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course of each experiment. Therefore the dispersion of indicator particles produced by the injection and sampling systems during each determination should have remained constant. Since the contribution to the dispersion of indicator is constant, the basic relationship of the SD of the dye curves obtained with different types of anesthesia will not be affected by the injection and sampling systems.

The anesthetic technic influences the relationship between the SD of the primary indicator-dilution curve and the TPR. Two possible mechanisms account for this relationship: (1) Changes in peripheral resistance influence the dispersive characteristics of the central circulation; or (2) Pharmacologic agents that change the peripheral vasculature also influence pulmonary circulation. Anesthetic agents could change the basic relationship by altering either or both of these. Further investigation will be necessary to determine the correct mechanism.

Indicator-dilution curves provide information about the cardiovascular system as well as about cardiac output. Our study indicates that the relationship between peripheral resistance and the shape of the dye curve is influenced by anesthetic technic. If this relationship holds for man, it would allow an alternative method of calculating cardiac output from a dye curve that does not require a direct calibration of the densitometer. The TPR could be directly calculated from the shape of the dye curve, and the cardiac output then calculated from the TPR and systemic pressure.

Another possible clinical application suggested by this study involves use of the shape of the dye curve to determine the adequacy of myocardial function. Other investigators have shown that the shape of the dye curve provides useful measurements of cardiac reserve.[6-9] Since our study showed that the shape of the curve varies with the type of anesthesia in the dog, these relationships may vary with the type of anesthesia. Further investigation will be necessary to determine the applicability of these measurements in man.

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Guest Discussion

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Relative Dispersion: A Characterizing Feature of Specific Vascular Beds

A framework for interpretation of the spread of indicator-dilution curves may be based on consideration of the physical processes involved.[1] Listing these in order from the microregion to the macroregion we have: (1) molecular diffusion (radial and axial in the vessel, and permeation of membranes by smaller or lipid-soluble molecules); (2) the intravascular velocity profile (the central stream having higher velocities than those at the wall); (3) disturbances of flow in large vessels (local eddies or turbulence, effects of orifices, pulsatile flow, branching); and (4) heterogeneities of path lengths or transit times via parallel routes (through capillary network of an organ, or through

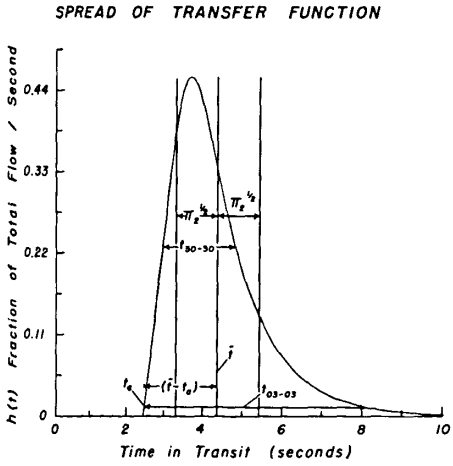

FIG 1. Measures of dispersion of an indicator-dilution curve. $\pi_2{}^1/_2$, the square root of the variance, shows the SD, and is given the symbol σ in this presentation. The width at 50% of peak height is $t_{50\text{-}50}$ and at 3% of peak heights is $t_{03\text{-}03}$. The mean transit time is $\bar{t}$. (Figure previously published in J Appl Physiol 22:879-888, 1967; reproduced with permission.)

the various organs). In addition to these biophysical events, there is also the spread due to a forceful injection or to prolongation of the injection.

The variations of measure of spread of an indicator-dilution curve are suggested by figure 1. One of the simplest is the width at ½ the peak height, $t_{50\text{-}50}$. This measure is quite similar to the standard deviation SD. (Ordinarily, unless recirculation is much delayed, calculation of the SD requires the fitting of a model to the dilution curve; the most commonly used model is monoexponential extrapolation of the downslope.) But the most useful is the relative dispersion, which is the SD (σ sec) divided by the mean transit time $\bar{t}$ both in seconds:

$$\text{Relative dispersion} = \frac{\sigma}{\bar{t}}$$

This is the same as the coefficient of variation, a standard statistical measure of spread. In the present context, it has a great advantage over the absolute SD, since its use allows one to distinguish between changes in dispersion due to the simple changes in flow or volume or mean transit time and changes due to an abnormality or to a change in the relative influence of the various dispersive physical processes.

