Responses of Pulmonary Allograft and Cheek Pouch Arterioles in the Hamster to Alterations in Extravascular Pressure in Different Oxygen Environments

MICHAEL J. DAVIS, JOSEPH P. GILMORE, AND WILLIAM L. JOYNER

SUMMARY The responses to changes in transmural pressure were investigated in pulmonary allograft and cheek pouch arterioles in two oxygen environments. Neonatal hamster lung tissue was transplanted into adult hamster cheek pouches. After vasculaxization (8-10 days), pulmonary and cheek pouch vessels were observed by intravital microscopy in hamsters anesthetized with pentobarbital. By gassing the suffusion solution (bicarbonate-buffered Ringer's) (pH 7.4 at 35-37°C) with either low oxygen (95% N₂/5% CO₂) or high oxygen (75% N₂/5% CO₂/20% O₂) and after sealing the top of the chamber, extravascular pressure was altered by varying the fluid volume of the closed chamber. Changes in arteriolar diameters in response to positive and negative square-wave pressure pulses were quantified using a video micrometer and close-circuit TV system. Pulmonary arterioles showed a passive dilation or constriction in response to increases or decreases in transmural pressure (±20 mm Hg). These responses were not altered either by changes in Po₂ or nitroprusside. In contrast, cheek pouch arterioles showed myogenic responses by constricting when transmural pressure was increased and vice versa. These responses were potentiated at high Po₂ and abolished with nitroprusside. It is concluded that a myogenic response is dominant in cheek pouch arterioles but not in pulmonary arterioles under these conditions. These latter observations are consistent with results obtained from isolated, intact lung. Circ Res 49:133-140, 1981

THE tendency for an organ to maintain constant blood flow despite changes in arterial perfusion pressure has been termed autoregulation. Since the first observations by Bayliss (1902), this phenomenon has been demonstrated in nearly every organ and tissue of the body. It is most obvious in the brain and kidney where blood flow is maintained nearly constant when perfusion pressure is between 80 and 140 mm Hg. The only two tissues that apparently do not show autoregulation are skin (Green and Rapela, 1964) and lung (Guyton and Lindsey, 1959).

Currently, two mechanisms are believed to account for the autoregulatory behavior of the microvasculature: (1) a pressure-sensitivity, i.e., a myogenic response, and (2) a flow-sensitivity, i.e., an accumulation of metabolic vasodilators. In most studies, however, since the autoregulatory stimulus is a change in perfusion pressure, both myogenic and metabolic mechanisms are called into play. For example, as arterial pressure is reduced, perfusion pressure falls and as blood flow decreases, metabolites accumulate. Thus, a stimulus is initiated so that both mechanisms may operate in the same direction, namely, to cause vasodilation. Therefore, it cannot be determined whether a myogenic or a metabolic mechanism is primarily responsible for autoregulation under these conditions.

Johnson (1967) and others (Baez et al., 1974; Johnson and Intaglietta, 1976) have used venous pressure elevation to put these two mechanisms into opposition. When venous pressure is elevated, intravascular pressure increases, favoring a myogenic vasoconstriction, while at the same time, blood flow falls and the consequent build-up of metabolites should favor vasodilation; the change in arteriolar diameter should reveal which mechanism dominates. With isolated, perfused cat mesentery and rat mesoappendix, the most consistent finding when venous pressure is raised is an increase in vascular resistance, i.e., a vasoconstriction, thus implicating the dominance of the myogenic response under these conditions.

Most proponents of a metabolic mechanism of autoregulation have argued generally that there must be some link between tissue metabolism and metabolites as they relate to tissue blood flow. A number of chemical mediators have been implicated and although there is considerable evidence that some are important in specific tissues, such as carbon dioxide in the brain and adenosine in the heart, no single mediator has emerged as the choice for all tissues. In any event, autoregulation me-
diated solely by either a metabolic or a myogenic
mechanism, seems doubtful for most tissues.

