Quantitative Studies of Microcirculatory Structure and Function

III. Microvascular Hemodynamics of Cat Mesentery and Rabbit Omentum

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SUMMARY We made simultaneous measurements of intravascular pressure and red blood cell velocity for vessels which make up the modular configuration of microvascular networks in mesentery and omentum. An analysis of these variables and the computed volumetric flow rates is presented for arterioles which had a maximum diameter of 56 μm through the "true capillaries" (typically 7 μm for mesentery and 8 μm for omentum) to 56-μm venules. The spatial variance of pressure and flow is related to topographical features of each network. Vascularization statistics for each network are presented and demonstrate a unique ratio of potential microvascular exchange area to module planar area, with values of 0.71 ± 0.22 (SD) for omentum and 0.19 ± 0.03 (SD) for mesentery. Analysis of the volumetric flow rate for each module demonstrates a linear relationship to the planar area of tissue serviced by each modular network. In situ perfusion rates of 1180 ml/min per 100 g and 105 ml/min per 100 g were determined for omentum and mesentery, respectively. The hemodynamic resistance of the omental and mesenteric circuitry was evaluated, and in the case of the omentum, found to be inversely proportional to the planar area of the module. The arterial to venous distribution of pressure and flow for the mosaic of contiguous modules in omentum and mesentery is described and related to the deployment of parallel and serial microvessels of each network.

MEASUREMENTS in situ of intravascular pressure and red blood cell velocity have become a primary tool in the assessment and quantification of microvascular structure and function. However, there are no studies which relate simultaneous measurements of pressure and velocity in the microcirculation to prominent anatomical features or to the topography of a given microvascular network. In a previous study on the distribution of intravascular pressure in the terminal bed of cat mesentery, it was shown that pressure-related phenomena have a strong dependence on the geometric features characteristic of a given tissue. A second study described the spatial variability of capillary pressure in the true capillaries.

The present report is an extension of these earlier investigations and is concerned with the relationship between pressure, velocity, and volumetric flow rate in two structurally different microvascular networks, with an emphasis on the dependency of these hemodynamic variables on the branching pattern and resultant hierarchy of vessels from arterial to venous vessels. The mesentery of the cat and the omentum of the rabbit were used because they are functionally similar in nature, yet substantially different in vascularity. The microvascular network geometry in both of these tissues can be defined completely by micrographic reconstruction. A major premise underlying the present approach is that nutritive networks serve the same basic function, i.e., bring volumetric flow rates and intravascular pressures within the true capillaries to levels commensurate with nutritional and metabolic demands. In addition, different nutritive networks are presumed to be subject to similar neural, hormonal, and myogenic regulatory mechanisms.

In an attempt to determine how these requirements are accomplished, we propose to examine the following for each bed: (1) the intravascular pressures and volumetric blood flow rates in representative segments of each bed, (2) the flow requirements per unit area of tissue, (3) the distribution of pressure, velocity, and flow rate throughout successive functional segments of a given network, and (4) the relationship between pressure and flow through discrete segments as a controlling mechanism.

The mesentery of the cat and the omentum of the rabbit are especially useful because of the ease with which one can measure the total flow to an almost planar (two-dimensional) microvascular array. The pattern of artery-vein pairs circumscribing discrete areas of mesentery in a modular configuration has been described previously. As pointed out, the mesenteric module usually appears as an irregular polygon (from four to six sides) with a number of separate arterioles and venules forming the module perimeter. "Self-contained" or modular units also have been observed in the rabbit omentum. These are characterized as a bulb-shaped network which in many cases has a single artery-vein pair at the hilus. Although the omental module can take on a three-dimensional vascular pattern when large deposits of fat are present, only those beds which were clearly two-dimensional were used in the present study.
Methods

The techniques of intravital microscopy used in the present study have been described previously for the cat mesentery\textsuperscript{4-6} and the rabbit omentum.\textsuperscript{5-7} These methods have been followed here with minor modifications and are summarized briefly as follows.

Cats weighing between 1.5 and 3.0 kg were anesthetized with sodium pentobarbital, 35 mg/kg body weight, iv. Supplementary doses of 5 mg/kg were given later as needed to maintain the initial depth of anesthesia. Rabbits weighing 1.0–2.5 kg were anesthetized with Inactin, 50 mg/kg body weight iv, and given supplementary doses as needed. Systemic pressures were monitored by Statham pressure transducers (P23-Dt) via catheters introduced into the carotid artery directed toward the aorta (for central arterial pressure) and in the superior vena cava, via a femoral vein (for central venous pressure).

