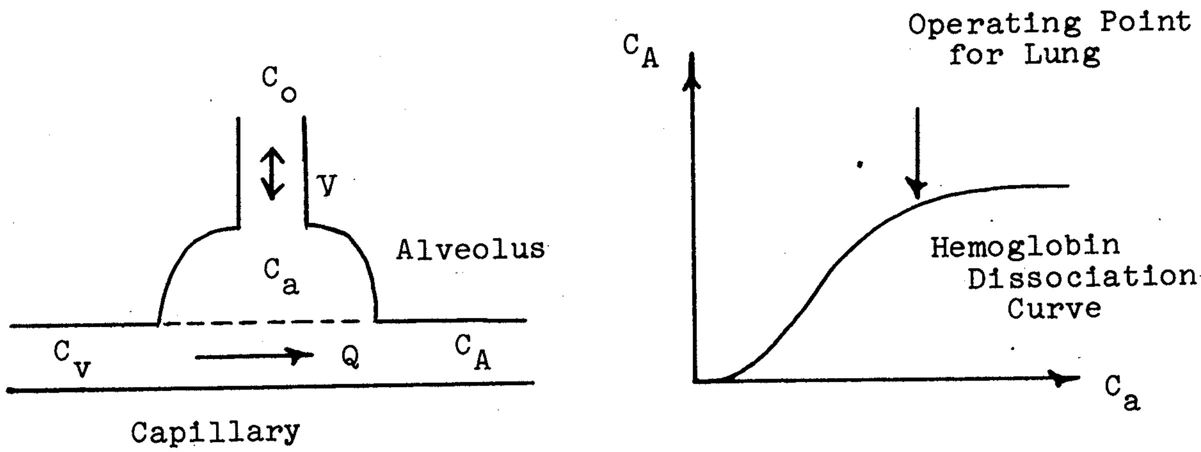
IV. Heart-Lung Interactions*

Ventilation/Perfusion Ratio



$$V_i(C_o - C_a^i) = Q_i(C_A^i - C_v) \qquad C_A^i = f(C_a^i)$$

(Steady-State).

i = index of alveolar unit

C = concentration of oxygen

C_o = atmospheric

C_a = alveolar

C_v = systemic veins (and hence pulmonary artery)

C_A = systemic arteries (and hence pulmonary veins)

V = alveolar ventilation

Q = blood flow.

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* J.B. West, Ventilation/Blood Flow and Gas Exchange, Oxford, Blackwell Publications, Ltd. 1965.

Remark: The hemoglobin dissociation curve is usually given as % saturation as a function of partial pressure of oxygen. At constant hemoglobin concentration, however, % saturation is proportional to the concentration of oxygen C_A. Similarly, at constant temperature in the alveolus the partial pressure of oxygen is proportional to the concentration of oxygen C_a. For the purposes of the discussion to follow here, we do not need the exact form of the hemoglobin dissociation curve, but only the fact that the arterial concentration is a function of the alveolar concentration of oxygen. The latter is true if equilibrium is attained during the passage of the blood through the alveolar capillaries.

The pair of equations:

$$\left.\begin{aligned} V_i(C_o-C_a^{\,i}) &= Q_i(C_A^{\,i}-C_v) \\ C_A^{\,i} &= f(C_a^{\,i}) \end{aligned}\right\}$$

determines $C_A^{\,i}$ and $C_a^{\,i}$ as a function of $r_i = \frac{Q_i}{V_i}$ (with C_o, C_v as parameters). To make this dependence explicit we write $C_A^{\,i} = g(r_i)$.

The ratio r_i of blood flow to air flow may differ in the different parts of the lung. As a design criterion one could seek to maximize the rate of oxygen extraction

$$E = \sum_i Q_i(C_A^{\,i} - C_v)$$

subject to V_i given (not necessarily equal for different i) and subject to the constraint

$$\sum_i Q_i = Q \quad .$$

Taking 1^{st} order variations we find

$$0 = \sum \delta Q_i (C_A^{\,i} - C_V) + Q_i \delta C_A^{\,i}$$

But

$$\delta C_A^{\,i} = g' \delta r_i = g' \frac{\delta Q_i}{V_i}$$

$$Q_i \; \delta C_A^{\,i} = r_i g' \; \delta Q_i \quad .$$

It follows that

$$0 = \sum_i \delta Q_i (g(r_i) + r_i g'(r_i) - C_V) \quad .$$

This must hold for arbitrary δQ_i consistent with

$$0 = \sum_i \delta Q_i \quad ,$$

which will be true if and only if the coefficient of δQ_i is independent of i. That is:

$$g(r_i) + r_i g'(r_i) - C_V \quad \text{independent of } i$$

or

$$r_i = r \quad \text{independent of } i$$

Thus the optimal choice of Q_i has the form

$$\boxed{Q_i = rV_i}$$

One can show that the foregoing solution yields an absolute maximum in the following way: Note that the problem has the form

$$E = \sum_i V_i h(r_i)$$

$$\sum_i V_i r_i = Q \text{ , constant.} \qquad V_i > 0$$

Let r_o satisfy $\sum_i V_i r_o = Q$ and let $E_o = \sum_i V_i h(r_o)$.

