Quantitative Studies of Microcirculatory Structure and Function

III. Microvascular Hemodynamics of Cat Mesentery and Rabbit Omentum

Benjamin W. Zweifach and Herbert H. Lipowsky

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.

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Methods

The techniques of intravital microscopy used in the present study have been described previously for the cat mesentery and the rabbit omentum. 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. Rabbids 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-Dh) 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.7

Morphometric studies of the modular vascularization patterns were performed by constructing photomontages from Polaroid prints at a magnification of 35× for the larger mesenteric modules and 100× 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. This was performed at an effective magnification of 900×, 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 servo-null technique as modified by Intaglietta et al. Intravascular velocity of red blood cells was measured as a variation in the ratio of \( \frac{V_{CL}}{V_m} \). 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 \( Q = V_{CL} \cdot \pi D^2/4 \).

Although both the pressure and velocity exhibited a pulsatile character in all of the microvessels, mean values were simply estimated from \( Q = V_{CL} \cdot \pi D^2/4 \).

Details of the modular configuration of microvessels in the omentum, described previously in an idealized form, are shown in Figure 1 for two outwardly dissimilar vascular networks.

Results

OMENTAL MODULAR NETWORK

Details of the modular configuration of microvessels in the omentum, described previously in an idealized form, are shown in Figure 1 for two outwardly dissimilar vascular networks.

![Figure 1: Representative modular networks in the rabbit omentum. The dashed line circumscribing each module encloses the planar tissue area serviced by each.](image-url)
lar patterns. A dashed line circumscribing each module approximates the area of tissue taken to be served by these networks. In all cases here, similar confines were constructed for each functional module. Areas of 0.48 mm² and 0.73 mm² were measured by planimetry for models A and B, respectively. In addition to the differences in vascularity, these modules also demonstrate the kind of modular irregularities which are encountered. For example, module B has a well defined single artery-vein pair supplying the tissue, whereas module A has a branch vessel (17-μm precapillary) which feeds a contiguous area of tissue. The differences in vascularity were examined by counting the number of vessel segments between each branching point in the network. Module A was composed of 82 vessels with an average length of 151.0 μm, while module B contains 220 vessels with an average length of 85.7 μm. If one considers the ratio of vessel surface area (all vessels except for feeding arteriole and collecting venule, representing the potential exchange area) to module tissue area, we find that for modules A and B, this ratio is essentially the same, 0.81 (see Table 3 for variation).

It should be noted that, in the present study, all comparisons between tissues are made on the basis of inscribed modular area and not on tissue volume. Histological cross sections show that local tissue thickness of mesentery and omentum varies, being as thick as 80 to 100 μm in regions directly surrounding large vessels. However, the tissue thickness was found to average between 40 and 60 μm in the interior of these modules where only small vessels were present. The variation in modular tissue area (planar area) ranged from 0.2 to 1.3 mm² in the omentum, and from 0.63 to 4.3 mm² in the mesentery (see Tables 3 and 4 for mean values). Inasmuch as these substantial differences in modular area represent the major factor influencing tissue volume, it was felt that area alone was suitable as a frame of reference for comparing volumetric flow levels.

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 spatial distribution of hemodynamic parameters corresponding to the labeled microvessels are presented in Table 1 for the mesentery and Table 2 for the omentum.

FIGURE 2 Schematic representations (obtained from overlay tracings of photomontages) of the modular networks of mesentery (a) and omentum (b). The spatial distribution of hemodynamic parameters corresponding to the labeled microvessels are presented in Table 1 for the mesentery and Table 2 for the omentum.

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same direction, with overestimation on the average ranging from 0 to 20%. Our calculations, which are based on the assumption that all of the vessels are circular in cross section, probably overestimate venular cross-sectional area and mean venular flow. Total flow to a module was taken as the average of inflow and outflow, e.g., $1.69 \times 10^{-3}$ mm³/sec for this module.

