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Determination of Histamine PC_{20}
Comparison of Linear and Logarithmic Interpolation

To the Editor:

Standardization of methodology related to both the performance and interpretation of bronchoprovocation tests is important. The results of bronchial inhalation tests with histamine or methacholine are usually expressed as the provocation concentration (or dose) producing a 20 percent reduction in FEV$_1$, termed the PC$_{20}$ (or PD$_{20}$). The method of calculating the PC$_{20}$ from the dose-response curve is one aspect of standardization which has not been critically examined. The last two points on the dose-response curve (ie, those bracketing the 20 percent fall in FEV$_1$) are generally used for the calculation of PC$_{20}$. The PC$_{20}$ may be determined either by linear or logarithmic interpolation between these two points, and either interpolation may be performed by means of an algebraic formula, or by manually graphing the dose vs response, or log dose vs response curve.

We have compared linear and logarithmic interpolation by formula in 72 histamine dose-response curves in which a greater than 20 percent FEV$_1$ reduction was achieved. We have also examined the graphed determination of histamine PC$_{20}$ both linearly and logarithmically in 12 of these curves and have compared the results to those obtained by formula. In addition, we have examined between-observer and the inter-observer variation in determination of PC$_{20}$ graphically.

Histamine inhalation tests were performed as previously described. Doubling concentrations of histamine from 0.03 to 8.0 mg/ml were inhaled for two minutes' tidal breathing at five minute intervals from a Wright nebulizer which was calibrated to deliver an output of 0.130 ml/min. We examined 72 consecutive tests in which the FEV$_1$ fell by ≥20 percent. This represented results in 55 with asthma, 12 with rhinitis, and five normal subjects with mildly hyperresponsive airways. The PC$_{20}$ was then calculated by two algebraic formulae, one linear and the other logarithmic, interpolating the last two points of the dose-response curve. The formulae used were as follows:

1. Linear: $PC_{20} = \frac{(20-R_1) (C_2-C_1)}{(R_2-R_1)} + C_1$
2. Logarithmic: $PC_{20} = \text{Antilog} \left( \frac{(20-R_1) (\log C_2 - \log C_1)}{(R_2-R_1)} + \log C_1 \right)$

C$_1$ is the histamine concentration producing less than a 20 percent FEV$_1$ fall and C$_2$ is that producing greater than a 20 percent FEV$_1$ fall. R$_1$ and R$_2$ are the percent FEV$_1$ reductions produced by C$_1$ and C$_2$ respectively.

Twelve of these dose-response curves were then blindly analyzed by two observers who were trained and experienced in measuring PC$_{20}$ on two separate occasions. On each occasion, the histamine dose-response curves were manually graphed on both linear and semi-log paper, and the PC$_{20}$ calculated by dropping a vertical line from the point representing a 20 percent FEV$_1$ fall to the horizontal (histamine concentration) axis.

The 72 linearly and logarithmically interpolated PC$_{20}$s are compared graphically in Figure 1. The linear interpolation resulted in a PC$_{20}$ which was consistently greater than or equal to that obtained by logarithmic interpolation. The difference, however, was small, ranging from 0 to 6 percent, mean 3.7±2.1 (SD) percent. The graphic interpolation of PC$_{20}$ logarithmically differed from the formula by 0 to 10 percent (2.8±2.9 percent) for observer 1 and by 0 to 5 percent (1.0±1.4 percent) for observer 2. The between-observer difference in PC$_{20}$ determination ranged from 1 to 5 percent (2.1±1.7 percent), and the within-observer differences ranged from 0 to 11 percent (2.8±3.2 percent) for observer 1 and from 0 to 2 percent (0.6±0.6 percent) for observer 2. Results for graphic linear interpolation were similar.

The important observation from this study is the small magnitude of the difference between PC$_{20}$s calculated logarithmically and linearly. This consistent difference is well within the range of nonconsistent variability over short or long periods in the measurement of FEV$_1$ or the consistent between-observer variation which may occur in calculation of FEV$_1$ from the same spirogram. Furthermore, the observed PC$_{20}$ difference is of the same order of magnitude as the difference between formula and graphic calculation of PC$_{20}$, and as the within-observer and between-observer variability in graphically calculating PC$_{20}$. Importantly, the PC$_{20}$ difference is much smaller than the observed difference in repeated PC$_{20}$ testing, which is as great as ± one doubling dilution.

