SUMMARY While it is known that β-adrenergic receptor stimulation is associated with an increase in venous return, the mechanism by which this increase is mediated has not been well defined. A total of 55 dogs were anesthetized, placed on cardiopulmonary bypass, and perfused at a constant rate. In 23 of these animals, changes in total systemic intravascular volume were measured as reciprocal changes in extracorporeal reservoir volume during isoproterenol (6 µg/min) or norepinephrine infusion (30 µg/min). At central venous pressures of 3, 8, and 13 cm H₂O, isoproterenol was associated with decreases in intravascular volume of 70 ± 20 (standard error of the mean) (P < 0.001), 50 ± 20 (P < 0.005), and 20 ± 30 (NS) ml, respectively, and norepinephrine was associated with decreases of 300 ± 60 (P < 0.001), 230 ± 30 (P < 0.001), and 190 ± 40 (P < 0.001) ml, respectively. The splanchnic vasculature was perfused selectively at a constant rate and drained separately in another 18 animals. In these dogs, an isoproterenol-associated decrease in splanchnic volume occurred concomitantly with a decrease in postsinusoidal hepatic vascular resistance from 38 ± 5 to 18 ± 3 cm H₂O-min/liter (P < 0.001). A norepinephrine-associated decrease in splanchnic volume occurred simultaneously with a decrease in hepatic vascular resistance from 33 ± 6 to 18 ± 2 cm H₂O-min/liter (P < 0.001). The decreases in total intravascular volume obtained with either isoproterenol or norepinephrine were abolished after the splanchnic vasculature had been removed in two other animals. Decreases in hepatic resistance, splanchnic volume, and total volume were abolished after propranolol. Thus, β-adrenergic receptor stimulation with either isoproterenol or norepinephrine is associated with a decrease in transsplanchnic vascular resistance and subsequent decreases in splanchnic and total systemic intravascular volume.

CARDIAC performance is dependent upon ventricular filling and, hence, upon venous return. Alterations in venous return are dependent upon changes in the capacitance vasculature. Thus, cardiac performance is importantly related to alterations in total systemic capacity. While the direct effects of β-adrenergic receptor stimulation on myocardial contractility, heart rate, and the arterial resistance vasculature have been well defined, the influence of β-adrenergic stimulation on total systemic capacity is less well understood. The present study was undertaken to examine this influence.

Kaiser et al. (1964) and Imai et al. (1978) have demonstrated that the infusion of isoproterenol is associated with an increase in venous return. Whereas Kaiser et al. postulated that the increase was due to β-adrenergically mediated venoconstriction and Imai et al. postulated that the increase was a result of decreased venous outflow resistance, neither study elucidated the mechanism of action of the beta adrenergically mediated increase in venous return. A possible mechanism of action has been suggested by Green (1977). He observed a decrease in splanchnic venous resistance and effective splanchnic back pressure with isoproterenol and speculated that such a decrease "may account, in whole or in part, for the increase in venous return associated with isoproterenol." Whether changes in splanchnic venous outflow resistance contribute to changes in venous return with β-adrenergic receptor stimulation has not been demonstrated to date. Furthermore, quantification of changes in splanchnic volume during β-adrenergic stimulation has not been accomplished.

In the present study, changes in splanchnic intravascular volume were correlated with changes in transsplanchnic vascular resistance measured directly during β-adrenergic receptor stimulation. β-Receptor stimulation was accomplished with both isoproterenol and norepinephrine, agents which have markedly different effects on the overall cardiovascular system but which we demonstrated to have similar effects on the transsplanchnic resistance vasculature. To ascertain whether vascular volume changes are dependent upon redistribution of regional arterial blood flows during β-receptor stimulation, we assessed volume changes under conditions of constant splanchic arterial inflow. Changes in total capacity were assessed at different levels of central venous pressure because of the potential effect of the level of central venous pressure on the
pressure gradient across the transhepatic resistance vasculature and subsequent intravascular volume changes. Thus, the effect of alterations in transhepatic resistance on splanchnic intravascular volume and total systemic capacity, during isoproterenol and norepinephrine administration, was examined quantitatively under controlled hemodynamic conditions.

