BLOOD VESSELS IN FAT TISSUE.
RELATION TO PROBLEMS OF GAS EXCHANGE*†

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Plates 8 and 9

Studies on the blood vessels of fat tissue are nearly coextensive with the development of knowledge of the tissue itself. The close topographic and functional relationship of fat to blood vessels is apparent on simple inspection. In areas where fat is selectively deposited and stored, the relationship, while seemingly obscure, clearly exists, especially during development, and is retained throughout life. In embryos, differentiation of sites occupied in adult life by fat consists of a rapid, circumscribed proliferation of mesenchymal cells honeycombed with sinusoid-like blood channels and capillaries. The capillary net appears to become coarser and less prominent as fat cells continue to be differentiated, until in well developed fat sites capillaries seem to be inconspicuous, at least in sections of tissue fixed in conventional ways (1, 2). In accordance with this seemingly suppressed vascularity and the relatively small cytoplasmic volume of fat tissue, it has been assumed that metabolic activity of the tissue is low.

More recent findings tend to conflict with the common view. It is now known that a variety of enzymes exists in fat cells: diastase, lipase, phosphatase, dehydrase, and other respiratory enzymes (3). Moreover, Schoenheimer and his colleagues (4) have revealed metabolic activities in fat tissues of undreamed variety, magnitude, and extent. Finally, there are indications that the capillary bed of well developed fat tissue is more extensive than commonly believed. For example, Occhipinti (5) showed that in injected preparations, the capillaries form "polygonal" meshes having

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† The experiments reported here constitute one aspect of a determined effort by members of the Institute to add to our understanding of the problems of gas exchange in the body with the purpose in mind of removing dangers to aviation and diving personnel and of increasing their efficiency. The experiments were conducted only under adequate anesthesia.

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dimensions of 50 to 60μ. Again, Bini (6) found that the capillary meshes frequently enclosed single fat cells. In lean fat, or in the fat of starved or cachectic animals, including man, the blood vessels are conceded by all workers to be dense (2, 7, 8). It should be emphasized that though virtually all morphologists comment on blood vessels in fat, no reliable quantitative studies have been reported.

The present study was undertaken to clarify our knowledge of the vascularity of fat tissue, primarily because of its importance for an understanding of gas exchanges that take place during compression to high pressure and after decompression.

The uptake (or elimination) curve of an inert gas for a tissue depends on the rate of blood flow, the gas concentration in the arterial blood, the solubility and rate of diffusion of the gas in plasma and other tissue and cell fluids, and the permeability of blood vessels and other barriers through which gas exchange takes place. The last named factor can be estimated when the ratio of the surface of the capillary bed to the volume of tissue supplied by the vessels \( S/V \) is known. There are several advantages of expressing capillary density in this way: (1) The values can be compared with values already published for other tissues. (2) The estimations of \( S/V \) for fat tissue enable approximations to be made of the permeability of the barrier to inert gases. This statement is based on the recent findings of Smith and Morales (9–11) that the product of the solubility of the gas in a tissue, the permeability of the barrier to the gas, and \( S/V \) are an experimentally demonstrable constant. Thus, since the solubilities of the common gases are known, determination of \( S/V \) for a tissue will make possible an approximation of the permeability of the barrier to the gas. As a special case, a more precise knowledge of the capillary bed of fat tissue will contribute to an understanding of the curves of uptake and elimination of excess nitrogen and other gases (12–14). Another special case where \( S/V \) values are applicable consists of observations on the effects of rapid decompression from high pressure atmospheres. It has been shown that only vascular bubbles occur when fat guinea pigs are rapidly decompressed from a pressure of 60 pounds per square inch; when they are decompressed from higher pressures, extravascular bubbles occur also, but only in fat tissue, adrenal cortex, and the myelin sheath of nerve fibers (15, 16). A knowledge of the \( S/V \) ratio of fat tissue thus contributes to the understanding of findings encountered in practical fields involving the exposure of individuals to high pressure and high altitude.

