artery, and the fibers were followed dorsally until close to the vertebral bodies. The vagosympathetic cardiac nerves we removed most of the left sympathetic trunk towards the heart. Stimulation of these fibers, of the ansa subclavia, and of the first thoracic ganglion were all tried. The most consistent response was obtained by stimulation of the ganglion with a bipolar electrode using square wave pulses at a frequency of 15 to 30 c.p.s., a duration of 20 msec., and a strength of 6 to 8 V. supplied by a Grass stimulator.

The peripheral end of the severed left and right vagi were stimulated individually with square wave pulses from a Grass stimulator using a frequency of 15 to 30 c.p.s., a duration of 20 milliseconds, and a strength of 4 to 8 V. The heart was driven during part of the experiments by a pair of fishhook electrodes attached to the right atrium as close as possible to the sinoatrial node using square wave pulses provided by a second Grass stimulator at a strength of 4 to 8 V. and frequencies of 1 to 3.5 c.p.s. as required to assume control of the heart rate. Pulse durations of 2 to 30 msec. were tried in the first few experiments; a duration of 20 msec. was found the most reliable and was used subsequently. In general the vagus stimulation was started in order to demonstrate that the vagus was effective; then, while continuing the vagal stimulation, the pacemaker was started. While continuing the pacemaker, vagal stimulation was stopped (fig. 4). For some experiments the heart rate was slowed by topical anesthesia of the sinoatrial node. This permitted the pacemaker to drive the heart at a slower rate without "escape."

Measurements. Coronary perfusion pressure and the phasic coronary flow curves were measured at three moments in the cardiac cycles: (1) approximately the end of isometric contraction (at a minimum point of the coronary inflow curve), (b) the end of systole (just at the moment of onset of pre-diastole), and (c) at the end of diastole (immediately before the onset of isometric contraction). The various parameters during vagal stimulation alone were compared with those in the nondriven heart before vagal stimulation was begun (table 2, line 6). The parameters during vagal stimulation plus pacemaker were compared with those obtained during the control period before vagal stimulation (table 2, line 7) and also with those obtained during continuation of the pacemaker action after stopping vagal stimulation (table 2, line 8). In some instances where the effect of vagal stimulation was observed without the use of the pacemaker and a marked slowing of the heart occurred, a second set of diastolic pressures and flows was measured at the point in diastole where the next systole would have started if the control heart rate had been maintained (table 2, line 6, column C2).

Calculations. Column A, tables 1 and 2, Isometric Contraction. Since the flows during isometric
## Table 1.—Control Data from Seven Experiments

<table>
<thead>
<tr>
<th>Pressure (mm. Hg.)</th>
<th>Flow (ml./min.)</th>
<th>PRU</th>
</tr>
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<tbody>
<tr>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
</tr>
<tr>
<td>123.0</td>
<td>5.4</td>
<td>24.0</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
</tr>
<tr>
<td>55 to 163</td>
<td>—1 to +13</td>
<td>7 to 70</td>
</tr>
<tr>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
</tr>
<tr>
<td>23</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
</tr>
<tr>
<td>115.5</td>
<td>7.4</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
</tr>
<tr>
<td>50 to 155</td>
<td>—1 to +17</td>
<td>3 to 16</td>
</tr>
<tr>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
</tr>
<tr>
<td>23</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
</tr>
<tr>
<td>119.3</td>
<td>18.1</td>
<td>12.06</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
</tr>
<tr>
<td>62 to 152</td>
<td>6 to 29</td>
<td>5 to 22</td>
</tr>
<tr>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
</tr>
<tr>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
<td><strong>Average</strong></td>
</tr>
<tr>
<td>119.3</td>
<td>18.1</td>
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</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
<td><strong>Range</strong></td>
</tr>
<tr>
<td>62 to 152</td>
<td>6 to 29</td>
<td>5 to 22</td>
</tr>
<tr>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
<td><strong>No.</strong></td>
</tr>
<tr>
<td>29</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Contraction in the control period were sometimes positive (forward flow) and sometimes negative (backflow) we expressed the data as the difference between experimental and control flows by subtracting the control flow from the experimental flow \((F_c - F_c)\). Thus a positive figure for the difference would indicate either a lesser degree of backflow or a greater forward flow, and vice versa for a negative difference. The same calculation was made for the effect of the control saline injections. The net effect of the drug was then expressed as the drug difference minus the saline difference:

\[
[(F_{ic} - F_{ic})_{drug} - (F_{ic} - F_{ic})_{saline}] = \Delta F_{ic}\text{net}.
\]

