Behavior of Vascular Beds in the Human Upper Limb at Low Perfusion Pressure


ABSTRACT
A technique of venous occlusion pressure plethysmography was used to examine the behavior of blood flow in the hand and forearm during reduced perfusion pressure. The trend of flow following sudden reduction in perfusion pressure was recorded, and steady-state pressure-flow curves were constructed. Epinephrine iontophoresis allowed discrimination between forearm skin and muscle blood flow. Pressure-flow curves for the hand were parabolic, convex to the pressure axis, and passing close to the zero point. There was no progressive change in flow once perfusion pressure and flow were initially reduced. Autoregulation was evident in forearm muscle and was more marked in chronically sympathectomized limbs. When perfusion pressure was reduced, blood flow fell, then rose to a new, steady level. Pressure-flow curves were concave to the pressure axis and intersected it at close to zero.

ADDITIONAL KEY WORDS blood flow epinephrine forearm muscles plethysmography skin sympathectomy

The behavior of blood flow in individual vascular beds when the systemic, or local, arterial pressure is low is of considerable practical consequence to man. The vascular beds of the limbs are readily accessible to study, but clinical situations are usually extremely complex. We sought therefore to gain an understanding of the behavior of human upper limb flow when perfusion pressure is reduced, but other variables are controlled.

Shepherd (1) reviewed the several studies in man in which limb arterial pressure was reduced by local external pressure and flow measured by plethysmography or calorimetry. In two important respects the results differed from those obtained in vascular beds of isolated limbs of animals. In man, a flow cessation pressure has commonly been described, though our work (2) suggests this may be attributable to artifacts inherent in the method of pressure plethysmography used. In animals, autoregulation of flow is prominent in skeletal muscle (3), but it has not been noted in man.

Method
The details of the method of venous occlusion pressure plethysmography, in which the entire upper limb is enclosed in a pressure box, have been described in a previous paper (2). Unless otherwise specified, the experimental conditions in the present study were identical. The subjects were volunteers from among us, our colleagues, and hospital outpatients.

Our main purpose was to seek evidence of autoregulation in the vascular beds of the hand and forearm muscle. This was accomplished by constructing pressure-flow curves for these beds, and also by observing the trend of blood flow after sudden reduction in perfusion pressure. The behavior of the forearm muscle was distinguished from that of the skin by minimizing the circulation in the latter by epinephrine iontophoresis, using a technique essentially identical to that of Cooper et al. (4). A 1:2,000 solution of epinephrine tartrate in distilled water was used. The skin of the forearm was cleaned with detergent and covered with an absorbent bandage soaked in the epinephrine solution. Aluminum foil bandaged in place acted as the positive electrode. Aluminum foil with ECG jelly contact was applied to the calf as the negative electrode. Current from a 24-v dry cell was increased by a
rheostat until discomfort was just tolerable and was maintained for 20 min, or until uniform skin blanching and piloerection were apparent. The effect appeared to persist unchanged for at least 2 hr, as judged by inspection and temperature measurement of the skin and by the unchanged low resting level of forearm flow. In no subject were changes in heart rate or blood pressure noted as a result of the procedure.

The usual sequence was to record 10 arterial inflow traces during a 3-min period at normal atmospheric pressure. The box pressure was then raised to a randomly selected level, and 10 more inflow curves were recorded. The box was then opened to the atmosphere, and when flow had returned to the control level, the sequence was repeated.

When pressure-flow curves were constructed, an English Electric KOF9 digital computer was used to derive the best second- or third-degree polynomial to fit the experimentally determined points.

Results

Hand

The hands of 4 normal subjects were tested, each at more than one level of sympathetic tone, which was varied from experiment to experiment by altering the room temperature over a range of 15 to 30°C. To reach thermal equilibrium, the subject was allowed 60 to 90 min in the room before each experiment. The range of blood flow at normal perfusion pressure between the extremes of room temperature was 1.0 to 17.0 ml/100 ml per min, and of palm skin temperature was 26.4 to 36.7°C. During any individual experiment, palm temperature remained constant to within ±0.5°C, and mean resting flow did not alter by more than ±15%. Hand volume ranged from 400 to 450 ml (mean 427).