**Methods and Materials**

The \( S/V \) ratio was determined for the inguinal and perirenal fat depots of two groups of rats: (1) lean, fed a minimal, nutritionally adequate diet, and (2) fat, fed the same diet supplemented with lard.

The vascular system was prepared for study in two ways: (1) by very rapid fixation of the fat and its contained blood by freezing and drying the tissue in unaltered animals, and (2) by arterial injection of the whole animal with India ink. The first procedure was designed
to estimate the number and dimensions of capillaries containing red blood cells at the moment of freezing. While these vessels do not necessarily correspond with those through which blood was circulating at the time, they must approximate them closely. The second procedure was designed to determine the total number of capillaries present in the tissue. While one can never be certain that all blood vessels are injected in any one preparation, the values may be regarded as approaching the maximum. Measurements were treated mathematically to yield $S/V$ values. Errors due to shrinkage resulting from the method of preparation were neglected.

The significance of the size and shape of fat cells in the transfer of substances between them and the surrounding tissue fluid is discussed briefly.

**TABLE I**

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Sex</th>
<th>Weight before dieting</th>
<th>Weight 1 mos. later</th>
<th>Weight 4 mos. later</th>
<th>Weight 6 mos. later</th>
<th>Specific gravity</th>
<th>Method employed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>♀</td>
<td>150</td>
<td>239</td>
<td></td>
<td></td>
<td>1.053</td>
<td>Freezing and drying</td>
</tr>
<tr>
<td>2</td>
<td>♂</td>
<td>144</td>
<td>313</td>
<td></td>
<td></td>
<td>1.057</td>
<td>&quot; &quot; &quot;</td>
</tr>
<tr>
<td>3</td>
<td>♀</td>
<td>121</td>
<td>180</td>
<td></td>
<td></td>
<td>1.059</td>
<td>&quot; &quot; &quot;</td>
</tr>
<tr>
<td>4</td>
<td>♂</td>
<td>145</td>
<td>331</td>
<td>370</td>
<td>398</td>
<td></td>
<td>India ink injection</td>
</tr>
<tr>
<td>5</td>
<td>♀</td>
<td>134</td>
<td>254</td>
<td>286</td>
<td>315</td>
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<td>&quot; &quot; &quot;</td>
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<tr>
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<td>154</td>
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<td>371</td>
<td>380</td>
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</tr>
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<td>♂</td>
<td>84</td>
<td>114</td>
<td></td>
<td></td>
<td>1.092</td>
<td>Freezing and drying</td>
</tr>
<tr>
<td>14</td>
<td>♂</td>
<td>140</td>
<td>120</td>
<td></td>
<td></td>
<td>1.092</td>
<td>&quot; &quot; &quot;</td>
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<td>152</td>
<td>138</td>
<td></td>
<td></td>
<td>1.105</td>
<td>&quot; &quot; &quot;</td>
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<td>♂</td>
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<td>146</td>
<td>137</td>
<td></td>
<td>India ink injection</td>
</tr>
<tr>
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<td>147</td>
<td>140</td>
<td></td>
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</tr>
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<td>♂</td>
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<td>113</td>
<td>130</td>
<td>148</td>
<td></td>
<td>&quot; &quot; &quot;</td>
</tr>
</tbody>
</table>

**Preparation of Lean and Fat Rats.**—One group of six rats was fed a restricted quantity of a basic diet, while a second group of six had access to a fat-rich supplement, in addition to the same quantity of the basic diet. The basic diet of both series consisted of 7 to 8 gm. per day of the following mixture:

- Brewers' yeast .................................................. 8 per cent
- Skim milk ...................................................... 25 per cent
- Whole wheat flour ................................................ 67 per cent
- One drop vitamin A concentrate per day.

The supplement consisted of:

- Lard.......................................................... 50 per cent
- Whole wheat flour.............................................. 50 per cent

Table I presents a brief summary of the weights of the animals during the preparatory phase, together with their specific gravity as determined after death. The latter serves as a measure of the degree of fatness of the rats in each series.