Methods

A total of 55 adult mongrel dogs of either sex weighing between 17 and 25 kg were anesthetized with chloralose (60 mg/kg, iv) and urethan (600 mg/kg, iv). After tracheal intubation, ventilation was provided by a Harvard respirator using 97% O₂ and 3% CO₂. A median sternotomy was performed, and heparin, 3 mg/kg, was administered intravenously. The specific experimental preparation used in the first series of experiments in 23 animals is shown in Figure 1. Total venous return to the reservoir of a pump oxygenator was accomplished by cannulating the superior and inferior vena cavae through the right atrial appendage with Argyle 32 French catheters. The azygos vein was securely ligated. Central venous pressure (CVP) was measured in the venous return line and was set at a predetermined level by adjusting the height of a venous overflow column. The roller pump (Cardiovascular Instruments), returning oxygenated blood to the femoral arteries of the dog, was set at a rate between 1.4 and 1.8 liters/min, and the rate was maintained constant throughout the course of each experiment. Blood was oxygenated using a Harvey model #H-1000 oxygenator (William Harvey) which was calibrated with whole blood in 100-ml increments up to a total volume of over 3000 ml before each experiment. Thus, any increase or decrease in the animal's systemic intravascular volume could be measured as a reciprocal change in oxygenator volume. Arterial pressure was measured with a cannula in the subclavian artery. The aorta was cross-clamped 2 cm above the aortic valve and the pulmonary hila were clamped to exclude the coronary, pulmonary, and bronchial circulations, and, hence, any contributions of the cardiac chambers or pulmonary vasculature to total systemic capacity. The adequacy of clamping was demonstrated by the absence of flow from drains placed in both ventricles.

To assess the influence of transhepatic vascular resistance on splanchnic intravascular volume during β-adrenergic receptor stimulation, the splanchnic and extra-splanchnic vasculatures were separately perfused and drained in another 18 dogs. In these experiments, the perfusion rate of each of these two regions was held constant. Splenectomy was performed in all of these animals to avoid the α-adrenergic constrictor effect of norepinephrine on the dog's muscular splenic capsule (Opdyke and Ward, 1973) (see Fig. 2). The cranial and caudal mesenteric arteries and the celiac axis were isolated and perfused at a constant rate by a separate variable speed-calibrated roller pump. A ligature was placed around the inferior vena cava below the hepatic vein, and the inferior vena cava was cannulated between the hepatic vein and the right atrium. This hepatic vein tubing, which carried the splanchnic outflow, was then passed to an overflow column and the blood from the column was led to the calibrated oxygenator. The peripheral vasculature was drained by cannulas in the superior vena cava and femoral veins after the inferior vena caval ligature was tightened below the hepatic veins. The tubing from these latter cannulas was passed to a second overflow column. Blood from these latter cannulas was drained to the same calibrated oxygenator into which the splanchnic vasculature drained. By adjusting the heights of the overflow columns, the peripheral CVP and hepatic venous pressure were set equal to each other at 8 cm H₂O. To eliminate all visible shunts from the portal venous circulation to the systemic arterial circulation, running sutures were placed in the esophagus and rectum, and the inferior mediastinum was divided. Blood flow through the diaphragm was eliminated by clamping the circumference of the diaphragm with multiple Kelly clamps. In one of these animals, Silastic (Canton Biomedical Products, Inc.) was infused into the
splanchnic arterial system at the conclusion of the experiment to document the lack of visible communication between the portal and systemic circulations. In this animal, the Silastic perfused to, but not beyond, the points of occlusion. Splanchnic (portal) venous pressure was measured via a catheter advanced from a small segmental gastric or splenic vein into the major splenic vein. Hepatic vein flows of 30 seconds duration were collected manually in graduated cylinders. Changes in splanchnic vascular capacity were determined by integrating the difference between the mean hepatic vein flow of the control period and the observed flows during and following each intervention. Transhepatic vascular resistance was calculated by dividing the difference between splenic and hepatic vein pressures by hepatic vein outflow. In two of these animals, the hepatic artery was cannulated and perfused separately at a constant flow to eliminate any possible arterial redistribution of blood flow between the hepatic and extra-hepatic mesenteric circulations.

To ascertain whether changes in transhepatic vascular resistance, splanchic volume, and total volume were due to redistribution of regional arterial blood flow during β-adrenergic receptor stimulation, studies were performed in eight additional dogs in which the splanchnic and peripheral vasculatures were separately drained, as described above, but not separately perfused. Splenectomies were not performed in these animals. Arterial perfusion was accomplished for both circulations by perfusing the femoral arteries as described in the first series of experiments. Splanchic and peripheral venous flows were measured with extracorporeal flow meters; the measurements were confirmed intermittently by volume collections in graduated cylinders over 30- to 60-second intervals. In two of these animals, hepatic sinusoidal pressures were obtained by means of hepatic sinusoidal wedge pressure determinations. A #7 Swan-Ganz catheter (Edwards Laboratories) was advanced through the splanchic outflow tubing to a hepatic vein, and the balloon was inflated intermittently in order to record hepatic sinusoidal wedge pressures. The wedge pressures were determined during control periods and during drug administration.

