A Comparison of the Effects of Vasodilator Stimuli on Peripheral Resistance Vessels in Normal Subjects and in Patients with Congestive Heart Failure

ROBERT ZELIS, DEAN T. MASON, and EUGENE BRAUNWALD
with the technical assistance of MIMI WINTERHALTER and CLARA KING

Cardiology Branch, National Heart Institute, National Institutes of Health, Bethesda, Maryland 20014

ABSTRACT The objective of this investigation was to characterize the mechanism of peripheral vasoconstriction observed in heart failure and to determine whether it can be attributed to the augmented sympathetic nervous activity, characteristic of this state. The response of the resistance bed in the forearm after release of inflow occlusion (reactive hyperemia), to hand exercise, and to local heating and the response of the calf resistance vessels to arterial occlusion and intra-arterial sodium nitrite and phentolamine were studied in 23 patients with congestive heart failure and 21 normal subjects. In the normal subjects, reactive hyperemia blood flow after varying periods of arterial occlusion greatly exceeded the values observed in patients with heart failure. Local anesthetic blockade and intra-arterial phentolamine did not significantly alter the reactive hyperemia response in heart failure patients, militating against the possibility that increased sympathetic vasoconstrictor activity is responsible for the reduction of this response. Following compensation, the reactive hyperemia response returned toward normal. The striking elevations of the forearm blood flow observed after hand exercise and heating of the forearm in normal subjects were also markedly attenuated in patients with heart failure. Following intra-arterial phentolamine and/or sodium nitrite, peak calf blood flow was still significantly reduced in heart failure.

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These observations indicate that (*1*) heart failure is characterized by a striking reduction in the response to a variety of endogenous and exogenous vasodilator stimuli; (*2*) circulating catecholamines and sympathetic vasoconstrictor activity are not solely responsible for the elevation of peripheral vascular resistance and the reduced response to vasodilator stimuli in heart failure; and (*3*) heart failure may increase systemic vascular resistance directly by altering the mechanical properties and reducing the dilating ability of the resistance vessels.

INTRODUCTION

It is generally acknowledged that abnormalities of the peripheral circulation occur commonly in patients with congestive heart failure; blood flow to many organs has been shown to be reduced, and since arterial pressure is generally normal, the resistance to blood flow through these vascular beds is elevated. It has been thought that arteriolar constriction, mediated by the sympathetic nervous system, is responsible for these elevations of vascular resistance and that this peripheral vasoconstriction is important in maintaining the perfusion pressure to vital organs, such as the heart and brain, in the face of a low cardiac output. However, it is clear that vascular resistance is determined not only by nervous influences but is affected profoundly by local metabolic stimuli as well as by the physical characteristics of the blood

vessels themselves. It is not known whether the alterations in the peripheral vasculature in congestive heart failure are due entirely to altered autonomic influences or whether abnormalities in the response of the vessels to metabolic vasodilator stimuli also play a role. Accordingly, the objective of the present investigation was to compare the effects of a variety of endogenous and exogenous vasodilator stimuli on normal subjects and patients with congestive heart failure.

METHODS

Studies were carried out in a total of 21 normal subjects between 19 and 50 yr of age (average, 27.3 ± 2.3 yr/SEM) and 23 patients with congestive heart failure between 23 and 56 yr of age (average, 43.8 ± 1.7 yr). All of the patients in the latter group were receiving digitalis glycosides. 21 patients had rheumatic heart disease, one had cor pulmonale, and one had idiopathic hypertrophic subaortic stenosis. All of these patients had hepatomegaly, venous pressures exceeding 15 cm H_2O, and were in functional Classes III or IV, according to the New York Heart Association. Peripheral edema was present in all patients in whom forearm blood flow was measured, but was absent in all patients in whom calf blood flow was measured. Mean arterial pressure averaged 82.5 ± 1.9 mm Hg in the normal subjects and 87.9 ± 2.5 mm Hg in the patients with congestive heart failure. Forearm and calf blood flow were measured with the limbs at heart level and the subject recumbent. The venous occlusion technique was employed (1, 2) utilizing a single strand mercury-in-rubber strain gauge plethysmograph as previously described by Holling, Boland, and Russ who validated the use of this method (3). Circulation to the hand or foot was arrested by inflating a cuff around the wrist or ankle for at least 1 min before each determination of blood flow (4). All measurements were performed with the subjects in the basal, postabsorptive state, with at least a 15 min period of equilibration being allowed to elapse after placement of all the instruments before blood flow recordings. Arterial pressure was measured in the opposite brachial artery through an indwelling needle or by the auscultatory method. Regional vascular resistance was calculated by dividing the difference between the mean arterial pressure and venous pressure by the blood flow. Minimal vascular resistance was estimated using the peak blood flow after release of 10 min of arterial occlusion.

I. Endogenous Vasodilator Stimuli

A. Reactive Hyperemia

Control blood flow was taken as the average of 6–10 flow measurements made at 15-sec intervals before each intervention. Ischemia of the forearm or calf was produced by inflating the upper cuff to suprasystolic pressure for 1, 3, 5, and 10 min. After release of arterial occlusion, blood flow was measured initially at 5 and 15 sec after release and every 15 sec thereafter until it returned to control values. Reactive hyperemia blood flow (RHBF), Fig. 1A, was defined as the total excess blood flow in ml/100 g above the control resting flow.

