PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 150, 65–70 (1975)

The Response of Blood Flow to Altered Perfusion Pressure in Canine Adipose Tissue[1] (38975)

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(Introduced by S. S. SOBIN)

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Blood flow in canine adipose tissue appears to be regulated by both neural and humoral factors, which determine a balance between the degree of vasoconstriction and vasodilatation (1, 2). These extrinsic stimuli exert strong influences on the transcapillary exchange functions of the microcirculatory bed in fat. The intrinsic ability of adipose tissue to maintain its blood flow at a relatively constant level, despite normal variations in blood pressure, i.e., to autoregulate, has been less well defined. Nielsen and Secher (3) reported that the vascular resistance in subcutaneous fat pads increased when venous pressure was raised and, conversely, declined during arterial hypotension. This would indicate a myogenic type of autoregulation. On the other hand, Intaglietta and Rosell (4) observed a linear relationship between blood flow and pressure in the canine subcutaneous fat pad, which suggests that autoregulatory responses are weak or absent in this preparation. In the human forearm, blood flow in the subcutaneous adipose tissue is regulated within a certain arterial blood pressure range where venous pressure is constant (5).

The experiments described herein were performed to test the response of blood flow in the isolated autoperfused canine fat pad to stepwise reductions in perfusion pressure and to increases of pressure above control levels. Autoregulatory behavior would be revealed by a tendency for blood flow to return toward control level in face of the altered pressures. We were able to observe only very weak autoregulatory responses in the isolated fat pad under the conditions of the experiments.

Methods. The experiments were performed on 25 mongrel dogs of either sex, anesthetized with sodium pentobarbital (30 mg/kg body wt, i.v.) with supplements as necessary. Body weights ranged from 8.6 to 20 kg with a mean of 14.9 kg. The trachea was intubated in order to assure a clear airway passage.

Complete vascular isolation of the inguinal subcutaneous fat pad was achieved as follows: The fat pad was palpated and a skin incision was made following the general outline of the pad. The tissue was dissected free from underlying structures with the artery, vein, and nerve intact. After the overlying skin was removed double ligatures were tied at the proximal and distal ends of the fat pad. In ten of the preparations the nerve was severed at this point. Hemostasis was maintained by ligation of all bleeding points on the surface of the isolated tissue. The fat pad was kept covered with plastic wrap and temperature was maintained at 37–38° with a heating lamp. Heparin (15,000–20,000 IU) was given to the whole animal about 15–30 min before the experimental run was started. Autoperfusion of the tissue was provided by a shunt from the right femoral artery to the adipose tissue artery, via a silicone filled drop chamber to measure flow. Perfusion pressure was measured from a side arm off the shunt cannula and recorded on a Statham model 421 ink writer. Mean arterial blood pressure was recorded on a printing digital voltmeter (Practical Automation Inc., model Series PDM-611).

In order to determine whether the fat pad autoregulated blood flow, the flow was recorded while perfusion pressure was (a) reduced stepwise by means of a screw clamp on the (femoral) arterial inflow to the tissue

[1] This investigation was supported in part by USPHS Grant HL 14329.