To continue the development of the conceptual approach, next consider the degree of dispersion (D) as a function of the distance between the site of an ideal injection and a sequence of positions, x, along the flow stream. In figure 2 are shown curves of concentration versus distance, $C(x)$, a succession of snapshots at differing times. The spreading process was assumed to be a random one, so that the curves in the left panel are symmetrical, Gaussian curves. Because the spreading progresses as the indicator travels downstream, an observer at a

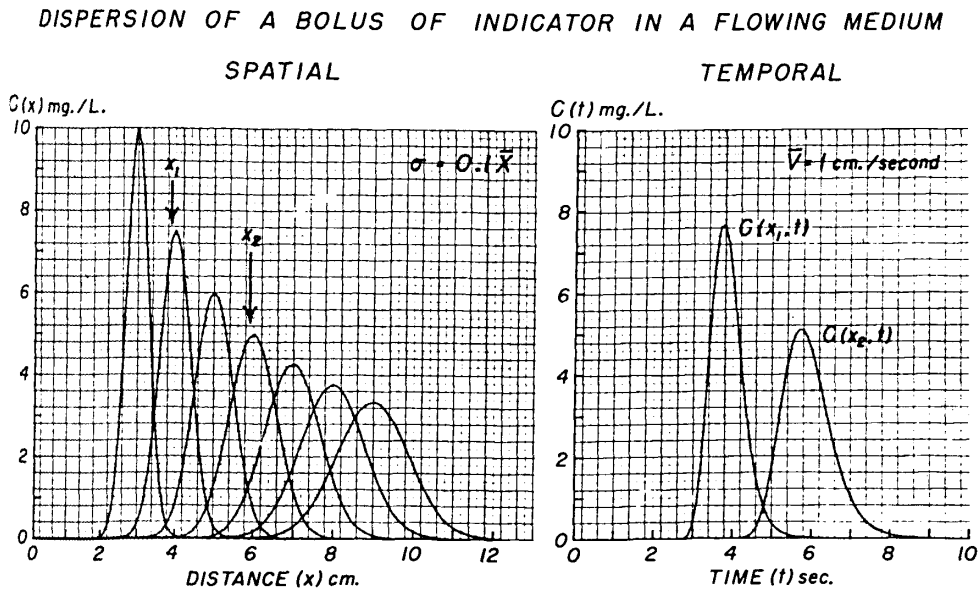

FIG 2. A random process causes spreading that is symmetrical with respect to distance around the centroid (left panel). But concentration-time curves obtained by sampling at a given point are always right-skewed (right panel).

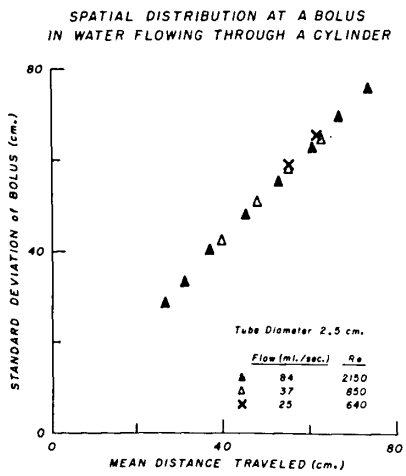

FIG 3. The dispersion (SD with respect to position x) in a large tube at 3 different flows can be seen to be wholly dependent on the mean distance travelled and not on flow. (The Reynold's number $Re = vr\rho/\eta$, where v = velocity, r = radius, ρ = density and η = viscosity.)

stationary location, x_1 or x_2, would see a right-skewed concentration-time curve, as shown in the right panel of figure 2.

The rate of spreading with distance is characteristic of the underlying physical phenomena. In turbulent flow or with spreading solely by molecular diffusion, the SD of $C(x)$ would be proportional to $x^{1/2}$, the square root of the mean distance travelled, or to the square root of time.[2] With streamline flow or even partially disturbed flow, the spread is proportional to time or to the mean distance travelled. The results of direct observation of spread of dye in disturbed flow in a tube are seen in figure 3; the linearity of the relationship shows that streamline flow characterizes the mass transport over a wide range of flow velocities (at the 3 different Reynold's numbers, Re). This appears also to be true of aortic flow[3] and denies any serious consideration of turbulence.