Three interventions were utilized to attempt to alter the reactive hyperemia response by modifying peripheral sympathetic tone. In the first, reactive hyperemia after 5 min of ischemia was studied before and after 1.0 mg of phentolamine was injected into the femoral artery. Arterial occlusion was applied 3 min after injection of the drug at a time when the blood flow had stabilized at its new resting level. Alpha adrenergic blockade with this dose of phentolamine was insured by observing marked reduction of the constrictor response to intra-arterial norepinephrine and to immersion of the hand in ice water. In the patients with heart failure, before the administration of phentolamine, the injection of 1 μg of norepinephrine and application of the cold pressor test reduced calf blood flow by averages of 44 and 26%, respectively; after phentolamine these responses were significantly less, averaging 16 and 5%, respectively. The second intervention consisted of observing the reactive hyperemia response of the forearm to 1, 3, and 5 min of arterial occlusion before and after blocking the median, ulnar, and radial nerves at the elbow with xylocaine. The presence of sympathetic blockade was confirmed by observing that resting blood flow increased and that the vasoconstrictor response to cold stimulation was abolished. This was documented by the finding in the patients with heart failure that before nerve blockade, forearm blood flow fell by an average of 35% during the cold pressor test. Nerve blockade resulted in a tripling of resting forearm blood flow and an actual reversal in the blood flow response to the cold pressor test; a 28% increase was observed, presumably as a consequence of reflex elevation of systemic arterial pressure. Third, norepinephrine was infused i.v. at a rate of 16 μg/min to elevate mean arterial pressure by 20–30 mm Hg. Circulating catecholamine concentrations were determined by the trihydroxyindole method (5). The reactive hyperemia response was studied before and during the norepinephrine infusion.

Venous congestion was produced by the method described by Wood, Little, and Wilkins (6), in which the arm was packed with blood by inflating the upper arm cuff to 70–95 mm Hg for 5 min before 10 min of arterial occlusion. The reactive hyperemia response was then measured.

The reactive hyperemia response was studied in five patients with heart failure shortly after admission and after compensation.

B. Active Hyperemia

The forearm was exercised by squeezing a hand dynamometer to 50 lb. pressure, once every second for 30 sec. The flow was recorded at 5 and 15 sec after the final contraction and then every 15 sec until it returned to control levels. The postexercise hyperemia in ml/100 g was calculated as the total blood flow in excess of resting blood flow (Fig. 1C).

C. Direct Heating

The upper forearm was heated by means of two 150 w tungsten lamps with internal reflectors, placed 30 cm from the arm and 180° from one another. The strain gauge was protected by an opaque shield which did not touch the arm. Comparisons were made on the basis of the total excess blood flow above control flow, observed during 5 min of heating and during the following 5 min of recovery (Fig. 1E).

II. Exogenous Vasodilator Stimuli

A. Vasodilator Drugs

Sodium nitrite ($NaNO_2$), 10, 30, and 50 mg, was injected through an indwelling Cournand needle in the femoral artery, and calf blood flow recorded every 15 sec until the peak effect had subsided. 15 min was allowed to elapse between injections. After the effects of the $NaNO_2$ had been dissipated, phentolamine (1 mg) was injected intra-arterially and calf blood flow was recorded every 15 sec. The peak response was noted, as well as the new steady level of resting blood flow, which was reached 3 min after the injection. This level was compared to the resting blood flow noted before adrenergic blockade. 5 min after the intra-arterial administration of phentolamine, 30 mg of $NaNO_2$ was again injected intra-arterially and the calf blood flow response compared with that produced by the same dose of sodium nitrite given before phentolamine. Again the presence of sympathetic blockade was confirmed as indicated above. Methemoglobin levels determined by the cyanide method (7) were found not to exceed 5% with these doses of $NaNO_2$.

RESULTS

I. *Basal vascular dynamics.* The basal forearm blood flow determined in 14 normal subjects averaged 4.12 ± 0.53 (SEM) ml/min per 100 g and was significantly greater than that observed in 17 patients with congestive heart failure, in whom it averaged 2.09 ± 0.19 ml/min per 100 g ($P < 0.01$). Forearm vasuclar resistance averaged 24.0 ± 1.5 mm Hg per ml/min per 100 g in the normal subjects and was significantly higher in the heart failure patients, 47.5 ± 5.1 mm Hg per ml/min per 100 g ($P < 0.01$), Fig. 3, left. Similarly, the calf blood flow of seven normal subjects was significantly higher (4.71 ± 0.35 ml/min per 100 g) than in six patients with congestive heart failure (2.93 ± 0.56 ml/min per 100 g), $P < 0.01$, whereas vascular resistance in the calf averaged 20.7 ± 1.3 mm Hg per ml/min per 100 g in normal subjects and 33.6 ± 3.6 mm Hg per ml/min per 100 g in patients with heart failure ($P < 0.01$).

