The following is the abstract of the article discussed in the subsequent letter:

**Venegas, José G., R. Scott Harris, and Brett A. Simon.** A comprehensive equation for the pulmonary pressure-volume curve. *J Appl Physiol* 84: 389–395, 1998.—Quantification of pulmonary pressure-volume (P-V) curves is often limited to calculation of specific compliance at a given pressure or the recoil pressure (P) at a given volume (V). These parameters can be substantially different depending on the arbitrary pressure or volume used in the comparison and may lead to erroneous conclusions. We evaluated a sigmoidal equation of the form, V = a + b[1 + e\(^{(\text{P} - \text{cV})/d}\)]\(^{-1}\), for its ability to characterize lung and respiratory system P-V curves obtained under a variety of conditions including normal and hypoxic pneumoconstricted dog lungs (n = 9), oleic acid-induced acute respiratory distress syndrome (n = 2), and mechanically ventilated patients with acute respiratory distress syndrome (n = 10). In this equation, a corresponds to the V of a lower asymptote, b to the V difference between upper and lower asymptotes, c to the P at the true inflection point of the curve, and d to a width parameter proportional to the P range within which most of the V change occurs. The equation fitted equally well inflation and deflation limbs of P-V curves with a mean goodness-of-fit coefficient ($R^2$) of 0.997 ± 0.02 (SD). When the data from all analyzed P-V curves were normalized by the best-fit parameters and plotted as (V - a)/b vs. (P - c)/d, they collapsed into a single and tight relationship ($R^2$ = 0.997). These results demonstrate that this sigmoidal equation can fit with excellent precision inflation and deflation P-V curves of normal lungs and of lungs with alveolar derecruitment and/or a region of gas trapping while yielding robust and physiologically useful parameters.

**Modification of a sigmoidal equation for the pulmonary pressure-volume curve for asymmetric data**

*To the Editor:* A sigmoidal equation to characterize the pulmonary pressure-volume (P-V) curve has been proposed by Venegas and coworkers (3) and is widely used for computerized analysis of P-V curves. It is based on a mathematical model introduced by Paiva et al. (1), amended to fit the entire curve even below functional residual capacity (FRC). The equation

$$V = a + b[1 + e^{(P - cv)/d}]^{-1} \quad (1)$$

where a represents lower asymptotic volume, b the upper asymptotic volume or vital capacity, c the pressure at the point of highest compliance (“true” inflection point of the sigmoidal curve), and d an adjustment parameter, provides a close proximity between observed and calculated P-V relations by using the Levenberg-Marquardt fitting procedure. This function is symmetrical with respect to the inflection point, but there is no physiological reason justifying the symmetry, prompting Venegas et al. to further develop the model so that it could be applied to asymmetric data as the product of a normal distribution-based recruitment function [R(P)]

$$R(P) = [1 + e^{(P - cv)/d}]^{-1} \quad (2)$$

times a function representing the compliant properties of the already-recruited lung above FRC, such as the one described by Salazar and Knowles (2)

$$V = (A - Be^{-kP}) \quad (3)$$

with A corresponding to total lung capacity (TLC) and parameters B and k reflecting the elastic stiffness of the lung. Venegas et al. (3) concluded that this would result in the following

$$V = (\text{TLC} - Be^{-kP})(1 - e^{(P - cv)/d}) \quad (4)$$

Choosing arbitrary parameters, Venegas et al. presented a simulated model of the shape of the resulting curve. However, the increase from four to five fitting parameters was judged to be disadvantageous.

The following comments have to be made about the mathematical modeling. In Eq. 4, the value of V for P = c is infinite, since the exponent $(-P - c)/d$ will become zero and $e^0 = 1$; therefore, the denominator will be zero, meaning that the function has a singularity at P = c. Using the same arbitrary values (TLC = 1, B = 1, k = 0.1, d = 2.5, and c = 15), we graphed of the function represented by Eq. 4 (see our Fig. 1).

To be mathematically correct, the denominator of Eq. 4 should read $1 + e^{(P - cv)/d}$ instead of $1 - e^{(P - cv)/d}$, which will never become zero, and thus the graphic of the function would have the same shape as that presented in Fig. 7 of the article by Venegas et al. (3). Another concern is regarding Eq. 3; the original equation by Salazar and Knowles (2) was expressed as

$$V = V_0(1 - e^{-kP}) \quad \text{or} \quad V = V_0 - Ve^{-kP} \quad (5)$$

with $V_0$ being the maximum lung volume, which is equal to $a + b$ observed in *Eq. 1*. Therefore, if we substitute Eq. 5 for Eq. 3 into the corrected Eq. 4, we get

$$V = (V_0 - Ve^{-kP})/(1 + e^{(P - cv)/d}) \quad (6)$$

with only four fitting parameters.

When we use the same arbitrary values for $V_0 = 1$, $k = 0.1$, $c = 15$, and $d = 2.5$ in *Eq. 6*, we obtain a function whose graphic is also plotted in Fig. 1, which
can also be compared with the graphic from Eq. 1, with $a = 0$, $b = 1$, $c = 15$, and $d = 2.5$.

Another point that needs clarification is the concept of convergence used to show that, in the upper limit of pressures, where $e^{-(P - c)/d} < 1$, Eq. 1 converges to Eq. 3 with $A = a + b$, $B = b e^{c/d}$, and $k = d$, since convergence is strictly related with the definition of limit.

Considering the fact that $0 < e^{-(P - c)/d} < 1$ for $P > c$ and that $e^{-(P - c)/d}$ converges to zero when $P$ takes higher values, Eq. 1 will converge toward the horizontal upper asymptote $a + b$.

Equation 3 has similar asymptotic behavior, within the same range of pressure values, and this function will also have a horizontal upper asymptote $A$; thus $A = a + b$.

In Eq. 3, parameter $B$ must always be positive and its value will influence the shape of the curve $V = -e^{-kP}$ before suffering a vertical translation associated to the vector $\mathbf{\alpha}$, and $k$ is a measure of adjustment. The same kind of geometrical transformations also occurs in Eq. 1.

With this kind of consideration, it is understandable that a correspondence exists between Eq. 1 and Eq. 3. The authors have shown that Eq. 1 and Eq. 3 have the same asymptotic behavior, but the way the parameters $B$ and $k$ were derived still remains unclear.

Equation 6 represents the correct mathematical model; however, it neither proves the underlying assumptions nor the physiologic correctness. These steps have yet to be done in future investigations.

REFERENCES


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REPLY

To the Editor: We appreciate the letter from Dr. Henzler and colleagues in which they point out a typographic error in the modified sigmoidal equation to allow for fitting of asymmetric data sets. By following the algebra postulated in the paper, it can be shown that the sign in front of the exponential term of the denominator of Eq. 4 should have been positive instead of negative. The authors also point out that, by using the original equation by Salazar and Knowles, which includes a single parameter $V_0$ instead of our two parameters $A$ and $B$, an alternative expression is made with only four parameters compared with our five. We contemplated that alternative but rejected it because it implies the condition that the volume of the respiratory system at atmospheric airway pressure is zero and thus does not allow for positive values of FRC. Using the model with parameters $A$ and $B$ allows for variations of FRC between different P-V curves, such as in comparisons between inspiratory and expiratory maneuvers where the end-expiration volume may be larger than the initial volume of the lung. Granted, in some special conditions, this equation may provide a better fit to experimental data, but that still remains to be tested.

We agree with their clarification of the convergence of Eqs. 1 and 3 at high values of pressure.

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