The mesentery and omentum were exteriorized via a midline abdominal incision and draped over a hollow support for transillumination. Each tissue was irrigated with Ringer-gelatin solution buffered to a pH of 7.2 and maintained at 37°C, to simulate the environment of the abdominal cavity.\textsuperscript{7}

Morphometric studies of the modular vascularization patterns were performed by constructing photomontages from Polaroid prints at a magnification of 35X for the larger mesenteric modules and 100X for those of the omentum. Areas of tissue circumscribed by the module boundaries were measured from the montages by a planimeter with an accuracy of 5%. Lengths of vessels within a module were also measured from the montage by use of a map measure. Photographs also were used to provide vessel internal diameters for vascularization statistics.

In addition, an electronic video image shearing technique was used to determine internal vessel diameter for all vessels in which pressure and velocity measurements had been made.\textsuperscript{8} This was performed at an effective magnification of 900X, as observed on a video monitor.

Intravascular pressure and red blood cell velocities were measured simultaneously in selected vessels of each tissue. Micropressures were obtained by the Wiederhielm servomotor technique\textsuperscript{9} as modified by Intaglietta et al.\textsuperscript{10} Inasmuch as we are applying this method to vessels with diameters ranging from 7 to 50 \textmu m in this study, and in view of the lack of suitable calibration factors for vessels smaller than 17 \textmu m, we have elected to treat the measured velocity (VcL) as a mean velocity (Vm) of cells plus plasma and not to include any correction factor. We believe that such a course is justified, since we are interested primarily in comparing intravascular flow factors between various segments of the arteriovenous hierarchy of vessels, as well as from one tissue to another. The range of the velocities and flow rates at these various sites was found to be considerably greater than any anticipated variation in the ratio of VcL/Vm. When a more definitive calibration becomes available, the data may be adjusted accordingly to obtain true mean velocities and volumetric flow rates. The volumetric flow rates presented herein were simply estimated from Q = VcL · (\pi D^2/4).

Although both the pressure and velocity exhibited a pulsatile character in all of the microvessels, mean values of these parameters were taken over several cardiac cycles and used throughout the presentation and analysis of the data.

Results

OMENTAL MODULAR NETWORK

Details of the modular configuration of microvessels in the omentum, described previously in an idealized form,\textsuperscript{5} are shown in Figure 1 for two outwardly dissimilar vascul-
HEMODYNAMICS OF THE MESENTERIC AND OMENTAL MODULAR NETWORK

The distribution of hemodynamic parameters throughout the mesenteric and omental modules is presented in Figure 2 as an overlay tracing of a representative module for the two tissues. The lower case letters (a and v) label the arterial and venous vessels for the mesentery and for the omentum. The vessel types, internal diameters, pressures, velocities, and volumetric flow rates are given for each labeled vessel in Table 1 for the mesentery and Table 2 for the omentum. The detailed pressure measurements tabulated in Table 1 are not as complete as the velocity measurements for practical reasons because of the considerable time needed to obtain micropressures. An estimate of the resistance to flow traversing the module interior was obtained by computing the average values of arteriole pressures (44.0 mm Hg) and venule pressure (32.7 mm Hg) for the arcuate side branches within the module interior. Based on the difference between these pressures, a resistance of $6.7 \times 10^{-3}$ mmHg/sec was computed.

This resistance can be attributed in part to the gradients in pressure and velocity around the mesenteric module perimeter, as illustrated by the values of pressure, velocity, and flow presented in Table 1 for 23 vessels. In general, these gradients are a reflection of the dual function of the arcuate vessels. First, we see hemodynamic differences between the paired artery and vein (e.g., A, B; C, D; E, F; etc.) which reflect their roles as perfusion manifolds to supply the needs of the immediately contiguous tissue. For example, arcuate artery A shows a pressure of 48 mm Hg, which represents the driving force for supplying the local tissue via precapillary vessel V. The local effluent is collected by arcuate venule B, with a pressure of 25 mm Hg. The intervening network between A and B must be structurally organized to permit the delivery of blood at an appropriate pressure and flow to the enclosed tissue area.

The arcuate vessels forming the boundary of mesenteric modules supply blood to many modules, depending upon the size and volumetric flow rate of the particular vessel. For example, arcuate artery H which has a high flow rate ($20.5 \times 10^{-3}$ mm/sec) perfuses a large number of modules, whereas artery F, which has only about 10% of the flow in H, perfuses only the two contiguous modules which it bounds. In this particular module, the greater portion of...
the flow in artery H (with a pressure of 79 mm Hg) is diverted into the neighboring modular region via the artery (a) between sides 3 and 4. The remainder of the flow is directed through artery F, a low pressure vessel (55 mm Hg) which, in turn, interconnects with artery C. A similar situation is seen in the venous vessels (e.g., G and E).

