Effects of Propranolol and Its Stereoisomers upon Coronary Vascular Resistance

By Leighton S. Whitsitt, B.S., and Benedict R. Lucchesi, Ph.D., M.D.

ABSTRACT

Responses of the coronary vascular bed to propranolol and its stereoisomers were studied in dogs anesthetized with allobarbital and urethane. The circumflex coronary artery was cannulated and perfused at a constant rate with blood from a femoral artery, coronary perfusion pressure being monitored as an index of coronary vascular resistance. dl-Propranolol (0.5 mg/kg iv) increased coronary vascular resistance and simultaneously reduced myocardial contractile force, heart rate, and systemic blood pressure. Approximately two thirds of the increase in coronary resistance was associated with the negative chronotropic action of propranolol. Intracoronary injections of dl-propranolol and l-propranolol increased coronary vascular resistance; d-propranolol increased resistance after an initial transient coronary dilatation. Intracoronary injections reduced contractile force in the pump-perfused area, but were without effects on heart rate and blood pressure. Reserpine pretreatment reduced, but did not abolish, the coronary vascular response to systemic propranolol; the chronotropic and inotropic responses were abolished. The responses to intracoronary d-propranolol were not altered. It was concluded that the increase in coronary vascular resistance following propranolol is due largely to the negative chronotropic effect of the drug and to an action of the drug which is unrelated to specific β-adrenergic receptor blockade.

ADDITIONAL KEY WORDS

coronary perfusion pressure
non-specific depression
myocardial contractile force

β-adrenergic receptor blockade
d-propranolol
intracoronary injections
l-propranolol
reserpine
cardiac rate
anesthetized dogs

A number of investigators have shown that propranolol and other β-adrenergic receptor blocking drugs reduce coronary blood flow, increase coronary vascular resistance, and convert the coronary vasodilatation usually observed following adrenergic stimulation to a vasoconstrictor response (1-5). The vasoconstrictor response to adrenergic stimulation is believed to be mediated through β-adrenergic receptors in coronary vascular smooth muscle, since it is abolished by blockade of α-adrenergic receptors (4-6). Parratt and Grayson (6) have suggested that the α-receptor mediated vasoconstriction following blockade of β-adrenergic receptors leads to an increase in coronary vascular resistance and a decrease in coronary blood flow. Alternatively, the profound reduction in heart rate and myocardial contractile force, leading to a decrease in the cardiac work load and energy requirements, could account for the reduction in coronary blood flow and the increase in coronary resistance observed following β-adrenergic receptor blockade. In fact, constriction of the coronary vascular bed would be the opposite effect to that classically sought in the treatment of patients with angina pectoris (7), unless the decrease in coronary blood flow was accompanied by a relatively greater decrease in the myocardial work load and oxygen requirement. The effectiveness of propranolol in the clinical management of angina pectoris is well documented (8-12), suggesting that the drug does lower the

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cardiac work load in anginal patients at rest or during exercise.

The present investigation was undertaken to study the mechanisms by which coronary vascular resistance is increased following propranolol; i.e., to determine if mechanisms other than direct α-adrenergic coronary constriction are involved. The availability of the dextroretorotary and levorotatory stereoisomers of propranolol made it possible to study those actions of the drug related to specific β-adrenergic receptor inhibition as well as those actions unrelated to it.