Calculations. Columns B and C, Tables 1 and 2. End Systolic and End Diastolic Resistance. The data on flows \((F = ml./min.)\) and pressures \((P = mm. Hg)\) at the end of systole and at the end of diastole were calculated as PRU = \(\frac{ml. Hg}{ml./min.}\) and were then expressed as the ratio of experimental PRU to control PRU for the drug. A similar calculation was made for the control saline injections. The net drug effect was then calculated as the ratio for the drug divided by the ratio for the saline times 100:

\[
\frac{P_{c} \text{ drug}}{P_{c} \text{ drug}} + \frac{P_{c} \text{ saline}}{P_{c} \text{ saline}} \times 100 = PRU\%_{c}\text{net}
\]

Calculations. Column D, Tables 1 and 2, Mean Arteriolar Resistance. Mean arteriolar resistance was calculated from the ratio of the mean coronary artery pressure \((\text{mm. Hg})\) to the mean coronary artery flow \((\text{ml./min.})\), and the data for the experimental period were then expressed as the per cent of control 'mean arteriolar resistance. The mean coronary artery pressure was obtained by mechanical integration of the phasic pressure record. The effects of the saline injections were compensated for in the same manner as for columns B and C.

Calculations. Column E, Table 2, Ratio of Net Per Cent of Mean Control Resistance to Net Per Cent of End-Diastolic Control Resistance Expressed as Per Cent. These figures indicate the degree of correlation between changes in mean flow and in end-diastolic flow as indices of the amount of arteriolar dilation produced by the drugs and nerve stimulations.

Calculations. Column F, Table 2, Mean Flow. The mean flows in the experimental period were expressed as per cent of the mean flow in the control period only for the vagal stimulations.

Calculations. Columns G and H, Table 1 and 2, Peripheral Coronary Pressure (PCP). The end-diastolic peripheral coronary pressure was measured at the fourth cycle after occluding the coronary inflow. The effects of the various agents on this pressure were expressed as the per cent of control (column G). This diastolic PCP may be a measure of the "critical closing pressure" of the coronary vessels. The amplitude of the systolic rise in the PCP above the preceding diastolic pressure was computed as the pulse pressure, and was also expressed as the per cent of the control pulse pressure (column H).

Interpretations. Coronary arteriolar dilation was considered to have occurred when the peripheral resistance at the end of diastole (coronary perfusion pressure divided by coronary artery flow) decreased as compared to the resistance in the control period, and constriction was considered to have occurred when the resistance increased. The end-diastolic point of the heart cycle was chosen since at this moment extravascular compression is at a minimum and is undergoing a minimum change with time; thus the inflow is minimally influenced by changes in the volume of blood contained in the arteries distal to the meter. Increased myocardial contraction is defined, for
Fig. 1. Simultaneous records of right atrial pressure (VCP); mean flow (MCF), lateral pressure (CP) and phasic flow (CF) in the descending ramus of the left coronary artery, and aortic pressure (AP) of an open-chested anesthetized dog during stimulation of the (Continued on opposite page)
the purposes of this paper, as a more rapid and
greater degree of shortening of the myocardial
fibers and decreased myocardial contraction as the
converse. Augmentation of the systolic rise of in-
tramyocardial tension occurring without a signifi-
cant rise of aortic systolic pressure would be
indicative of such increased contraction. Qualita-
tive evidence of increased systolic intramyocardial
tension would be: (a) the occurrence in the flow
curves of a greater degree of reduction of inflow,
or the occurrence of backflow during isometric con-
traction and an increase in the computed resistance
to inflow at the end of systole; (b) the observation
in the pressure curves of a shortening of the ejec-
tion phase of systole; and (c) registration in the
PCP curves of a more abrupt rise and fall of
pressure and of an increase in the amplitude of
the pulsation (PCP, pulse, column H of tables
1 and 2).

Mean flows were originally thought to be of
minimal value in themselves in estimating coro-
nary arteriolar constriction or dilation, since mean
flow would be influenced not only by changes in
the arteriolar lumen but also by the varying extra-
vascular compression which occurs during systole
and early diastole and by variations in the dura-
tion of diastole with respect to that of the heart
cycle. However, the mean flow could indicate the
extent to which the balance between these factors
has been modified by a given drug injection or
other procedure, and thus could quantitate the
over-all effects on the flow. The phasic flow pat-
terns are the best indication of the primary action
of the agent whose effect is being studied, i.e., of
whether the effect is basically a change in vascular
tone, myocardial contraction, cycle length, or a
combination of these.