II. *Reactive hyperemia.* The ability of the fore-

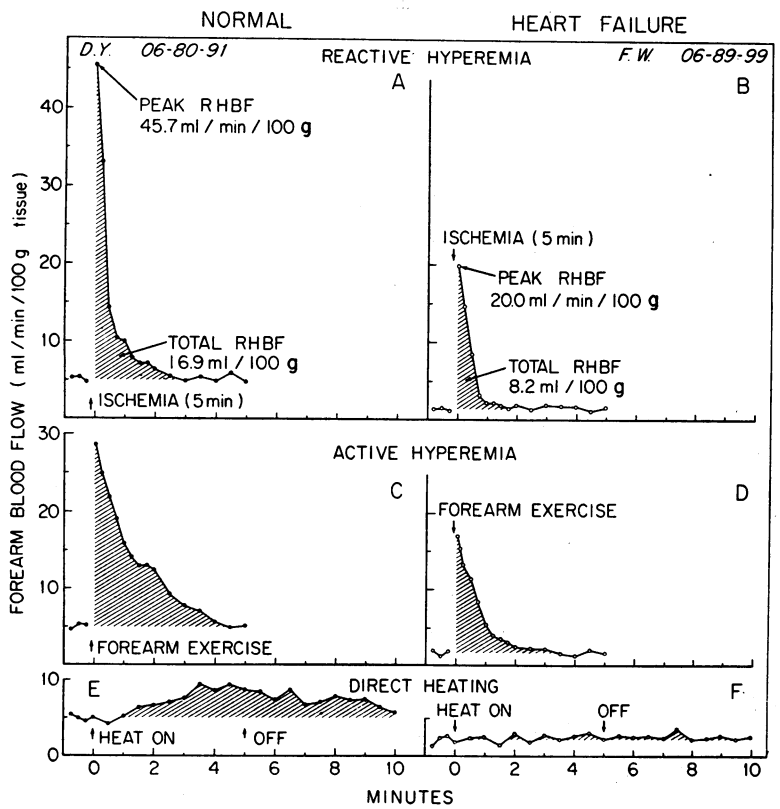

Figure 1 Serial forearm blood flow measurements in normal subject (left) and a patient with congestive heart failure (right). A and B, blood flow recorded before and after a 5 min period of ischemia. RHBF, reactive hyperemia blood flow. Total RHBF refers to the shaded area under the curve. Peak RHBF refers to the highest blood flow recorded after release of arterial occlusion. C and D, blood flow recorded before and after completion of 30 sec of rhythmic forearm exercise. E and F, blood flow recorded before, during, and after 5 min of direct heating of the forearm.

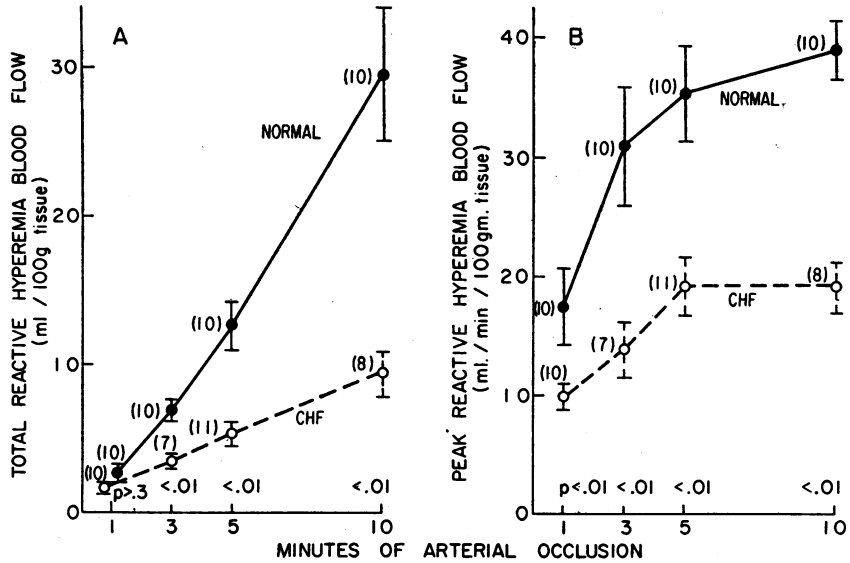

FIGURE 2 A, total reactive hyperemia blood flow (± SEM). B, peak reactive hyperemia blood flow after release of 1, 3, 5, and 10 min of arterial occlusion. Solid Circles, normal subjects. Open Circles, patients with congestive heart failure.

arm vascular bed to dilate in response to an ischemic stimulus in the normal subjects and patients with heart failure was compared on the basis of two measurements: the total RHBF response (Figs. 1A, 1B, and 2A) and the peak RHBF (Figs. 1A, 1B and 2B). The total RHBF in the patients with congestive heart failure was substantially less than in the normal subjects. The