To examine effects on the extra-splanchnic peripheral vasculature, ligatures were securely placed around all arteries and veins supplying the mesenteric vasculature in two additional animals. Thus, the celiac, cranial mesenteric, and caudal mesenteric arteries and veins were ligated, thereby excluding the splanchnic and hepatic vasculatures from the preparation. Pressures in all experiments were monitored with Statham P23Db pressure transducers; the frequency response of the pressure measurement system was linear up to 30 cycles/sec. In experiments in which flowmeters were used, Statham SP2202 Blood Flowmeters with 20-mm extracorporeal flow probes were employed. The meters were calibrated with known blood flows at the start of the experiment, and the calibrations were confirmed intermittently throughout the course of each experiment. Pressures and flows were recorded on a Hewlett-Packard model #7700 eight-channel recorder.

Ganglionic blockade was produced in all 55 animals by the administration of 100 mg mecamylamine (Inversine; Merck, Sharpe & Dohme) to the pump reservoir over 10 minutes. This dose was adequate to abolish entirely 50 mm Hg rises in perfusion pressure obtained by clamping a single carotid artery below the carotid bifurcation in preliminary experiments. Bilateral cervical vagectomy was also performed in all animals.

Isoproterenol (Isuprel; Winthrop Laboratories), 6 µg/min, and norepinephrine (Levophed; Winthrop Laboratories), 30 µg/min, were each infused intraarterially with a parenteral Fluid Delivery System (IV 5000, Valley Lab.) for 10–21 minutes. Each drug was diluted in normal saline at a concentration that allowed for infusion of the solution at 2 ml/min. Reservoir volume and arterial pressure were unchanged from the baseline during 20-minute infu-
sions of normal saline alone at 2 ml/min in two animals. β-Adrenergic receptor blockade was achieved with propranolol (Inderal, Ayerst Laboratories), 20–200 mg, administered intravenously. The adequacy of blockade was assessed by noting systemic arterial pressure responses to 12 μg isoproterenol administered intra-arterially before and after blockade. Complete blockade was confirmed before and after each infusion administered in the presence of β-adrenergic blockade by noting the absence of changes in blood pressure with isoproterenol boluses.

In the dogs with separate splanchnic and peripheral arterial perfusion, the splanchnic circulation was perfused at 500 ml/min and the peripheral circulation at 800–1000 ml/min. Isoproterenol, 2 μg/min, or norepinephrine, 10 μg/min, was infused into the splanchnic arterial circulation alone in these studies. These concentrations were selected in order to approximate the concentrations of drugs delivered to the splanchnic vasculature in the animals without separate splanchnic perfusion.

A double-tailed paired Student’s t-test was used for all statistical analyses. Significance was assumed only with \( P < 0.05 \).

**Results**

In the dogs on total cardiopulmonary bypass without separate splanchnic perfusion or drainage and in which volume changes were measured at different CVPs, isoproterenol and norepinephrine each were associated with decreases in total intravascular capacity. Isoproterenol administration was associated with losses of 70 ± 20 (standard error of the mean) (\( P < 0.02 \)), 50 ± 20 (\( P < 0.05 \)), and 20 ± 30 (NS) ml of blood at CVPs of 3, 8, and 13 cm H₂O, respectively (Fig. 3). Norepinephrine was associated with losses of 300 ± 60 (\( P < 0.001 \)), 230 ± 30 (\( P < 0.001 \)), and 190 ± 40 (\( P < 0.001 \)) ml of blood from the animals at CVPs of 3, 8, and 13 cm H₂O, respectively (Fig. 4). In two animals in this group, control blood pressures were 97 and 98 mm Hg before isoproterenol administration at a CVP of 8 cm H₂O and were associated with decreases in intravascular capacity of 90 ml on both occasions with isoproterenol. In the same two animals, control blood pressures were 105 and 82 mm Hg before norepinephrine administration at a CVP of 8 cm H₂O and were associated with decreases in intravascular capacity of 270 and 280 ml, respectively, with norepinephrine.