Recently, we modified a chamber technique
(Greenblatt et al., 1969) which allows us access to
the microcirculation of normally unobservable tis-
sues by transplantation of these tissues into the
tissue of the hamster (Cick et al., 1979; Davis
et al., 1981). In the first series of studies (Davis et
al., 1981), we described the dimensional responses
and pressure redistributions in pulmonary allograft
and cheek pouch microcirculations to different ox-
ygen environments. This study is concerned with
testing the responses of pulmonary and cheek pouch
arterioles to changes in transmural pressure. In
contrast to other studies of this nature, this one is
unique in several respects: systemic arterial pres-
sure remains unchanged, so there are no systemic
neural or hormonal reflexes, and transmural pres-
sure can be increased as well as decreased.

The aim of the present study was 3-fold: (1) to
compare the responses of pulmonary and cheek
pouch arterioles to an extravascular pressure stim-
ulus, (2) to compare the effect of different oxygen
environments on these responses, and (3) to deter-
mine, if possible, the relative importance of meta-
bulic and myogenic mechanisms in these two mi-
crocirculations.

Methods

Pulmonary tissue from neonatal hamsters was
transplanted into the cheek pouch of adult female
hamsters according to the techniques described pre-
viously (Davis et al., 1981). Eight to 14 days after
transplantation, when the allograft was fully vas-
cularized and had brisk pulmonary capillary flow,
the hamster was anesthetized and prepared for
experimentation. The trachea, femoral artery, and
femoral vein were cannulated and a 5 μl/min infu-
sion of 6% dextran in 0.9% NaCl was started. Addi-
tional anesthetic was administered intraperitone-
ally when necessary (3 mg/100 g per hr). After the
Saran wrap was removed from the chamber and the
exposed tissue covered with Ringer’s bicarbonate
solution, a plastic cover slip was epoxied over the
top half of the chamber. For suffusion, two 16-gauge
needle hubs were secured tightly into holes on each
side of the chamber. After the epoxy had hardened,
one needle hub (the outflow side) was allowed to
drain into a beaker. The sealed chamber was then
filled and suffused (Fig. 1) with Ringer’s bicarbon-
ate solution which had been heated to 36°C in an
column and gassed with either a low oxygen (95% N2/5% CO2) or a high oxygen (75% N2/5% CO2/20% O2) mixture.

Since in some experiments we wished to investi-
gate the responses of cheek pouch arterioles in the
absence of pulmonary tissue, the identical trans-
plantation procedure was followed with the excep-
tion that the pulmonary tissue was omitted. These
preparations were observed at 8-14 days after in-
sertion of the chamber. In terms of vessel size and
branching pattern, the cheek pouch circulation did
not appear to be affected by the chronic presence
of the chamber. These chronic (8-14 day) chamber
implants were used to investigate the responses of
cheek pouch arterioles, since a minimum of 4-5
days appeared to be necessary for proper “air-tight”
sealing of the chamber. This presumably required
proliferation of the connective tissue layer around
the chamber edges in contact with the cheek pouch
membrane.

After surgical preparation of the hamster, the
cheek pouch membrane was allowed to stabilize for
15-20 minutes under continuous suffusion. In one-
half of the experiments, this solution had been
equilibrated initially with the low oxygen mixture,
whereas in the other half of the experiments the
solution was equilibrated with the high oxygen mix-
ture.

After stabilization, the following experimental
protocol was rigidly observed. An arteriole was se-
lected for viewing under the microscope and its

\[ \text{diameter was recorded on line for 5 minutes.} \]

The system was closed by turning stopcocks on both the
inflow and outflow sides of the chamber (Fig. 1); one
side was connected with a Statham Pb23BB
transducer for recording chamber pressure, while
the other side was attached to a 500-ml Ringer’s
filled flask. Into this flask, a small volume of fluid
(=1.0 ml) could be injected or withdrawn, thus
changing the pressure inside the chamber. Then, a
1-minute square-wave pulse of either increased or

\[ \text{FIGURE 1 Schematic diagram of the sealed-
chamber preparation used for altering ex-
travascular pressure. This figure is not}
\]

drawn to scale.
decreased extravascular pressure (20 mm Hg) was applied while the diameter of the vessel was monitored continuously for the duration of the pulse and for another 2 minutes. The procedure was repeated on the same vessel using the opposite pressure pulse and then the chamber was re-opened to the column and suffusion was continued for at least 5 minutes. This allowed the preparation to equilibrate while another vessel was selected for study. After three to four branching orders of vessels had been tested, the oxygen mixture was changed and the procedure repeated. In this manner, 7-10 cheek pouch or pulmonary arterioles usually could be observed during the course of an experiment.