The next question is whether a pharmacologic intervention or a pathophysiologic state induces a change in the characteristic dispersion of a particular vascular bed: Is the *relative* dispersion changed?

The need for using relative rather than absolute dispersion can be seen from figure 4. Changing flow through a system dominated

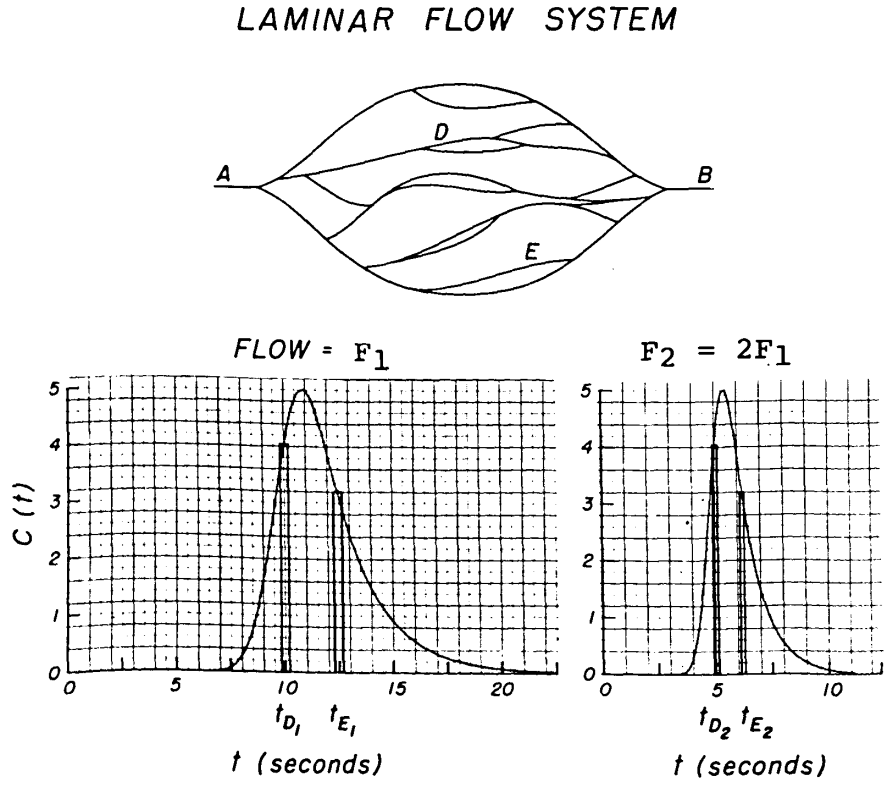

FIG 4. In a laminar-flow situation such as exists between points A and B in the upper panel, doubling the flow causes halving of each transit time, so that the absolute dispersion is halved. The basic shape and the relative dispersion, are unchanged by changing flow. (Figure reproduced from Circ Res 19:333-346, 1966; by permission of The American Heart Association, Incorporated.)

by streaming flow results in a proportional change in SD (or any other measure of spread). The basic shapes of the 2 indicator-dilution curves at the 2 flows are identical: the *relative dispersion,* and the other commonly used statistical measures of shape, such as skewness and kurtosis, are *constant.*

The SD (σ) itself changes in proportion to mean transit time, $\bar{t}$; changes in either, flow (F ml/sec) or volume (V ml), therefore, result in changes in $\bar{t}$:

$$\bar{t} = V/F$$

which means that σ is governed by V and F in the same way:

$$\sigma = \frac{V}{F} K_D$$

where K_D is the dimensionless constant characteristic of the particular bed. Given this situation, admittedly a simplified one, then the parameter of fundamental interest is K_D, since it is independent of V and F:

$$\text{Relative dispersion} = \frac{\sigma}{\bar{t}} = \frac{K_D V/F}{V/F} = K_D$$

These arguments demonstrate that, for a system with constant volume, the SD, σ, is inversely proportional to flow. Thus to relate this to the observations of Davis et al., when pressure is regulated so that it doesn't change greatly and peripheral resistance is calculated as pressure/flow, then the SD can be expected to be directly proportional to peripheral resistance and to the reciprocal of cardiac output. One might expect the correlation to be better with the 1/F than with resistance if V were truly constant, but either resistance of 1/F should give closer correlation than would be obtained directly with F, which is in accord with their observations.