**Methods**

Male mongrel dogs weighing between 8 and 18 kg were anesthetized with 60 mg of alobarbital (Dial) /kg, and 240 mg/kg of urethane iv. One group of animals was pretreated with reserpine, 0.1 mg/kg per day subcutaneously for 3 days; these animals required less anesthesia. Positive pressure respiration was maintained through an endotraceal tube by a Harvard respirator pump. Systemic arterial blood pressure was measured in the left common carotid artery by a Statham pressure transducer. In most experiments the cervical vagi were severed bilaterally. The heart was exposed through a thoracotomy in the left fifth intercostal space. A 5-mm segment of the circumflex branch of the left coronary artery was dissected free near its origin. Henarin was administered in an initial dose of 3 mg/kg iv and then in hourly doses of 1.5 mg/kg. The circumflex artery was cannulated with a polyethylene cannula and perfused from a femoral artery (Fig. 1). The blood flow through the circumflex coronary artery was maintained constant at any desired level (between 10 and 27 ml/min in these experiments) by a Sarns Bilateral Roller Pump (pulsatile flow pattern). In each experiment circumflex blood flow was adjusted to produce a resting coronary perfusion pressure slightly less than the prevailing mean arterial blood pressure. Coronary perfusion pressure was measured with a Statham pressure transducer from a sidearm of the coronary artery cannula near the heart. No drugs were given until at least 1 hr after the coronary perfusion pressure had stabilized at the desired level. The temperature of the perfusing blood was maintained constant at 36 to 37°C by means of a heat exchanger interposed between the perfusion pump and the heart. The temperature was monitored continuously with a thermistor probe inserted into the blood stream near the heart. Brody-Walton strain gauges were sutured to the right ventricle (autoperfused area) and to

![Schematic diagram](http://circres.ahajournals.org/)

**FIGURE 1**

Schematic illustration of the technique used. The circumflex coronary artery was perfused from a femoral artery using a constant flow pump; coronary perfusion pressure was measured as an index of coronary vascular resistance. Blood temperature was monitored using a thermistor inserted through a sidearm of the coronary artery cannula near the heart; intracoronary injections were made proximal to the pump. CIRC = circumflex branch; AD = anterior descending branch of the left coronary artery (LCA); LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium; and A = aorta.
PROPRANOLOL ON CORONARY VASCULAR RESISTANCE

Effects of dl-propranolol on coronary vascular resistance following intravenous administration in a vagotomized animal. The increase in coronary perfusion pressure was accompanied by a reduction in heart rate and myocardial contractile force in the autoperfused area; contractile force in the pump-perfused area increased slightly. The point of injection is indicated by an arrow in this and subsequent figures. Values for coronary perfusion pressure and systemic blood pressure are expressed in millimeters of mercury. The black area of the heart indicates the pump-perfused area of the left ventricle in this and subsequent figures.

systemic arterial blood pressure, coronary perfusion pressure, and myocardial contractile force on a Grass polygraph.

All drugs were administered either intravenously into an external jugular vein, or by intracoronary injections of small volumes (less than 0.1 ml) into a sidearm of the extracorporeal circulation, as shown in Figure 1.

Coronary vascular resistance (CVR) was expressed as coronary resistance units (CRU), (CRU = CPP/CBF) and varied directly with coronary perfusion pressure (CPP) since coronary blood flow (CBF) was kept constant. The data were analyzed according to the method described by Hill for paired comparisons (13).

**Results**

**EFFECTS OF INTRAVENOUS dl-PROPRANOLOL**

The intravenous administration of dl-propranolol, 0.5 mg/kg, to a group of 10 vagotomized dogs resulted in an increase in coronary vascular resistance (+37.1%), which reached a peak within 20 to 40 min after injection. The increase in resistance was accompanied by a decrease in cardiac rate and contractile force, and by a slight fall in blood pressure. All changes were statistically significant. These data are presented in Table 1, and the results of a typical experiment are shown in Figure 2.

Similar results were obtained in a series of 6 animals without prior bilateral midcervical vagotomy. These data are summarized in Table 1. The differences between the responses of the two groups of animals were not statistically significant.

The dose of dl-propranolol administered in these experiments was previously shown to inhibit the increase in cardiac rate and contractile force that follows adrenergic stimulation; i.e., to produce β-adrenergic receptor blockade (14, 15). The responses to systemic injections of d- and l-propranolol were not studied because of the limited supply of these stereoisomers.