In contrast, the omental module shows exact agreement of inflow and outflow, 1.14 x 10^-3 mm^3/sec. Since the pressure drop from arteriole A to venule H is 13 mm Hg, the total modular resistance is 11.4 x 10^-6 mm Hg/(mm^3/sec). Pressure and velocity gradients reflect the change in effective cross-sectional area through successive ramifications of the network as shown in Table 2 for a number of representative vessels. The omental module can be depicted more faithfully in terms of the classical succession of feeding arteriole, precapillary, postcapillary, etc., due to the single artery-vein arrangement servicing the module (vessels A and H). A more orderly reduction in intravascular pressure is found within the successive functional segments, together with a progressive decrease in velocity and flow in individual arterial vessels of decreasing diameter. The 6:1 reduction in flow seen from feeding arteriole A to capillary C, and an 11:1 reduction in flow from A to postcapillary E are indicative of the presence of numerous parallel circuits.

A feature common to both the mesentery and omentum is the presence of vessels which may represent shunt vessels by virtue of their topographical location. For example, in the mesenteric module of Figure 2a, vessels K, M, X, R, and W show a relatively short pathway between arcuate artery and vein. However, due to their small diameters and high resistance, the velocity and flow in these vessels do not appear to be unusually high compared to other vessels in the network. Much higher velocities have been observed in vessels of this type in other modules in which the shunting vessel was sufficiently larger (20 μm in diameter) to permit a shunt flow velocity on the order of 25 mm/sec between arcuate artery and vein. Such high flow

### Table 2 Intravascular Pressures and Flows for a Representative Module of Omentum

<table>
<thead>
<tr>
<th>Site</th>
<th>Vessel type</th>
<th>Diameter (μm)</th>
<th>Pressure (mm Hg)</th>
<th>Velocity (mm/sec)</th>
<th>Flow (10^-3 mm^3/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Feeding arteriole</td>
<td>23.0</td>
<td>40.0</td>
<td>2.74</td>
<td>1.14</td>
</tr>
<tr>
<td>B</td>
<td>Precapillary</td>
<td>20.0</td>
<td>38.0</td>
<td>1.23</td>
<td>0.39</td>
</tr>
<tr>
<td>C</td>
<td>Capillary</td>
<td>13.0</td>
<td>33.0</td>
<td>1.32</td>
<td>0.18</td>
</tr>
<tr>
<td>D</td>
<td>Postcapillary</td>
<td>15.0</td>
<td>30.0</td>
<td>1.10</td>
<td>0.19</td>
</tr>
<tr>
<td>E</td>
<td>Postcapillary</td>
<td>13.0</td>
<td>29.0</td>
<td>0.77</td>
<td>0.10</td>
</tr>
<tr>
<td>F</td>
<td>Collecting venule</td>
<td>17.0</td>
<td>28.0</td>
<td>0.78</td>
<td>0.18</td>
</tr>
<tr>
<td>G</td>
<td>Collecting venule</td>
<td>13.0</td>
<td>30.0</td>
<td>3.31</td>
<td>0.44</td>
</tr>
<tr>
<td>H</td>
<td>Venule</td>
<td>23.0</td>
<td>27.0</td>
<td>2.74</td>
<td>1.14</td>
</tr>
</tbody>
</table>
shunts have been observed in a small percentage of all mesenteric modules. Similar anastomosing vessels also have been observed in the omentum.

**VASCULARIZATION STATISTICS**

The extent of vascularization of each type of module was mapped out in detail for 9 omental and 10 mesenteric modules. The data are presented in Table 3 for omentum and Table 4 for mesentery. Omental modules 1, 3, and 6 of Table 3 correspond to those of Figures 2b, 1A, and 1B, respectively, while mesenteric module 6 in Table 4 corresponds to that of Figure 2a. The vascularization statistics are listed in order of ascending modular area. Statistics for potential exchange vessels (vessels which satisfy nutritional and/or metabolic needs) are given in terms of exchange vessel length, vessel exchange area (wetted surface area), the number of exchange vessels, and the average length per exchange vessel. For the rabbit omentum, those vessels within the interior of a module with diameters less than or equal to 12 μm were taken as exchange vessels. In larger vessels, the muscular coat becomes perceptibly thicker and these vessels were arbitrarily excluded. Actually, the larger vessels constituted less than 5% of the total microvascular surface area. The exchange vessel length was determined by running a map measure over the linear length of all relevant microvessels photographed at 200x. The total exchange area was computed from the product of πDL, where D represents the mean exchange vessel diameter which was found to be 10 ± 2 (SD) μm with a range of 8-12 μm. The number of vessel segments and average length per vessel also were measured and computed.

