Correspondence

Time Constants in Anesthesiology

To the Editor:—We were intrigued by the novelty of Dr. Fink's [1] concept of the "decimal" time constant, as opposed to the "natural" time constant; that is, the time in which an exponential decay becomes one-tenth incomplete as opposed to the time in which it becomes $1/e = 1/2.7$ incomplete.

This concept has the obvious advantage that 10 is an easier number to remember than 2.7 but in making the change to decimal time constant some very convenient properties of the natural time constant are lost.

The most important of these is that the natural time constant of any particular exponential decay can often be quite easily worked out if it is simply remembered that the (natural) time constant is the time in which the decay would be complete if the initial rate of decay were maintained. In other words, the natural time constant of a variable can be determined by dividing the initial value of the variable by its initial rate of change. For instance, in the passive deflation of the lungs the initial volume of gas in the lungs (above the end-expiratory level) is PC where P is the pressure in the alveoli (cm. of water) and C is the compliance (liters/cm. of water). The initial rate of change of volume (that is, the initial flow) is P/R where R is the airway resistance (cm. of water per (liter/second)). Therefore the natural time constant (initial value divided by initial rate of change) is PC divided by $P/R = CR$. Thus, for the passive deflation of the lungs, the natural time constant is simply equal to the product of the compliance and the resistance of the lungs. Similarly, in the washout of nitrogen from the lungs the initial volume of nitrogen in the lungs is equal to the functional residual capacity of the lungs, V, multiplied by the alveolar concentration of nitrogen $F_{A_{N_2}}$, that is, $VF_{A_{N_2}}$. The initial rate of change is equal to the alveolar ventilation $\dot{V}_A$ multiplied by the alveolar concentration $F_{A_{N_2}}$, that is, $\dot{V}_AF_{A_{N_2}}$. Therefore the natural time constant (initial value divided by initial rate of change) is $VF_{A_{N_2}}/\dot{V}_AF_{A_{N_2}} = V/\dot{V}_A$. That is, for nitrogen washout of the lungs, the natural time constant is simply equal to lung volume divided by alveolar ventilation. If it is desired to use the decimal time constant the natural time constant must first be determined in the manner just described and then multiplied by 2.3.

Another advantage of the natural time constant is that it provides more information about the process of decay *in the range of clinical interest.* The last 5 per cent of any decay process is rarely of any clinical importance so that once an exponential change is 95 per cent complete it can be regarded as fully complete for most clinical purposes. The only information which the decimal time constant provides in this range is that after one decimal time constant the variable has already fallen right down to 10 per cent of its initial value. On the other hand when the natural time constant is used it is known that: after one natural time constant the variable has fallen to $1/e = 37$ per cent of its initial value; after two natural time constants the variable has fallen to $1/e^2 = 13.5$ per cent of its initial value; after three natural time constants the variable has fallen to $1/e^3 = 5$ per cent of its initial value. This provides relatively detailed information about the progress of the decay. This point is perhaps brought out more clearly by the two graphs in figure 1. Both represent the exponential decay of a variable down to 5 per cent of its initial value but, in the first, (a) the decimal time constant has been used so only one point can be plotted (where the variable has fallen to 10 per cent of its initial value) whereas, in the second, (b) the natural time constant has been used and points have been plotted where the variable has fallen to 37, 13.5 and 5 per cent of its initial value. If, in addition, it is remembered that this initial rate of decay of an exponential is such that it would reach zero in one (natural) time constant it is

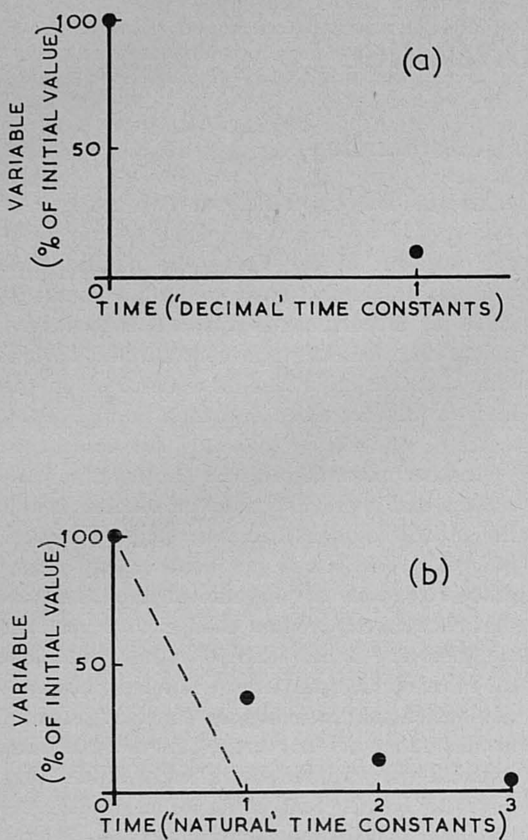

FIG. 1. Points which can be plotted for the first 95 per cent of an exponential decay when either the "decimal" time constant (a) or the "natural" time constant (b) is used.

evident that the decay curve must start along the broken line in figure 1 (b). Clearly, a freehand curve, drawn to start along the broken line in figure 1 (b) and then to go through the plotted points, would be much more likely to lie close to the true exponential curve than one drawn through the two points in figure 1 (a). Of course, neither approach is satisfactory for precise research work for which recourse must be had to tables of exponentials. However, for clinical work and even for everyday approximations in research, we submit that the natural time constant has much to commend it.