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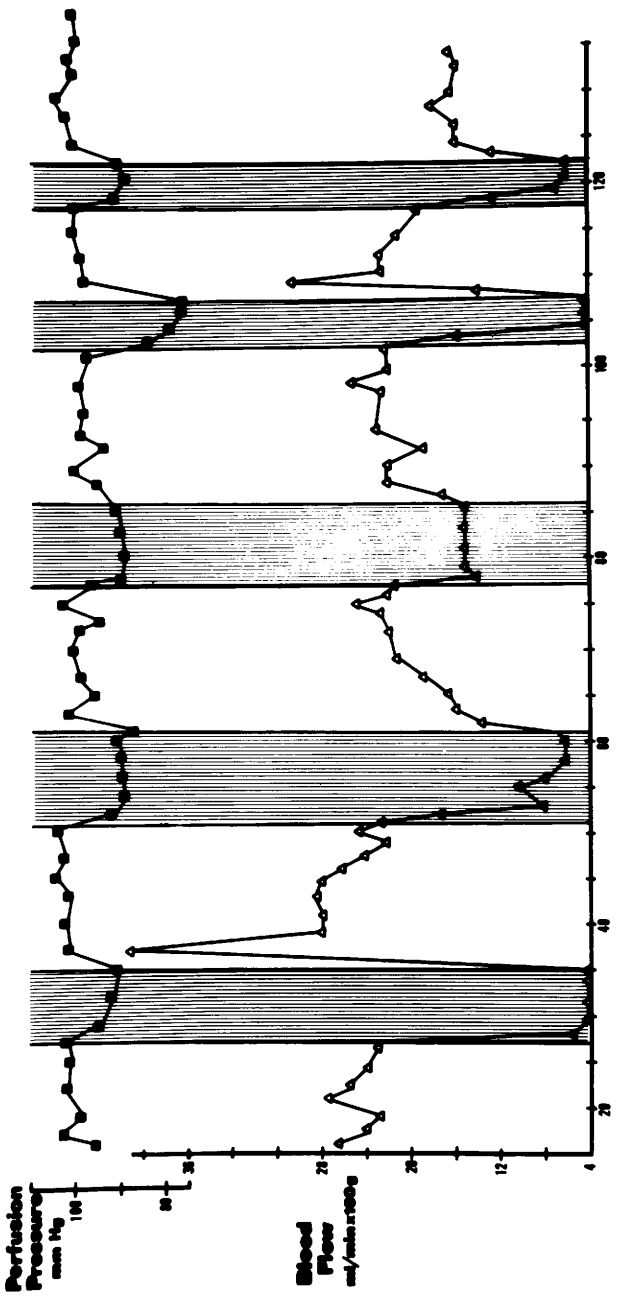

FIG. 1. Blood flow responses to reduced perfusion pressure in a representative experiment. The shaded areas show the period of femoral artery occlusion.

