# DETERMINATION OF DIFFUSING CAPACITY OF CARDIAC CAPILLARIES IN DOGS BY A DOUBLE INDICATOR METHOD

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An urgent task in the investigation of the microcirculation is the study of the exchange function of the capillaries by a method based on the ability of the capillary wall to allow various substances to pass through it. The rate of outflow of low-molecular-weight water-soluble substances is determined by the permeability of the capillary wall and the surface area of the capillary bed accessible for diffusion of these substances from the blood into the tissue, i.e., the number of perfused capillaries. To assess these parameters in different organs and tissues, a diffusion indicator method has been developed [1-4].

The use of this method for quantitative evaluation of the functional state of the terminal vascular system of the heart in a dog with intact circulation and a closed chest is examined in this paper.

The method is based on injection of a mixture of two (or more) indicators in known initial concentrations into the vascular system of the heart. The mixture includes a test indicator capable of diffusing through the capillary wall ($^{3}H$-glucose, $^{24}Na$, $^{42}K$, or $^{86}Rb$, for example) and a relative or nondiffusing indicator (T-1824, Evans' blue, $^{131}I$-albumin), which is used to calculate the dilution of the test label in the blood stream (F). Changes in the concentration of the indicators in the venous outflow from the heart are recorded. Changes in concentration of the indicators after simultaneous injection of a mixture are illustrated in Fig. 1. As a result of diffusion of the test substance from the blood into the tissue its concentration curve does not coincide with that of the relative indicator.

The rate of diffusion of the indicator depends on the permeability of the capillaries (P), the surface area of perfused capillaries (S), and the blood flow. The product of the permeability index and the area of capillary surface (P•S) characterizes the possibilities for exchange of materials between blood and tissue in the capillary bed under the given conditions. In other words, the index PS is an integrative index of the diffusing capacity system, which determines the functional state of the microcirculation of the organ under investigation.

The course of the arguments during deduction of an equation for calculating the index is illustrated in Fig. 2. Arterial blood with test indicator in a concentration of $C_a$ enters the capillary, venous blood with concentration $C_b$ leaves the capillary, and the arteriovenous difference ($C_a - C_b$) is created by diffusion of the indicator along the whole length of the capillary. Let $\Delta_x$ represent an infinitely thin transverse section through the capillary. If the diffusion indicator enters the infinitely thin section with the blood in a concentration of $C_x$, the total quantity of indicator entering the section per unit time will be $F \cdot C_x$. From the section indicator is either carried away by the blood in an amount equal to $F \cdot C(x + \Delta x)$ or it diffuses through the wall of the section in an amount determined by Fick's first law:

$$\frac{dm}{dt} = -DS\frac{C_x - C_{inter}}{\Delta l}, \quad (1)$$

where dm/dt is the quantity of substance diffusing in unit time; D the coefficient of diffusion; S the surface area of the capillary; $\Delta l$ the thickness of the capillary wall; and $C_x - C_{inter}$ the concentration difference of indicator diffusing through membrane ($C_{inter}$ can be

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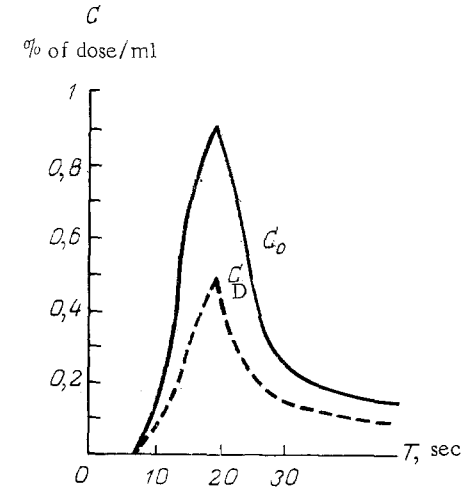


Fig. 1. Concentrations of indicators in blood flowing from organ after simultaneous injection of a mixture of them into an artery. $C_D$) Concentration of diffusing, and $C_o$) concentration of relative indicator. To plot indicator concentration curves with time the activity of each sample is expressed as a ratio of the injected activity and divided by its volume. Dimensionality of ordinate: return fraction in %/ml blood.