Calculations of vascularization statistics for the mesenteric modules were based on all vessels within the module interior, excluding the arcuate artery-vein perimeter. The mean exchange vessel diameter was 9 ± 2 (SD) μm with a range of 7-15 μm. Also shown in Tables 3 and 4 are the means, standard deviations, and coefficients of variation for all data in each sample. It should be emphasized that these vascularization

**Table 3** Vascularization Statistics-Omentum

<table>
<thead>
<tr>
<th>Module no.</th>
<th>Area (mm²)</th>
<th>Total exchange vessel length (mm)</th>
<th>Total exchange area* (mm²)</th>
<th>No. of exchange vessels</th>
<th>Average length per vessel (μm)</th>
<th>Ratio, exchange area to module area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.225</td>
<td>4.29</td>
<td>0.135</td>
<td>41</td>
<td>104.5</td>
<td>0.600</td>
</tr>
<tr>
<td>2</td>
<td>0.429</td>
<td>16.19</td>
<td>0.508</td>
<td>217</td>
<td>74.6</td>
<td>1.184</td>
</tr>
<tr>
<td>3</td>
<td>0.476</td>
<td>12.39</td>
<td>0.389</td>
<td>82</td>
<td>151.0</td>
<td>0.810</td>
</tr>
<tr>
<td>4</td>
<td>0.658</td>
<td>12.85</td>
<td>0.404</td>
<td>128</td>
<td>100.4</td>
<td>0.614</td>
</tr>
<tr>
<td>5</td>
<td>0.718</td>
<td>16.23</td>
<td>0.526</td>
<td>217</td>
<td>77.1</td>
<td>0.733</td>
</tr>
<tr>
<td>6</td>
<td>0.725</td>
<td>18.86</td>
<td>0.592</td>
<td>220</td>
<td>85.7</td>
<td>0.811</td>
</tr>
<tr>
<td>7</td>
<td>0.737</td>
<td>14.95</td>
<td>0.470</td>
<td>198</td>
<td>75.5</td>
<td>0.663</td>
</tr>
<tr>
<td>8</td>
<td>0.849</td>
<td>10.91</td>
<td>0.343</td>
<td>137</td>
<td>79.6</td>
<td>0.404</td>
</tr>
<tr>
<td>9</td>
<td>1.277</td>
<td>23.46</td>
<td>0.737</td>
<td>212</td>
<td>110.7</td>
<td>0.577</td>
</tr>
<tr>
<td>Mean</td>
<td>0.677</td>
<td>14.512</td>
<td>0.456</td>
<td>161.3</td>
<td>95.5</td>
<td>0.708</td>
</tr>
<tr>
<td>SD</td>
<td>0.297</td>
<td>5.381</td>
<td>0.169</td>
<td>67.1</td>
<td>24.8</td>
<td>0.219</td>
</tr>
<tr>
<td>C.V.†</td>
<td>0.439</td>
<td>0.371</td>
<td>0.371</td>
<td>0.416</td>
<td>0.260</td>
<td>0.309</td>
</tr>
</tbody>
</table>

* Based on a mean exchange vessel diameter of 10 μm (range = 8-12 μm).
† Coefficient of variation = SD/mean indicates the spread of data.