Then

$$E-E_o = \sum_i V_i[h(r_i)-h(r_o)]$$

$$= \sum_i V_i\{h'(r_o)(r_i-r_o) + \tfrac{1}{2} h''(r_i^*)(r_i-r_o)^2\}$$

$$\text{where } r_i^* \in [r_i, r_o]$$

But

$$\sum_i V_i(r_i-r_o) = 0 \quad .$$

Therefore one need only show that $h'' < 0$ everywhere. But $h = C_o-C_a$, since the oxygen extraction in each alveolus is $V_i(C_o-C_a^i)$. Therefore $h'' = -C_a''$ and we want to show that $C_a'' > 0$.

Dropping the index i the pair of equations which determines C_a is

$$(C_o-C_a) = r(C_A-C_V)$$

$$C_A = f(C_a) \quad .$$

Differentiate with respect to r

$$-C_a' = (C_A-C_V) + rC_A'$$

$$= C_A-C_V + rf'C_a'$$

$$C_a'(1 + rf') = -(C_A - C_V) .$$

Therefore $C_a' < 0$ since $C_A > C_V$. Differentiating again:

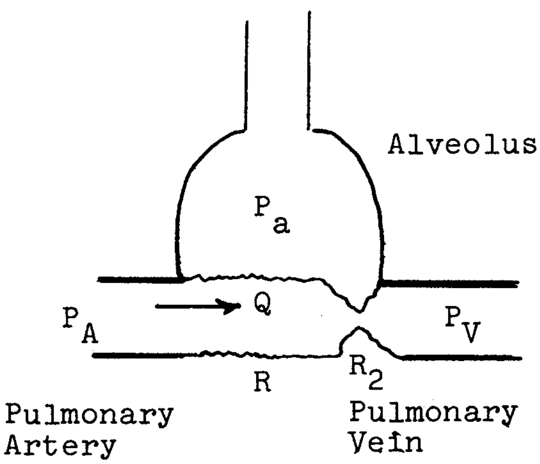
$$C_a''(1 + rf') + C_a'(rf''C_a' + f') = -C_A' = -f'C_a'$$

or

$$C_a''(1 + rf') = -C_a'(2f' + rf''C_a')$$

In the region where $f'' < 0$ (which is certainly true in the lung), we have $C_a'' > 0$ as required. This completes the proof.

Mechanical Influences on the Distribution of Ventilation and Perfusion *



In a collapsible but inextensible tube with end pressure P_A, P_V and side pressure P_a, three separate flow regimes may be distinguished. In the following assume that $P_V < P_A$.

I. $P_A < P_a \rightarrow$ Collapse of the tube $Q = 0$

II. $P_V < P_a < P_A \rightarrow$ Partial Collapse (at end of tube)

$$P_A - P_a = RQ$$

($P_a - P_V = R_2 Q \rightarrow P_A - P_V = (R + R_2)Q$, but R_2 depends on flow)

III. $P_a < P_v \rightarrow$ Tube open $(P_A - P_V) = RQ$

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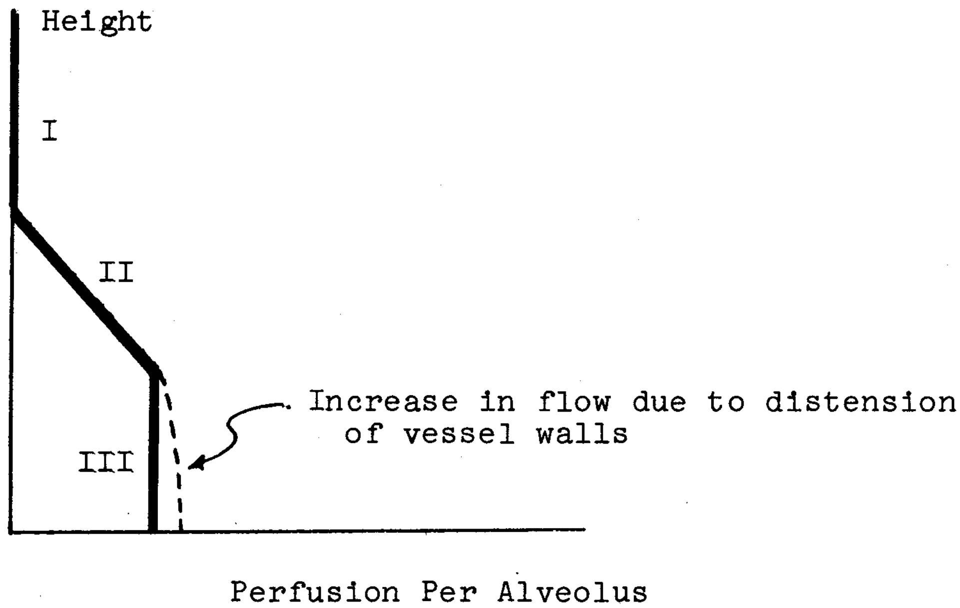
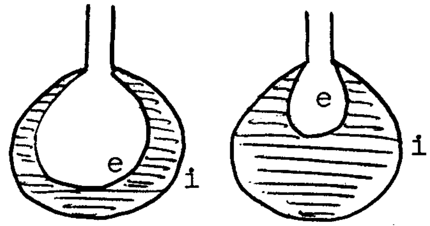
* West (cited above), also see
S. Rubinow, Mathematical Methods in the Biological Sciences, (SIAM).