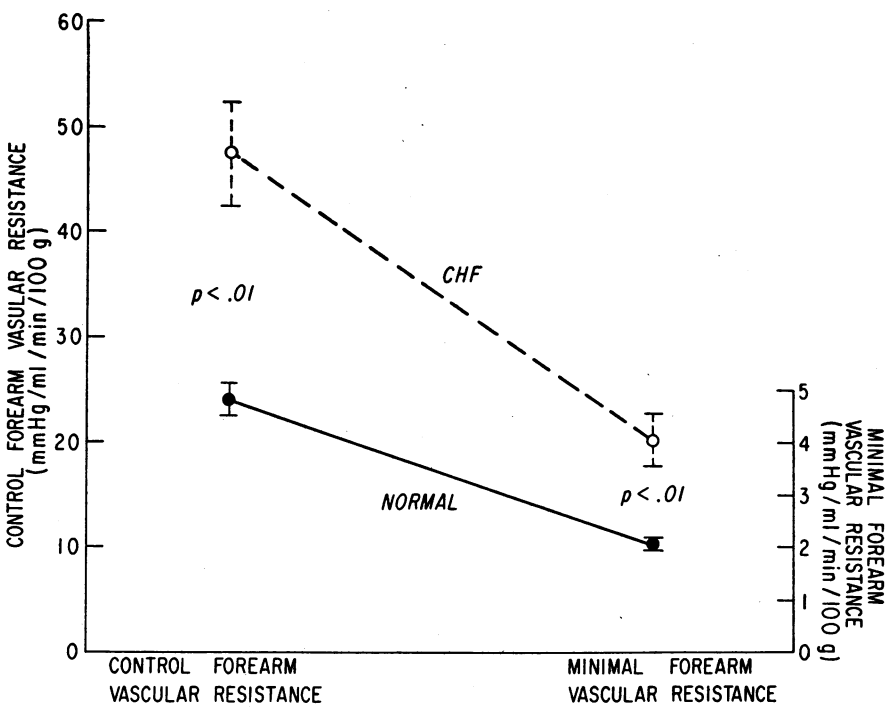

FIGURE 3 Control and minimal forearm vascular resistance in normal subjects (closed circles) and patients with congestive heart failure (open circles). Peak flow after release of 10 min of arterial occlusion was used to calculate minimal forearm vascular resistance.

peak RHBF after 10 min of ischemia approaches the maximum that can be observed with an ischemic stimulus of any duration. After this period of ischemia, the total RHBF in the patients with heart failure averaged only 31.9% of that observed in normal subjects, $P < 0.01$, (Fig. 2A). Similarly, the peak RHBF was markedly reduced in patients with heart failure, as compared with normal subjects. After 10 min of ischemia this value in the patients with heart failure averaged 47.7% of that observed in the normal subjects (Fig. 2B). The minimal peripheral vascular resistance in the forearm estimated from the peak RHBF after 10 min of ischemia is shown in Fig. 3. In normal subjects peripheral vascular resistance fell to 2.06 $\pm$ 0.14 mm Hg per ml/min per 100 g, whereas in the patients with heart failure the minimal resistance was significantly higher, and averaged 4.05 $\pm$ 0.56 mm Hg per ml/min per 100 g ($P < 0.01$).

In order to determine whether the reduced RHBF of patients with heart failure resulted from augmented sympathetic constrictor activity, the effects of nerve blockade on the response to ischemia was studied in four patients with congestive heart failure. Peak RHBF was essentially identical before and after nerve blockade (Fig. 4A); total RHBF was also not significantly affected. In four other patients with heart failure, adrenergic blockade with phentolamine similarly did not alter peak RHBF (Fig. 4B) or total RHBF in the calf. In four normal subjects the infusion of norepinephrine raised the catecholamine concentration of arterial blood to between 1.39–2.44 μg/liter and elevated forearm resistance from 25.3 to 40.2 mm Hg per ml/100 g per min. However, this heightened vasoconstrictor tone did not interfere with the peak RHBF (Fig. 4C) or the total RHBF response.

In order to determine whether the reduced RHBF in patients with heart failure was related to alterations in arteriolar tone produced by the elevated venous pressure, the effects of ischemia were determined with and without prior venous congestion. In seven normal subjects, total RHBF after release of 10 min of arterial occlusion was reduced by 9.1% with venous congestion, $P < 0.05$, (Fig. 5A). In six patients with heart failure,

