DEDUCTION OF PULMONARY MICROVASCULAR
HEMATOCRIT FROM INDICATOR DILUTION CURVES

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We have developed a new model describing the relationship between plasma and red cell tracers
flowing through the lung. The model is the result of an analysis of the transport of radiolabeled
plasma albumin between two flowing phases and shows that differences between red cell and
plasma tracer curves are related to microvascular hematocrit. The model was tested in an
isolated, blood-perfused dog lung preparation in which we injected $^{51}$Cr-labeled red cells and
$^{125}$I-labeled plasma albumin into the pulmonary artery. From the tracer concentration-time
curves at the venous outflow, we calculated $h_r$, the ratio of microvascular hematocrit to
large-vessel hematocrit. In 18 baseline experiments, $h_r = 0.92 \pm 0.01$ (mean \pm sem) at a blood flow
rate of $10.7 \pm 0.3$ ml s$^{-1}$. We determined the effects of (a) glass bead embolization, (b) alloxan,
and (c) lobe ligation on $h_r$. Embolization attenuated the separation between plasma and red cells
(increased $h_r$), probably as a consequence of passive vasodilation. Alloxan enhanced separation
of plasma and red cells (decreased $h_r$), possibly as a result of arteriolar vasoconstriction.
Ligation of a fraction of the perfused tissue at constant flow did not cause significant change in $h_r$ in the
remaining perfused tissue. The model assumes that large-vessel transit times are uniform and
that all dispersion occurs in the microvasculature. A theoretical analysis apportioning dispersion
between large and small vessels disclosed that the error associated with these assumptions is
likely to be less than 15\% of the measured $h_r$. We conclude from this study that the microvascular
hematocrit model describes experimental plasma and red cell curves. The results imply that $h_r$
can be readily deduced from tagged red cells and plasma and can be accounted for in calculating
permeability-surface area in diffusing tracer experiments.

1. Introduction. For reasons not thoroughly understood, hematocrit is
usually lower in the microvasculature than in large vessels (Gaehtgens, 1980;
Duling and Desjardins, 1987; Pries and Gaehtgens, 1989). Pries and
Gaehtgens (1989) identify two categories of phenomena that can lead to
hematocrit reduction. The first category is comprised of those phenomena
associated with the inherent heterogeneity of the suspension of red cells in
plasma. For example, red cells are thought to be excluded from a relatively
stationary plasma cuff near the wall and to concentrate in the central, fast-
moving portion of the flow—the "vessel Fahraeus effect" (Cokelet, 1974;
Effros, 1984). Partial blockage or acceleration of erythrocytes at the capillary
entrance may also affect their transit time. The second source of hematocrit
reduction is the architectural heterogeneity of the vascular network itself (Pries
and Gaehgens, 1989), such that path lengths, velocities and red-cell and plasma transit times may vary throughout the microvascular bed, leading to an overall tissue hematocrit which will in general be different from the large-vessel hematocrit.

There have been a number of approaches to the measurement of the ratio of microvascular hematocrit to large-vessel hematocrit, a ratio we will call \( h_r \); the results of some of these are shown in Table 1. Capen et al. (1987) categorized the methods as "direct" and "indirect". The direct methods involve viewing individual capillaries using such techniques as photomicroscopy and epillumination or trans-illumination video-microscopy. There are several indirect methods. Hogg et al. (1985) used a combination of post-mortem morphometry and indicator dilution methods to quantify red cell transit times and microvascular hematocrit in various sections of the dog lung. Parker et al. (1984) estimated small vessel hematocrit by measuring labeled albumin and red cell volumes within tissue samples. Lee et al. (1985) used a blood densitometric approach in which one raises perfusion pressure to a lung lobe and observes the transient increase in the density of venous blood; the density transient is then converted into a corresponding change in hematocrit. In the multiple indicator dilution technique, labeled tracers (usually tagged plasma and red cells) are injected into an organ, and the transit times are calculated from the output concentration profile of the tracers. Brigham et al. (1975) used this method to demonstrate that variations between red cell and albumin flow through sheep lungs could be explained by the Fahraeus–Lindqvist effect.

We applied a new theoretical approach to indicator dilution methodology in

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Organ</th>
<th>( h_r )</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gibson et al. (1946)</td>
<td>Dog lung</td>
<td>0.83</td>
<td>Cell counting</td>
</tr>
<tr>
<td></td>
<td>Dog spleen</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dog muscle</td>
<td>0.48</td>
<td></td>
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<tr>
<td>Lipowsky et al. (1980)</td>
<td>Cat mesentery</td>
<td>0.21</td>
<td>Micro-occlusion</td>
</tr>
<tr>
<td>Sarelius and Duling (1982)</td>
<td>Hamster cheek pouch</td>
<td>0.30</td>
<td>Transillumination Videomicroscopy</td>
</tr>
<tr>
<td>Pries and Gaehgens (1989)</td>
<td>Cat mesentery</td>
<td>0.30</td>
<td>Videomicroscopy</td>
</tr>
<tr>
<td>Lee et al. (1985)</td>
<td>Isolated dog lung</td>
<td>0.80</td>
<td>Densitometry</td>
</tr>
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<td>Parker et al. (1984)</td>
<td><em>In vivo</em> dog lung</td>
<td>0.92</td>
<td>Tracer cell counting</td>
</tr>
<tr>
<td>Hogg et al. (1988)</td>
<td>Dog lung</td>
<td>0.95</td>
<td>Morphometry</td>
</tr>
</tbody>
</table>

\( h_r = \frac{H_{mv}}{H_v} \) = ratio of microvascular to large vessel hematocrit.