In six animals with a CVP 8 cm H₂O with or without separate splanchnic drainage in which large changes in systemic capacity occurred, isoproterenol was associated with a decrease in vascular capacity of 385 ± 144 ml (\( P < 0.05 \)) before β-adrenergic receptor blockade with propranolol and 13 ± 17 ml (NS) after propranolol. In four animals in which isoproterenol was infused twice in succession without β-adrenergic blockade, the decrease in vascular capacity was not attenuated with the second infu-
When splanchnic inflow was held constant, isoproterenol was associated with a decrease in splanchnic intravascular capacity of 295 ± 73 ml (P < 0.01) concurrent with a decrease in transhepatic vascular resistance from 38 ± 5 to 18 ± 3 cm H₂O • min/liter (P < 0.001). Norepinephrine was associated with a decrease in splanchnic intravascular capacity of 392 ± 90 ml (P < 0.01) concurrent with a decrease in transhepatic vascular resistance from 33 ± 6 to 18 ± 2 cm H₂O • min/liter (P < 0.001).

Before blockade in these five animals, isoproterenol was associated with a decrease in splanchnic capacity of 130 ± 50 ml (P < 0.05) and a decrease in hepatic resistance from 35 ± 8 to 18 ± 2 cm H₂O • min/liter (P < 0.03). After blockade, isoproterenol administration was not associated with any significant change in either splanchnic capacity or hepatic resistance. In seven of the dogs that received norepinephrine, the norepinephrine infusion was repeated after β-adrenergic blockade. Before blockade in these seven animals, norepinephrine was associated with a decrease in splanchnic capacity of 164 ± 28 (P < 0.02) and a decrease in hepatic resistance from 36 ± 8 to 28 ± 7 cm H₂O • min/liter (P < 0.05). After blockade, norepinephrine was associated with small but statistically insignificant increases in splanchnic capacity and hepatic resistance.

In one animal in which hepatic arterial flow was held constant, isoproterenol was associated with a decrease in splanchnic volume of 547 ml before β-adrenergic blockade and a small increase of 68 ml after blockade. Hepatic resistance decreased from 51 to 12 cm H₂O • min/liter before blockade and increased slightly from 112 to 123 after blockade. In the other animal with hepatic arterial flow maintained constant, norepinephrine was associated with a decrease in splanchnic volume of 476 ml before blockade and an increase of 132 ml after blockade. Hepatic resistance decreased from 52 to 15 cm H₂O • min/liter before blockade and increased from 78 to 94 after blockade.

In the four dogs in which the portal vein was vented, isoproterenol administration was associated with a small decrease in splanchnic volume of 25 ± 2 (P < 0.001) and norepinephrine with a small increase in splanchnic volume of 47 ± 13 (P < 0.02). Splenic vein pressure remained constant during all drug infusions in these four animals, except during norepinephrine infusion in one animal, when splenic vein pressure increased by 6 cm H₂O.

The hemodynamic changes associated with infusions of isoproterenol and norepinephrine in dogs in which both total systemic capacity and splanchnic hemodynamics were monitored are enumerated in Table 1. In these animals, the splanchnic and peripheral circulations were separately drained but not separately perfused. Figures 7 and 8 present representative data from a single animal. As seen in Table 1A and the upper panels of Figure 7, isoproterenol-induced decreases in systemic capacity were always associated with decreases in transhepatic resistance. Both the decreases in capacity and the lowering of hepatic resistance were abolished after β-adrenergic blockade with propranolol (Table 1A). As seen in Table 1B and the upper panels of Figure 8, norepinephrine-induced decreases in systemic capacity also were always associated with decreases in systemic capacity.
in hepatic resistance. Note that in all animals, splanchic inflow either changed little or decreased with isoproterenol administration and increased with norepinephrine. Hepatic wedge pressures, in the two of these animals in which they were determined and in which both isoproterenol and norepinephrine were administered, were consistently within 1.5 cm H$_2$O of splenic vein pressure and usually within 1 cm H$_2$O, despite large decreases in splenic vein pressure.

In the two dogs in which the entire splanchic and hepatic arterial vasculatures had been ligated, neither isoproterenol nor norepinephrine infusion was associated with any change in systemic capacity, although arterial pressure fell from 54 ± 19 to 41 ± 6 mm Hg with isoproterenol and rose from 54 ± 3 to 96 ± 24 mm Hg with norepinephrine.

**Discussion**

Administration of either isoproterenol or norepinephrine is associated with a decrease in total intravascular capacity. These decreases in total capacity are associated with decreases in splanchic intravascular capacity. The decreases in splanchic capacity appear secondary to decreases in resistance to splanchic venous outflow. The decreases in resistance, splanchic capacity, and total capacity are mediated by $\beta$-adrenergic receptor stimulation.