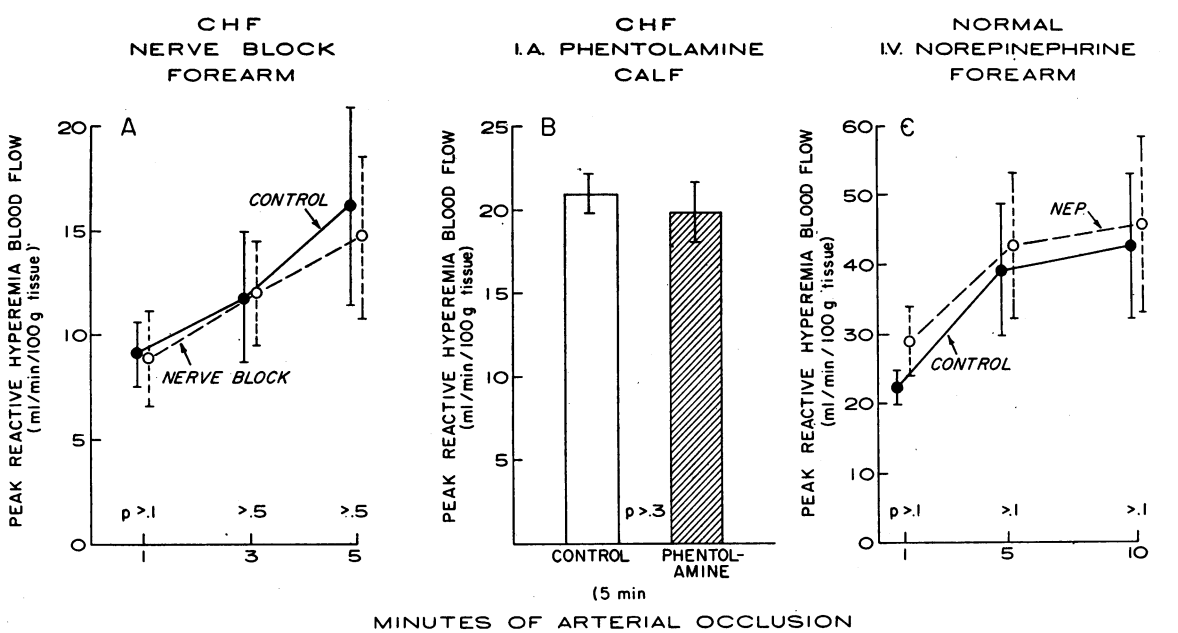

FIGURE 4 A, peak reactive hyperemia blood flow after various periods of forearm ischemia before (solid circles) and after (open circles) deep nerve blockade of the forearm in patients with congestive heart failure. B, Peak reactive hyperemia blood flow in the calf of patients with congestive heart failure after release of 5 min of arterial occlusion. White bar, control. Shaded bar, after intra-arterial phentolamine. C, peak reactive hyperemia blood flow after various periods of forearm ischemia in normal subjects before (solid circles) and during (open circles) an i.v. norepinephrine infusion.

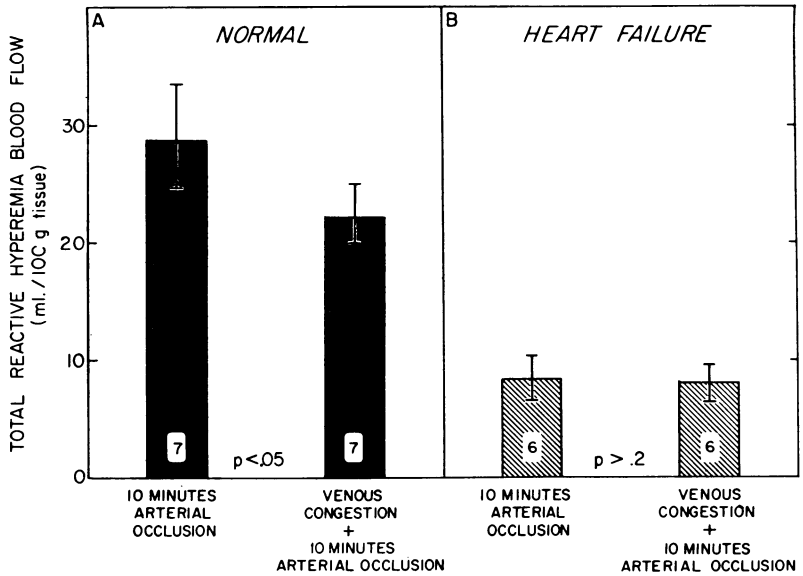

FIGURE 5 Total reactive hyperemia blood flow after release of 10 min of arterial occlusion with and without 5 min of prior venous congestion in normal subjects (panel A, solid bars) and in patients with congestive heart failure (panel B, shaded bars).

however, the total RHBF was not significantly altered by prior venous congestion (Fig. 5B). Furthermore, the total and peak RHBF after ischemia with venous congestion in normal subjects greatly exceeded the values observed in patients with heart failure, regardless of whether venous congestion had been carried out in them (Figs. 5A and 5B).

III. *Effects of compensation.* The reactive hyperemia response was restudied in five patients after compensation of their congestive heart failure, an average of 17 days after the initial study. At the time of the second investigation these patients all had normal venous pressures, a decrease in hepatomegaly, no edema, and diuresis had resulted in weight loss that averaged 6.8 kg less than that present at the time of the first study. After compensation, total and peak RHBF were significantly higher following 1, 5, and 10 min of arterial occlusion (Fig. 6).

IV. *Postexercise hyperemia and direct heating.* The total forearm postexercise hyperemia blood flow was markedly reduced in patients with heart failure, as compared to normal subjects (Fig. 7A), as was the total excess forearm blood flow induced by direct heating (Fig. 7B).