**Table 4** Vascularization Statistics-Mesentery

<table>
<thead>
<tr>
<th>Module no.</th>
<th>Area (mm²)</th>
<th>Total exchange vessel length (mm)</th>
<th>Total exchange area* (mm²)</th>
<th>No. of exchange vessels</th>
<th>Average length per vessel (μm)</th>
<th>Ratio, exchange area to module area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.628</td>
<td>4.00</td>
<td>0.113</td>
<td>22</td>
<td>181.8</td>
<td>0.181</td>
</tr>
<tr>
<td>2</td>
<td>0.727</td>
<td>5.27</td>
<td>0.149</td>
<td>24</td>
<td>219.7</td>
<td>0.205</td>
</tr>
<tr>
<td>3</td>
<td>0.831</td>
<td>6.28</td>
<td>0.177</td>
<td>41</td>
<td>153.1</td>
<td>0.213</td>
</tr>
<tr>
<td>4</td>
<td>0.878</td>
<td>8.09</td>
<td>0.229</td>
<td>42</td>
<td>192.6</td>
<td>0.260</td>
</tr>
<tr>
<td>5</td>
<td>0.971</td>
<td>6.68</td>
<td>0.189</td>
<td>39</td>
<td>171.3</td>
<td>0.194</td>
</tr>
<tr>
<td>6</td>
<td>1.642</td>
<td>9.46</td>
<td>0.267</td>
<td>42</td>
<td>225.1</td>
<td>0.163</td>
</tr>
<tr>
<td>7</td>
<td>1.844</td>
<td>9.09</td>
<td>0.257</td>
<td>36</td>
<td>252.5</td>
<td>0.140</td>
</tr>
<tr>
<td>8</td>
<td>2.077</td>
<td>12.18</td>
<td>0.345</td>
<td>49</td>
<td>248.6</td>
<td>0.166</td>
</tr>
<tr>
<td>9</td>
<td>4.218</td>
<td>28.55</td>
<td>0.807</td>
<td>84</td>
<td>339.8</td>
<td>0.192</td>
</tr>
<tr>
<td>10</td>
<td>4.300</td>
<td>25.09</td>
<td>0.709</td>
<td>83</td>
<td>302.3</td>
<td>0.165</td>
</tr>
<tr>
<td>Mean</td>
<td>1.812</td>
<td>11.47</td>
<td>0.324</td>
<td>46.2</td>
<td>228.7</td>
<td>0.188</td>
</tr>
<tr>
<td>SD</td>
<td>1.382</td>
<td>8.45</td>
<td>0.239</td>
<td>21.3</td>
<td>59.0</td>
<td>0.034</td>
</tr>
<tr>
<td>C.V.†</td>
<td>0.763</td>
<td>0.737</td>
<td>0.738</td>
<td>0.461</td>
<td>0.258</td>
<td>0.181</td>
</tr>
</tbody>
</table>

* Based on a mean exchange vessel diameter of 9 μm (range = 7 to 15 μm).
† Coefficient of variation = SD/mean indicates the spread of data.
statistics correspond to relatively fat-free areas of mesentery and omentum so that all vessels within the modules could be accounted for.

For both the mesentery and omentum, the trend is that of increasing vasculature with module area, although the number of exchange vessels in each case does not exhibit a consistent monotonic trend. Instead, the progressive increase in exchange area is accomplished at the expense of the average length per vessel by the addition of both serial and parallel pathways which, for the omentum, are rather uniformly distributed for the 9 modules. Thus, when module 1 is compared with 9 and 10 in the mesentery, we see a 6- to 7-fold increase in total exchange vessel length for the approximately 7-fold increase in modular area, which serves to preserve the constancy of the ratio of exchange vessel length to modular area.

A particularly interesting parameter for each of the tissues is the ratio of exchange area to module area. For the omentum, this ratio was 0.708 ± 0.219 (sp) with a coefficient of variation (sp/mean) of 0.309, compared to the mesentery in which the ratio was approximately 70% lower, 0.188 ± 0.034 (sp) but which had a coefficient of variation of only 0.181. The coefficient of variation17 indicates the spread of the data and reflects the certainty of the mean values. When the variance of the data is on the order of the mean, their significance becomes questionable. The substantial difference between these two tissues is believed to reflect their respective functional roles, i.e., the omentum being primarily a fat-storage organ, hence requiring a greater perfusion per unit area of tissue, whereas the intestinal mesentery has primarily a supportive or mechanical function. The omental modules studied here, although comparatively free of fat, represent a developing substrate for fat deposition in young animals and, hence, the microvascular system can be considered to be in a state of increasing vascularization consistent with future tissue function.

MODULAR FLOW AND AREA

With the establishment of a framework for the comparison of modular function, an analysis was made of the volumetric flow rates servicing these modules. Figure 3 is a plot of flow vs. modular area for both the mesentery and omentum. These data correspond to the modules in Tables 3 and 4. Nine additional mesenteric modules were included, for which only partial vascularization statistics were obtained. Also shown are linear regression lines for each tissue and the resultant statistics for the equation of best fit and correlation coefficient. For the mesentery, these measurements correspond to 19 modules from nine cats, in which central arterial pressure averaged 114.8 mm Hg ± 21.9 (SD) mm Hg for all modules. During the course of measurement, central arterial pressure remained essentially the same within ±5.4 mm Hg. For the rabbit population, each of the modules was observed in a different rabbit, and central arterial pressure averaged 77.1 mm Hg ± 11.3 mm Hg, with the central arterial pressure being maintained within ±3.0 mm Hg during the period of measurement.