**EFFECTS OF INTRAVENOUS dl-PROPRANOLOL WITH HEART RATE MAINTAINED CONSTANT**

A series of 7 animals was studied to assess
### TABLE 1

**Effects of dl-Propranolol on Coronary Vascular Resistance in Anesthetized Vagotomized and Nonvagotomized Dogs**

<table>
<thead>
<tr>
<th></th>
<th>Vagotomized (n = 10)</th>
<th>Nonvagotomized (n = 6)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>After dl-propranolol 0.5 mg/kg</td>
</tr>
<tr>
<td>Contractile force autoperfused area (%)</td>
<td>100.0 (±3.7)*</td>
<td>69.1 (±3.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contractile force pump-perfused area (%)</td>
<td>100.0 (±5.6)</td>
<td>82.0 (±5.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Systemic blood pressure (mm Hg)</td>
<td>102.0 (±4.2)</td>
<td>93.1 (±4.0)</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beat/min)</td>
<td>157.7 (±3.7)</td>
<td>118.3 (±3.8)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>Coronary perfusion pressure (mm Hg)</td>
<td>101.9 (±2.1)</td>
<td>139.8 (±3.4)</td>
</tr>
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<tr>
<td>Coronary vascular resistance (units)</td>
<td>7.0 (±0.9)</td>
<td>9.6 (±1.2)</td>
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*Values in parentheses represent standard error of the mean (±SEM).
the role of changes in heart rate in the coronary vascular response to propranolol. The heart was paced electrically at a rate slightly above the existing spontaneous heart rate during the intravenous administration of dl-propranolol, 0.5 mg/kg. Once the peak response had developed the electrical pacing was stopped, allowing the heart rate to fall to the lower spontaneous rate produced by propranolol. Changes in coronary vascular resistance, as well as in the other variables, were determined during constant and spontaneous heart rates. These data are summarized in Table 2.

Approximately one third of the total increase in coronary vascular resistance produced by propranolol occurred during the period in which the heart rate was maintained constant (+15.3%). The other two thirds developed only when the heart rate was permitted to fall to the lower spontaneous level (27.6% below control). The negative inotropic and depressor responses to propranolol occurred during the period when heart rate was maintained constant; only negligible changes occurred when electrical pacing was stopped and the heart rate was allowed to decrease. The secondary increase in coronary resistance is presumably due to a lower myocardial oxygen consumption associated with the reduced heart rate (16,17), rather than to any physical influence of the negative chronotropic action. The total increase in coronary vascular resistance (+40.3%) agrees with that obtained in the control group (Table 1).

**EFFECTS OF dL-, lL- AND dl-PROPRANOLOL FOLLOWING INTRACORONARY ADMINISTRATION**

dl-Propranolol and its stereoisomers were administered by intracoronary injection to restrict their effects to that part of the myocardium supplied by the pump-perfused circumflex coronary artery. This permitted a study of the effects of these agents on coronary vascular resistance and myocardial contractile force without accompanying changes in heart rate, blood pressure, and contractile force in the autoperfused area. Changes in these variables in a few experiments indicated that the systemic effects of the drug were slight and were only observed following the larger doses. The volume injected was always less than 0.1 ml, since larger volumes of saline solution

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<tbody>
<tr>
<td><strong>Role of Heart Rate Changes in the Coronary Vascular Response to dl-Propranolol (7 Dogs)</strong></td>
</tr>
<tr>
<td><strong>Constant heart rate</strong></td>
</tr>
<tr>
<td>Contractile force</td>
</tr>
<tr>
<td>Autoperfused area (%)</td>
</tr>
<tr>
<td>Pump-perfused area (%)</td>
</tr>
<tr>
<td>Systemic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
</tr>
<tr>
<td>Coronary perfusion pressure (mm Hg)</td>
</tr>
<tr>
<td>Coronary vascular resistance (units)</td>
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</tbody>
</table>

*Maintained constant by means of electronic pacer. Values in parentheses represent standard error of the mean (±SEM).

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produced a transient decrease in coronary resistance.

\(\textit{d}\)-Propranolol, which lacks significant \(\beta\)-adrenergic receptor blocking activity (15, 18), produced an initial transient reduction in coronary vascular resistance in 15 animals in doses of 0.01 to 50 \(\mu\)g/kg. The magnitude of the response appeared to be dose-dependent; the response lasted for 20 to 60 sec. Following the initial dilatation, coronary resistance returned to a level above control in 10 of 15 experiments; i.e., a net increase in coronary resistance which averaged 19.2\% (± 4.3 SEM). In the remaining 5 experiments coronary resistance returned to control levels or slightly below. A typical experiment is shown in Figure 3, which shows an increase in coronary vascular resistance without changes in heart rate or in myocardial contractile force in the autoperfused area. A transient reduction in contractile force in the pump-perfused area which accompanies the increase in resistance can also be seen in Figure 3. The transient reduction in coronary resistance does not ap-