**Preparation of Tissues.**—Adipose tissue from the fat and lean groups of rats was prepared in two ways for study: (1) by freezing and drying the tissue, and (2) by injection of India ink (Table I). In the first process the rat's hind limb was extended. On the inguinal
region of one side was placed one end of an oval-shaped copper tube about 3 cm. long and 1 cm. wide, which had been chilled by immersion in liquid air. The tube was immediately filled with isopentane, chilled to \(-150\) to \(-160\) °C, which was allowed to escape by lifting the oval ring slightly, and at the same time replacing the outflow with freshly chilled isopentane. The excess was permitted to flow directly along the dorsum of the animal, thus anesthetizing it. When the inguinal region was frozen the animal was anesthetized and killed. The inguinal tissues were then broken out together with the subjacent muscle, transferred to the drying chamber, and dried at \(-25\) °C. (17). The tissue was then transferred to absolute alcohol at \(-25\) °C, and after 24 hours allowed to warm up to room temperature. Tissues other than the inguinal fat pad were removed, and the fat pad with some supporting tissue was embedded in nitrocellulose and sectioned at 40μ thick serially. The sections were stained lightly with hematoxylin and mounted in clarite.

The second series of animals was killed with illuminating gas and injected with a cannula through the left ventricle under a pressure head of about 6 feet. The ink was allowed to flow through the vascular system and leave by a small opening in the right auricle. When the flow ceased, the animal was immersed in formaldehyde (40 per cent) chilled to about \(+3\) °C.; the inguinal skin was incised, and the anterior abdominal wall cut. After about 2 days, perirenal and inguinal fat pads were removed, dehydrated, embedded in nitrocellulose, and sectioned serially at 30μ. The sections were stained lightly with hematoxylin and mounted in clarite.

Measurement of Capillaries in Sections.—Different methods were used for the sections of frozen-dried tissues and the ink-injected tissues. In the former, camera lucida drawings were made of the endothelium of capillaries containing red blood cells in 15 to 30 fields selected at random from different sections. The surface area of each capillary was measured with a planimeter, as well as the area of the whole field which was drawn. In the latter, the sections were projected on a screen; 7 to 15 fields were selected at random and the capillaries drawn as lines. The drawings were then magnified by projection on a screen with a delineascope and the length of the lines determined with a map measurer. The area of the field was measured with a planimeter.

Calculation of S/V, Frozen-Dried Material.—Since capillaries in fat are distributed in all planes, we may assume that the axes of the capillaries are randomly distributed (Fig. 14). Thus, 50 per cent of them will make angles with the line of sight greater than \(45°\) and 50 per cent will make angles less than \(45°\) C. Accordingly, we may assume that the "typical" capillary has its axis at \(45°\) with the line of sight. The area viewed through the microscope and subject to planimeter measurement is the planar area normal to the line of sight. It is clear from Fig. 14 that this area divided by \(\cos 45°\) (i.e., multiplied by 1.4142) is equal to the planar area through the capillary cylinder. Let this latter area be \(2 π r h \) cm.². Then \(π\) times this area will be the cylindrical surface of the capillary, for \(2 π r h \) is the internal surface of a cylinder whose radius is \(r\) and whose length is \(h\). Thus we see that

\[ 1.4142 \times (\text{True planar area}) \times π = (\text{Cylindrical surface area of capillary}) \]

The true planar area is in turn obtainable from the areas measured on the camera lucida drawings. Evidently

\[ (\text{True planar area}) = \frac{(\text{Area on drawing}) \times (\text{Planimeter constant})}{(\text{Magnification})} \]
Thus, combining our results we have

\[
\frac{1.4142\pi \times (\text{Planimeter constant}) \times (\text{Area of one capillary on the drawing})}{(\text{Total cylindrical area of one capillary}) \times (\text{Magnification})}
\]  

(1)

The total capillary cylindrical surface area is thus obtained from the total planimeter surface area by a simple summation of similar equations. The volume of the tissue supplied by these capillaries is the area of the section multiplied by the depth of the section, minus the volume of the capillaries. The latter quantity may be considered negligible for this purpose, and has been omitted. Thus,

\[
\text{(Volume of tissue)} = (\text{Area of section}) \times (\text{Planimeter constant}) \times (\text{Magnification}) \times (\text{Thickness of section})
\]  

(2)

Putting together (1) and (2), we have

\[
\frac{S}{V} = \frac{1.4142\pi \times (\text{Planimeter constant}) \times (\text{Total area of capillaries on drawing})}{(\text{Volume of tissue}) \times (\text{Thickness of section})}
\]

We may illustrate this by a numerical example.

