Linearity of the Vascular Pressure-Volume Relationship of the Canine Intestine

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SUMMARY To test whether the pressure-volume relationship of the canine small intestinal vasculature is linear over the normal range of portal venous pressures (5 to 35 mm Hg), we used two methods to measure volume: (1) the integral of inflow minus outflow (IFD), and (2) tissue activity of $^{51}$Cr-labeled erythrocytes (Cr-51). Venous pressures were changed in steps of 5 mm Hg with a servo-controlled system. The tissue was perfused at a constant rate. With venous pressures of 3.6 to 38.6 mm Hg, the vascular compliance was $2.19 \pm 0.42$ (SD) ml/kg • mm Hg using IFD, and $1.87 \pm 0.50$ ml/kg • mm Hg using Cr-51. Although a quadratic term significantly improved the fit, the effect was small (less than 3 ml/kg with a 30 mm Hg venous pressure change). The control blood volume of the intestinal loop at a venous pressure of $8.6 \pm 1.5$ (SD) mm Hg was $86.2 \pm 19.1$ ml/kg tissue weight using the mean transit time of a step input of indocyanine green at a perfusion pressure of 106 ± 29 mm Hg and a flow of 556 ± 147 ml/min • kg. We conclude that there is no significant change in compliance over the normal venous pressure range of 5-35 mm Hg. Circ Res 47: 551-558, 1980

THE LINEARITY of the small capacitance vessel pressure-volume relationship (P/V) over the physiological operating range is uncertain. In the latest edition of Ruch-Patton's *Physiology and Biophysics*, Rowell (1974, p. 228) represents the pressure and volume relationship of splanchnic veins as highly nonlinear over the range of 0-15 mm Hg. For large veins not tethered by tissue, there is a large change in volume with little change in transmural pressure at low pressures, since volume can be removed from unstressed vessels by changes in geometry, i.e., from a circular to elliptical cross-section, without an appreciable change in pressures. At high pressures, most large blood vessels become progressively stiffer (Bergel, 1972; Oberg, 1967; Wesly et al., 1975). For the vasculature within organs, even within the physiological range (ca. 5-25 mm Hg transmural pressure), Alexander's (1954) early work and that of Oberg (1967) strongly suggested a marked nonlinearity of the pressure-volume relationship. Gauer and Henry (1976, p. 151) assumed the venous vasculature to be nonlinear, and Koubenc et al. (1978) stated: “Since the pressure and volume relationship of the two compartments [intrathoracic and lower body] are nonlinear, the effective compliance of the total circulation cannot be predicted.” Mitzner and Goldberg (1975) concluded that the compliance of the splanchnic bed was twice as large at a hepatic venous pressure of 4 mm Hg as at 12 mm Hg, but Laust and Greenway (1976), using a plethysmograph, reported that the compliance of the liver of cats was much lower (13 ml/mm Hg • kg tissue weight) at a hepatic venous pressure of 2.3 mm Hg than the compliance (34 ml/mm Hg • kg) at 9.4 mm Hg. Clearly, the liver may have characteristics different from that of the intestinal bed or there may be great species differences.

Lutz (1969) found only small nonlinearities, with a lower compliance between 0 and about 5 mm Hg and above about 22 mm Hg than in the linear range of about 5-20 mm Hg. Johnson and Hanson (1963) concluded that the relationship was linear, but occasionally found a decreased compliance in the range of 0 to 5 mm Hg venous pressure and above 30 mm Hg. We have found a remarkably constant total body vasculature compliance over the range of 5-25 mm Hg in mean circulatory filling pressure (Drees and Rothe, 1974). The technique of estimating venous resistance from the vascular compliance and the time constant of outflow after a pressure change (Green, 1977; 1979) is predicated on a constant venous compliance, i.e., a linear P/V relationship.