\textbf{FIGURE 3}

\textit{Effects of intracoronary (ic) injections of \textit{d}-propranolol (upper tracing) and \textit{l}-propranolol (lower tracing) injected at 5-min intervals. The transient reduction followed by a slow increase in coronary perfusion pressure (expressed in millimeters of mercury) produced by \textit{d}-propranolol is accompanied by a transient reduction in contractile force in the pump-perfused area. In the lower tracing, an increase in coronary vascular resistance is produced by \textit{l}-propranolol. This effect is accompanied by an abrupt and sustained decrease in contractile force in the pump-perfused area and by a slight fall in heart rate and contractile force in the autoperfused area (\(\beta\)-adrenergic receptor blockade). These effects were not observed after \(\textit{d}\)-propranolol (upper tracing).}
Pear to be related to a reduction in extravascular resistance, since it was observed at low dose levels which did not depress myocardial contractile force in either area of the heart.

L-Propranolol was administered to a group of 14 animals in doses of 0.01 to 20 µg/kg. In 12 of 14 experiments only a progressive increase in coronary vascular resistance was observed as the dose was increased until a peak elevation was obtained which averaged 15.8% (±3.4 SEM). Larger doses produced an initial transient dilatation similar to that observed with d-propranolol, followed by a return to control levels or slightly above. Figure 3 shows the progressive increase in coronary resistance following repeated intracoronary injections of l-propranolol, 5 µg/kg, at 5-min intervals. A slight systemic response can be seen, manifested by a reduction in heart rate and in contractile force in the autoperfused area, in contrast to the d-isomer which had no effect on these variables (top tracing). Figure 3 also shows that l-propranolol produced a rapid and sustained decrease in myocardial contractile force in the pump-perfused area; this is characteristic of β-adrenergic receptor blockade. Subsequent injections of l-propranolol produce only a transient depression of contractile force, similar to that produced by d-propranolol and thus, unrelated to inhibition of β-adrenergic receptors.

Intracoronary injections of dl-propranolol (3 experiments) altered coronary vascular resistance in a manner similar to l-propranolol, in that all dose levels increased coronary resistance, and similar to d-propranolol, in that the initial transient dilatation appeared at a lower dose level for dl-propranolol than for l-propranolol, presumably because of the presence of the dextrorotatory isomer. Thus, a dose of 1.0 µg/kg increased coronary resistance by 14.5% (±3.0 SEM); higher doses produced an initial reduction in resistance followed by a sustained increase in resistance.

**EFFECTS OF dl-PROPRANOLOL AND ITS STEREOISOMERS FOLLOWING PRETREATMENT WITH RESERPINE**

Reserpine pretreatment abolished the negative chronotropic and negative inotropic responses to intravenous dl-propranolol, 0.5 mg/kg. However, pretreatment with reserpine reduced, but did not abolish, the increase in

<table>
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<tr>
<th>TABLE 3</th>
<th>Effect of Reserpine Pretreatment on the Coronary Vascular Response to dl-Propranolol in Vagotomized Dogs</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>Contractile force</td>
<td></td>
</tr>
<tr>
<td>autoperfused area (%)</td>
<td>100.0</td>
</tr>
<tr>
<td>Contractile force</td>
<td></td>
</tr>
<tr>
<td>pump-perfused area (%)</td>
<td>100.0</td>
</tr>
<tr>
<td>Systemic blood pressure (mm Hg)</td>
<td>97.0</td>
</tr>
<tr>
<td>Heart rate (beat/min)</td>
<td>112.8</td>
</tr>
<tr>
<td>Coronary perfusion pressure (mm Hg)</td>
<td>103.7</td>
</tr>
<tr>
<td>Coronary vascular resistance (units)</td>
<td>4.2</td>
</tr>
</tbody>
</table>

*Values in parentheses represent standard error of the mean (±SEM).
Segments of a record showing the responses to intravenous dl-propranolol in an animal pretreated with reserpine. Note the progressive increase in coronary perfusion pressure, unaccompanied by significant changes in rate or force. The time after injection is indicated at the top of each segment.
coronary vascular resistance following propranolol. These data are summarized in Table 3, which shows that coronary resistance increased by 16.7% in this series of 5 vagotomized animals, as compared with 37.1% in the control series (Table 1, left side). This value is comparable to that obtained in control animals during the period in which heart rate was maintained constant (Table 2). Figure 4 shows the results of a typical experiment.