RESULTS

Twenty-one experiments were undertaken.
The sympathetic nerves usually became non-
responsive after an hour or two whether or
not they were stimulated, and the vagi some-
times failed to respond after prolonged stimu-
lation. Some animals failed to maintain a
satisfactory blood pressure, thus producing
abnormal coronary flow patterns; a few went
into ventricular fibrillation, and some had the
coronary artery embedded in the myocardium
so that a satisfactory cannulation was not
achieved. In general the responses that were
elicited by the drug injections and nerve stim-
ulations appeared to be normal in these de-
fective preparations. However, in view of the
extensive dissection and the rather long
time required to complete the procedure, it
was thought best to discard experiments in
which any of the above complications de-
veloped prematurely. The following data is
from 7 experiments that were considered to
be satisfactory by the above criteria.

Control Data. The control data, just prior
to the drug injections or stimulations at rep-
resentative points in the seven satisfactory
experiments, were similar to those in a pre-
vious study2 (table 1).

Sympathetic Nerve Stimulation. Stimula-
tion was limited to the left nerves in order to
minimize changes in heart rate. The first
effect was a progressive diminution of inflow
during late systole (fig. 1A, C and D,
and table
2, line 1, column B) ; this was followed by an
increase in end-diastolic flow and pressure
and, on the average, by an insignificant de-
crease in end-diastolic resistance (table 2, line
1, column Cj). On the average, mean flow
increased more than did end-diastolic flow.
Also mean resistance decreased more than did
the end-diastolic resistance; i.e., the mean per
cent of control resistance was 88.2 per cent
of the end-diastolic per cent of control resist-
ance, which was just significantly different
from 100 per cent (table 2, line 1, column C1,
D and E.) However, the difference was not
prominent in the record chosen for illustra-
tion (fig. 1). These changes in mean flow were

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TABLE 2.—Changes in Parameters of Coronary Circulation in Response to Various Agents

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av.</td>
<td>PLG (ml./min.)</td>
<td>No.</td>
<td>No.</td>
<td>NF</td>
<td>No.</td>
<td>No.</td>
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<tr>
<td>1. Stimulation</td>
<td>1.96</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>2. Acetylcholine</td>
<td>5.76</td>
<td>11.8</td>
<td>7</td>
<td>8</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>3. Acetylcholine</td>
<td>8.4</td>
<td>4.6</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>4. Acetylcholine</td>
<td>6.0</td>
<td>7.8</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>5. Acetylcholine</td>
<td>11.2</td>
<td>51.1</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>6. Vagus vs. control without PM</td>
<td>1.3</td>
<td>6.6</td>
<td>9</td>
<td>7</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>7. Vagus with PM*</td>
<td>0.12</td>
<td>129.5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>8. Vagus with PM*</td>
<td>0.25</td>
<td>147.5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>9. Acetylcholine</td>
<td>6.0</td>
<td>2.2</td>
<td>5</td>
<td>4</td>
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<table>
<thead>
<tr>
<th>H</th>
<th>PCP (% C) Pulse</th>
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<tbody>
<tr>
<td>121.0</td>
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</tr>
<tr>
<td>100.5</td>
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<td>101.6</td>
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<td>63.0</td>
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<td>11.8</td>
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<td>92.5</td>
<td>6.0</td>
</tr>
<tr>
<td>97.2</td>
<td>4.2</td>
</tr>
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</table>

Due to the fact that the flow accelerated more rapidly following closure of the aortic valve in the experimental than in the control period; this early diastolic acceleration more than compensated for the greater reduction of flow during systole in the experimental, as compared with the control period. The early diastolic acceleration of flow occurred simultaneously with the more rapid decrease in the PCP pressure during early diastole in the experimental phase of the records (fig. 1A, D and B). The effects of sympathetic stimulation increased progressively during the first 20 to 25 sec. of stimulation and persisted up to 4 min. after cessation of stimulation (fig. 1B).

Levarterenol. One μg. intracoronary artery injections of levarterenol produced changes similar to those reported previously (fig. 2). The effects were qualitatively similar to those obtained with sympathetic nerve stimulation, but quantitative differences were noted. As compared with sympathetic nerve stimulation it was noted that with levarterenol: 1. The effects appeared and disappeared more rapidly. 2. The inflow during isometric contraction was reduced more or converted to a greater degree of backflow. 3. End-systolic resistance always decreased, whereas with sympathetic stimulation it always increased. 4. The mean resistance was decreased to a lesser, though still significant degree. 5. End-diastolic PCP remained unchanged. 6. PCP pulse pressure was increased to a greater degree. 7. There was no significant difference in the effects on end-diastolic resistance (table 2, lines 1 and 2).