As shown in Figure 3, a surprisingly good fit of the variation of flow with modular area was obtained, as evidenced by the correlation coefficients. These results are also consistent with the vascularity statistics; i.e., for omentum, the exchange area to module area ratio is approximately 4 times greater than that of mesentery. The mean value of flow per unit area for the data of Figure 3 is 9.843 ± 3.445 (sp) ~10^-3 mm^3/sec per mm^2, which is on the order of 11 times greater than that for mesentery, 0.872 ± 0.433 (sp) ~10^-3 mm^3/sec per mm^2. The slopes of the flow vs. area curves are approximately 16 times greater for the omentum than the mesentery.

MODULAR RESISTANCE

In conjunction with measurements of modular flow rates, pressure recordings were taken to facilitate the computation of modular resistance. These were done for eight omental modules which were tended by one major artery-vein pair feeding the unit, and two mesenteric modules for which the arteriovenous pressure differential was computed on the basis of an electrical mean of arterial pressures and venous pressures in the several inflow and outflow vessels. The resistance, R, was computed from the average arteriovenous pressure differential of the module, ΔP, from R = ΔP/Q. These data are presented in Figure 4 as resistance vs. module area. Also shown is a least squares regression (solid line) for a power law functional relationship of the omentum data. The resistance, R, is expressed in units of 10^8 mm Hg/(mm^3/sec). (A correlation coefficient of ~0.757 was computed for the best fit in the linear transform plane, indicating that 57.3% of the variance in the data is represented by the regression line.)

The modular resistance for the omentum is almost inversely proportional to modular area. For decreasing modular area, the number of parallel microvascular pathways is reduced and the modular resistance is increased accordingly, approaching that of a single unbranched vessel. For example, for a single unbranched vessel, 10 μm in diameter and 100 μm in length (as suggested by the mean...
The data thus far have established some of the characteristics of individual modules comprising the omental and mesenteric microvascular systems. In view of the variation of modular size in individual tissues, we then examined the distribution of pressure, velocity, and volumetric flow throughout the entire syncytium of modular units. In order to display these data in terms of network function and topographical features, we have characterized the successive divisions and confluences of the network in terms of vessel diameter. Although this is not an ideal scheme, it does lead to a reasonable representation.\(^1\) Hemodynamic measurements were obtained in arterial and venous vessels ranging in diameter from 8 to 50 \(\mu\)m. In perspective, the afferent and efferent vessels of the omental modules presented here had mean arterial diameters of 34.7 \(\pm\) 8.85 (SD) \(\mu\)m and venous diameters of 42.4 \(\pm\) 11.9 \(\mu\)m. Similar arterial and venous arcuate vessels which form the perimeter of the mesenteric modules had diameters of 25.1 \(\pm\) 11.6 and 32.12 \(\pm\) 15.6 \(\mu\)m. These values are consistent with modular vessel sizes reported earlier for mesentery\(^2\) and omentum.\(^3\)

Figure 5 presents the distribution of intravascular pressure (mm Hg) and centerline velocity (mm/sec) measured simultaneously in 435 vessels in over 40 animals. Each data point represents the mean of from two to five measurements for several vessels at the indicated discrete diameter (abscissa). The solid curves represent a piecewise cubic “spline fit,” which is a least squares estimate of the smoothest (least curvature) curve representing the trends in the data from artery to vein.\(^18\) This type of fit is analogous to a “mathematical french curve,” and is useful for data with large amounts of scatter, yet not related by a specific functional form for regression analysis. The central arterial pressure of the group of cats studied under pentobarbital anesthesia averaged 123.9 \(\pm\) 18.1 (SD) mm Hg. It should be noted that animals under pentobarbital anesthesia have a somewhat higher arterial blood pressure (10-15 mm Hg) than animals studied under the influence of other anesthetic agents. A comparison of the microvascular pressures in vessels below 30 \(\mu\)m in diameter showed them to be essentially the same (\(\pm\) 3 mm Hg) in a group of 20 cats with an arterial blood pressure range of 95-110 mm Hg (ketamine) as in a group of 18 cats with an arterial blood pressure range of 115-130 mm Hg (pentobarbital).

We observe in Figure 5 that the rate at which the pressure drops from artery to vein is greatest in the 16 to 40-\(\mu\)m arteriolar vessels with an attendant rapid reduction in velocity. Velocities as low as 1-2 mm/sec are seen in postcapillary vessels approximately 14 \(\mu\)m in diameter. In the subsequent confluences of the venous vessels, velocity is increased, reaching a value of 10 mm/sec in the largest vessels. The pressure in the venous portion of the circuit falls gradually in line with the degree of convergence of the venous vessels.