The pulmonary vascular bed in dogs is characterized by a K_D of approximately 0.46, as suggested by figure 5.[4] The slope of the graph of the SD versus $\bar{t}$ is K_D. The question raised by the data and presentation of Davis' group at this symposium is whether the changes in SD which they observed are merely those accompanying changes in flow or volume or are indicative of a change in the pulmonary bed. The linear relationships they observed between SD and total systemic arterial resistance are clearly provocative; however, they are not, in this form, diagnostic of any changes in the central circulation, and may only indicate the status of the cardiac output and peripheral vasodilation. Further analysis might clarify this point.

It is worth noting that each circulatory region normally has a different characteristic relative dispersion, as is shown in figure 6. In moderate-sized arteries of the human arterial system lying between the femoral and dorsalis pedis arteries (shown by the plus signs): $K_D = 0.18 \pm 0.04$, n = 57 (mean ± SD, n = number of observations).[5] In the dog aorta (the open circles) K_D averaged 0.31 ± 0.13, n = 162.[3] Across capillary beds, K_D is naturally larger. The coronary system of dogs, from coronary artery

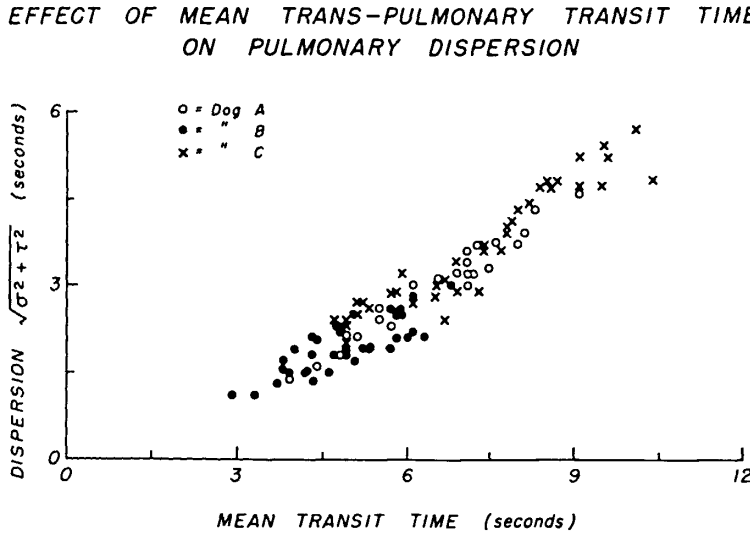

FIG 5. Transpulmonary dispersion is very nearly proportional to mean transit time in anesthetized dogs; the ordinate is the SD. Relative dispersion (K_D) is the ratio of ordinate to abscissa, or the slope, and is nearly constant. (Figure previously published in J Appl Physiol 27:36-43, 1969; with permission.)