Following this protocol, we examined the responses of arterioles in 11 pulmonary allografts and 13 chronic pouch preparations. In some of these experiments which contain both types of vessels sodium nitroprusside (5.0 x 10^{-4} M) was added to the suffusate after the initial observations and after 4-5 minutes of equilibration, arteriolar responses to the same pressure protocol were recorded. In all experiments, pulmonary arterioles were distinguished according to their anatomical arrangement within the mass of pulmonary tissue, as described in the preceding paper.

Video System

The cheek pouch was transilluminated with a polished lucite rod and 100-W Hg lamp. The entire microscope, opticvar, and image rotator were made by Zeiss (Collins Microscope Co.). Leitz 10x and 20x objectives projected the image through the scope into a CCTV system, consisting of a Cohu 4410 camera, Conrac monitor, and JVC videocassette recorder. Static and dynamic vascular dimensions were measured through the CCTV system with a Colorado Video micrometer.

Results

Cheek Pouch Arterioles

Of the 139 cheek pouch arterioles tested, 133 vasoconstricted in response to a negative extravascular pressure. For these same arterioles, 94 vasodilated in response to a positive extravascular pressure. Figure 2 depicts the time course for a response of a second order cheek pouch arteriole to both a negative and positive pulse (20 mm Hg) in extravascular pressure at low oxygen suffusion. This vessel exhibited the typical behavior which was characteristic of almost all cheek pouch arterioles. When the square-wave pulse was applied, there was an initial transitory response which was passive. This was followed rapidly by an active response which decreased vessel diameter during a negative extravascular pressure pulse and increased vessel diameter during a positive extravascular pressure pulse. The time course and magnitude of the response (percent of control) for all orders of cheek pouch arterioles to both positive and negative extravascular pressure pulses at low and high oxygen suffusion are shown in Figure 3. The percent of control vessel diameter is given at 30-second intervals for a 3-minute period. The pulse of extravascular pressure was applied during the 1st minute. After an initial transitory response (not shown), the arterioles began to actively constrict or dilate within 4-6 seconds and reached a maximum response by 30 seconds. When the extravascular pressure was returned to atmospheric, arteriolar diameters generally returned to control within 1 minute without significant overshoots or undershoots. Generally, it appears that larger arterioles had relatively smaller responses to these stimuli than did the smaller arterioles (third and fourth order). The arteriolar responses to positive pulses of extravascular pressure were not as great in amplitude as those to negative pulses of extravascular pressure. Further, the response to both positive and negative pulses of extravascular pressure appears to be potentiated at high oxygen suffusion. The maximum responses to negative and positive pulses of extravascular pressure in low and high oxygen suffusion for each order of cheek pouch arteriole are shown in Table 1 as the absolute maximum change in arteriolar diameter and the percent of control diameter. First order arterioles consistently showed the greatest absolute responses to negative and positive pulse of extravascular pressure, whereas third order arterioles maintained the greatest change in terms of the percent of control diameter. Suffusion with high oxygen solutions potentiated all of these responses in the first three orders of arterioles. Nitroprusside dilated cheek pouch arterioles and abolished active responses in all arterioles regardless of the type of oxygen suffusion (Fig. 2, Table 2).