V. *Response to exogenous vasodilator stimuli.* Immediately after intra-arterial injection of phentolamine, blood flow rose to peaks which were significantly lower in patients with congestive heart failure than in normal subjects (Fig. 8B); and after stabilization of blood flow following phentola-

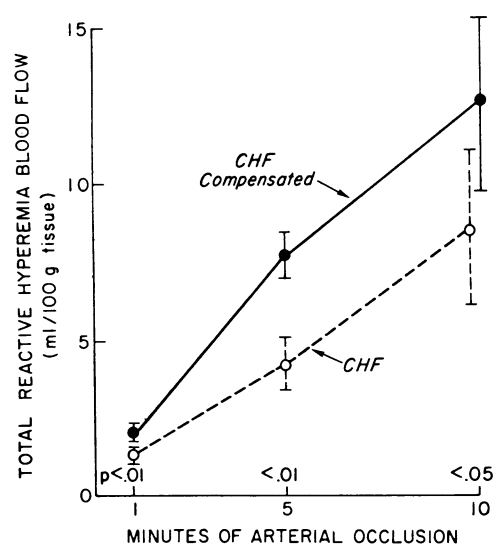

FIGURE 6 The effect of compensation of heart failure on modifying the total reactive hyperemia blood flow response after release of various periods of arterial occlusion. Open circles, heart failure–uncompensated. Solid circles, heart failure–compensated.

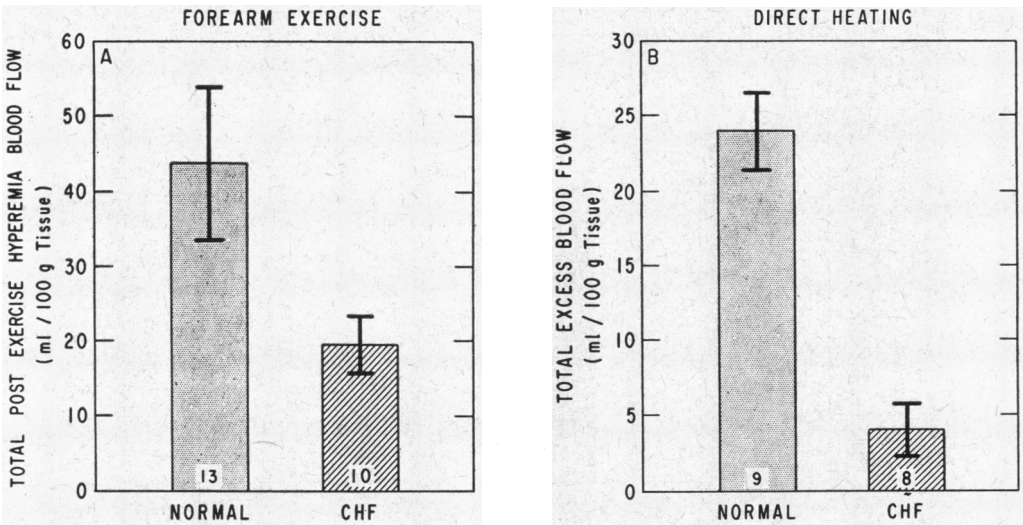

FIGURE 7 A, total postexercise hyperemia blood flow. This was calculated as the shaded areas under the curves in Figs. 1C and 1D. B, total excess blood flow during 5 min of direct heating and 5 min of recovery. This was calculated as the shaded area under the curves in Figs. 1E and 1F. Fine Strippled bars, normal subjects. Cross hatched bars, patients with congestive heart failure.

mine, it remained at a significantly lower level in the patients with heart failure (Fig. 8C). The peak blood flow after intra-arterial injections of three doses of $NaNO_2$ was significantly lower in patients with heart failure than in normal subjects (Fig. 9), regardless of whether the $NaNO_2$ was administered before or after phentolamine (Fig. 8D).

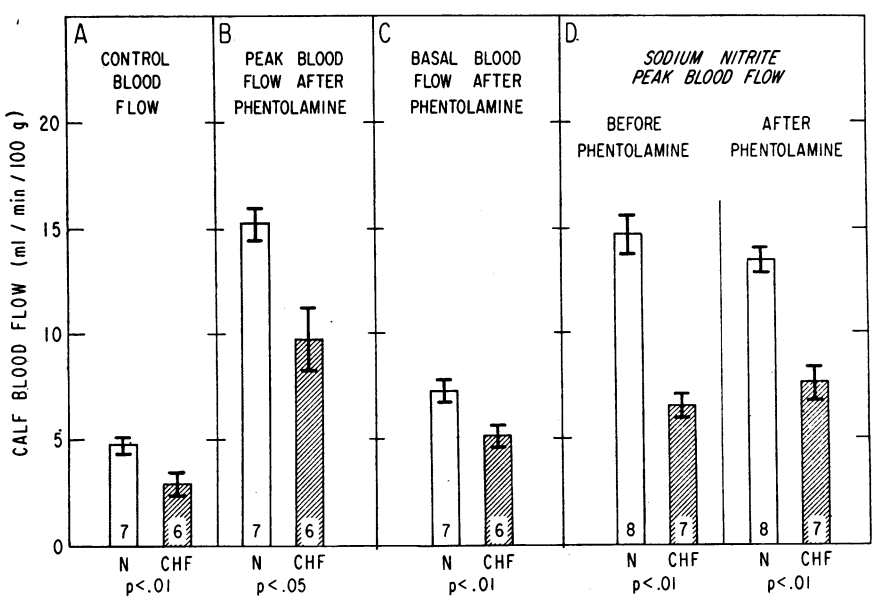

FIGURE 8 Peak calf blood flow response to intra-arterial vasodilators. A, control calf blood flow. B, peak calf blood flow after 1 mg of intra-arterial phentolamine. C, basal calf blood flow after stabilization of blood flow after intra-arterial phentolamine. D, peak calf blood flow response to 30 mg of intra-arterial sodium nitrite before (left) and after (right) adrenergic blockade with intra-arterial phentolamine. Fine stippled bars, normal subjects (N). Cross hatched bars, patients with congestive heart failure (CHF).