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 $6.7 \times 10^3$ mm Hg/(mm³/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 ($2.05 \times 10^{-3}$ mm³/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, $1.14 \times 10^{-3} \text{ mm}^3/\text{sec}$. Since the pressure drop from arteriole A to venule H is 13 mm Hg, the total modular resistance is $11.4 \times 10^3 \text{ mm Hg/(mm}^3/\text{sec)}$. 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-vene network 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 mm in diameter) to permit a shunt flow velocity on the order of 25 mm/sec between arcuate artery and vein. Such high flow

<table>
<thead>
<tr>
<th>Side</th>
<th>Site</th>
<th>Vessel type</th>
<th>Diameter ($\mu$m)</th>
<th>Pressure (mm Hg)</th>
<th>Velocity (mm/sec)</th>
<th>Flow ($10^{-3} \text{ mm}^3/\text{sec}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>Arcuate artery</td>
<td>14.0</td>
<td>48.0</td>
<td>3.11</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Arcuate venule</td>
<td>16.0</td>
<td>25.0</td>
<td>1.66</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>V</td>
<td>Precapillary</td>
<td>9.5</td>
<td>2.52</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>U</td>
<td>Precapillary</td>
<td>8.0</td>
<td>1.49</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>W</td>
<td>Venule</td>
<td>12.5</td>
<td>0.51</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>Arcuate arteriole</td>
<td>16.0</td>
<td>1.25</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>Arcuate venule</td>
<td>12.0</td>
<td>1.55</td>
<td>0.17</td>
<td></td>
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<tr>
<td>2</td>
<td>C</td>
<td>Arcuate arteriole</td>
<td>13.5</td>
<td>22.85</td>
<td>3.27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>Arcuate venule</td>
<td>24.0</td>
<td>2.94</td>
<td>1.31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K</td>
<td>Precapillary</td>
<td>9.5</td>
<td>3.02</td>
<td>0.21</td>
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<tr>
<td></td>
<td>J</td>
<td>Venule</td>
<td>18.0</td>
<td>2.17</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>Arcuate artery</td>
<td>50</td>
<td>1.00</td>
<td>1.96</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>Arcuate venule</td>
<td>34.5</td>
<td>5.58</td>
<td>5.21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>Arteriole</td>
<td>11.5</td>
<td>5.61</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>Venule</td>
<td>18.0</td>
<td>2.17</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>Arcuate Artery</td>
<td>51.0</td>
<td>10.42</td>
<td>20.53</td>
<td></td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>Arcuate vein</td>
<td>50.0</td>
<td>9.47</td>
<td>18.66</td>
<td></td>
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<tr>
<td></td>
<td>X</td>
<td>Terminal arteriole</td>
<td>12.0</td>
<td>4.28</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>Postcapillary</td>
<td>9.5</td>
<td>1.22</td>
<td>0.09</td>
<td></td>
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<tr>
<td></td>
<td>O</td>
<td>Venule</td>
<td>11.0</td>
<td>1.27</td>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>P</td>
<td>Postcapillary</td>
<td>7.5</td>
<td>2.20</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q</td>
<td>Venule</td>
<td>13.5</td>
<td>0.88</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>Venule</td>
<td>14.0</td>
<td>1.33</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Site</th>
<th>Vessel type</th>
<th>Diameter ($\mu$m)</th>
<th>Pressure (mm Hg)</th>
<th>Velocity (mm/sec)</th>
<th>Flow ($10^{-3} \text{ mm}^3/\text{sec}$)</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 lineal length of all relevant microvessels photographed at 200×. 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>
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<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>
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<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>
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<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>
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<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>
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<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>
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<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>
</tbody>
</table>

Mean: 0.677 14.512 0.456 161.3 95.5 0.708
sd: 0.297 5.381 0.169 67.1 24.8 0.219
C.V. †: 0.439 0.371 0.416 0.260 0.309

* 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>0.625</td>
<td>4.00</td>
<td>0.113</td>
<td>22</td>
<td>181.8</td>
<td>0.181</td>
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<tr>
<td>2</td>
<td>0.727</td>
<td>5.27</td>
<td>0.149</td>
<td>24</td>
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Mean: 1.812 11.47 0.324 46.2 228.7 0.188
sd: 1.382 8.45 0.239 21.3 59.0 0.034
C.V. †: 0.763 0.737 0.738 0.461 0.258 0.181

* 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 vascularity 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 8 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 (sd) 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 (sd) but which had a coefficient of variation of only 0.181. The coefficient of variation 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 for each module, 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 (sd) × 10⁻³ mm³/sec per mm², which is on the order of 11 times greater than that for mesentery, 0.872 ± 0.433 (sd) × 10⁻³ mm³/sec per mm². 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 10⁸ mm Hg/(mm²/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
values of Table 3), the resistance has been measured to be $10 \times 10^3$ mm Hg/(mm$^3$/sec), which agrees favorably with the trends of Figure 4.