Acetylcholine. Acetylcholine in all doses increased the phasic flow and reduced the phasic resistance at all points in the cycle.
and increased the mean flow and reduced the mean resistance; the phasic flow curve appeared to be simply shifted upward from its level during the control period. As a consequence: 1. The end-systolic resistance decreased more than the end-diastolic. 2. The difference between experimental and control flow during isometric contraction was strongly
positive. With the 2 larger doses the PCP pulse pressure diminished, but there was no significant qualitative change in contour of the PCP curves. With the exception of the smallest dose, the changes in mean resistance were not significantly different from those of the end-diastolic resistance (table 2, lines 4 and 5). The maximum effects appeared rapidly, within 2 to 3 sec, and disappeared equally rapidly (fig. 3). There was no evidence of a dose-response correlation with the three doses of aceylcholine that were used.

Vagal Stimulation. The resting vagal tone was low, as indicated by minimal effects of vagal section per se. The various vagal stimulations were sufficient either to slow or stop the heart. Since changes of heart rate seemed to alter significantly the flows and resistances at various points in the heart cycle, we attempted to keep the heart rate constant by driving the atrium with an artificial pacemaker. However, the resting rate was frequently so high that it was difficult to "take over" the sinoatrial pacemaker function with the artificial pacemaker (fig. 4, A and C).

The normal reduction of flow during isometric contraction was not significantly affected by vagal stimulation. On the average, end-systolic resistance was increased, but the change was not significant. The resistance at the end of diastolic was slightly increased in the undriven heart and slightly decreased in the driven heart, but these changes were not significant. The mean resistance also was not significantly changed, although on the average the mean flow decreased (table 2, lines 6, 7 and 8).

Atrial Pressure. Sympathetic stimulation elevated right atrial pressure (fig. 1). It was the only agent that caused any significant change (figs. 2-4).

DISCUSSION

Levarterenol and Sympathetic Stimulation. At maximum effect, levarterenol and sympathetic stimulation appear to affect the myocardium in a quantitatively similar manner, as shown by the increases in PCP pulse pressures; for each, the strength of contraction is increased noticeably. The differences between the values of isometric contraction flow and the end-systolic flow suggest that levar-
terenol causes a more rapid onset of systolic contraction and more rapid relaxation; the pulsatile flow contour records support this interpretation. These differences may, however, be partly due to the fact that the levarterenol had a localized effect, limited to the portion of the myocardium supplied by the metered artery, whereas the sympathetic stimulation affected the whole ventricular myocardium.

The values of resistance change also uphold the concept that the flow contour of systole is altered by sympathetic stimulation and levarterenol. The mean resistance became less but the end-diastolic resistance did not change significantly (table 2, lines 1 and 2, columns C, D, and E). If the end-diastolic resistance is indicative of the arteriolar tone, it would seem that these sympathetic agents have only a minor effect directly on the arterioles. The increase in mean coronary flow seems to be accomplished by a shortening of diastole relative to the cycle length and by a more rapid increase in flow to its maximum value during isometric relaxation of the ventricles (fig. 2C). These results are similar to those reported by Gregg and Shipley.

Acetylcholine. Even in the smallest dose used (0.1 μg.), acetylcholine appears to be primarily a coronary arteriolar vasodilator since: 1. The mean level of the flow throughout the heart cycle was elevated. 2. Both end-diastolic and mean resistances were decreased without evidence of increased myocardial contraction. Acetylcholine appears to have a minimal depressant effect on myocardial contraction since: 1. The PCP pulse pressure was slightly diminished. 2. The flow during isometric contraction was reduced to a lesser degree than that in the control. It is possible that the effects on flow during isometric contraction and on the PCP pulse pressure were due to the accompanying coronary arteriolar dilation; however, opposite changes accompanied the coronary arteriolar dilation which followed levarterenol and sympathetic nerve stimulation. The lack of a dose-response curve suggests that the 0.1 μg. dose was sufficient to cause full vasodilation.

**Vagal Stimulation.** With vagal stimulation alone there were a small drop in mean flow, and small elevations in end-systolic, end-diastolic, equivalent diastolic and mean resistances, but none of these changes was significant. Vagal stimulation induced even less change in these parameters when the heart rate was kept at the control level (table 2, lines 6, 7 and 8). It appears, therefore, that, in contrast to acetylcholine, the vagus has no effect on ventricular contraction or on the coronary arterioles, and that changes in the pulsatile flows and pressures are due solely to slowing of the heart rate. These effects of vagal stimulation and of acetylcholine are in agreement with those obtained by Schreiner et al.

**Summary**

Coronary flow is determined primarily by the coronary arteriolar tone, and secondarily by the contractile effort of the heart and by the aortic pressure.