Our data localize the effects on capacity of isoproterenol and norepinephrine to the splanchic vasculature, since administration of either agent is not associated with a change in total intravascular volume after the splanchic vasculature has been removed. The decreases in splanchic volume could be mediated by several possible mechanisms. Brooksby and Donald (1972) have described passive decreases in splanchic venous pressure and volume subsequent to decreases in splanchic vascular inflow. Since splanchic inflow is noted to decrease with isoproterenol administration in animals with separate splanchic and peripheral venous drainages, it is possible that the isoproterenol-mediated decrease in splanchic volume occurs passively. The flow decrement with isoproterenol, however, is small. Furthermore, when splanchic inflow is maintained at a constant rate during isoproterenol administration, splanchic capacity still decreases substantially. With norepinephrine administration, splanchic inflow increases and substantial decreases in splanchic capacity still occur. Thus, neither the isoproterenol- nor norepinephrine-associated decrease in splanchic capacity is mediated by a decrease in splanchic inflow. In addition, the decrease is not due to alterations in hepatic arterial flow, since splanchic volume and outflow resistance decrease with isoproterenol or norepinephrine even when hepatic arterial flow is maintained constant.

It is possible that the decreases in capacity with...
FIGURE 7  Hemodynamic changes associated with isoproterenol administration in a single dog in which the splanchnic and peripheral venous outflows have been separated. The isoproterenol-induced decrease in systemic capacity is associated with a decrease in hepatic resistance. Abbreviations: BP = systemic arterial pressure, CVP = central venous pressure.

FIGURE 8  Hemodynamic changes associated with norepinephrine administration in the same dog from which the data for Figure 7 were obtained. The norepinephrine-induced decrease in systemic capacity is associated with a decrease in hepatic resistance. Abbreviations are as in Figure 7.
these agents are due to splanchnic vеноconstriction. If so, one would expect that splanchnic venous pressure would increase with isoproterenol and norepinephrine administration. Our data, however, demonstrate a fall in splanchnic venous pressure with administration of either agent. Furthermore, if splanchnic vеноconstriction accounts for the decreases in volume, the decrements in splanchnic capacity should be unaffected after venting the portal vein. Changes in splanchnic volume, however, were very small after portal vein venting. Finally, studies in isolated veins demonstrate that isoproterenol administration causes vеноdilation (Folkow, 1960; Abboud et al., 1965; Zsoter and Tom, 1967; Johnson and Öberg, 1968; Guimarães and Osswald, 1969; Webb-Peploe and Shepherd, 1969). Thus, it is unlikely that either isoproterenol or norepinephrine causes a decrease in splanchnic volume by means of splanchnic vеноconstriction.

Thus, the decrease in splanchnic capacity is due to the observed decrease in transhepatic vascular outflow resistance with subsequent passive decreases in splanchnic pressure and volume. In terms of total splanchnic volume changes, this decrease in transhepatic vascular resistance far outweighs any vasodilation or vasoconstriction in the more proximal splanchnic vasculature, as has been observed with administration of isoproterenol and norepinephrine, respectively, in an isolated jejunal preparation (Rothe et al., 1978). The major portion of the splanchnic outflow resistance lies distal to the hepatic sinusoids, since hepatic sinusoidal pressure, as measured by hepatic wedge pressure determinations, always was within 1.5 cm H2O of splenic vein pressure with administration of either isoproterenol or norepinephrine. Hepatic wedge pressure determinations have been well documented by others to reflect hepatic sinusoidal pressures (Friedman and Weiner, 1951; Price et al., 1964).

Under some circumstances, a decrease in hepatic post-sinusoidal resistance may not cause a decrease in total volume. Note, in Figure 3, which presents data from a group of dogs in which the systemic capacity changes were relatively small, that isoproterenol is not associated with a statistically significant decrease in total systemic intravascular capacity at a CVP of 13 cm H2O. This lack of a decrease is likely to be due to a decreased pressure gradient across the post-sinusoidal resistance vasculature prior to the administration of isoproterenol. Thus, with isoproterenol administration, the change in pressure gradient between splanchnic and hepatic veins is insufficient to cause volume shifts from the splanchnic vasculature to the hepatic veins and extracorporeal reservoir. Therefore, agents which decrease post-sinusoidal vascular resistance would be expected to have less effect on venous return under conditions of an elevated central venous pressure.