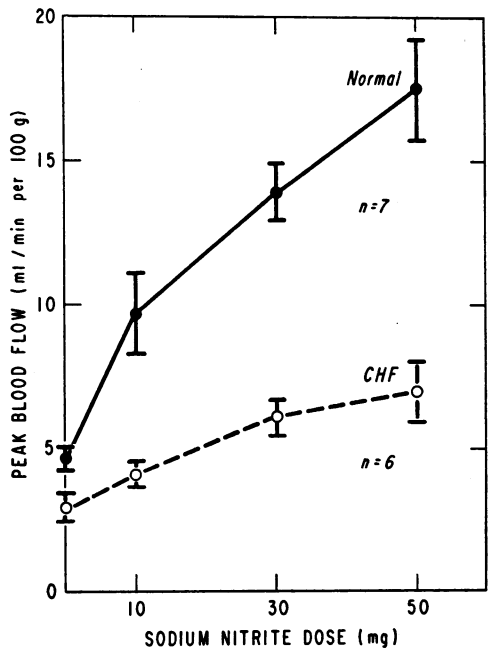

FIGURE 9 Peak calf blood flow response after intra-arterial injections of various doses of sodium nitrite. Solid circles, normal subjects. Open circles, patients with congestive heart failure.

DISCUSSION

The major finding of this investigation is a striking, heretofore unrecognized, reduction in the capacity of the resistance vessels of patients with congestive heart failure to respond to a wide variety of vasodilator stimuli. It was observed that both the peak and total RHBF following various periods of ischemia were markedly reduced in patients with congestive heart failure (Figs. 1A, 1B, and 2). Consequently, after a maximal ischemic stimulus, the calculated forearm vascular resistance in patients with heart failure declined to levels approximately twice as high as those levels observed in normal subjects (Fig. 3). Also, the vasodilation, which normally occurs after muscular exercise and direct heating of the limb, was markedly attenuated by the heart failure state (Fig. 7). Exogenous humoral vasodilator stimuli, such as $NaNO_2$ and the immediate response to phentolamine, an agent which not only blocks alpha adrenergic receptors but also exerts a direct, dilating effect on smooth muscle (8), also evoked a less prominent vasodilating effect in patients with congestive heart failure as compared with normal subjects (Figs. 8 and 9). These differences occurred despite the fact that the lower levels of blood flow in the control state in patients with heart failure afforded a greater opportunity for exposure of the vascular smooth muscle to these vasodilating drugs.

It is well known that forearm and calf blood flow are reduced and the resistance in these vascular beds elevated in patients with congestive heart failure in the basal state (1, 9, 10) and the results of the present investigation are consistent with these findings. Since, in the past, the higher vascular resistance has been attributed to higher sympathetic activity in patients with heart failure (11–14), we considered the possibility that the reduced responsiveness to dilator stimuli might merely be another manifestation of their increased sympathetic vasoconstrictor activity. Indeed, recent reports have indicated that elevated sympathetic tone will decrease the reactive hyperemia response (15, 16). In order to test this hypothesis, three types of experiments were undertaken (Fig. 4). In the first two, sympathetic vasoconstrictor tone to the limb was abolished in patients with congestive heart failure by direct nerve blockade and markedly reduced by the intra-arterial administration of the alpha adrenergic blocking drug phentolamine. The effectiveness of the nerve blockade was documented by observing that the vasoconstrictor response to the cold pressor test was abolished and that, in fact, reversal occurred with forearm blood flow increasing with immersion of the opposite hand in ice water and control blood flow tripling. The effectiveness of phentolamine was reflected in the significant reduction of the constrictor response to injected norepinephrine and to the cold pressor test. However, these maneuvers did not restore the response to dilator stimuli to normal; the total and peak RHBF after an ischemic stimulus were no higher after sympathetic blockade than before (Figs. 4A and B). It is unlikely that any residual sympathetic activity after either method of blockade could have been responsible for the striking difference observed between the normal subjects and the patients with heart failure, in view of the finding of Strandell and Shepherd that peak active hyperemia blood flow is little affected by intense reflex vasoconstriction (17). Furthermore, this postulation is consonant with the findings in experimental animals by Remensnyder, Mitchell, and Sarnoff (18) that

even marked sympathetic vasoconstriction does not reduce vasodilatation resulting from muscular activity.

In the third experiment, norepinephrine was infused into normal subjects and the circulating catecholamine concentration elevated to levels comparable with those observed in patients with congestive heart failure during exhaustive exercise (12). Despite the fact that the maneuver elevated forearm vascular resistance to levels observed in the basal state in patients in heart failure, the RHBF was not affected (Fig. 4C). From these studies it is concluded that sympathetically mediated vasoconstriction is not responsible for the markedly abnormal vasodilator responses observed in heart failure.