For animal 1, section 33,

Area of field drawn = 3487 planimeter units
Area of sum of capillaries = 47 planimeter units
Thickness of section 40\(\mu\) = 4 \(\times\) 10\(^{-4}\) cm.

Then

\[
\frac{S}{V} = \frac{47 \times 1.4142\pi \times 10^6}{3487 \times 4} = 14.9 \text{ cm}^{-1}
\]

**India Ink-Injected Material.**—The calculation of \(S/V\) from India ink drawings is a different problem, for these observations give only the total planar length of the cylinder. Accordingly an assumption must be made regarding the average radius of the cylinder. We have taken this quantity as 3\(\mu\) or 3 \(\times\) 10\(^{-4}\) cm. (see p. 225). Now,

\[
\frac{(\text{Cylindrical surface of capillaries})}{(\text{Cylindrical surface of capillaries on drawing})} = \frac{(\text{Planar length of capillaries on drawing}) \times (\text{Linear magnification})}{(\text{Cylindrical surface of capillaries on drawing})} \times (\text{Radius of capillaries})\]

\[
(\cos 45^\circ)
\]
Blood vessels in fat tissue

As before,
\[
\text{Volume of \( \text{section} \)} = \left( \frac{\text{Planimeter area \( \text{of section} \)}}{\text{Constant}} \right) \times \left( \frac{\text{Planimeter \( \text{of section} \)}}{\text{Linear \( \text{magnification} \)}} \right) \times \left( \frac{\text{Thickness \( \text{of section} \)}}{\text{Planimeter \( \text{constant} \)}} \right)
\]

and combining,
\[
\frac{S}{V} = \frac{\left( \frac{\text{Planar \( \text{length of capillaries} \)}}{\text{Planimeter \( \text{area of section} \)}} \right) \times \left( \frac{\text{Linear \( \text{magnification} \)}}{\text{Planimeter \( \text{constant} \)}} \right) \times 2\pi \times 1.4142 \times \left( \frac{\text{Radius \( \text{of capillary} \)}}{\text{Planimeter \( \text{area \( \text{of section} \)}} \right) \times \left( \frac{\text{Thickness \( \text{of section} \)}}{\text{Planimeter \( \text{constant} \)}} \right)}{\text{Planimeter \( \text{constant} \)}}
\]

Again, we may illustrate numerically.
For animal 22, section 44,
- Planar length of capillaries = 973 cm.
- Planimeter area of section = 2524 planimeter units.
- Planimeter constant = 0.1289 cm. -1 (planimeter units) -1.
- Thickness of section = 3 \times 10^{-4} cm.

\[
\frac{\text{Planar \( \text{length of capillaries} \)}}{\text{Planimeter \( \text{area \( \text{of section} \)}} \right) \times \left( \frac{\text{Linear \( \text{magnification} \)}}{\text{Planimeter \( \text{constant} \)}} \right) \times 2\pi \times 1.4142 \times \left( \frac{\text{Radius \( \text{of capillary} \)}}{\text{Planimeter \( \text{area \( \text{of section} \)}} \right) \times \left( \frac{\text{Thickness \( \text{of section} \)}}{\text{Planimeter \( \text{constant} \)}} \right) = 138.0 \text{ cm.}^{-1}
\]

Fat cells (Fig. 15).—For a prolate spheroid whose semimajor axis is \( a \) cm. and whose semiminor axis is \( b \) cm., the ratio of surface area to volume is,
\[
\frac{S}{V} = \frac{2\pi \left( \frac{a^3}{3} + \frac{ab \sin^{-1} E}{E} \right)}{4\pi \frac{ab^2}{E}} = 1.5 \left( \frac{1}{a} + \frac{1}{b} - \frac{\sin^{-1} E}{E} \right) \text{ cm.}^{-1}
\]

where \( E \) is the eccentricity of the ellipsoid, defined as
\[
E = \frac{a^3 - b^3}{a^3}
\]