In the lung of a person who is standing, hydrostatic effects lead to the conclusion that P_A and P_V decrease linearly with height, while P_a is constant because of the negligeable density of the air. Consequently all three regimes occur and the distribution of perfusion with height looks like this:



Ventilation also increases going down the lung because in the lung at maximal expiration the alveoli near the bottom are more collapsed probably because of the weight of the lung. Then at maximal inspiration the alveoli all stretched maximally and are roughly equal in volume. The <u>change</u> in volume is greater lower down, and this determines the ventilation.



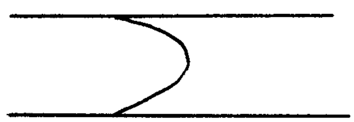
Top Bottom

i = inspiration

e = expiration

Shear Stress and Pulmonary Vascular Diameter*

For steady flow in cylindrical tubes of radius a



$$u = u_o\left(1 - \frac{r^2}{a^2}\right)$$

$$Q = 2\pi \int_0^a r u_o\left(1 - \frac{r^2}{a^2}\right) dr$$

$$= \frac{\pi}{2} a^2 u_o$$

Shear stress at the wall is given by

$$\sigma = -\eta \frac{\partial u}{\partial r}\bigg|_a = \frac{2\eta u_o}{a}$$

$$\frac{\sigma}{Q} = \frac{4\eta}{\pi a^3}$$

Now suppose that in a system of symmetrically branching tubes

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* P. Grassman, "Chemical Engineering and Medicine" The Chemical Engineer, June 1969 CE233-240.

$$\sigma = \text{constant}$$

and

$$Q_{k+1} = \frac{1}{2} Q_k$$

where k is an index giving generation number. Then

$$a_{k+1}^3 = \frac{1}{2} a_k^3$$

$$a_{k+1} = 2^{-1/3} a_k$$

and this branching law is observed in the pulmonary arterial tree.

Functional explanations:

(i) Let

P_k = pressure drop across k^{th} generation of vessels

$N_k = 2^k$ = number of vessels in the k^{th} generation.

L_k = length of vessels in the k^{th} generation.

Assume that $L_k \sim a_k$. Then

$$P_k \sim \frac{N_k^{-1} L_k}{a_k^4} \sim 2^{-k} a_k^{-3} \quad .$$

The total pressure drop P is given by

$$P = \sum P_k \sim \sum_k \frac{1}{2^k a_k^3}$$

The volume occupied by the aggregate of vessels in the k^{th} generation is $\sim a_k^3 2^k$ since $L_k \sim a_k$ so we might pose the problem.

$$\text{Minimize } \sum_k \frac{1}{2^k a_k^3}$$

subject to the constraint

$$\sum_k 2^k a_k^3 = \text{constant}$$

or, equivalently,

$$\text{minimize } \sum \frac{1}{x_k} \text{ subject to } \sum x_k = \text{constant.}$$

The solution is obviously to make x_k independent of k, that is,

$$a_k^3 \sim 2^{-k} \rightarrow \frac{a_{k+1}}{a_k} = \frac{1}{\sqrt[3]{2}}$$

as before.

(ii) Regulation of size of vessels using wall stress σ as a stimulus. In a vessel with given flow, holding $\sigma = \sigma_o$ amounts to setting

$$a^3 = \frac{4\eta Q}{\pi\sigma_o}$$

Thus the vessel radius is regulated according to flow. One can even imagine a simple control system like $\frac{da}{dt} = k(\sigma-\sigma_o)$. Then since $\sigma = \frac{4\eta Q}{\pi a^3}$ we get stable equilibrium when a, Q are related as above.

The time scale of the foregoing is very slow, since a growth phenomenon is involved. Two examples which would be qualitatively explained by the existence of such a control mechanism are:

Increased diameter of pulmonary arteries in cases of left-to-right shunt with large pulmonary flow.

Development (actually enlargement) of collateral circulations when a main vessel is obstructed, e.g. coarctation of the aorta.

Regulation of Blood Flow to Individual Alveolar Units

Constriction of small arteries leading to the pulmonary capillaries appears to occur in response to

(i) low oxygen - to maintain ventilation/perfusion ratio

(ii) high pulmonary venous pressure, e.g. from initial stenosis or from left heart failure - to protect against fluid being pressed out of pulmonary capillaries into air spaces of the lung.