The responses to the intracoronary administration of a series of doses of d-propranolol in
3 animals were unaltered by reserpine pretreatment. As shown in Figure 5, the transient decrease in coronary resistance, the net increase in resistance, and the brief negative inotropic responses to d-propranolol were still observed in animals pretreated with reserpine. In 2 animals, the intracoronary administration of l-propranolol produced an insignificant increase in coronary resistance and failed to reduce myocardial contractile force in the pump-perfused area of the left ventricle except after the largest doses, in which case a transient cardiac depression was observed.

Discussion

The present study with propranolol confirms previous reports (2, 6, 19) that /β-adrenergic receptor blocking drugs increase coronary vascular resistance. Although the mechanism by which it is increased was not determined in these earlier studies, Parratt and Grayson (6) suggested that it may be due to "active" coronary vasoconstriction mediated through α-adrenergic receptors in the coronary vascular bed, unmasked by blockade of myocardial β-adrenergic receptors. Alternatively, the increase in coronary resistance following propranolol could be largely a "passive" response to a decrease in the cardiac work load and oxygen requirement.

The present investigation was undertaken to study the mechanisms by which propranolol increases coronary vascular resistance. Table 1 shows that the increase in resistance following intravenous dZ-propranolol is accompanied by simultaneous reductions in myocardial contractile force, heart rate, and systemic blood pressure. These effects are presumably due to inhibition of sympathetic nervous tone, rather than to direct myocardial depression (20), since they were not observed in animals pretreated with reserpine (Table 3). Similar findings have been reported by other investigators (12, 19, 21). In view of the known relationships between heart rate and other cardiac contractile events, myocardial oxygen consumption, and coronary blood flow (1, 16, 17, 22, 23), these actions of propranolol would be expected to reduce the cardiac work load, myocardial oxygen requirement, and therefore, the metabolic stimulus for compensatory dilatation of the coronary vascular bed (24). The resulting "passive" coronary vasoconstriction, supplemented by blockade of /β-adrenergic vasodilator receptors in the coronary vascular bed (4, 25), could account for the increase in coronary vascular resistance observed after propranolol in this and previous reports, and for the reduction in coronary blood flow reported by other investigators (2, 6, 12, 19).

The decrease in heart rate accounted for approximately two thirds of the increase in coronary vascular resistance following the intravenous administration of d/z-propranolol (Table 2). The remaining one third, which occurred during the period in which heart rate was held constant, was quantitatively similar to the increase produced by intracoronary injections of l- or d-propranolol when heart rate changes were negligible. It was also similar to the increase in resistance produced by either intravenous d/z-propranolol or intracoronary d-propranolol following pretreatment with reserpine.

The portion of the increase in coronary resistance that was independent of changes in heart rate could be due to the reduced metabolic demand associated with the decrease in contractile force; however, the physical effects of a reduction in extravascular compression might tend to oppose an increase in coronary vascular resistance (26). Alternatively, the increase in resistance could be attributed to stimulation of α-adrenergic receptors unmasked by cardiac β-adrenergic receptor blockade, or to a "nonspecific" action of propranolol which is unrelated to blockade of β-adrenergic receptors. The first of these two alternatives is supported by the observation that propranolol increases the coronary arteriovenous oxygen difference (19), which is considered to be indicative of "active" coronary vasoconstriction. The second alternative is supported by the results of the present investigation in which d-propranolol, which has negligible β-adrenergic receptor blocking activity (15, 18), produced an increase in
coronary resistance equivalent to that which occurred when heart rate was maintained constant. In addition, dL-propranolol still increases coronary vascular resistance after reserpine pretreatment.