INTERORGAN COMPARISON OF INTRAVASCULAR TRANSPORT

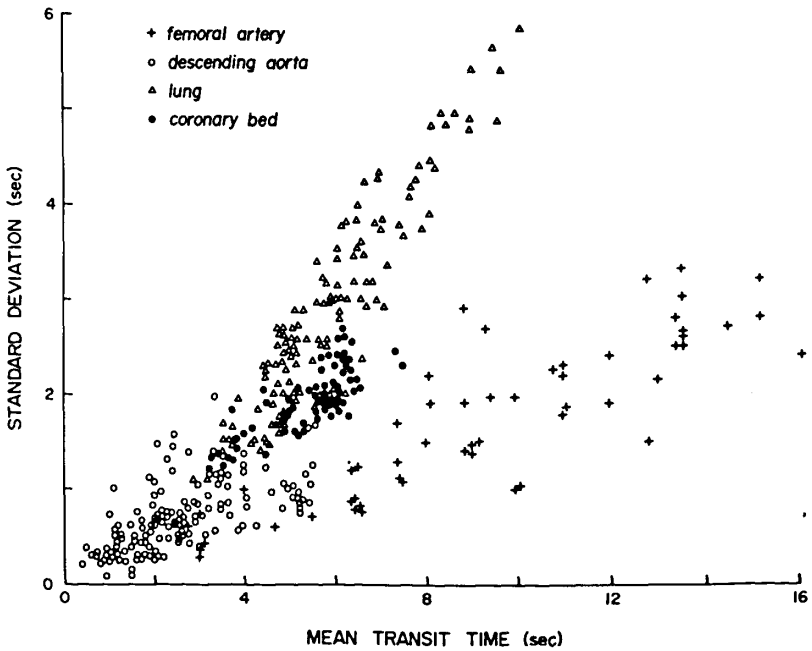

FIG 6. Dispersive characteristics of different vascular beds. The SD of the distribution of transit times plotted against the mean shows a roughly linear relationship in each bed. The leg arterial data are from awake humans, the other data from anesthetized dogs. (Figure appearing in Ann Biomed Eng 4:44-59, 1976; with permission.)

inflow to the coronary sinus (the closed circles) showed a K_D of 0.38 ± 0.05, n = 60.[6] The pulmonary vascular bed in anesthetized closed-chest dogs (the open triangles) shows a still larger K_D, 0.46 ± 0.06, n = 144 (data from fig 5). For the lung, Maseri's group[7] obtained K_D = 0.48 ± 0.08, n = 16. (All these data are from experiments where indicator-dilution curves were recorded from both inflow and outflow, so that there is no artifactual influence on the relative dispersion by the form or force of the injection.) From data on the renal vascular bed, Gomez and coworkers[8] give a value (half width divided by mean) of 0.66 ± 0.06, n = 10, which is approximately the same as the $t_{50\text{-}50} / \bar{t}$ of 0.7 found by Bassingthwaighte and Ackerman[3] in the dog aorta; Gomez' measure of dispersion includes that due to the injection. Other beds have not been studied, so far as I know.

As for the central circulation, one can expect some secondary influences on K_D. Permutt and colleagues[9] found that raising pulmonary-vein pressure decreases the relative dispersion, which accords with our data in figure 5—the K_D's were somewhat less when mean transit times were short, which occurred with high flow and minor elevation of pressure. It also seems likely that the dispersive characteristics of the chambers of the heart might change, even dramatically, with changes in ventricular volumes accompanying changes in contractility or in peripheral vascular resistance.

Is the approach useful? Very likely, yes. It appears that the dispersion of intravascular tracer in passing through a vascular bed is characteristic of the normal status of particular segments of the circulation. A search for changes in dispersion, or probably better yet, relative dispersion, with changes in pathophysiologic status, is therefore very much in order. While this approach has not yet been proved of diagnostic or therapeutic value, the technic should certainly be explored. Moreover, it should not be regarded as necessarily invasive, for the general approach can be applied to externally detected tracer-dilution curves or to videoangiographically determined contrast-dilution curves. Given the continuing development of these

relatively noninvasive approaches, the evaluation of indicator dispersion as a diagnostic test appears very worthwhile.

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SHOULDER PAIN. The efficacy of acupuncture therapy vs placebo was evaluated in 42 patients with shoulder pain due to periarticular disease or osteoarthritis. All received 1 treatment for 3 weeks. Half the patient received treatments performed in a positive atmosphere (enthusiastic therapist) and the other patients were treated by a not-very-friendly and unenthusiastic therapist. Placebo therapy was accomplished by pricking the needle against the skin as use of sham points has been criticized since beneficial effects may be obtained with needle insertion other than that corresponding to the traditional points. One week after the last treatment subjects returned for reevaluation. The placebo therapy was convincing as only 2 patients thought they had received imitation treatment. Sixty-nine percent felt the shoulder pain was decreased but there was no difference between acupuncture and placebo treatments. Despite subjective improvement the range of shoulder motion was not changed from pretreatment values. Greatest subjective relief occurred in patients previously demonstrated to manifest increased hypnotic susceptibility. The authors are skeptical that acupuncture has a role in modern medicine. *(Moore ME, Berk SN: Acupuncture for chronic shoulder pain. An experimental study with attention to the role of placebo and hypnotic susceptibility. Ann Int Medic 84:381-384, 1976)*