Although there are no data to support which method (linear vs logarithmic) is "right," it is customary to plot results as log dose vs
response, and logarithmic interpolation (graphically) of $P_{e}$ has been recommended by a national standardization committee. We suggest that, considering the repeatability of $P_{e}$ determinations, either linear or logarithmic interpolation may be used without significantly influencing the result. Furthermore, algebraic formulae are described which can be used to accurately interpolate $P_{e}$ by either method. Although up to a ± 10 percent error was found in manually graphically interpolating $P_{e}$, this method is considered accurate enough for clinical use.

We suggest that for both accuracy and simplicity, the formulae are preferable to manual determination of $P_{e}$. Either linear or logarithmic interpolation may be used with only minor differences in result. The only advantage of one method over the other is that less sophisticated equipment is needed for the linear method.

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REFERENCES


Bedside Calibration of Pulmonary Artery Catheters

To the Editor:

I should like to expand on my discussion of bedside calibration of pulmonary artery catheters and point out some newer modifications since publication of my letter to the editor (Chest 1981; 79:718-19).

Accurate pulmonary artery catheter calibration is extremely important because one is working in the range of very low pressures (0-30 mm Hg). In order to have the system properly calibrated, both

The transducer and the monitor need to be calibrated. Presently, the monitors are calibrated by a voltage check done through a calibration button usually on the monitor (Fig 1). In most institutions, as well, the transducer is calibrated periodically by using a mercury or anaeroid manometer and applying a specific pressure. It is assumed that the transducer remains in calibration between the intermittent checks.

Problems may occur due to many factors leading to inaccurate pressure readings. The transducers do not always stay in calibration. They may be affected by age, handling or sterilization. The calibration check is often performed at relatively high pressures, such as 50 or 100 mm Hg. These pressures are often significantly above the desired physiologic range to be measured. Also, there is often significant error (1 to 2 cm of water or sometimes greater) in placing the zero reference point for the transducer at the same place as the mid-catheter (left atrial approximate) by using a long level from the transducer to the bed.

Fortunately, there is a much simpler and, in fact, more accurate way of calibrating the entire system. This also circumvents the necessity for monitoring teams, etc., and allows the physician and nurses to be confident of the numbers that are obtained.

Most pulmonary artery catheter setups now have the catheter leading to a piece of tubing with a stopcock on it (often used to obtain blood gases, etc), and then another piece of tubing from the stopcock to the transducer. In my previous letter I mentioned that one can disconnect this stopcock and hold the tip of the line at the left atrial approximate and then zero the transducer. However, it is, of course, unnecessary to physically disconnect the catheter (Fig 2). One merely needs to turn the stopcock "off" to the patient and open to air and then the same thing is done. This is a significant improvement in that it assures more sterility, as the line does not have to be broken. The combined catheter, transducer, and monitor can then be zeroed at exactly the left atrial approximate.

To assure that the instrument "gain" is correct, a known mechanical pressure must be applied. This is simply done by lifting the tube and stopcock from the initial zero position vertically up a ruler 13.6 cm. Exactly 10 mm Hg pressure will then be applied and should be indicated on the monitor. Then it can be lifted up another 13.6 cm which will be 20 mm Hg, etc. If the monitor does not read accurately, one can adjust the "gain" if the manufacturer has made provision for this, or one can mark the proper numbers on the oscilloscope where the trace is seen (Fig 1) and make use of the wave-form on the oscilloscope calibrated appropriately to obtain measurements, or one can change the transducer in an attempt to obtain more accurate readings. In this way, very accurate pressures are obtained, as well as very accurate zero reference pressures in the normal range of pulmonary artery pressures.

We hope this technique will soon become common practice throughout ICUs. However, it is very important that physicians first

![Diagram of catheter calibration](http://journal.publications.chestnet.org/pdfracess.ashx?url=/data/journals/chest/21379/ on 06/21/2017)