\( E \) may be taken as the best single measure of the shape of the ellipsoid (as abstracted from its volume). To illustrate, for rat 2 we obtain the following information:

\[
\begin{align*}
a &= 4.7 \text{ cm. on drawing} \\
b &= 1.5 \text{ cm. on drawing}
\end{align*}
\]

* For convenience of drawing, a two-step magnification was necessary. Thus, in the numerical examples, this factor is not the square root of the magnification used in determining \( V \).

† \( \sin^{-1} E \), "the angle whose sine is \( E \)," must be expressed in radians. \( 1^\circ \) is equivalent to \( \pi/180^\circ \) radians.
Magnification = 63 mm. apparent is equivalent to 0.1 mm. true. Substituting into (2)
we see that

\[ E = \frac{21.2 - 2.25}{21.2} = 0.895 \]  (4)

Putting (3) and (4) into (1),

\[ S = \frac{1.5}{1.587 \times 10^{-3}} \left( \frac{1}{4.7} + \frac{1}{1.5 \times 0.895} \right) = 953 \text{ cm}^{-1} \]  (5)

RESULTS

The capillaries of the fat depots of the rat, unlike those in muscle and nerve,
show no particular orientation, but form loose meshes which run in all direc-
tions in the reticular connective tissue that encloses the fat cells. It is doubtful
if many fat cells escape close contact with at least one capillary (Figs. 1–9)
(5, 6, 18). The capillary density increases as the fat cells become smaller;
in other words, the capillary meshes are of smaller caliber when the fat cells
are smaller. There is always considerable variation from region to region in
the number of capillaries. (Compare for example, Figs. 5 and 8, Figs. 2 and
4, as well as Figs. 6 and 9.) This has been expressed as surface area of capil-
laries in Text-fig. 1. There seems to be no significant difference in capillary
density in the fat depots in the same animal; for example, capillary surface
area estimations in different parts of the inguinal fat depot show as great a
variation over the same range as may occur in different regions of the lateral
perirenal fat. In the perirenal fat of the rat, a greater capillary density of the
brown fat along the mid-line is found as compared with that in the more
laterally disposed fat (8). This is illustrated in Fig. 3, where the richer capil-
lary supply appears at the right and in the lower portion of the figure.

The same generalizations apply also when one considers only that fraction
of the total capillary bed which is open during ordinary activity. This is
illustrated in Figs. 10 to 13, which show camera lucida drawings of fields of
inguinal fat prepared by freezing and drying. They were reduced to the same
magnification as the photomicrographs for easy comparison. This has also
been expressed as surface area of open capillaries in Text-fig. 2.

The mean diameter of capillaries in adipose tissue fixed by freezing and
drying is 6μ (fat-rich) and 7μ (fat-poor). The tendency toward reduction
in capillary diameter during differentiation and development has been noted
by all investigators. It is also said to take place in inanition. These dimen-
sions are greater than those estimated from ink-injected tissue (about 4μ).