Presented in Figure 6 is the corresponding distribution of volumetric flow rate throughout the sequence of micro-
VOLUMETRIC FLOW RATE DISTRIBUTION

ARterial

VENous

MESENTERY CAT

FIGURE 6 Arterial to venous distribution of intravascular volumetric flow rate in mesentery. The volumetric flow rates were computed from the velocity data of Figure 5 and are similarly presented. The dashed curve represents ±1 SD about the solid line (fairing) of the data.

Intravascular pressure shows a gradual decline from 43 mm Hg in a 50-μm artery to 19 mm Hg in a 50-μm vein. If one compares the pressures in two equal-sized arterioles (e.g., 50 μm) of the omentum and mesentery, they are found to be 43 mm Hg vs. 90 mm Hg, respectively. These arteriolar pressures are 56% and 73% of systemic arterial pressure for the rabbit and cat, respectively. This difference is essentially due to the serial deployment characteristic of parent artery-vein pairs which feed successive omental modules. The relatively small drop in pressure in the vessels supplying the mesenteric modules is due to the highly parallel arrangement of these parent vessels and their larger size.

Velocity likewise undergoes a gradual decrease, from 9 mm/sec in the larger arterioles to 3 mm/sec in the large veins. Unlike the mesentery, velocity in the omentum does not show a substantial minimum in the immediate postcapillaries, although a modest upturning of the velocity curve is observed between 40 and 50 μm on the venous side. The vessels immediately contiguous with the capillary network proper range in diameter from 15 μm on the arterial side to 15-μm venous vessels and have a mean centerline velocity of 3.52 ± 4.05 (SD) mm/sec.

The attendant volumetric flow rates in the omentum were presented in Figure 8 with the minimum flow of 2.64 ± 1.86 x 10^-4 mm³/sec in the postcapillary vessels. Such flows are approximately 1.6 times greater than in comparable vessels of the mesentery. The U-shaped nature of the curve appears to follow a square law dependency on vessel internal diameter.

In order to obtain an insight into possible regulatory mechanisms, i.e., their flow rate or pressure dependency, a plot was made of volumetric flow rate vs. intravascular pressure for the mesentery (Fig. 9A). Included in the data are arterial vessels with a maximum diameter of 42 μm and venous vessels with a maximum diameter of 50 μm.

A feature of immediate interest in the mesentery is the decrease in scatter from arterial to capillary level, with a relative invariance of flow vs. pressure over a range of pressures of 30 to 45 mm Hg. An increasing scatter of the data again is seen in the venous vessels. It should be noted that there is an interlacing of data for arterial and venous vessels. The considerable variance of flow rates is illustrated, in addition to the spline fairing, by dashed lines which demarcate ±1 SD about the fairing. A log-log plot of the data shows a square law variation with vessel diameter. A striking feature is the attendant decrease in scatter as the bloodstream approaches the true capillary network. The standard deviations tend to decrease in proportion to the magnitude of the flow. This is believed to be due to the vessels taking on a more singular function as the true capillary level is reached. At this level, the vessels deliver flow only to a specific region of tissue and do not, as in the case of the larger feeding vessels, transmit flow to other parts of the network (e.g., contiguous modules). The lowest flow rate occurs in the postcapillary vessels (8–13 μm in diameter) with a minimum value of 1.66 ± 0.77 (SD) x 10^-4 mm³/sec. Centerline velocity in this group of vessels was 1.93 ± 0.96 (SD) mm/sec. When larger arterial and venous vessels of similar diameter are compared, the higher flows on the arterial side reflect a reduced number of parallel arterial vessels on the assumption that the two segments receive the same total flow (conservation of mass).

For comparison, pressure and velocity distributions for the omentum are shown in Figure 7. These data represent 308 simultaneous measurements of pressure and velocity in 30 rabbits. Mean systemic arterial pressure for these young rabbits was 76.6 ± 11.2 (SD) mm Hg. The distribution patterns of pressure and flow are considerably different for the omentum when compared to the mesentery. Intravascular pressure shows a gradual decline from 43 mm Hg in a 50-μm artery to 19 mm Hg in a 50-μm vein.
vessels on either side of the capillary line (34 mm Hg). If one were to speculate on the type of network geometry which would result in this overall behavior, the following would be evident. Given a completely serial network, but with changing diameters in the constituent vessels, spatially random observations of pressure and flow would reveal a random distribution of pressure (bounded by the perfusion and effluent pressures) with the same flow at every point where measurements are made. The opposite would be true for a purely parallel system of conduits in which flow would change depending on the number and relative diameter of the vessels. Hence, in Figure 9A, the reduction in scatter for vessels comprising the interior of a network emphasizes the essentially serial deployment of these vessels, with a more parallel structure in the attendant arcuates which bound the module.

