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In Reply:—While it is true that the earlier report by Cherala and Ovassapian described the passage of a bronchoscope through the Murphy eye of an endotracheal tube, in none of the three cases was there any mention of difficulty in advancing of the tube/scope combination into the trachea as was the case in our report. Instead, they reported an inability to withdraw the bronchoscope once successful intubation had been accomplished. As was stated in our letter, our concern was that repeated or forceful attempts to advance the endotracheal tube in a situation where the bronchoscope has exited through the Murphy eye may result in traumatic injury to the glottic structures. We retain this concern and feel that our letter serves as an important reminder that difficult passage of an endotracheal tube over a bronchoscope may be due to more than a narrow nasal passage or failure to adequately lubricate the bronchoscope.

With regard to their comments that the bronchoscope should be advanced after the endotracheal tube has been positioned in the posterior pharynx, we feel that this is a matter of personal preference and that successful intubations may be achieved either in this manner or by first positioning the bronchoscope and then advancing the endotracheal tube.

MARK H. ZORNOW, M.D.
Assistant Clinical Professor of Anesthesiology
KATHLEEN P. NICHOLS, M.D.
Resident in Anesthesiology
Department of Anesthesiology
UCSD Medical Center
225 Dickinson Street
San Diego, California 92103

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A Statistic for Inferences Based upon Negative Results

To the Editor:—The letter by Benefiel[1] *et al.* calls attention to an important concept of probability related to the strength of a clinical inference based upon the nonoccurrence of a disease in a series of patients. However, the equation for such is incorrect, as printed. Hence, I would like to derive the correct formula while presenting the simple underlying concepts.

If R is the rate of occurrence or incidence of the condition in a general population, (1 − R) is the fraction of the population free of the condition and represents the probability that observation of a single patient will be negative. Then, the probability P of a negative observation in n consecutive patients is $(1 - R)^n$, or

$$(1 - R)^n = P \quad (1)$$

The P in equation 1 is indeed our familiar P value, usually taken at 0.05 or 5%, representing the probability that the observed result occurred by chance alone. The corresponding level of confidence, $1 - P$, is 0.95 or 95%.

Depending upon the question asked, equation 1 may be rearranged into several useful forms, as shown below.

$$(1 - R)^n = P \quad (1)$$

Taking the n^{th} root on both sides of the equality yields:

$$1 - R = P^{1/n}. \quad (2)$$

Solving for R:

$$R = 1 - p^{1/n}, \quad (3)$$

or

$$R = 1 - \sqrt[n]{P}, \quad (4)$$

which is the correct equation for the letter of Benefiel *et al.* using his notation for the n^{th} root of P. The form of equation 3 or 4 is useful for calculating, in the general population, a condition's expected rate of occurrence corresponding to a desired P value and the number n of consecutive negative observations made.

Another useful form of equation 1 is obtained as follows:

$$(1 - R)^n = P. \quad (1)$$

Taking the logarithm on both sides of the equality

$$n \cdot \log (1 - R) = \log P.$$

Solving for n

$$n = \frac{\log P}{\log (1 - R)}. \quad (5)$$

The form of equation 5 enables calculation of the number of consecutive negative observations (*i.e.*, condition absent) needed to confirm a known or assumed rate of occurrence R at a chosen P value.

To one who has not used these relationships quantitatively, it is surprising to learn the number of consecutive negative observations needed to confirm or infer a low rate of occurrence in the population of a condition under scrutiny. To familiarize the reader with the relation between the rate of occurrence (R) and the number (n) of consecutive negative observations, table 1 presents several milestone values of R and the corresponding values of n for the commonly-used $P = 0.05$ (confidence level 0.95).

For example, if we adopt a new procedure or administer a drug, and we wish to show that the rate of untoward effects is not greater than 10%, we need to observe 28 consecutive cases where the undesirable side effects have not occurred. Observation of 13 consecutive cases without an occurrence only permits the inference of a maximum rate of 20% in the general population of patients. And, as Benefiel *et*

TABLE 1

$P = 0.05$	
R	n
0.20 or 20%	13
0.15 or 15%	18
0.10 or 10%	28
0.05 or 5%	59

al. pointed out, the observation reported by Sears, Abdul-Rasool, and Katz[2] of eight consecutive patients without cardiac dysrhythmia who received a second dose of succinylcholine following induction with ketamine, permits inference of a rate of occurrence as great as 31%, approximately 1 in 3. This statistic does not give one much solace, and indeed the authors' letter of response[3] to Benefiel indicates their clinical confidence in the pharmacologic regimen lay elsewhere.

JOSEPH GRAYZEL, M.D.
Attending Physician, Cardiology
Division of Internal Medicine
Bergen Pines County Hospital
Paramus, New Jersey 07652

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In Reply:—The authors wish to thank Dr. Grayzel for deriving the correct formula that yields R as a function of n and *P*, his equation 4. He has also provided another useful equation, his equation 5, which enables the determination of the number of negative observations required to determine the upper limit of occurrence of an event (R) based on the *P* value.

We also note Dr. Grayzel's agreement with our results and the conclusions drawn from them.

DAVID J. BENEFIEL, M.D.
Director of Cardiovascular Anesthesia

EDWARD A. EISLER, M.D.
Director of Obstetrical Anesthesia

RODGER SHEPHERD, M.D., M.P.H.
Department of Epidemiology

Pacific Presbyterian Medical Center
Clay at Buchanan Street
San Francisco, CA 94120

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An Effect of Temperature on Anesthetic Solubility and Partial Pressure: Clinical Importance

To the Editor:—Ori, Ford-Rice, and London suggest that opioid receptors represent a possible target influenced by general anesthetics, although they add that this influence might not produce the anesthetic state.[1] They find that 100% nitrous oxide and 2% halothane (the latter more than the former) decrease the density of binding sites for κ receptors from guinea-pig brain, and that halothane also decreases binding affinity. Both nitrous oxide and halothane decrease μ binding affinity.

It is not clear to me that these findings are relevant to anesthetizing concentrations of anesthetics. Although Ori, Ford-Rice, and London used what appear to be reasonable concentrations of anesthetic for equilibration of their homogenates, equilibration was accomplished at 0° C. Because an increase in temperature decreases the solubility of gases, including anesthetics, the subsequent increase in temperature applied by Ori, Ford-Rice, and London would increase the anesthetic partial pressure. The partial pressure of halothane that would result at 37° C would be about 8.9% of an atmosphere.[2] Such a partial pressure is eight times that required for anesthesia. Indeed, this interpretation would apply at any temperature because a decrease in temperature decreases anesthetic requirement.[3] Perhaps we should reserve judgment on the effect of general anesthetics on opioid receptors until these elegant studies can be repeated at anesthetizing partial pressures.

EDMOND I. EGER, II, M.D.
Professor of Anesthesiology
Department of Anesthesia
Science-455, Box 0464
University of California
San Francisco, CA 94143-0464

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