The purpose of this study was to measure and assess the linearity of the pressure-volume relationship of the canine intestinal vasculature. We used two independent methods to estimate the magnitude of changes in contained blood volume. One was based on the integral of the difference between measured inflow and outflow (IFD) and extrapolation of the subsequent ramp volume change to the start of the pressure change. The other used loading of the vasculature with $^{51}$Cr-labeled erythrocytes and monitoring the radioactivity (Cr-51). We used constant-flow perfusion and so assumed that all of...
the venous pressure changes were transmitted to the capacity vessels. A measure of the total contained volume under control conditions was obtained as the product of the mean transit time (MTT) of an albumin tag and the flow (Rothe et al., 1978).

Methods

Nine male mongrel dogs weighing 11.4 ± 1.7 (SD) kg were anesthetized by intravenous injection of methohexital, 12.5 mg/kg (Brevital sodium, Lilly), and were maintained by methoxyflurane (Metho-
fane, Pitman-Moore) administered endotracheally to the spontaneously breathing animal using a small-animal anesthesia machine (Snyder Veterinary Products; model SAAM). The body temperature was held at 37.7 ± 0.8°C by heating the table and using a warming pad. A left femoral artery and vein were cannulated, using 3.5- and 4.8-mm OD polyethylene tubing, respectively. The systemic arterial blood pressure was monitored via the arterial cannula. A 24-gauge Teflon catheter was inserted coaxially through the venous cannula and advanced to the level of the right atrium for injection of indocyanine green for cardiac output determinations.

To provide rapid mixing of the erythrocyte tag throughout the vasculature and to stabilize the blood isotope concentration, the dogs underwent splenic isolation before the isotope was injected. Through a midline abdominal incision the common splenic artery was located and injected with 0.5 to 1 mg of epinephrine (Parke-Davis). After contraction, vascular isolation of the spleen was completed by ligating the remaining vasculature.

For 51Cr labeling of the red blood cells, 50 ml of arterial blood from the animal were added to 5 ml acid citrate dextrose solution (ACD, Squibb). Next, 0.5 or 1.0 mCi sodium chromate Cr-51 (New England Nuclear) was added to the blood-ACD solution and it was incubated at 37°C for 30 minutes. One hundred milligrams of ascorbic acid were then added to the mixture. The tagged blood was centrifuged and washed 2 times in cold saline. When the tagging was completed, 20 ml of blood containing 51Cr-labeled red cells were returned to the dog by way of the femoral vein. An interval of 30 minutes was allowed for complete distribution of the labeled cells.

A loop of jejunum (165 ± 63 (SD) cm from the stomach and 78 ± 49 cm from the cecum) was vascularly and neurally isolated. It weighed 34.6 ± 5.4 g and was 14.4 ± 2.4 cm long. To keep the lumen open and to ensure isolation, both ends of the jejunal segment were cannulated with 15 mm OD plastic cannulas. The tissue was placed on a warmed tissue tray and covered with a thin polyethylene sheet to keep it warm and moist. Hemostasis and luminal continuity of the remaining small intestine was established by rejoining the free ends with a third cannula. Heparin sodium (Elkins-Sinn, Inc.) at an initial dose of 500 U/kg and at least 2000 U/hour maintenance dosage was used as an anticoagulant.

The vasculature of the isolated denervated loop was cannulated and perfused with the dog’s own blood using a previously described circuit (Rothe et al., 1978). Because the perfusion pump motor had a set of tachometer windings independent of the motor windings, the speed could be monitored accurately as well as held constant with a high-gain feedback circuit (<0.5% variation). Perfusion rates were calibrated by collecting outflow in beakers for 1 minute, using pneumatically controlled valves and a timing circuit, and by assuming a blood density of 1.05 g/ml. The perfusion system outflow decreased only 1 % per 100 mm Hg increase in outflow pressure, and showed a 5% increase per 100 mm Hg inflow pressure increase. A second channel in pump (8.7% of the total flow) added saline, or saline plus the norepinephrine, to the blood. This was used for a separate set of experiments. Pressures were monitored with Statham P23De or P23Db transducers and recorded on Beckman Type R, direct-writing oscillographs.