In contrast, a comparable plot of flow vs. pressure for the omentum in Figure 9B shows considerable scatter throughout. This is in line with the parallel nature of the network in the interior of the omental module. The poor correlation in the larger serial vessels is in part due to some bias in the sampling, since emphasis was placed on measurements in small vessels immediately associated with the peritoneal network. The marked disparity between the flow vs. pressure trends of omentum and mesentery suggests that the network topography (vessel lengths, diameters, and branching patterns) by itself represents a major feature regulating flow to a given area of tissue in the normal flow state.

Discussion

Until recently, structure and function relationships for the microcirculation have been established on purely anatomical grounds due to the unavailability of suitable instrumentation for direct hemodynamic measurements. Qualitative estimates of network function, as deduced from the spatial deployment of the constituent vessels and their geometry, have formed the basis for numerous quantitative assessments of the relationship between network topography and hemodynamic variables. The present data provide a means of bridging these two approaches and illustrate the type of information which can be derived from an intensive in vivo hemodynamic study. The approach has been to examine the perfusion requirements and the attendant distribution of hemodynamic variables in representative detailed modular networks and the distribution throughout the entire mosaic of modular networks, for two tissues with similar functions but with different vascular patterns.
Resting tissue perfusion was used as a basic frame of reference in making a comparison of these two vascular beds. Basal or steady state requirements differed substantially in omentum and mesentery, as well as in other tissues for which comparable data have been obtained from whole organ studies. Based on an average tissue thickness of 50 μm and a tissue density of 1 g/cm³, perfusion rates of 1180 ml/min per 100 g and 105 ml/min per 100 g for the modular tissue areas of omentum and mesentery, respectively, were computed from the data of Figure 3. In both cases, the values are an order of magnitude greater than those reported in the literature on the basis of whole organ studies for several tissues. For example, resting regional blood flows of 35 ml/min per 100 g have been estimated for the gastrointestinal tract and a value of 6 ml/min per 100 g for white adipose tissue.

Differences between whole organ studies and those of direct in situ measurement would appear to be due primarily to microvascular inhomogeneity. For example, the omentum has fairly large avascular areas. The modular structures discussed here supply 20-30% of the omental tissue. If the weight of these avascular areas had been included in calculations of the perfusion rate per 100 g of tissue, this value would be substantially reduced. One can question the normality of the flows in exteriorized preparations, but there is no evidence to indicate that pressure-flow relationships would be distorted to that extent. The consistent responsiveness of individual vessels, together with autoregulatory activities and a predictable response to both constrictor and dilator influences, supports the contention that such beds are in fact maintained close to normal steady state conditions in situ measurements of pressure and flow. Although we have obtained large numbers of simultaneous measurements of pressure and flow for individual vessels, we have found that, for a large enough sampling in a standardized tissue preparation, the arteriovenous relationship between pressure and flow can be approximated closely by separate measurements of these parameters. However, the number of such individual measurements must be increased greatly.

In view of the clear dependency of the distribution data and corresponding pressure-flow diagrams in the network topography for the two tissues, investigations aimed at determining the sensing mechanism for regulation and control should take into account the spatial distribution of flow throughout successive functional divisions. Even though the pressures in the successive branchings of the terminal arterioles and in the capillary network proper differ by as much as 15 mm Hg, flow remains comparatively constant. This suggests that there are a number of possible sites that could serve to adjust the local distribution of flow. The omentum, however, would appear to have a more localized feedback mechanism for flow throughout its network. Regardless of the mechanism that dominates control, the substantial differences in the pressure-flow patterns between these two tissues clearly indicate the passive role of the network in its resting state with the precise distribution determined by topographical features.

This concept is consistent with the hypothesis that the resting state of the microvascular system is maintained with the least expenditure of energy. Active responses to perturbations in pressure and flow would then operate around this network configuration. The logical site for such active modulation would be one which has the greatest mechanical leverage. There is evidence that, in the mesentery, the arcading arteriolar vessels (50-150 μm) on the periphery of the module are concerned with adjustments of pressure, whereas the smaller vessels (< 40 μm) within the module proper tend to keep flow in a narrow range. The fact that pressure and flow in the successive portions of the microvascular system can be characterized by a numerical resistance term makes it possible to analyze in a systematic way singular perturbations of the terminal vascular bed.
Acknowledgments
We thank Steven Kovalcheck, John Firrell, and William Brown for their technical assistance.

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*Circ Res.* 1977;41:380-390
doi: 10.1161/01.RES.41.3.380

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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