To document any possible changes in intravas-
circular pressure during application of an extravascular pressure stimulus, the following procedure was performed: a small hole was cut in the coverslip before it was epoxied to the top of the chamber; after the chamber had been prepared and with the aid of a micromanipulator, the tip of a micropipette was lowered through the hole over an arteriole; after successful penetration of the arteriole, the shank of the pipette was epoxied to the cover slip. In this manner simultaneous measurement of intravascular and extravascular pressures could be made. Because of the tedious nature of this maneuver, intravascular pressure measurements were not made routinely in these experiments. However, interesting results were obtained: in a first order arteriole, negative 20 mm Hg extravascular pressure did not significantly alter intravascular pressure, whereas positive 20 mm Hg chamber pressure increased intravascular pressure by 10 mm Hg. This latter effect appeared to be due to partial collapse of the venous system. Consequently, in these experiments, the effective extravascular pressure stimulus during application of positive (20 mm Hg) extravascular pressure was only 10 mm Hg. This may

TABLE 1 Responses of Cheek Pouch Arterioles to Alterations in Extravascular Pressure during High and Low Oxygen Suffusion

<table>
<thead>
<tr>
<th>Vessel* order</th>
<th>Control diameter</th>
<th>Negative pressure†</th>
<th>% Control diameter</th>
<th>Positive pressure†</th>
<th>% Control diameter</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Maximum change</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low oxygen suffusion§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 CPA</td>
<td>105 ± 6 (20)</td>
<td>-14 ± 3</td>
<td>-11 ± 2</td>
<td>+4 ± 1</td>
<td>+3 ± 1</td>
</tr>
<tr>
<td>2 CPA</td>
<td>49 ± 4 (16)</td>
<td>-9 ± 2</td>
<td>-18 ± 3</td>
<td>+4 ± 2</td>
<td>+2 ± 3</td>
</tr>
<tr>
<td>3 CPA</td>
<td>29 ± 1 (28)</td>
<td>-8 ± 1</td>
<td>-28 ± 3</td>
<td>+4 ± 2</td>
<td>+13 ± 2</td>
</tr>
<tr>
<td>4 CPA</td>
<td>12 ± 1 (9)</td>
<td>-3 ± 1</td>
<td>-26 ± 6</td>
<td>+2 ± 1</td>
<td>+6 ± 1</td>
</tr>
<tr>
<td>High oxygen suffusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 CPA</td>
<td>93 ± 4 (16)</td>
<td>-20 ± 3</td>
<td>-23 ± 3</td>
<td></td>
<td>+8 ± 2</td>
</tr>
<tr>
<td>2 CPA</td>
<td>47 ± 4 (26)</td>
<td>-14 ± 2</td>
<td>-24 ± 3</td>
<td></td>
<td>+6 ± 1</td>
</tr>
<tr>
<td>3 CPA</td>
<td>26 ± 1 (18)</td>
<td>-8 ± 1</td>
<td>-36 ± 3</td>
<td></td>
<td>+5 ± 1</td>
</tr>
<tr>
<td>4 CPA</td>
<td>12 ± 1 (5)</td>
<td>-2 ± 1</td>
<td>-23 ± 4</td>
<td>+1 ± 1</td>
<td>+12 ± 6</td>
</tr>
</tbody>
</table>

All values are means ± SE; numbers in parentheses = number of observations.
* CPA = cheek pouch arterioles.
† Negative and positive pressure (±20 mm Hg extravascular pressure).
‡ Maximum change (μm).
§ Low = 0%O₂/5%CO₂/95%N₂, High = 20%O₂/5%CO₂/75%N₂
¶ Indicates significant difference between low and high oxygen suffusion using a paired Student's t-test with a confidence level of P < 0.05.
TABLE 2  Responses of Cheek Pouch Arterioles to Alterations in Extravascular Pressure after Nitroprusside

<table>
<thead>
<tr>
<th>Vessel order</th>
<th>Control diameter</th>
<th>Negative pressure†</th>
<th>Positive pressure†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Maximum change</td>
<td>% Control diameter</td>
</tr>
<tr>
<td>1 CPA</td>
<td>108 ± 6</td>
<td>+7 ± 2</td>
<td>+7 ± 2</td>
</tr>
<tr>
<td>2 CPA</td>
<td>66 ± 3</td>
<td>+3 ± 1</td>
<td>+5 ± 1</td>
</tr>
<tr>
<td>3 CPA</td>
<td>35 ± 1</td>
<td>+3 ± 1</td>
<td>+8 ± 2</td>
</tr>
<tr>
<td>4 CPA</td>
<td>13 ± 3</td>
<td>+3 ± 1</td>
<td>+23 ± 9</td>
</tr>
</tbody>
</table>

All values are means ± SE. Numbers in parentheses = numbers of observations, combined for both levels of oxygen suffusion after nitroprusside (10^-5 M).