*Arteriolar Tone.* Acetylcholine consistently reduced coronary arteriolar tone. Vagal stimulation has neither a constrictor nor a dilator effect upon arteriolar tone. Sympathetic nerve stimulation, like levarterenol, is accompanied by only a slight and rather delayed coronary arteriolar dilation.

*Myocardial Contraction.* Vagal stimulation exerts no significant effect on myocardial contraction although acetylcholine may diminish it slightly. Levarterenol and sympathetic stimulation augment both myocardial contraction and the speed and completeness of myocardial relaxation; while these effects reduce flow during systole, they augment early diastolic flow and increase the relative duration of diastole.

*Summated Effects.* Mean flow is increased and mean resistance reduced by acetylcholine due primarily to its dilator effects on the arterioles and secondarily to its slight depressant effect on myocardial contraction. Mean flow is also increased by levarterenol and by sympathetic stimulation, partly by moderation of arteriolar tone and partly by marked alteration of the ventricular contractile pattern.
Under the influence of levarterenol and sympathetic stimulation the greater systolic reduction of flow is more than balanced by the more abrupt augmentation of flow in early diastole and the lengthening of the relative duration of the diastole, so that the direct effect of the augmentation of cardiac contraction may be a small increase in mean flow.

Changes in coronary arteriolar tone are fairly closely reflected by alterations in mean coronary flow and resistance, whereas evaluation of myocardial contraction requires techniques, such as registration of phasic coronary flow curves and/or peripheral coronary pressure curves.

**ACKNOWLEDGMENT**

The anesthetic was composed of equal parts of (a) a solution containing 60 mg./ml. of sodium pentobarbital and (b) Dial with urethane. The latter contains in each ml.: diallylbarbituric acid 0.1 Gm., urethane 0.4 Gm., and monooethylurea 0.4 Gm., and was supplied by Ciba Pharmaceutical Products, Inc., Summit, N.J.

The anticoagulant was Treburon (mepesulfate) supplied in a solution containing 250 mg./ml. with 0.5 per cent phenol by Hoffman-La Roche, Inc., Nutley, N.J.

The levarterenol (Levophed Bitartrate) was supplied in 4 ml. ampules containing 0.2 per cent of the salt. The dose was expressed in terms of the base. This was obtained from Winthrop Laboratories, Inc., Baltimore, Md.

**SUMMARIO IN INTERLINGUA**

Le fluxo coronari es determinate primariamente per le tono coronari-artoriolar e secundarimente per le effortio de contraction in le corde e per le pression aortica.

*Tono arteriolar.* Acetylcholina resultava uniformalmente in un reduction del tono coronari-artoriolar. Stimulation vagal exerce nulle effeeto constrittori e nulle effeeto dilatatori super le tono arteriolar. Stimulation de nervos sympatiches—como le administration de levarterenol—es accompaniante per solmente leve grados de satis retardate dilation coronari-artoriolar.

*Contraction myocardial.* Stimulation vagal exerce nulle effeeto significative super le contraction myocardial, ben que acetylcholina pare capace a reducir lo al minus levemente.

Tanto levarterenol como etiam stimulation sympathetic augmenta le contraction myocardial e le rapiditate e le grado de completessa del relaxation myocardial. Durante que iste effectos reduce le fluxo in systole, illos aumenta lo levemente in pro-diastole. Illos etiam augmenta le duration relative del diastole.

**Effectos summate.** Le fluxo medie es augmentate e le resistencia medie es reducida per acetylcholina. Isto resulta primarimente del effecto dilatatori del droga super le arteriolas e secundarimente de su leve effeeto depressori super le contraction myocardial. Le fluxo medie es etiam augmentate per levarterenol e per stimulation sympathetic, in parte in consequentia del moderation del tono arteriolar e in parte in consequentia del marchate alteratzion del comportamento contractional del ventricle.

Sub le influentia de levarterenol e de stimulation sympathetic le plus grande reduction del fluxo in systole es plus que compensate per le abrupte augmentation del fluxo in pro-diastole e le prolongation del duration relative del diastole, de manera que le effecto directe del augmento in le contraction del corde pote esser un micre augmento del fluxo medie.

Alteratziones del tono coronari-artoriolar es satis nettemente reflectite in alteratziones del valores medie de fluxo coronari e de resistencia, durante que le evaluatzion del contraction myocardial require technicas special, como per exemplo le registration de curvas phasic del fluxo coronari e/o del pression periphero-coronari.

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Effects of Autonomic Nerves and Their Mediators on the Coronary Circulation and Myocardial Contraction

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