The pressure at the reservoir end of the venous cannula was held to the desired level by a servo system implemented with an analog computer (Electronics Associates, model TR20) using both proportional and integral control. The dynamic response of the venous pressure servo system provided a 90% response within 0.16 ± 0.07 second, a 4.7 ± 1.3% overshoot at 0.5 ± 0.1 second and settled within 1% of the final value by 0.8 second. The steady state uncertainty, including the venous pressure transducer drift, was about 1 mm Hg.

By connecting the perfusion cannulas (2.0 mm OD, tapered to a minimum of about 1.0 mm OD) end-to-end with a silicone rubber T-connection just before cannulating the vessels, the pressure drop, ΔP, across each cannula and its connecting tubing was measured to compute cannula resistance (R = ΔP/F). The arterial cannula resistance averaged 0.38 ± 0.07 (SD) mm Hg·min/ml; the venous, 0.25 ± 0.04. Correction was made for the pressure drops across the cannulas and for the hydrostatic head between the transducer and tissue.

Changes in vascular volume were monitored as the integral of the difference between inflow, determined by the calibrated tachometer output of the perfusion pump, and outflow, determined by an electromagnetic flowmeter (Carolina Medical Electronics, model 322; Fig. 1, top panel). The flow difference was integrated on the analog computer patched for automatic reset (<5 msec) when the integral reached full scale. Any drift during control conditions was subtracted from the response. Before and after each experimental series, the tissue was bypassed (Rothe et al., 1978) to measure the instrumentation drift from mismatch of inflow- and outflow-measuring systems at control flow rates.
and at zero flow. The integral of flow difference (IFD) provided a measure of transient changes in vascular volume, as well as loss of fluid across the capillaries, secretions, or hemorrhage. The system also was calibrated by injecting or removing 2 ml of blood with a calibrated syringe. (The coefficient of variation of the calibration factor was 2.2%.) The response, 40-60 seconds after the pressure change, was extrapolated linearly to the beginning of the pressure change to provide an estimate of volume change corrected for capillary filtration (Fig. 1, 2nd panel). We assumed a constant rate-of-loss by 40 seconds.

Continuous monitoring of the tissue segment for $^{51}$Cr activity was a second, independent method used for determining changes in blood volume. A 3 x 3 inch NaI (Tl) scintillation detector (Hewlett-Packard, model 10612A) was centered less than 1 cm above the tissue. The detector, by way of a linear amplifier (Canberra, model 816), was connected to a single-channel analyzer (Hewlett-Packard, model 5583A), with a window setting optimal for the $^{51}$Cr energy peak, and to a ratemeter (Canberra, model 1481). Output from the ratemeter was recorded on the Beckman Type R oscillograph (Fig. 1, bottom panel). At the levels of activity used, the sensitivity of the detector at its margins was about 30% of that at its center. The activity of the tissue ranged from 500 to 900 counts/sec, and the 90% response time of the detection plus recording system was about 6 seconds. The system was calibrated periodically throughout the experiment by placing 1 ml of labeled arterial blood in a planchette under the detector near the tissue. To reduce the background radioactivity, it was necessary to shield the tissue from the dog with at least 2 cm of lead. Steady state changes in activity after each pressure change were estimated independently by two observers using photocopies of the data, and the results were averaged.

A selector switch incorporated into the venous pressure servo system allowed for manual switching of venous pressures over a range of −10 to +30 mm Hg in increments of 5 mm Hg. A preselected sequence of venous pressure changes (Fig. 2) was made early and late in the experiment. Between these runs, we conducted a study of the time course of changes in vascular capacity over a 5-minute period.

The vascular volume of the tissue was also determined before and after each series of runs by measuring the mean transit time of a 1-minute infusion of indocyanine green, using a technique previously described (Rothe et al., 1978).

Statistical analysis of data was by analysis of variance of multiple regression models. $P < 0.05$ was considered significant.