The ratio of the total surface of capillaries to the total volume of fat tissue
was estimated from ink-injected preparations (Text-fig. 1). The S/V values
are significant in experimental work on gas exchanges such as take place in
diving operations. In such work, it is assumed that the volume of the tissue
**Text-Fig. 1.** Ratio of the total surface of capillaries (open and closed) to the volume of fat tissue in the fat depots of lean and fat rats. The ratio $S/V$ as calculated for different fields varies greatly from place to place in each animal (lower) and in different animals. Yet it is evident from the chart summarizing the individual animal measurements, that the surface of capillaries is much smaller in fat of fat-rich regions ($\text{mean } S/V = 51.9$) than that of fat tissue of lean animals ($\text{mean } S/V = 222.2$). These generalizations apply to the total capillary supply of the tissue, since they are based on ink-injected preparations in which the maximal number of open and closed capillaries were rendered visible.
**Text-Fig. 2.** Ratio of the surface of open capillaries to the volume of adipose tissue of inguinal fat depots of lean and fat rats. The variability from field to field in the same animals and in different animals is as marked as for total capillary surface of open and closed vessels (lower). The upper portion shows that the surface of open capillaries is much smaller in fat-rich tissue (mean $S/V = 23.5$) than in fat-poor tissue (mean $S/V = 64.1$). A comparison of these results presented in Text-fig. 1 shows that in ordinary activity about one-half (in fat-rich tissue) to one-third (in fat-poor tissue) of the total capillaries are open, and contain circulating blood.
corresponds to the total volume of the fat inclusions, since the volume of protoplasm is relatively small and may be neglected. In well developed fat tissue $S/V$ is small (mean = 51.9) and shows a small range of variability in different fields. In poorly developed (or potential) fat depots, $S/V$ is great (mean = 222.2) and shows a greater range of variability in different regions. There is a slight overlap in the $S/V$ values in the two groups.

The study of material prepared by freezing and drying makes possible an estimate of the surface of open capillaries which presumably contained circulating blood. In well-developed fat tissue, the mean $S/V$ is 23.5, while in lean fat tissue, it is 64.1. This is reflected in the gross color differences of the two kinds of tissue in the rat; when fresh the former is yellow-white, the latter is orange-red. The surface area of capillaries per unit volume of fat during ordinary activity is about one-half (in fat-rich depots) to one-fourth (in fat-poor or potential depots) of the total possible surface available for exchange of gas, electrolyte, fluid, etc. The same general ratio of open to closed capillaries also is found in muscle (18).

The ratio of the surface of capillaries of fat tissue to the volume of tissue can be compared with similar values obtained for muscle by calculations made from certain data in the literature (19). Such comparisons are important in studies on gas exchange in the body. Assuming an average capillary diameter of $d$, $S/V$ for muscle can be given as follows: for total capillary surface, $S/V = 190-513$ for rabbit muscle (20), 150 and 295 for rabbit musculus semitendinosus and musculus adductor magnus (21), and 494 for dog muscle (19); for open capillaries $S/V = 186-254$ and 304-507 for the gastrocnemius and masseter muscles of the guinea pig, and 486-640 and 726-923 for the same muscles of the mouse (18). Thus, the total capillary bed of fat-rich adipose tissue is about one-third that of the most poorly supplied muscles, while that of fat-poor tissue has about the same capillary density as the most poorly supplied muscle in the examples given above. The surface of capillaries expected to function in ordinary activity, is one-half to one-third of the relative values. This comparison points up the "inadequacy" of the capillary bed of fat for the transfer of inert gases. It becomes more significant in view of the fivefold greater solubility of nitrogen in fat than in plasma. This estimate is subject to correction, when and if it is shown that gas permeability of capillaries, rate of blood flow, etc., are different from that in other tissues. It is not surprising then to find that in guinea pigs rapidly decompressed from high pressure atmospheres the capillaries of the fat are so inadequate to carry away the gas as to result in extravascular gas bubbles, and that a greater number are distended with gas than in any other tissue. This capillary inadequacy probably explains in part why, in certain stages of decompression unaccompanied by extravascular bubbles, many more intravascular bubbles are present in fat tissue than in muscles (15). The quantitative estimation of
the capillary inadequacy of fat tissue justifies the assumption made by physiologists who have studied the effects of diving operations (22) that the capillary circulation in fat is poor.

The relations of the surface area of capillaries are pertinent to the exchange of gas between capillary and fat cell, but are misleading when applied to the transfer of metabolites or other substances such as water or salts which are confined largely or entirely to the protoplasm. For this purpose the relationship between the surface of capillaries and the volume of protoplasm (of fat cells) is applicable and may be calculated in the following way (Fig. 15):

\[ \frac{\text{Volume of cell}}{\text{Volume of shell}} = \frac{1}{1 - \alpha^a} \]

where \( a \) = mean semimajor axis, \( b \) = mean semiminor axis, and \( t \) = thickness of the protoplasmic shell of fat cells. The values for \( a \) (47\( \mu \)) and \( b \) (28\( \mu \)), were determined from a number of cells selected at random from fat tissue fixed by freezing and drying. The value for \( t \) (0.25\( \mu \)), was estimated from the same material.