From the moment that the atmospheric pressure in the box was changed, it was 20 to 30 sec before the next arterial inflow trace could be recorded. Whatever the change in perfusion pressure, there was no evidence of a progressive change in blood flow once the new perfusion pressure was reached (Fig. 1). Following exposure to very low perfusion pressures, there was sometimes an overshoot of flow.

When blood flow was plotted against perfusion pressure, the distribution of points always took a parabolic form, convex to the pressure axis (Fig. 2). Blood flow never reached zero at a perfusion pressure of more
UPPER LIMB FLOW AT LOW PERFUSION PRESSURE

Perfusion pressure vs. blood flow in a normal hand. Open circles = room temperature 29.5°C; closed circles = room temperature 16°C. Curves fitted by 2nd polynomials.

FIGURE 2

Perfusion pressure vs. blood flow in a normal hand, whatever the level of sympathetic tone.

FOREARM MUSCLE

We studied 6 normal subjects, whose skin circulation beneath the forearm plethysmograph had been minimized by epinephrine iontophoresis. The volume of the forearm segments was 428 to 540 ml (mean 490). Resting flow ranged from 2.0 to 4.2 ml/100 ml per min (mean 2.8) among the individual subjects. The corresponding levels of perfusion pressure were 62 to 77 mm Hg (mean 68). As with the hand, it was 20 to 30 sec from commencement of the change in perfusion pressure before flow measurements could again be made. Following a decrease in perfusion pressure, there was always a sharp reduction in arterial inflow, followed by a rise for 60 to 90 sec to a new stable level (Fig. 3). Flow usually returned immediately to the resting level when perfusion pressure was restored to normal. When flow was reduced to less than 1.2 to 1.6 ml/100 ml per min, two other events were often observed. During this low-flow period, in 4 subjects there was a rise in the mean systemic arterial pressure by an average of 9 mm Hg (Fig. 3). Following the low-flow period, in all subjects the first inflow was 2 to 5 times the control level (Figs. 3 and 4).

Three additional subjects were tested who had undergone cervicodorsal ganglionectomy at least 6 months previously for digital artery thrombosis. There was no other evidence of arterial or systemic disease. Total loss of sweating persisted in forearm and hand despite provocative whole-body heating. The vol-

FIGURE 3

Behavior of muscle blood flow in a normal forearm (after epinephrine iontophoresis), with change in perfusion pressure. Symbols as in Figure 1.
Behavior of blood flow in a sympathectomized forearm (after epinephrine iontophoresis), with change in perfusion pressure. Symbols as in Figure 1.

Pressure-flow plots for forearm muscle. Left, 6 normal subjects; right, 3 subjects whose arm had been sympathectomized. Values of pressure and flow normalized with respect to control conditions.

The pressure-flow relationship was plotted for forearm muscle in the 6 normal and 3 sympathectomized subjects (Fig. 5). For this purpose, the blood flow after perfusion pressure was lowered was derived from the mean of five successive inflow traces, once a new, steady rate of flow had been reached. Blood flow and perfusion pressure were normalized as a percentage of resting control values, to allow grouping of the individual results.

In all the subjects whose arm had been sympathectomized, blood flow remained very close to the control level until the perfusion
pressure had fallen by nearly 50%, to a level of 45 to 50 mm Hg. Thereafter, flow declined, to approach zero at a perfusion pressure of less than 10 mm Hg. In the normal subjects, the individual pattern was more variable, and only at the lower range of perfusion pressures was the curve concave to the pressure axis.

Because forearm muscle vascular resistance fell when perfusion pressure was lowered, we thought it important to exclude hyperemia as a result of increased muscle tone as an artifactual cause. There was no subjective sensation of this (the subjects frequently slept during the procedure), nor did electromyographic recordings from the forearm musculature give evidence of increased activity at raised box pressures.

**Discussion**

A number of factors make it difficult to answer the question whether autoregulation takes place in the skin of the hand; not the least of these is the considerable minute-to-minute variation of blood flow in the normal, intact hand. However, under the conditions of our experiments, we could find no satisfactory evidence of this phenomenon. Thus no rising trend of flow followed sudden reduction in perfusion pressures. The pressure-flow curves under all circumstances were convex to the pressure axis, and of a general shape remarkably similar to those which Green et al. (5) described for the isolated, perfused, pure-skin vascular bed of the canine lower limb.