**Results**

The control blood volume of the tissue averaged $86.2 \pm 19.1$ ml/kg of tissue (Table 1). After correcting for the pressure drop in the cannula (ave. = 4.8 mm Hg) and the hydrostatic head (5 cm water), the venous pressure at the cannula tip averaged 8.6 ± 1.4 mm Hg under control conditions, a value similar to the normal portal venous pressure. The perfusion rate averaged $556 \pm 147$ ml/kg-min.

The pressure-volume relationship of the intestinal vasculature was linear over the range of venous pressures from 5 to 35 mm Hg (Fig. 3), assuming that all of the cannula pressure change was trans-
TABLE 1 Cardiovascular Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early</th>
<th>Late</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>9</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Time after anesthesia (min)</td>
<td>213 ± 18</td>
<td>350 ± 15</td>
<td></td>
</tr>
<tr>
<td>Systemic blood pressure (mm Hg)</td>
<td>79.9 ± 9.6</td>
<td>72.9 ± 14.7</td>
<td>76.4 ± 12.4</td>
</tr>
<tr>
<td>Tissue wt (g)</td>
<td>557 ± 152</td>
<td>554 ± 151</td>
<td>556 ± 147</td>
</tr>
<tr>
<td>Tissue blood flow (ml/min • kg)</td>
<td>8.58 ± 1.50</td>
<td>8.52 ± 1.46</td>
<td>8.55 ± 1.43*</td>
</tr>
<tr>
<td>Control venous pressure (mm Hg)</td>
<td>100 ± 26</td>
<td>112 ± 32</td>
<td>106 ± 29</td>
</tr>
<tr>
<td>Control perfusion pressure (mm Hg)</td>
<td>6.2 ± 3.3</td>
<td>5.7 ± 3.3</td>
<td>6.0 ± 3.2</td>
</tr>
<tr>
<td>Vascular conductance</td>
<td>92.0 ± 17.4</td>
<td>80.4 ± 20.1</td>
<td>86.2 ± 19.1†</td>
</tr>
<tr>
<td>Control blood volume (ml/kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure/volume relationship by integral of flow difference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linear slope (ml/kg • mm Hg)</td>
<td>2.04 ± 0.31</td>
<td>2.33 ± 0.48</td>
<td>2.19 ± 0.42*</td>
</tr>
<tr>
<td>Intercept (ml/kg)</td>
<td>1.2 ± 1.9</td>
<td>2.0 ± 1.8</td>
<td>1.6 ± 1.8</td>
</tr>
<tr>
<td>RMSE fit (ml/kg)</td>
<td>5.4 ± 2.0</td>
<td>4.9 ± 2.2</td>
<td>5.1 ± 2.1</td>
</tr>
<tr>
<td>Compliance at 8.6 mm Hg</td>
<td>2.37 ± 0.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compliance at 23.6 mm Hg</td>
<td>1.63 ± 0.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure/volume relationship by Cr-51</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Linear slope (ml/kg • mm Hg)</td>
<td>1.94 ± 0.51</td>
<td>1.80 ± 0.52</td>
<td>1.87 ± 0.50</td>
</tr>
<tr>
<td>Intercept (ml/kg)</td>
<td>-0.4 ± 1.9</td>
<td>0.2 ± 1.5</td>
<td>-0.1 ± 1.6</td>
</tr>
<tr>
<td>RMSE fit (ml/kg)</td>
<td>4.0 ± 1.8</td>
<td>3.7 ± 1.4</td>
<td>3.9 ± 1.6</td>
</tr>
<tr>
<td>Compliance at 8.6 mm Hg</td>
<td>1.51 ± 0.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compliance at 23.6 mm Hg</td>
<td>1.74 ± 0.53</td>
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* Results are expressed as mean ± SD.
† < 0.05 probability that early and late runs different using paired t-test.
‡ < 0.01 probability.