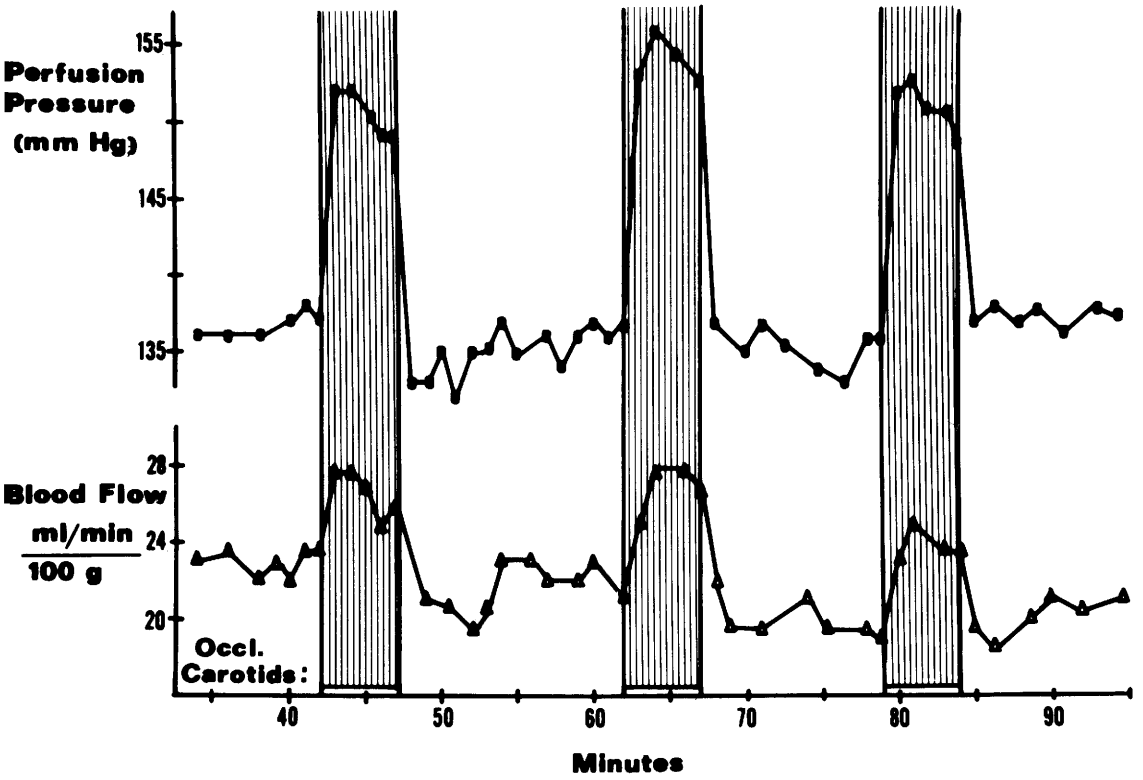

FIG. 2. Blood flow responses to increased perfusion pressure in a representative experiment. The shaded areas show the period of bilateral carotid occlusion.

or (b) increased by single or bilateral occlusion of the carotid arteries. Pressure was allowed to return to the original level between each step change. The study was extended over a wide range of pressures by employing two variations on the basic protocols: (a) perfusion pressure was reduced during sustained high systemic control pressure and (b) the animals were vagotomized before bilateral carotid occlusions to maintain high systemic pressures; perfusion pressures were reduced during the sustained hypertension. All experiments were placed into two groups according to femoral artery occlusion intervals. Group I = 1–5 min and Group II = 6–14 min. The mean experimental values were calculated from the flows during steady state conditions, which were reached when both pressure and flow levels had attained a new equilibrium following the alteration of perfusion pressure.

Results. The mean resting blood flow was 16.7 ml/min × 100 g tissue (range = 3.7–29.4 ml/min × 100 g). Although the denervated preparations had slightly lower mean flows than the innervated tissues, statistically they were not significantly different ($P = >.10$).

Group I (arterial inflow reduced for 1–5 min). A decrease in perfusion pressure produced by reducing the femoral arterial inflow resulted in reduced blood flow in the adipose tissue with little observable tendency to return to control values during the occlusion period. Figure 1 shows the pressure and flow responses of one preparation. At pressures where the blood flow was essentially zero, postocclusion hyperemia was observed. Hyperemia was greatly attenuated or absent in preparations perfused at pressures which produced less than complete stoppage of blood flow. Blood flows were also maintained at the respective new steady state after increasing the perfusion pressure by occlusion of the carotids (Fig. 2) or, alternatively, after reducing