A second possibility that must be considered to account for the difference between normal subjects and patients with heart failure is the presence of occlusive vascular disease in the latter group, a significantly older population than the normal subjects. Thus, if the lumen of the major arteries were severely compromised, limb blood flow could not rise to normal levels after vasodilator stimuli even if the peripheral vessels exhibited a normal dilator response (19, 20). However, this possibility can also be excluded, since none of the patients with heart failure in this study had ischemic or hypertensive heart disease, intermittent claudication, or any manifestations of peripheral arteriosclerosis. Finally, the diminished hyperemia responses were observed in all extremities and were as striking in the forearm as in the calf. The differences in their responses to vasodilator stimuli cannot be attributed simply to these differences in age, since in both groups of individuals there was no correlation between age and resting blood flow, peak and total RHBF, and peak response to $NaNO_2$. All of the patients with heart failure were receiving maintenance doses of cardiac glycosides at the time of study. Since these drugs are known to be mild vasoconstrictor agents (21) it was considered that their administration might be responsible for a reduction in the vasodilator responses. However, this possibility was excluded by studies in five additional subjects without heart failure who received cardiac glycosides, but who exhibited normal forearm vascular dynamics in control state and after being exposed to vasodilator stimuli.

A fourth possibility considered to account for the difference to the dilating stimuli relates to the difference in venous pressure in the patients with heart failure and in normal subjects. The myogenic hypothesis, proposed by Bayliss, suggests that when intraluminal pressure falls after arterial occlusion, arteriole tone diminishes (22). It might be argued that the elevated venous pressure which exists in patients with heart failure would prevent intraluminal pressure from declining to the same level during occlusion in these patients, thus resulting in a lesser tendency for the arterioles to dilate during the period of occlusion. That change in venous pressure can, in fact, alter the level of blood flow after a period of ischemia was demonstrated in normal subjects (Fig. 5A) in whom RHBF was slightly, though significantly, reduced when the veins were congested before occlusion of arterial inflow; and this response is consistent with that described by Wood et al. (6). However, this reduction in RHBF by elevating venous pressure markedly was very slight and did not lower RHBF to those levels observed in the presence of heart failure (Fig. 5). Furthermore, when a comparison was made between the RHBF in normal subjects and patients with heart failure, in whom venous pressure had been elevated to similar levels, the aforementioned differences persisted. Therefore, whereas the elevated venous pressure of heart failure may play a small role in the reduced RHBF, it certainly cannot be considered responsible for the major changes observed. Also, elevation of venous pressure would not explain the diminished response exhibited by these patients to the several other vasodilator stimuli tested.

The possibility was also considered that reduction in the diffusion of vasodilator metabolites to the vascular wall might account for the impairment in the vasodilator response observed after ischemia and exercise (25). Certainly, if the interstitial fluid volume were greatly augmented this could occur. However, the finding that vasodilation was as reduced in the arms as in the legs would militate against this possibility. More importantly, the finding that vasodilation was reduced after the intra-arterial administration of two exogenous vasodilators, sodium nitrite and phentolamine, points to an abnormality in the vessel wall itself. Indeed, the lower blood flow existing in patients with heart failure insured that their resistance vessels were actually exposed to these vasodilators in

higher concentrations and for longer periods of time than normal subjects.

In considering the last named possibility, i.e. that the difference in vascular responsiveness results from a structural abnormality in the wall of the resistance vessels in heart failure, studies in hypertensive subjects must be considered. Tobian, Janecek, Tomboulian, and Ferreira and Olson and Chesley have demonstrated an increased sodium and water content in the arterioles of hypertensive rats and humans, and suggested that this might produce a structural abnormality in the vessel and increase resistance to flow (24, 25). Conway's finding of a reduced reactive hyperemia response in the forearm of patients with hypertension is consistent with this suggestion (26). It is possible that in heart failure the resistance vessels participate in the generalized retention of salt and water. This could be accompanied by swelling, engorgement, and stiffening of these vessels, which, in turn, could lead to an inability to dilate appropriately when stimulated. The observation that treatment of hear failure by diuresis tended to restore the dilating response toward normal (Fig. 6) provides support for this suggestion. In any event, further studies particularly in animals with experimentally produced heart failure, will be required to throw further light on this question.

Regardless of the specific mechanism responsible for the marked reduction in the response to vasodilator stimuli which exists in patients with congestive heart failure, it is interesting to speculate upon the possible physiologic effects of this abnormality. In heart failure the dilatation of vascular beds supplying skeletal muscle would tend to be reduced during and after the contraction of these muscles. As a consequence, arterial pressure might not fall despite an inadequate elevation of cardiac output. A larger fraction of the cardiac output would then be available for perfusion of more vital organs than would be the case if the resistance vessels supplying the exercising muscles dilated normally. Presumably, increased extraction of oxygen by the peripheral tissues could compensate for the lack of dilation that occurs in patients with heart failure (10). This would be more economical in the face of a limited total cardiac output than that of the normal dilatation, which may not be essential (27).

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