It appears from the formula

\[
\frac{\text{Volume of cell}}{\text{Volume of shell}} = \frac{1}{1 - \alpha^a}
\]

that the protoplasm occupies 2.4 per cent of the total volume of the fat cell. Stated in another way, the volume of the cell is 41.6 times the volume of the protoplasm. This means that \( S/V \) for the protoplasm of fat cells of fat-rich tissue is 41.6 times greater than \( S/V \) of fat tissue as a whole. Thus, for metabolic studies of fat-rich tissue a relationship of capillary surface to volume of protoplasm of fat cells is an \( S/V \) value of 2159.0 (51.9 \times 41.6) for the total available capillaries, and 977.6 (23.5 \times 41.6) for the capillaries open at any one time. The \( S/V \) ratio for the protoplasm of the fat tissue of lean animals is not increased proportionately, because of the relatively larger volume of protoplasm contained in the fat cells (Text-fig. 3). The values are greater than those for muscle, the tissue most richly supplied with capillaries. It is obvious, then, that for metabolic purposes fat tissue is well supplied with capillaries. This can be correlated with the great variety of activities known to take place in fat tissue.

A similar reconsideration of the oxygen consumption of fat tissue can be made, based on the apparently low values reported (23) (approximately 0.07 c.mm. per mg. fat tissue wet weight per hour). Fat-rich fat tissue with fat cells having the same mean semimajor axes given above would have an oxygen consumption that can be calculated as follows:

\[
Q_{O_2} \text{ protoplasm} = \frac{\text{Volume of fat cell}}{\text{Volume of protoplasmic shell}} \times Q_{O_2} \text{ measured}
\]

\[
Q_{O_2} \text{ protoplasm} = 41.6 \times 0.07 = 2.9 \text{ c. mm. per hour per mg. wet weight}
\]
This tissue correction compares favorably with oxygen consumption values of muscle.

An important consideration is the rôle played by the shape and size of the fat cell in the exchange of substances (gaseous, fluid, or crystalloid) between it and the tissue fluid. Transfer of substances across the cell barrier is effected more rapidly in proportion as the surface of the cell is increased with respect to its volume. The efficiency of transfer must therefore be related to the ratio of surface to volume; as might be expected from its shape, the ratio is high. It is greater for the smaller fat cells of fat-poor tissue (mean $S/V = 2043.2$) than for the larger fat cells of fat-rich tissue (mean $S/V = 1250.9$). It is obvious, also, that the transfer of substances from the cell membrane to the fat inclusion through cytoplasm is slower in a smaller fat cell than a larger one, assuming the rate of movement through cytoplasm to be the same in both cases.

Presumably the general relations of capillaries to fat cells in rats can be extended to man. If so, they might then be used to derive estimates of permeability to inert gases of blood-tissue barriers, and to explain the origin of gas bubbles in divers decompressed too rapidly from high pressure atmospheres. The general concept of $S/V$ (protoplasm) of fat tissues in the rat is important also in clarifying the mechanisms involved in rapid loss or gain of weight in man through changes in fat depots. Finally, comparison of $S/V$ ratios of fat and muscle tissues may be useful in considerations of the effect of excess adiposity on the cardiac load.
SUMMARY AND CONCLUSIONS

1. The ratio of the surface of the capillary bed to the volume of tissue supplied by the vessels (S/V ratio) for both open and closed capillaries in fat-rich tissue of the rat is 51.9, in fat-poor tissue of the same sort 222.2. About one-half of the capillaries in fat-rich tissue, to one-fourth in fat-poor tissue, are open during ordinary activity. The total capillary bed of fat-rich tissue is one-third as great as in muscle; the total capillary bed of fat-poor tissue has about the same density as that of the most poorly supplied muscle. This establishes the fact quantitatively that the capillary bed of fat is relatively inadequate, compared to other tissues, for transferring inert gases from fat tissue at a sufficiently rapid rate to prevent the occurrence of extravascular bubbles following rapid decompression from high pressure atmospheres. It also explains the greater distention of the blood vessels in fat tissue, due to gas, than in any other tissue following decompression. The observations have a bearing also on the estimation of the permeability of the blood-fat barrier to inert gases.