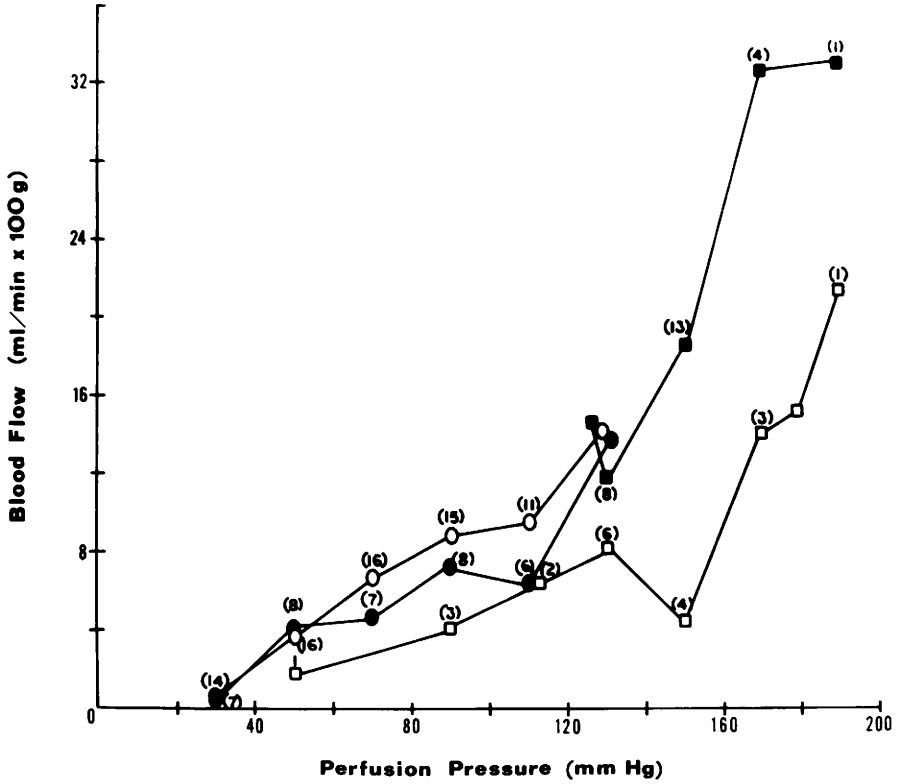

FIG. 3. Pressure–flow responses of all the experiments. The means are plotted. Small numbers over the data point indicate the number of preparations. Data points without numbers indicate controls. Group I: ○ = femoral artery occluded, □ = femoral artery occluded during hypertension produced by vagotomy and/or bilateral carotid occlusion, ■ = bilateral carotid occlusion. Group II: ● = femoral artery occluded.

pressure from a high initial control level. A plot of the means of blood flows vs perfusion pressures ranging 30–200 mmHg revealed a curvilinear relationship convex to the pressure axis for each type of intervention (Fig. 3). All of the above indicate little or no autoregulatory behavior in these preparations.

Group II (reduction for 6–14 min). The closed circles plotted in Fig. 3 show that the flow response to more prolonged femoral arterial occlusion was similar to that observed during 1–5 min clamping, i.e., a curvilinear relationship of flow vs pressure.

In order to determine whether extrinsic neural activity could override autoregulatory behavior, we compared ten preparations with severed nerves with four innervated tissues. (Fig. 4). Autoregulation was weak in the denervated as well as in the neurally intact fat pad.

It appeared that passive narrowing of the vascular bed occurred when perfusion pressure was lowered. The calculated vascular resistance for the innervated tissues was greater than the control values, over the pressure range of 44–103 mmHg. The resistance values for the denervated preparations were also greater than the control values. The increased resistance suggests that the adipose tissue did not actively regulate its blood flow in response to the reduced inflow pressure, but instead, acted as a passive vascular bed. Nielsen and Secher (3) found a direct relationship between pressure resistance over perfusion pressure ranges between 45 and 95 mmHg. However, their experimental design was somewhat different from the one used in the present study.

Resting blood flows varied widely from one fat pad to another due to differences in the adiposity among the animals (6).