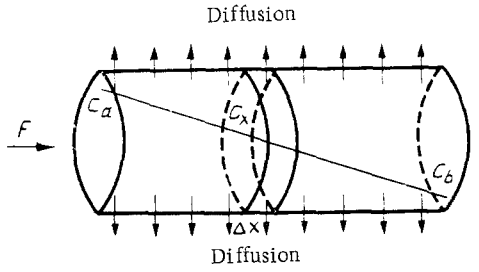


Fig. 2. Model of a single capillary. F) Blood flow; $C_a$) concentration of test indicator in arterial blood at entrance into capillary; $C_b$) concentration of test indicator in venous blood at exit from capillary; $\Delta_x$) infinitely thin transverse section through capillary; $C_x$) concentration of test indicator in blood entering infinitely thin section through capillary.

taken to be zero, for the volume of interstitial tissue is large compared with the volume of the capillary).

The total quantity of indicator entering the section in unit time is thus:

$$F \cdot C_x = \frac{dm}{dt} + F \cdot C(x + \Delta x), \tag{2}$$

or

$$-D \cdot S \frac{\Delta C}{\Delta l} = F \cdot [C_x - C(x + \Delta x)], \tag{2a}$$

where $d/\Delta l$ is the permeability (P) of the capillary wall. Integration along the whole length of the capillary from 1 to 0 and between concentration of $C_b$ and $C_a$ leads to the equation $PS/F = \ln (C_b/C_a)$.

Since $E = (C_a - C_b)/C_a$ and $C_b/C_a = 1 - E$,, where E stands for extraction of indicator from the blood,

$$PS = F \ln(1 - E), \tag{3}$$

where ln denotes the natural logarithm. Equation (3), deduced from a model of a single capillary, can be used to assess the index of the terminal vascular system of a whole organ on the assumption that all capillaries of the organ are equivalent to the sum of such single capillaries. Extraction of the diffusing indicator is calculated from experimentally obtained values by the equation:

$$E = \frac{\frac{[D]}{[O]}_a - \frac{[D]}{[O]}_b}{\frac{[D]}{[O]}_a}, \tag{4}$$

wher $[D]_a$ and $[D]_b$ are the concentrations of diffusing indicator in arterial and venous blood, respectively; $[O]_a$ and $[O]_b$ the concentrations of the relative indicator in arterial and venous blood, respectively.

The method described above was used to determine the diffusing capacity PS of cardiac capillaries of a dog with a closed chest. In mongrel dogs weighing 18-25 kg, anesthetized with pentobarbital, blood from the femoral artery was pumped into an airtight constant-temperature vessel, to which a manometer was connected, so that pressure within the vessel could be measured and varied. This vessel—manometer system enables a constant perfusion blood flow to be maintained. The blood flow from the vessel was directed through a catheter introduced under x-ray control along the carotid artery into the left coronary artery. In this way the coronary artery can be perfused. Throughout the period of injection of indicators and collection of blood samples the blood flow must be kept constant. Catheterization of the coronary sinus by means of a catheter with inflatable cuff was carried out through the jugular vein. The mixture of indicators $^{42}K$ and $^{131}I$-albumin (2:1), in a total volume of 0.2-0.3 ml, was injected as quickly as possible (0.5-1 sec) by a syringe through the coronary catheter. At the same time as the indicators were injected, collection of samples of venous blood from the coronary sinus began. Samples were obtained in a collector consisting of 30 cells, arranged on a rotating disk. The rate of blood sampling was once per second. Activity of each of the isotopes was determined in the venous blood samples and also in a standard solution of the original mixture of indicators on a $\gamma$-counter. Extraction and PS of the cardiac capillaries in the perfused region were calculated by equations (3) and (4). Depending on the rate of the blood flow, PS amounted to 30-80 ml/min/100g. For comparison it may be pointed out that according to data in [3] PS for skeletal muscle at rest is 2-5 ml/min/100g.

## LITERATURE CITED


1. C. Crone, Acta Physiol. Scand., 58, 292 (1963).
2. P. Martin de Julian and D. L. Yudilevich, Amer. J. Physiol., 207, 162 (1964).
3. E. M. Renkin, Amer. J. Physiol., 197, 1205 (1959).
4. D. L. Yudilevich and P. Martin de Julian, Amer. J. Physiol., 208, 959 (1965).