The change in volume is in ml per kg of tissue. The pressure change is in mm Hg and is from zero pressure at the servo end of the cannula. The control vascular conductance (G), based upon arterial pressure, cannula (servo) pressure and flow, is in ml/(min-kg-mm Hg). R² is the fraction of total variance explained by the regression equation. Although the ΔPv² and G terms in Equations 2 and 3 were statistically significant (P < 0.001), they provided only a slightly better (0.03 in R²) fit. The square root of the error-mean-square (RMSE) of an
capillary filtration. The method of calculating 
flow difference was 2.00 ± 0.44 ml/kg-mm Hg and 
using Cr-51, it was 1.63 ± 0.40 ml/kg-mm Hg. At 
the higher pressure (23.5 mm Hg at the vein), 
the compliance was significantly less (1.63 ± 0.54 ml/kg-
mm Hg) than when the venous pressure was lower 
(2.37 ± 0.60) using the integral of flow difference 
approach. However, no significant difference (P >
0.10) was found using the 51Cr-labeled erythrocytes 
(1.51 ± 0.39 at P = zero; 1.74 ± 0.53 at P = 15 mm
Hg). These data are consistent with those presented 
in Figure 3, except that the compliance at high 
pressure, using IFD, was less than that expected 
from the slope of the IFD data (Fig. 3) at 15 mm 
Hg (1.63 ml/mm Hg-kg vs. 2.21, respectively).

Pooling all of the slope coefficients from both the 
IFD and 51-Cr techniques, the compliance of the 
 canine intestine under the conditions of these ex-
periments averaged 2.03 ± 0.46 (sd) ml/kg-mm Hg 
with only a slight deviation from linearity over the 
range of 5–35 mm Hg venous pressure.

A negative 10 mm Hg was applied to the cannula 
during the experiment, but this resulted in only a 
17.9 ± 5.1 and 11.1 ± 4.3 ml/kg reduction in vascular 
volume by IFD and Cr-51, respectively. Further-
more, the system oscillated and the vein could be 
seen to collapse. With this collapse, the full venous 
pressure change cannot be transmitted from the 
cannula tip to the capacity vessels because the 
vascular resistance is greatly increased at the point 
of collapse. Thus the venous P/V relationship can-
not be estimated. Because the vein just upstream 
from the cannula collapsed when the cannula 
(servo) pressure was —10 mm Hg and the venous 
pressure (based on the cannula resistance correc-
tion) averaged —1.4 mm Hg, but did not collapse at 
—5 mm Hg when the pressure drop-corrected ve-
 nous pressure averaged 3.6 mm Hg, we concluded 
that the estimate of cannula resistance was reason-
able.

Capillary Filtration

The rate of fluid loss from the intestinal loops 
between 40 and 60 seconds after the venous pressure 
change was measured relative to the slope before 
the change in cannula pressure, by using the line 
that was extrapolated to zero time for the estimate 
of vascular volume change. From cannula pressure 
changes of 10, 20, and 30 mm Hg, the rates were 
26.8 ± 11.3, 63.4 ± 21.6, and 82.3 ± 22.6 ml/min-
kg tissue, respectively. The average slope of a linear 
fit for each of the early and late runs for cannula 
pressure changes to —5, 5, 10, 15, 20, and 30 mm Hg 
(n = 8) was 2.79 ± 0.91 ml/min/kg tissue per mm 
Hg cannula pressure change, and the intercept was 
1.73 ± 4.76 ml/min-kg. A cannula pressure of —5 
caus ed the rate of fluid loss to be only —0.3 ± 2.0 
ml/min-kg tissue. A quadratic equation signifi-
cantly fit the data better, but the predicted differ-
ence in rate of fluid loss at 30 mm Hg was only 9% 
higher than that for the linear fit and no different 
at 0 and 20 mm Hg. Because the change in outlet 
pressure was not transmitted 100% to the capillaries 
because of distension of the veins and thus reduc-
tion in venous resistance, and because interstitial 
hydrostatic and oncotic pressures were changed

The rate of fluid loss from the intestinal loops
somewhat by the filtration of fluid into the interstitial space by 40 seconds, the above slope of 0.279 ml/min-mm Hg·100 g is correspondingly less than the true capillary filtration coefficient. The total volume accumulated in the intestinal loop at 1 minute after the change in venous pressure was 52.4 ± 15.2, 111.6 ± 28.7, and 149.2 ± 30.6 ml/kg at 10, 20, and 30 mm Hg, respectively.