* CPA = cheek pouch arteriole.
† Negative and positive pressure (± 20 mm Hg extravascular pressure).
‡ Maximum change (μm).

explain why the magnitude of the response in the arterioles averaged only about half of that described for negative (20 mm Hg) pulses of extravascular pressure.

Pulmonary Allograft Arterioles

Pulmonary allograft arterioles behaved passively (Fig. 4). Out of 27 pulmonary arterioles tested, all 27 showed a passive dilation in response to negative pulses of extravascular pressure. For these same arterioles, 21 out of 24 showed a passive constriction in response to positive pulses of extravascular pressure. There were no significant differences in the responses of pulmonary arterioles under low or high oxygen (Table 3 and Fig. 4). As might be expected, nitroprusside vasodilated pulmonary arterioles but did not significantly alter the responses of these pulmonary arterioles to changes in extravascular pressure (Table 3).

As discussed in the preceding paper (Davis et al., 1981), pulmonary arterioles and cheek pouch arterioles also behaved in opposite manners in response to changing oxygen tension: cheek pouch arterioles were dilated during low oxygen suffusions, whereas pulmonary arterioles were constricted under low oxygen suffusion.

Discussion

The major goal of this study was to compare the responses of cheek pouch and pulmonary allograft arterioles to an extravascular pressure stimulus. The results indicate that pulmonary arterioles respond passively to changes in transmural pressure, whereas cheek pouch arterioles show a myogenic response.

Response of Pulmonary Arterioles

Whereas there is little doubt that peripheral arterioles can respond actively to changes in transmural pressure, the extent to which this mechanism contributes to the total autoregulatory response of a given tissue is widely disputed (Johnson, 1977; Lombard and Duling, 1977). However, the small arterioles of the lung apparently do not exhibit such behavior. In contrast to the systemic circulation, where the arterial beds of several tissues (large and small intestine, liver, skeletal muscle) have been shown to constrict when venous pressure is elevated (Hanson and Johnson, 1967), an elevation of left atrial pressure causes a decrease in pulmonary vascular resistance (Borst et al., 1956; Kuramoto and Roubard, 1962). This suggests that the pulmonary vasculature may respond passively to changes in perfusion pressure. Our findings support these conclusions. When transmural pressure was changed in either direction, pulmonary allograft arterioles always responded in a passive fashion; diameters increased as transmural pressure increased and decreased as transmural pressure decreased. Whereas it may be argued that our preparation was unre-
responsive to any stimuli, other evidence does not support this: (1) cheek pouch arterioles in the same chamber showed active responses to the same stimuli, (2) afferent arterioles in renal allografts respond to transmural pressure stimuli in a manner similar to cheek pouch arterioles [that is, they respond actively (Gilmore et al., 1980)], (3) the same pulmonary arterioles responded to hypoxia with vasoconstriction (Davis et al., 1981), (4) these pulmonary arterioles dilated when nitroprusside has been published on hamster cheek pouch vessels. Our results indicate that cheek pouch arterioles respond actively to changes in transmural pressure. Increased transmural pressure elicits vasoconstriction, whereas a decreased transmural pressure elicits vasodilation. Only one other study of this nature has been published on hamster cheek pouch vessels. Lombard and Duling (1977) evaluated the relative contributions of active and passive mechanisms to arteriolar dilation during microocclusion of single cheek pouch arterioles. The only evidence for a myogenic response in these experiments came from a series of short (3- to 6-second) occlusions and because the average dilation observed after such an occlusion was only about 110% of control diameter, these authors suggested that a myogenic response contributed a maximum of only 23% to the peak flow following occlusion release. The rest of the response was attributed to an interplay of passive and metabolic factors. Similar observations were made by Johnson and Intaglietta (1976) in the isolated, perfused cat mesentery. They concluded that, under the conditions of downstream arteriolar occlusion, myogenic mechanisms do not predominate; however, they can be shown clearly in the same arteriole merely by using another stimulus. Perhaps this is not surprising since several factors are operating simultaneously during a local occlusion: passive and metabolic factors oppose myogenic ones upstream, whereas metabolic and myogenic factors oppose passive ones downstream.