d-Propranolol produced a transient reduction in coronary resistance followed by a progressive increase to a level above control following intracoronary injection. The coronary responses were accompanied by a transient depression of myocardial contractile force in the pump-perfused area, with no significant change in either heart rate or systemic blood pressure. These effects were unaltered by pretreatment with reserpine. The transient decrease in coronary resistance has also been observed following large doses of intracoronary dL-propranolol in this and other studies (3). Shanks (27) has reported a transient dilatation in the peripheral vascular bed following d-propranolol and suggested that it may be related to the "local anesthetic" action of the drug. These observations with d-propranolol, and with both d- and dL-propranolol in reserpine-pretreated animals, suggest that the dextrorotatory isomer of propranolol exerts a nonspecific action on coronary vascular resistance which is independent of cardiac blockade of β-adrenergic receptors, an hypothesis in agreement with an earlier suggestion that propranolol possesses actions unrelated to adrenergic receptor inhibition (20, 28, 29). The nonspecific action of d-propranolol, and therefore, of dL-propranolol, could explain the increase in coronary vascular resistance produced by intravenous dL-propranolol when heart rate was maintained constant (Table 1), and in animals pretreated with reserpine (Table 2), because the magnitude of the response was about the same in both cases.

The nature of the nonspecific coronary vascular actions of propranolol (or more specifically, dL-propranolol) could not be determined from the present experiments. Propranolol, and particularly the dextro-isomer, may alter cardiac metabolism and further decrease myocardial oxygen consumption, and therefore, coronary blood flow. Nayler et al. (30) reported that propranolol decreased the coronary arteriovenous oxygen difference, suggesting that the drug decreases oxygen consumption to a greater extent than it decreases coronary blood flow. This disproportion was greater at larger dose levels (much larger than required for blockade of β-adrenergic receptors). Pronethalol has been reported to alter the myocardial metabolism of free fatty acids and glucose with a resulting shift to less oxygen-consuming carbohydrate metabolism (31). This may be due to blockade of myocardial fatty acid extraction (32), rather than to the well known inhibition of catecholamine-induced release of free fatty acids. A metabolic shift of this type would be expected to increase the cardiac respiratory quotient, as has been reported by McKenna (19) following propranolol.

The nonspecific and transient myocardial depression produced by dL-propranolol, and by large doses of dL-propranolol, is distinctly different from the immediate and sustained decrease in contractile force which is characteristic of specific inhibition of β-adrenergic receptors. The mechanism of this depression is unknown but it may be related either to the metabolic alterations already mentioned or to the ability of propranolol to inhibit lipid-facilitated transport of calcium across the cell membrane (33). Blinks (20) has shown a similar separation of specific and nonspecific types of depression of myocardial contractility using isolated atrial and papillary muscle preparations.

Tables 1 and 2 show that contractile force in the autoperfused area decreased about twice as much after propranolol as in the pump-perfused area of the left ventricle, even when heart rate was maintained constant. The reason for this discrepancy is unclear, but it may be due to the fact that blood flow is held constant in the pump-perfused area despite the coronary vasoconstriction, whereas coronary blood flow may fall in the autoperfused area owing to an increase in coronary vascular resistance. The reduction in blood flow in the autoperfused area would supplement the negative inotropic effect of propranolol in this area, and therefore, produce...
a greater total reduction in myocardial contractile force. The extent of blockade of β-
adrenergic receptors is believed to be the same in both areas of the myocardium since additional dl-propranolol did not further reduce contractile force in either region, except transiently.

The results of the present study suggest that the increase in coronary vascular resistance which occurs following dl-propranolol or one of its stereoisomers is not related entirely to specific β-adrenergic receptor blockade. Likewise, the negative inotropic action of d-propranolol is suggestive of a nonspecific myocardial depressant effect which occurs independently of receptor inhibition. The major part of the increased coronary resistance appears to be associated with the reduced myocardial energy requirements resulting from cardiac slowing following dl-propranolol (16, 17). Although the quantitative contribution of unmasked α-adrenergic receptors to the total coronary vascular response to propranolol was not determined in this study, it appears to be of little importance in normal animals since reserpine pretreatment, which eliminates both α- and β-adrenergic receptor activity, did not prevent the increase in coronary vascular resistance after dl-propranolol or its dextrorotatory or levorotatory isomers.

Acknowledgment

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References

during ventricular contraction and relaxation.
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