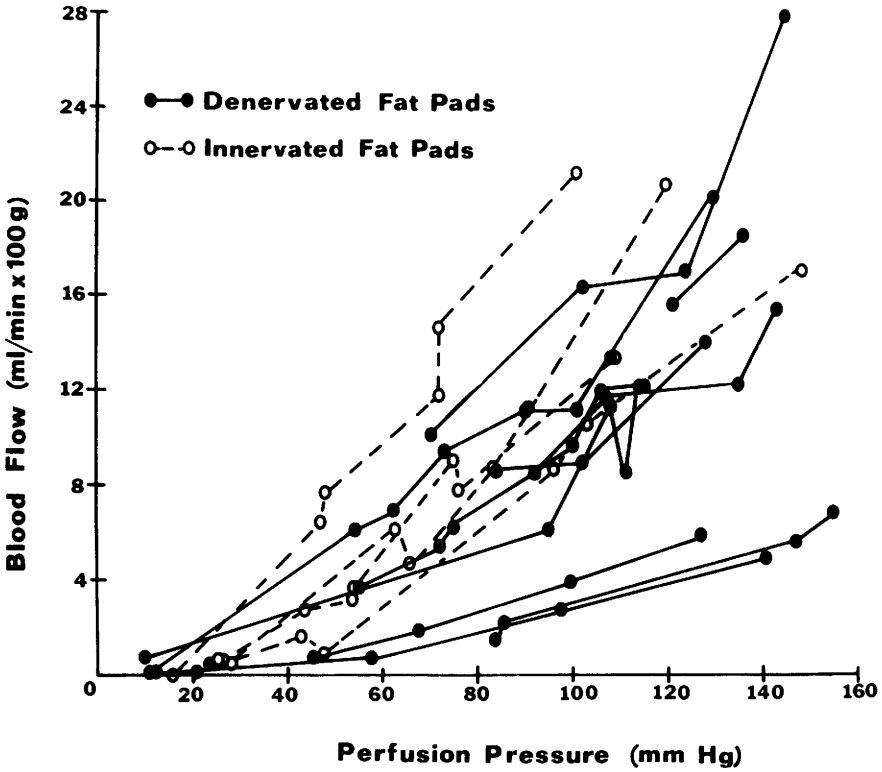

FIG. 4. Comparison of pressure–flow responses in four innervated and ten denervated fat pads.

Some of the scatter was reduced by calculating the percent change from control flow (mean = 16.7 ml/min × 100 g) and the corresponding percent pressure change. The data in Table I show the steady state mean values and the standard errors of the means for all the experiments in which perfusion pressure was reduced. Values from experiments in which pressure was raised are not included in the table.

TABLE I. PERCENTAGE OF CHANGE FROM CONTROL PRESSURES AND FLOWS.[a]

Number of experiments	Perfusion pressure (% Δ)[b]	Blood flow (% Δ)[b]
37	−15.98 ± 1.10	−25.84 ± 2.68
47	−36.46 ± 1.11	−52.58 ± 1.89
18	−60.57 ± 1.43	−73.88 ± 2.72
16	−82.86 ± 1.33	−88.46 ± 4.49

[a] Values given are mean ± standard error of the mean.

[b] Percent change = (Experimental-Control/Control) × 100.

Discussion. The phenomenon of autoregulation has been studied in a number of vascular beds and several experimental criteria have been established in order to determine the existence of the response. In pressure–flow studies, for example, certain transient responses in the blood flow may occur in a tissue that possesses autoregulatory behavior. A sudden reduction in perfusion pressure may result in an initial transient decrease in blood flow. Soon after this transient response, however, the flow will begin to rise toward control levels due to dilatation of the resistance vessels. Pressure–flow plots show a curvilinear relationship which is concave or convex to the pressure axis except over certain pressure ranges where it is parallel to this axis, e.g., 60–90 mmHg for skeletal muscle, and 80–180 mmHg for the kidney. In the fat pad, the relationship between flow and reduced pressure produces a curve convex to the pressure axis. This is a response typically found in passive vascular beds. The shape of the curve is partially due

to the degree of compliance and elastic recoil of the vascular elements and surrounding tissue.

It has been reported that experimental conditions may significantly affect the results by abolishing the autoregulatory response or at least reducing it. For example, Johnson (7) states that the use of artificial perfusion circuits and pumps may eliminate or lessen the response. Hinshaw (8) did not find the presence of autoregulation in the pump perfused leg and intestine. Rapela and Green (9) also explain that surgical, traumatic, or perfusion procedures may abolish the autoregulatory response. No artificial pumps or perfusion circuits were used in the experiments described herein. However, we cannot completely exclude the possibility that surgical trauma or mechanical handling, or both, weakened an autoregulatory response which might be present in the intact tissue. This is especially true in the case of adipose tissue which is highly sensitive to handling.

Summary. It is concluded that subcutaneous adipose tissue autoregulates its blood flow only weakly or not at all in the range of perfusion pressures employed in our studies. Instead, these experiments demonstrate that when perfusion pressure is altered in the fat pad, vascular resistance must change in an opposite direction since there is little tendency for the flow to return to control values. Therefore, the vascular bed is responding passively. Furthermore, there was little evidence of autoregulation in denervated tissues indicating that the extrinsic neural control does not mask an underlying ability to modulate flow.

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Received April 7, 1975. P.S.E.B.M., 1975, Vol. 150.