It had occurred to us that if "nutritive" vessels in skin exhibited autoregulation, while "shunt" vessels did not, the behavior of the former might be masked by the ordinarily much greater flow through the latter. We therefore also examined hands under cold environmental conditions because we supposed this would minimize flow through arteriovenous anastomoses, but autoregulation was not demonstrated.

We supposed the modest overshoot of flow after exposure to very low perfusion pressures (Fig. 1) to be a manifestation of autoregulation in the 15% (6) of skeletal muscle in the normal hand.

Thus we conclude that autoregulation is not a marked feature of, is extremely slow to develop, or is absent from, the vessels of the skin of the hand. Indeed, because minute-to-minute variations in blood flow in response to reflex stimulation persist in the intact hand even at a low perfusion pressure (Fig. 1), it seems probable that the sympathetic nervous system dominates the control of flow so overwhelmingly that any minor degree of rapidly occurring autoregulation would be meaningless.

In contrast, in our preparation of normally innervated forearm skeletal muscle autoregulation of blood flow does appear to exist. This statement is based both on the shape of the pressure-flow curves (Fig. 5), which differs from that of the "passive" curves of the hand (Fig. 2), and on direct observation of the tendency for flow to return toward the control value when perfusion pressure is lowered (Fig. 3).

We are not able to comment on the importance of local vascular smooth-muscle stretch responses in this regard. There is, however, some evidence of the importance of a metabolic factor in the observation that only when autoregulation failed to maintain flow at a level greater than 1.2 to 1.6 ml/100 ml per min did relative hypertension develop in normal subjects, and was an overshoot of flow observed on return to normal perfusion pressure. Staunton et al. (7) have identified hypertension as a reflex response to muscle ischemia of the upper limb, and the overshoot of flow may well be a form of reactive hyperemia.

The implication from this is that a flow rate of greater than 1.2 to 1.6 ml/100 ml per min in the normal forearm may be necessary for the metabolic requirements of its muscle, and that at perfusion pressures of less than about 20 mm Hg, further autoregulation to maintain this flow may be impossible. This suggestion receives indirect support from the observations of Holling and Verel (8), who measured forearm blood flow when the upper limb
was elevated. They found no reactive hyperemia following reduction of perfusion pressure to 45 to 58 mm Hg, and of flow to 1.3 to 1.4 ml/100 ml per min. At such flow rates, oxygen extraction as gauged by the deep venous oxygen saturation was increased, but calculated oxygen consumption was normal.

It is clear that the degree to which autoregulation is manifest in normally innervated forearm muscle varies among individuals, but is near-perfect over a considerable range of perfusion pressures in chronically sympathectomized muscle (Fig. 5). In most studies made on isolated, pure-muscle vascular beds in animals, the preparation has been denervated. In these circumstances the pressure-flow curves resemble closely those we found in sympathectomized forearm muscle. Thus Folkow (9) derived an equation $F = cP^{0.65}$ to describe the steady-state pressure-flow relation in the denervated, skinned lower leg of the cat. Stainsby and Renkin (10) derived a similar curve from perfused isolated muscle groups in the dog, though with a flow cessation pressure of about 10 mm Hg. From the data of Jones and Berne (11), who used a similar preparation, pressure-flow curves can be constructed that are distinguished from those of Stainsby and Renkin only by the fact that there was no flow cessation pressure. They did compare innervated with chronically denervated muscle (though in anesthetized animals), and their values for steady-state vascular resistance suggest that autoregulation was less pronounced in the innervated preparation.

There seem to be two possible and related explanations for the difference in shape of the pressure-flow curves for normal versus chronically sympathectomized muscle that we observed. On the basis of work that he and his colleagues have undertaken, Hyman (12) has suggested that cholinergic vasodilator fibers influence only shunt vessels. He also adduces evidence to support the thesis that during postischemic hyperemia in muscle, blood flow is increased only in “nutritive” pathways, and to a degree which repays exactly the metabolic debt. Despite the relaxed state of our subjects there may have been some cholinergic drive, and a “passive” curve from shunt vessels may be superimposed on the autoregulatory curve from nutritive vessels. Conversely, if autoregulation in muscle has a metabolic basis, our pressure-flow curves imply that blood flow in chronically sympathectomized muscle is largely restricted to “nutritive” channels.

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