Responses of Cheek Pouch Arterioles

Our results indicate that cheek pouch arterioles respond actively to changes in transmural pressure. Increased transmural pressure elicits vasoconstriction, whereas a decreased transmural pressure elicits vasodilation. Only one other study of this nature has been published on hamster cheek pouch vessels. Lombard and Duling (1977) evaluated the relative contributions of active and passive mechanisms to arteriolar dilation during microocclusion of single cheek pouch arterioles. The only evidence for a myogenic response in these experiments came from a series of short (3- to 6-second) occlusions and because the average dilation observed after such an occlusion was only about 110% of control diameter, these authors suggested that a myogenic response contributed a maximum of only 23% to the peak flow following occlusion release. The rest of the response was attributed to an interplay of passive and metabolic factors. Similar observations were made by Johnson and Intaglietta (1976) in the isolated, perfused cat mesentery. They concluded that, under the conditions of downstream arteriolar occlusion, myogenic mechanisms do not predominate; however, they can be shown clearly in the same arteriole merely by using another stimulus. Perhaps this is not surprising since several factors are operating simultaneously during a local occlusion: passive and metabolic factors oppose myogenic ones upstream, whereas metabolic and myogenic factors oppose passive ones downstream.

In contrast to the occlusion studies just described, the extravascular pressure pulse applied in our experiments provided a simultaneous stimulus for both myogenic and metabolic mechanisms to act in concert, since both pressure and flow would be changed in the same direction. There are, however, two pieces of evidence with which to distinguish between these two mechanisms. Although not shown clearly in Figures 2 and 3, the half-time of the response to a negative extravascular pressure stimulus was approximately 3-5 seconds; the half-time of the response to a positive extravascular pressure stimulus was slightly longer, approximately 7-8 seconds. These numbers are in close agreement with the time course of a myogenic response suggested by the experiments of several other investigators. Smiesko (1971), following a 1-second decrease in perfusion pressure, found the average time for onset of an increase in blood flow was 4.4 seconds. Likewise, the onset of the tension increase in response to quick stretch of umbilical artery strips averaged 9.2 seconds (Sparks, 1964). The second piece of evidence from our experiments in support of a myogenic mechanism is the potentiation of the response under high O2. Since an increase in the oxygen content of the suffusion solution should be associated with an improved oxygen supply to both the vascular smooth muscle and the parenchymal tissue around it, the contribution of anaerobic parenchymal cell metabolites or vascular smooth muscle hypoxia to the response would be minimized and myogenic mechanisms should become more apparent (Lombard and Duling, 1977). This is indeed what happens, as shown in both Figure 3 and Table 1. Also, the present results are consistent

<table>
<thead>
<tr>
<th>Oxygen suffusion</th>
<th>Control diameter</th>
<th>Maximum change</th>
<th>% Control diameter</th>
<th>Positive pressure†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>27 ± 3</td>
<td>+4 ± 1</td>
<td>+15 ± 2</td>
<td>-4 ± 1</td>
</tr>
<tr>
<td></td>
<td>(13)</td>
<td></td>
<td></td>
<td>-11 ± 3</td>
</tr>
<tr>
<td>High</td>
<td>33 ± 3</td>
<td>+4 ± 1</td>
<td>+10 ± 2</td>
<td>-4 ± 1</td>
</tr>
<tr>
<td></td>
<td>(14)</td>
<td></td>
<td></td>
<td>-9 ± 3</td>
</tr>
<tr>
<td>POST-N procedure§</td>
<td>Low</td>
<td>+3 ± 1</td>
<td>+9 ± 4</td>
<td>-6 ± 1</td>
</tr>
<tr>
<td></td>
<td>(4)</td>
<td></td>
<td></td>
<td>-15 ± 1</td>
</tr>
</tbody>
</table>

All values are means ± SE; numbers in parentheses = number of observations.