**Distended Volume**

To provide an estimate of the distending volume under control flow, we stopped perfusion at the end of the experiment and measured the progressive reduction in vascular volume. The final reduction in volume averaged 25.2 ± 6.7 (s.d) ml/kg by IFD (n = 6) and 20.9 ± 5.5 ml/kg by Cr-51 (n = 7). Assuming a linear compliance of 2.0 ml/kg-mm Hg from the control capacitance vessel pressure to the pressure at zero flow, the equivalent pressure required to store this much blood was 11.5 ± 2.9 mm Hg by IFD and 11.9 ± 2.4 mm Hg by Cr-51. Since the cannula resistance caused an average pressure drop of 4.8 mm Hg, the venous resistance pressure drop was at most 7 mm Hg because some fluid reabsorption was included in the volume reduction. At the time of these experiments, the total tissue blood volume was 78.5 ± 19.9 ml/kg by mean transit time of indocyanine green, and the perfusion rate was 553 ± 148 ml/min·kg. Subtracting the stop-flow volume loss from the total blood volume provided an estimate of the unstressed vascular volume that amounted to 55 ml of blood per kg of tissue.

**Venoarteriolar Response**

The vascular resistance increased in response to venous pressure increases using constant perfusion flow. The 10 mm Hg increase in venous pressure caused the perfusion pressure to increase by 26.5 ± 16.8 mm Hg. We had seen an increase of 33.5 ± 15.8 mm Hg in our earlier study (Rothe et al., 1978). In response to the 20 mm Hg venous pressure change, the arterial pressure increased by 45.0 ± 20.5 mm Hg, and in response to 30 mm Hg, the change was 64.6 ± 31.1 mm Hg.

**Cardiovascular Effects of Methoxyflurane**

Two hours after the start of anesthesia and after the abdominal surgery, the systemic blood pressure averaged 93 ± 25 mm Hg and the cardiac output was 149 ± 42 ml/min·kg. The hematocrit averaged 39.1 ± 3.6%. Although the use of methoxyflurane for human anesthesia is restricted because the fluoride released in metabolism causes renal damage (Samuelson et al., 1976), we have found it easy to use. It does not cause the high arterial blood pressure and heart rate that we see when using pentobarbital. The level of anesthesia is self-regulating in that, when respiration becomes depressed, the reduced ventilation automatically reduces the intake of anesthetic.

**Discussion**

The canine intestinal vascular compliance of 2.03 ± 0.46 (s.d) ml/kg-mm Hg found in this study was less than that reported earlier (Johns and Rothe, 1978) of 2.55 ml/kg-mm Hg, or 2.67 ± 0.32 ml/kg-mm Hg (Rothe et al., 1978). The vascular volume of 86.2 ± 19.1 ml/kg also was less than that reported before: 102.3 ± 7.4 ml/kg (Johns and Rothe, 1978) and 104 ± 14 ml/kg (Rothe et al., 1978). Venoconstriction related to the anesthetic or cool tissue might have been the cause.

It appears that the capacitance system for the intestinal bed, as well as for the body as a whole, is linear over the normal operating pressure range. Our data are consistent with those of Johnson and Hanson (1963), although our value for compliance is appreciably lower than the 3.4 ± 0.7 (s.d) ml/mm Hg·kg that they reported. We did not use Pro-Banthine (1 mg/kg) or any other depressant of intestinal motility.