It is likely that the larger decrease in intravascular volume with norepinephrine administration (Fig. 4) compared to the decrease with isoproterenol (Fig. 3) was due to the α-adrenergic constrictor effect of norepinephrine on the muscular capsule of the dog spleen (Odpynes and Withrington, 1973). In the experiments in which the splanchnic and peripheral circulations were separately perfused and drained and in which splenectomies were performed, the effects of isoproterenol and norepinephrine on splanchnic vascular capacity were comparable (Fig. 5 and 6).

Stimulation of β-adrenergic receptors is responsible for the observed decreases in total capacity, splanchnic capacity, and hepatic resistance for the following reasons. The decrease in total capacity associated with isoproterenol administration is abolished after β-adrenergic blockade. The abolition of the decrease is not due to tachyphylaxis since repetitive administration of isoproterenol without blockade is associated with no attenuation of the isoproterenol-mediated response, and capacity does not decrease with isoproterenol when pranopanol is administered to an animal before administration of isoproterenol. Whether β-adrenergic receptor stimulation is accomplished with isoproterenol or norepinephrine, decreases in splanchnic capacity and hepatic resistance are abolished after β-adrenergic blockade.

The β-adrenergic receptor stimulation with isoproterenol and norepinephrine is due to direct stimulation of adrenergic receptors and is not due to reflex-induced changes. Ganglionic blockade with mecamylamine was present in all animals. Furthermore, in the experiments in which the splanchnic and extrasplanchnic vasculatures were perfused separately, drugs were delivered only to the splanchnic vasculature, whereas the splanchnic outflow was diverted into a separate extra-corporeal reservoir for the first 75 seconds of drug infusion. Even with this exclusion of the drugs from the extrasplanchnic circulation, splanchnic capacity and hepatic resistance decreased during the first 75 seconds of drug administration (Fig. 5 and 6), thereby indicating that a reflex mechanism, with the afferent limb originating in the extrasplanchnic circulation, is unlikely. In addition, these data suggest it is unlikely that the observed hemodynamic changes with isoproterenol and norepinephrine are due to release of other vasoactive substances from the extrasplanchnic circulation.

Anatomical evidence exists for the presence of post-sinusoidal hepatic sphincters in both dog and man. In the dog, the walls of the hepatic venules are invested with thick smooth muscle that is predominantly longitudinally oriented; at the junction of the hepatic venules with the hepatic veins, this muscular wall thickens and some of the fibers become circumferential (Arey and Simonds, 1920; Walker et al., 1960). In humans, the junction of central veins with hepatic venules has been described by Popper (1931) as being “funnel-like.” Elias and Popper (1955) noted that thin-walled hepatic venules in the human constricted on entering thick-walled vessels. Furthermore, at the level
of the hepatic veins in humans, the veins have been shown to have longitudinally oriented smooth muscle (Elias and Feller, 1926; Miyake, 1929). Finally, in neoprene casts of the hepatic venous system in humans the junctions of central venules and hepatic veins sometimes are retracted (Gibson, 1959). Since these junctions are numerous, Gibson (1959) concluded that junctional constriction is probably the "chief venous sphincter mechanism in the human liver."

It is possible that these post-sinusoidal hepatic sphincters are physiologically important in humans. Since \(\beta\)-adrenergic receptor stimulation causes a sustained increase in cardiac output (Goodman and Gilman, 1975), such stimulation also may be associated with a decrease in vascular capacity that would be necessary to sustain the increment in venous return. Shepherd and Vanhoutte (1975, 1978) have emphasized that the cutaneous, skeletal muscle, and splanchnic vasculatures constitute the important portions of the capacitance vasculature in man. Numerous studies, however, have demonstrated little, if any, influence of \(\beta\)-adrenergic stimulation on the forearm capacitance vasculature (Eckstein and Hamilton, 1957; Eckstein et al., 1965; Abboud et al., 1968), which is composed of cutaneous and skeletal muscle vasculature. Thus, it is possible that the \(\beta\)-adrenergically induced increases in cardiac output are importantly related to alterations in the splanchnic capacitance vasculature in humans.

In summary, the present study demonstrates that \(\beta\)-adrenergic receptor stimulation with isoproterenol or norepinephrine in the dog is associated with a decrease in hepatic post-sinusoidal vascular resistance. The decrease in hepatic resistance accounts for a substantial decrease in splanchnic intravascular capacity and a subsequent decrease in total capacity.

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