2. The volume of protoplasm of fat cells may be very small; a method is presented for estimating it quantitatively. Since it alone is important in metabolism, recalculation of the basic data on a basis of the ratio of surface area of capillaries to volume of protoplasm of fat cell in fat tissue yields a more useful figure. For fat-rich fat tissue S/V (protoplasm) = 2159.0 (for total capillary surface) or 977.6 (for open capillary surface). This means that for purpose of metabolism, the capillary bed is far richer than that of muscle.

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**EXPLANATION OF PLATES**

**PLATE 8**

Photomicrographs of sections of fat depots of rats perfused with India ink. Sections 30μ thick, stained lightly with hematoxylin. They are selected from various animals to show the inverse relationship of capillary density and the size of the fat cell. Magnification × 61. A quantitative measure of the mean capillary density of the whole fat depot is the ratio of the surface area of the capillaries to the volume of the tissue (*S/V*). These values are given with each figure.

**Fig. 1.** Rat 12 (fat), inguinal fat, mean *S/V* = 51.8.

**Fig. 2.** Rat 5 (fat), inguinal fat, mean *S/V* = 66.3.

**Fig. 3.** Rat 5 (fat), perirenal fat, mean *S/V* = 66.3.

**Fig. 4.** Rat 5 (fat), inguinal fat, mean *S/V* = 66.3.

**Fig. 5.** Rat 21 (lean), inguinal fat, mean *S/V* = 256.6.

**Fig. 6.** Rat 22 (lean), inguinal fat, mean *S/V* = 284.3.
(Gersh and Still: Blood vessels in fat tissue)
FIGS. 7 to 9 prepared and described as in Figs. 1 to 6.

Fig. 7. Rat 23 (lean), inguinal fat, mean $S/V = 180.0$.

Fig. 8. Rat 21 (lean), inguinal fat, mean $S/V = 256.6$.

Fig. 9. Rat 22 (lean), perirenal fat, mean $S/V = 284.3$.

Figs. 10 to 13. Camera lucida drawings reduced to $\times 61$ for comparison with photomicrographs. The inguinal fat depot was frozen with isopentane and dried in a vacuum at $-25^\circ$ C. From the drawings of different fields selected at random, measurements were made that make possible an estimate of the ratio of the surface area of open capillaries to the volume of the tissue ($S/V$). The mean values are given for each animal, as well as the lowest and highest individual field and some intermediate ones.

Fig. 10. Rat 2 (fat), mean $S/V = 27.4$.

$S/V_a = 14.0, S/V_b = 20.7, S/V_c = 28.9, S/V_d = 37.3, S/V_e = 63.5$

Fig. 11. Rat 3 (fat), mean $S/V = 28.5$.

$S/V_a = 10.9, S/V_b = 26.6, S/V_c = 33.8, S/V_d = 38.8, S/V_e = 90.1$

Fig. 12. Rat 13 (lean), mean $S/V = 64.1$.

$S/V_a = 38.3, S/V_b = 50.0, S/V_c = 72.8, S/V_d = 83.5, S/V_e = 134.6$

Fig. 13. Rat 15 (lean), mean $S/V = 66.1$.

$S/V_a = 12.8, S/V_b = 34.2, S/V_c = 60.7, S/V_d = 138.5, S/V_e = 202.5$

Fig. 14. Diagram used to illustrate method of calculation of ratio of surface of capillaries to volume of tissue (see p. 222).

Fig. 15. Diagram used to illustrate method of calculation of ratio of surface of fat cell to volume of the cell (see p. 224).