Lutz (1969) reported an intestinal compliance for cats of 2.06 ml/mm Hg·kg over the range of 0-15 cm water and 1.56 ml/mm Hg·kg over the range of 15-30 cm water. Our study of the compliance around an 8.6 or 23.6 mm Hg venous pressure does not support the conclusion of Lutz (1969) of a less compliant vasculature at low pressures, compared to that at moderate (7 to 22 mm Hg) pressures. Lutz (1967) also used a constant flow perfusion preparation. He considered the volume change to be the integrated outflow deficit or overshoot measured by drop counter compared to the venous outflow rate found at 2 minutes. We confirmed the findings of Lutz (1969) that the volume of blood recovered on returning the venous pressure to control was not significantly different from the volume that distended the veins.

Other investigators using plethysmographs have used the rapid volume change that was apparently completed by 40-50 seconds (Mellander, 1960; Wallentin, 1966; Oberg, 1967) as a measure of vascular volume change to study capillary filtration, but made no specific correction for the transcapillary shifts that occurred during this interval.

To estimate vascular compliance, measurements of both the change in volume and change in transmural pressure are needed. Using a constant flow preparation, we have assumed that the venous resistance was constant and that the change in venous pressure was transmitted without decrement to the capacity vessels, capillaries, and arteries. If, as we found, there is an increase in overall vascular resistance (venoarterial reflex), then at a constant flow the arterial perfusion pressure will increase without necessarily influencing the postcapillary pressures. However, to the extent that venous resistance to flow is decreased as a result of a volume increase, the assumption of 100% transmission of venous pressure change will not be met. Furthermore, since volume is related to the square of the
vessel diameter and vascular conductance is related to the fourth power of diameter, the conductance of each segment will be increased as the square of the volume relative to control, and the pressure-drop from the capillaries to the vein will decrease as the conductance increases. Using a 2.03 ml/kg-mm Hg estimate of compliance and a control vascular volume of 86.2 ml/kg, then a venous pressure change of 20 mm Hg will cause vascular volume to be 1.47 times control and the venous conductance 2.16 times control. Since the flow was held at normal levels, we assumed that the Fahraeus-Lindqvist effect and viscosity were constant. Assuming a mean capillary pressure of 15 mm Hg, a venous pressure of 8.6 mm Hg, and no change in flow, and assuming that the pressure drop across venous resistance was 15 - 8.6 = 7.4 mm Hg and decreased in proportion to the change in resistance (or 1/G) then, with a venous pressure change of 20 mm Hg, the venous resistance drop would decrease to 3.4 mm Hg and the capillary pressure would change to 32 mm Hg, or 91% of the expected increase with 100% transmission of pressure (15 ± 20 mm Hg). However, the capacity vessels, being downstream from the capillaries, would have an even larger proportion of the venous pressure transmitted to them. Mortillaro and Taylor (1976), using an auto-perfused cat small intestine preparation, provided data indicating that the control venous resistance-pressure drop was 9.3 mm Hg, 69% of the venous pressure change was transmitted to the capillaries, and the venous conductance at a venous pressure of 20 mm Hg, compared to zero, was 1.94 times the control values. At 30 mm Hg, they reported virtually no pressure-drop from capillaries to vein. Johnson and Hanson (1963) assumed that 100% of the venous pressure change was transmitted to the veins. Mitzner and Goldberg (1975) reported that the splanchnic venous resistance was relatively pressure independent over the range of 2-12 mm Hg. Analysis of the data of Wiedeman (1963) for the bat wing and Green (1944) for the dog mesentery by Schmid-Schoenbein (1972) suggests that the resistance and thus the pressure drop across the postcapillary venules is about 20 mm Hg and so is much more than that of the larger venules and small veins (20-40 μm) that contain over 40% of the total blood volume. The studies of rat intestine by Gore and Bohlen (1977) and Bohlen and Gore (1977) suggest a pressure drop of only about 3 mm Hg from the mucosal capillaries to the small veins and a 5 mm Hg drop in pressure in the muscularis venules. From our stop-flow studies, we calculated a venous resistance pressure drop of less than 7 mm Hg. Thus it would appear that there is a pressure drop of about 6 mm Hg or less from the average of the capacity vessels to the outlet vein. This progressive decrease in transmitted pressure, as venous pressure is raised, would tend to make even more linear the pressure-volume relationship (Fig. 3) determined by IFD and would suggest a small, progressive increase in compliance at high venous pressures using the Cr-51 data.