Only two modular resistances are shown in Figure 4 for the mesentery. These resistances are on the order of 5 times greater than those in the omentum. The findings are consistent with the observations that, although the omental modules have twice the pressure drop observed in the mesentery, they have only one-fifth the resistance. Hence, the omentum has 10 times the flow in the mesentery. The lower omental resistance appears to be a direct result of the 4-fold greater vascularity, as evidenced by the ratios of exchange vessel area to module area and by the fact that these additional omental pathways occur in parallel.

**ARTERIAL-VENOUS PRESSURE AND FLOW DISTRIBUTIONS**

The data thus far have established some of the characteristics of individual modules comprising the omental and mesenteric microvessels. 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. Hemodynamic measurements were obtained in arterial and venous vessels ranging in diameter from 8 to 50 $\mu$m. In perspective, the afferent and effluent vessels of the omental modules presented here had mean arterial diameters of 34.7 ± 8.85 (SD) $\mu$m and venous diameters of 42.4 ± 11.9 $\mu$m. Similar arterial and venous arcuate vessels which form the perimeter of the mesenteric modules had diameters of 25.1 ± 11.6 and 32.1 ± 15.6 $\mu$m. These values are consistent with modular vessel sizes reported earlier for mesentery and omentum.

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. 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 ± 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 (± 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 microvessels.
VOLUMETRIC FLOW RATE DISTRIBUTION

VOLUMETRIC FLOW RATE $\times 10^4$ mm$^3$/sec

ARTERIAL

VENOUS

MESENTERY

$\times \chi$FAIRING

$\times \chi$SD 170

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 $\pm$ 1 SD about the solid line (fairing) of the data.

vessels. The considerable variance of flow rates is illustrated, in addition to the spline fairing, by dashed lines which demarcate $\pm$ 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 $\mu$m in diameter) with a minimum value of $1.66 \pm 0.77$ (SD) $\times 10^{-4}$ mm$^3$/sec. Centerline velocity in this group of vessels was $1.93 \pm 0.96$ (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 $76.6 \pm 11.2$ (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-$\mu$m artery to 19 mm Hg in a 50-$\mu$m vein.

If one compares the pressures in two equal-sized arterioles (e.g., 50 $\mu$m) 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 $\mu$m on the venous side. The vessels immediately contiguous with the capillary network proper range in diameter from 15 $\mu$m on the arterial side to 15-$\mu$m venous vessels and have a mean centerline velocity of $3.52 \pm 4.05$ (SD) mm/sec.

The attendant volumetric flow rates in the omentum are presented in Figure 8 with the minimum flow of $2.64 \pm 1.86 \times 10^{-4}$ mm$^3$/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 $\mu$m and venous vessels with a maximum diameter of 50 $\mu$m.

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

FIGURE 7 Arterial to venous distribution of intravascular pressure and velocity in omentum. The data are presented in a format similar to that shown for mesentery (Fig. 5).
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 modular 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 \( \mu m \) and a tissue density of 1 g/cm\(^3\), 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. Furthermore, the reasonably good linear correlation of modular flow vs. modular area (Fig. 3) for many different animals suggests that the tissue preparation did not suffer from exposure, and both vascular and tissue compartments were in a viable state of equilibrium. It also is pointed out that similar high perfusion rates (750 ml/min per 100 g) have been estimated previously for the rabbit omentum, based upon an average tissue thickness of 50 \( \mu m \) and a tissue density of 1 g/cm\(^3\), 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.  

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 arcing arteriolar vessels (50-150 \( \mu m \)) on the periphery of the module are concerned with adjustments of pressure, whereas the smaller vessels (< 40 \( \mu m \)) 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

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