Book for People with Lung Cancer and Their Families

To the Editor:

Living with Lung Cancer: A Reference Book for People with Lung Cancer and Their Families is the title of a little book produced by two of my colleagues (Barbara G. Cox, B.S., and Robert E. Lee, M.D.) and me under a contract with the National Cancer Institute. Five thousand copies of the volume have been distributed to cancer centers and physicians caring for patients with cancer of the lung. The book has been of great help in the care of these patients.

Living with Lung Cancer has been reprinted and is again available to physicians who wish to use it to supplement their discussions with patients and their relatives. The book answers many questions that these people have about their problem and its management.

Further information about the availability of copies of the book may be obtained by writing to the Mayo Comprehensive Cancer Center, Rochester, Minn 55901.

David T. Carr, M.D.
Comprehensive Cancer Center
Mayo Clinic, Rochester, Minn

Tests of Bronchodilator Therapy

To the Editor:

The report by Light and colleagues1 in Chest raises several key issues which deserve thoughtful comment. Since work from our laboratory is directly quoted, I feel compelled to make observations which, I trust, may be of general interest.

The quoted statement regarding the essential need for measurement of airway resistance (Raw) by body plethysmograph grew out of a study comparing patients with chronic obstructive disease and normal subjects, all of whom were tested with a variety of pharmacologic agents having actions upon bronchomotor tone.2 Analysis showed that although there was no statistically significant difference in the spirometric indices of airflow (the forced expiratory volume in one second [FEV₁], the maximum expiratory flow rate, and the ratio of the FEV₁ over the forced vital capacity times 100) in normal subjects following aerosol therapy with isoproterenol, subcutaneous administration of epinephrine, or intravenous administration of theophylline (compared to control levels following aerosol administration of physiologic saline solution), the specific Raw reflected changes that were significant at the 5 percent confidence level. In patients with obstruction of airflow, the spirometric indices (FEV₁, the maximum expiratory flow rate, and the forced vital capacity [FVC]) were significantly improved and correlated with changes in the specific


888 COMMUNICATIONS TO THE EDITOR
We concluded that using the more sensitive test of bronchomotor tone, the specific Raw, we could detect responses to therapy with bronchodilator agents which were similar in magnitude between normal subjects and patients with obstruction of airflow. In no way did we negate the value of the FEV₁ as an index of measurement in patients.

Some years later, Stanescu et al² critically evaluated the response of patients to aerosol therapy with isoproterenol (isoprenaline) using the Raw and the maximum expiratory flow rates measured from flow-volume curves. A linear discriminant analysis⁴ was used to compare the relative value of the indices used and to estimate the amount of independent information provided by each of these indices. The conclusion of Stanescu et al² was that two measurements, the Raw and the maximum flow at 75 percent of the expired FVC, provided maximum and independent information regarding bronchomotor tone; that is, a measurement of Raw, probably providing information from the central airways, and a measurement of flow from a portion of the flow-volume curve nearing residual volume best characterized the bronchomotor tone and the response to therapy with bronchodilator agents.

In short, our study was directed toward detecting changes in bronchomotor tone in both normal subjects and patients. Our data clearly reflected that both normal subjects and patients responded in similar fashion to the tested drugs as far as specific Raw was concerned, but that different measurements correlated differently with each other in the two groups. As tests related to events largely occurring in airflow from terminal airways developed, measurements of flow derived from the later portion of the flow-volume curve have been shown to reflect events not necessarily the same as shown by Raw or specific Raw.

The "best test" for measuring a patient's response to therapy with bronchodilator drugs may well be the FEV₁, because of its general availability, technical simplicity, and low cost, but these issues are not directly addressed by Light et al.¹ Obviously, the "best" method depends upon the type of information that one is seeking to obtain.

Charles B. Payne, Jr., M.D., F.C.C.P.
Assistant Professor of Medicine
Case Western Reserve University, Cleveland

REFERENCES

To the Editor:

We would like to call attention to what we believe to be a significant error in the report entitled "The One Best Test for Evaluating the Effects of Bronchodilator Therapy" by Light and his associates¹ in Chest. The error arises in the use of statistics in the report. An objection to the statistical analysis presented by Light et al¹ is that inappropriate interpretations are made regarding time-dependent data. One cannot say that the persistence of the effects of a drug at 300 minutes represents an absolute superiority of the forced expiratory volume in one second (FEV₁) over other tests of pulmonary function. Successive measurements of many physiologic characteristics tend to be positively correlated, and it is improper to imply that these observations may be treated as if they were independent.

It is also misleading to state that the F value for the time-weighted mean is significantly greater for FEV₁ than for other spirometric measurements. The univariate F ratios presented in the report by Light et al¹ range from about 5 to 10.

All of these F ratios are significant. What is the meaning of one F ratio being larger than another? One fact to keep in mind is that the smaller the standard deviation, the larger the F ratio. It is well known that the standard deviation of the FEV₁ is small and, indeed, is smaller than the standard deviation of the specific airway resistance (specific Raw). Remember that the more sensitive a measurement is, the larger the coefficient of variation and the larger the standard deviation (i.e., the experimental "noise" is larger). Since the FEV₁ has a smaller standard deviation, and the FEV₁ and specific Raw are strongly correlated, it is not surprising that the univariate F ratio for the FEV₁ is higher. One additional possibility that Light et al¹ failed to consider is that the observed differences among the univariate F ratios may simply be due to chance. Insufficient information is presented in their report to conclude otherwise.

What statistical methods could take such differences into account? A more appropriate and standard method of assessing the additional power of one variable while controlling for differences explained by another variable is to apply multivariate discriminant analysis.³ This has been done, and the Raw and the flow from a terminal portion of the forced vital capacity (FVC) together have been found to provide maximum information about bronchomotor tone.

In conclusion, we believe that Light et al¹ are wrong in stating that the FEV₁ is the best test to evaluate the response to bronchodilator therapy. We do believe that the use of body plethysmographic studies and the mean forced expiratory flow during the middle half of the FVC are useful in evaluating the response of the airways, as we have previously stated.⁴,⁵ We believe that the view of the superiority of the FEV₁ espoused by Light et al¹ is incompatible with our findings.⁴,⁵ It is