Because the rate of volume gain by the intestine between 40 and 60 seconds after a venous pressure change was a reasonably linear function of venous pressure change and because the total volume gained by the intestine 1 minute after the pressure change of 20 and 30 mm Hg averaged 2.15 ± 0.04 (SE, n = 18) and 3.04 ± 0.13 (n = 17) times as great as that at 10 mm Hg, respectively, then either most of the venous pressure change was transmitted to the capillaries using our constant flow perfusion preparation or the capillary filtration coefficient increased at the higher distending pressures. Granger et al. (1979) claim that the capillary filtration coefficient progressively decreases at larger elevations of venous pressure.

In marked contrast to the early stabilization that occurred using the 51Cr-labeled RBC technique (Fig. 1), the integral of inflow and outflow method is sensitive to both vascular volume change and transcapillary fluid exchange. Thus separation of vascular and transcapillary events was necessary. For our extrapolations to time zero, we assumed that a constant rate-of-change of total volume was attained by about 40 seconds, but viscoelastic creep of vascular volume still may have been occurring (Johns and Rothe, 1978) as well as changes in interstitial hydrostatic and oncotic pressure. Johnson and Hanson’s gravimetric approach required data collection for about 5 minutes to reach a plateau in weight change in which the drip from lymph and secretions from the preparation matched the transcapillary filtration at elevated venous pressures, and extrapolation of the logarithm of the difference between the weight and the plateau to time zero. From a computer simulation of the hypothesized system (Rothe, unpublished), linear extrapolation to time-zero of the gravimetric data of Johnson and Hanson (1963) is unreasonable; extrapolation of the log transformed data from about 0.3 to 5 minutes is essential.

Sato et al. (1975) have suggested that there is an intermediate exponential transcapillary event in the gracilis muscle vascular response to venous pressure changes. Thus, some error may be associated with the visual extrapolation of what was considered to be a linear ramp (Fig. 1) to zero time, because the data pattern might also contain a second exponential with a 30-second time constant. Thus, because of the complex nature of the vascular and interstitial pressure-volume relationship, using a small part of it may not give an adequate basis for extrapolation, and so more careful delineation of this relationship is needed than has heretofore been available.

Because of the noise in the Cr-51 data and the long ratemeter time constant used, it was not possible to describe clearly the possibly exponential
pattern of the rapid vascular volume change using that approach, but the time constant was less than 5 seconds. The time constant of the IFD data was about 3 seconds; Johnson and Hanson (1963) reported 7.6 seconds. The venous time constant was much less than 23 seconds for the slow—splanchnic—compartment reported by Caldini et al. (1974), or the 15-second time constant for the splanchnic bed found by Green (1977). Hepatic characteristics may account for the difference.

Because the venules and small veins are surrounded by tissue, the pressure-volume characteristics of these capacity vessels are thus appreciably different from those of large veins not so supported. Their pressure-volume relationship appears to be linear throughout the range of 5 to 35 mm Hg, but at yet higher nonphysiological pressures, the compliance is most likely decreased (Lutz, 1967; Gaethgens and Uekermann, 1971). The estimate of 55 ml of blood per kg of tissue at zero flow and zero cannula pressure is similar to the estimate of residual blood volume of 60 ml/kg of “bowel” reported by Gibson et al. (1946) and the 64.9 ml/kg estimated by us in earlier experiments (Rothe et al., 1978). In contrast to large veins that can be collapsed easily, a large negative pressure may be required to remove this “unstressed volume” from the small veins located within the mass of tissue.

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