* Low = 9%O2/5%CO2/95%N2; High = 20%O2/5%CO2/75%N2.
† Negative and positive pressure (±20 mm Hg extravascular pressure).
‡ Maximum change (μm).
§ PRE-N = before nitroprusside; POST-N = after nitroprusside (10^-4 M).

Table 3. Responses of Pulmonary Arterioles to Alterations in Extravascular Pressure during Low and High Oxygen Suffusion before and after Nitroprusside
with those obtained by Bouskela and Wiederhiem (1979) in wing arterioles of unanesthetized bats. When transmural pressure was elevated, there was a reduction in arteriolar blood flow and vasoconstriction. This reduction of flow in the face of an elevated arterial pressure is important, since it is incompatible with a metabolic mode of control for these vessels. Further, Tuma et al. (1977) reported that, in the cat tenuissimus muscle, peak hyperemic velocities in capillaries were not attenuated by exposure of the muscle to high oxygen, even though control velocities were dramatically reduced. Thus, it is apparent that myogenic mechanisms are operative in control of arterioles in the cheek pouch of the hamster and in other vasculature.

A detailed analysis of the time course of the response can best be made by using a radius-tension diagram similar to that of Johnson (1968). The response of a third order cheek pouch arteriole is shown in Figure 5. Pressure isobars represent both chamber pressure and transmural pressure. Transmural pressure was calculated using the data from micro-pressure measurements made in the preceding study (Davis et al., 1981). Circumferential wall tension was calculated from the Laplace relation. Point a is the control state, in which chamber pressure is 0 mm Hg, intravascular pressure is 60 mm Hg, and vessel radius is 20 μm. When extravascular pressure is decreased suddenly to -20 mm Hg, there is initially a passive increase in vessel radius to 21.5 μm (point b), which reflects the elastic properties of the vessel wall. This is followed by an increase in the tone of the vascular smooth muscle, constricting the vessel to 17.5 μm (point c). When extravascular pressure is restored suddenly, the arteriole transiently collapses along the radius-tension curve appropriate to its new state (point d) and then dilates back to control. The same type of response pattern is observed with a pulse of positive extravascular pressure. Thus, a brief pressure transient will move the operating point of the vessel along its steady state elastic curve appropriate for the new state of vascular tone. These observations are highly consistent with those made for mesenteric arterioles (Johnson, 1968). In addition, we could observe some responses which he was merely able to predict: as vascular tone increases (i.e., in response to increased transmural pressure) a point is reached when all smooth muscle fibers are responding maximally to the stimulus and any further increase in transmural pressure will lead to an increase in radius along the elastic curve of the maximally contracted vessel (c-d). Arterioles which were dilating in response to a pulse of positive extravascular pressure would often begin to collapse when a critical value of pressure was reached. At this point the arterioles collapsed along a curve appropriate for a passive, elastic vessel and this could be confirmed by generating such a curve after all vascular tone had been abolished by nitroprusside. The active behavior of arterioles in our preparation was, therefore, generally consistent with that predicted by the myogenic tension-sensor hypothesis (Johnson, 1977).

These experiments strongly suggest that a myogenic response predominates in cheek pouch arterioles under these conditions. This does not imply necessarily, however, that autoregulation in the hamster cheek pouch is achieved predominately via a myogenic “mechanism.” Indeed, autoregulation, in the strictest sense of the word, describes the maintenance of a constant blood flow to an organ, and therefore cannot correctly be applied to the observed behavior of single vessels within that organ. We are unable to state with certainty what variables, if any, besides arteriolar diameter, were being regulated in these experiments, since neither arteriolar pressure nor flow could be measured during the interventions. These experiments do indicate that a myogenic response can be powerful in the hamster cheek pouch under the appropriate stimulus, and that in several respects it is consistent with the tension-sensor hypothesis. The importance of this response in blood flow autoregulation, however, remains to be defined clearly.

Acknowledgments

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