The only disadvantage of the natural time constant is that the degrees of completion of the change after one, two or more time constants are not simple numbers. However, if the three numbers 37, 13.5 and 5 are remembered, for the percentages of the initial value remaining after one, two and three natural time constants respectively, this will be adequate for most purposes. If even this is too great a burden on the memory it may well be adequate to round off e (=2.72) and call it 3, and say that: after one time constant 1/3 remains; after two time constants 1/3 of 1/3 = 1/9 remains; after three time constants 1/3 of 1/3 of 1/3 = 1/27 remains.

Dr. Fink says, "Ultimately the choice of time constants is a matter of convenience" and "Anesthesiologists . . . should choose the base that suits their purpose best." We agree. The object of this letter is to point out some factors which may make anesthesiologists think that the "natural" time constant is, on balance, the most convenient. These, and other factors, have been treated more extensively, but still simply, elsewhere.[2]

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1. Fink, R. B.: Time constants in anesthesiology, ANESTHESIOLOGY 27: 838, 1966.
2. Waters, D. J., and Mapleson, W. W.: Exponentials and the anaesthetist, Anaesthesia 19: 274, 1964.

To the Editor:—The recent article by Dr. B. R. Fink (Time Constants in Anesthesiology, ANESTHESIOLOGY 27: 838, 1966) presented the concept of utilizing the base 10 rather than the base e. Most anesthesiologists will find this constant more understandable and easier to work with. Dr. Fink is to be commended for advancing this idea.

However, in attempting to demonstrate the derivation of the natural time constant Dr. Fink may have inadvertantly confused some readers. Starting with the differential equation of

$$\frac{dx}{x} = -\,kdt,$$

he attempts to find a value of x at any time t, by integrating between t_0 and t. This cannot be done since

$$\int_{t_0}^{t} \frac{dx}{x} = \ln x \Big]_{t_0}^{t} = \ln t - \ln t_0$$

which eliminates x from the equation.

The definite integral should not be used, but rather the indefinite integral, thus:

$$\int \frac{dx}{x} = -\int kdt$$

$$\ln x = -\,kt + C$$

where C is the constant of integration. Its value is found by noting that at the moment x, the partial pressure, begins to decrease, its value is 100% or 1, and the time, $t = 0$. At this moment then $\ln 1 = -\,k \times 0 + C$. Since $\ln 1 = 0$, C must $= 0$. The general equation thus becomes: $\ln x = -\,kt$.

This is the same equation used by Dr. Fink but I believe this is the correct mathematical derivation.

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To the Editor: I wish to thank Dr. Engel for his kind comment on my paper. He is, of course, correct in insisting that, strictly, the constant of integration ought to be included in the definite integral, and then eliminated in the next step of my development. I telescoped the steps in order to simplify the presentation and make it less forbidding to the non-mathematical reader.

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Methoxyflurane and Renal Function

To the Editor:—We read with interest Dr. Crandall's article on the possible relationship of Methoxyflurane to renal function. During the past six years our hemodialysis unit has treated approximately 40 patients a year for acute renal problems and during the past two years we have noted 6 cases of acute high output renal failure. This was of interest, because during the previous four years we had seen none. Of the 6 cases we observed, 5 had received Methoxyflurane anesthesia. One of the patients died with peritonitis and septicemia so that the relationship with Methoxyflurane in this case, if any, is obscure. In the remaining 4 patients, 3 were known to have had normal BUN's at the time of admission and developed high output renal failure with rising BUN's. All of these patients were dialyzed; 3 of them expired. Postmortem examination showed no consistent picture, except for the finding of oxalate crystals in the renal tubules. In one of these patients there was an episode of hypotension followed by a one day period of low urine output; however, in no other istance was there shock nor had the patients received any nephrotoxic agents. All of our patients were in the older age group and had long operative procedures. In the 6th patient we observed with high output renal failure, ether anesthesia was used and the patient was operated on for a repair of an abdominal aneurysm.

This observation of high output renal failure in patients receiving Methoxyflurane is not conclusive but tends to complement the observations made by Dr. Crandall.

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