

ment with very large doses of steroids, such as methylprednisolone, 1 g, intravenously, may be effective in preventing an anaphylactic response, whereas smaller doses may not be effective. These experiences also suggest that the optimal time for pretreatment is half an hour to several hours prior to challenge. Intravenous administration of diphenhydramine does not appear to be effective in preventing the anaphylactic response,<sup>4-6</sup> although it may be helpful in decreasing the severity of the response.<sup>7</sup> Of course, other unknown situational factors may be very important in preventing anaphylaxis, and it is not possible to determine these factors from small numbers of anecdotal reports such as these. Both Drs. Millbern and Bell's report and our experience underscore the importance of having suitably trained personnel in attendance in situations where an anaphylactic response is likely or expected. Proper preparation for the eventuality and prompt, appropriate intervention can markedly affect the eventual outcome.

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### Averaging pH vs. H<sup>+</sup> Values

*To the Editor:*—In a recent letter to the editor, Giesecke<sup>1</sup> criticized statistical methods used by Stoelting<sup>2</sup> in reporting gastric-fluid pH changes following several preanesthetic medication regimens. Stoelting measured pH in gastric aspirates and derived mean and standard deviation values. Giesecke claimed that pH must first be converted to a real number, then statistically manipulated, and finally reconverted to pH form. Although details of the transformation were not given, it would appear Giesecke meant one should convert the pH to a derived hydrogen ion concentration ([H<sup>+</sup>]), average, take the negative logarithm, and call the result the average pH. He maintained that only a real number can be meaned and that pH, being a logarithm, is not real. (Parenthetically, a logarithmic transformation of a real number is most assuredly also a real number.) We believe that Giesecke is in error, and fear that acceptance of his letter by the editors of *ANESTHESIOLOGY* might reflect a new standard for the review of statistical procedures involving pH.

Both Stoelting and Giesecke seem to implicitly accept pH as the expression of gastric-fluid acidity. We agree with them. Although many have called for the abolition of pH notation and for the use instead of

a derived [H<sup>+</sup>] in describing acidity,<sup>3-5</sup> a consideration of thermodynamics applied to biologic systems confirms the superiority of pH over [H<sup>+</sup>] in relating acidity to physiologic function.<sup>6,7</sup> Although pH was originally defined as  $pH = \log 1/[H^+]$ , pH is now accepted as the measure of acidity without regard to that definition.<sup>7</sup> pH is an independently determined variable; [H<sup>+</sup>] is a derived, dependent variable. Within certain tight constraints, it still remains true that  $pH = -\log a_{H^+}$ , where  $a_{H^+} = \gamma [H^+]$ : hydrogen ion activity;  $\gamma$ : activity coefficient). It is likely that most physiologic processes affected by hydrogen ion respond in a manner proportional to the logarithm of the hydrogen ion activity.<sup>6</sup>

A series of pH measurements can be summarized by a sample mean and sample standard deviation. It is erroneous to take the antilog of the pH, invert, average, take the negative logarithm of the average, and call this number the mean pH.<sup>7</sup> Let us consider a simple example. Given two samples of gastric fluid of equal volumes with pH 1 and 6, the mean pH is 3.5. When Giesecke's method is used, the following calculations have to be made. First, the pH values are converted to [H<sup>+</sup>]; thus, pH 1 yields [H<sup>+</sup>] = 10<sup>-1</sup> mol/l and pH 6 gives [H<sup>+</sup>] = 10<sup>-6</sup> mol/l. Next, the average of

the  $[H^+]$  values  $(10^{-1} + 10^{-6})/2 \cong 5 \times 10^{-2}$  mol/l is obtained. Finally, the negative logarithm of this average is the mean  $pH$ :  $-\log 5 \times 10^{-2}$ , or  $pH = 1.3$ . Since  $10^{-6}$  is far smaller than  $10^{-1}$ , its contribution to the average is trivial and changes little the calculated mean  $[H^+]$ . Obviously,  $pH = 1.3$  is a far different result from  $pH = 3.5$ . Since  $pH$  is linearly related to chemical potential, then an average value of  $pH$  should properly represent the average value of the disposition of hydrogen ion to participate in the physiologic state being studied.<sup>6,7</sup> Thus, in our example, the appropriate mean  $pH$  is 3.5, not 1.3.

This recent notion that  $pH$  should be converted to  $[H^+]$  for averaging arises from the assumption that random variations of  $[H^+]$  have a normal distribution. No experimental or theoretical evidence supports this assertion.<sup>6,7</sup> To the contrary, theoretical considerations suggest that it is  $pH$  that is normally distributed.<sup>6,7</sup>

In some circumstances use of  $[H^+]$  rather than  $pH$  is needed.<sup>6</sup> For example, if Stoelting had measured gastric acid production (by use of titration methods in gastric-fluid samples), then the results should have been expressed as  $[H^+]$ , not  $pH$ . Any statistical manipulations (mean, standard deviation, standard error, confidence intervals) should have also been expressed in terms of  $[H^+]$ . We strongly recommend that in re-

porting  $pH$  results, usual statistical calculations are correct and appropriate without any data transformations.

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*In reply:*—I have read with sustained fascination the correspondence by Pace *et al.* and others regarding mean  $pH$  as an expression of the central tendency of acidity in gastric specimens. Many arguments have been presented in favor of meaning  $pH$  values by adding them all together and dividing by "n" exactly the same as one would derive the mean of any other set of numbers.<sup>1,2</sup> These arguments were so eloquent that I began to doubt my own conviction that this mathematical manipulation was not scientifically valid.<sup>3-5</sup> My conviction was based largely on the knowledge that when one adds logarithms the antilogs that they represent are multiplied, not added. Further, when one divides a logarithm by a number "n", then one achieves the "n-th root" of the antilog which is represented. The controversy boils down to a simple question: "Which of the following is the best expression of the central tendency of acidity in a series of solutions of different  $pH$ ?"

$$\bar{X} = \frac{\sum x}{n}$$

or

$$\bar{X} = \sqrt[n]{X \cdot X \cdot X \cdots}$$

I decided to test the question physically rather than just speculate on the theoretical mathematics. In the laboratory I added 100 ml of distilled water to each of five beakers. Using a continuously reading  $pH$  meter, I added hydrochloric acid or sodium hydroxide dropwise until the  $pH$  values of the five solutions read 2.045, 3.114, 4.131, 5.192 and 6.063. Triplicate observations and constant stirring were used to assure accuracy of the readings. To determine the central tendency of acidity of the solutions, I poured 25 ml of each of the five solutions together in a mixing flask and measured the  $pH$  of the resulting solution. If mean  $pH$  were a valid expression of the central tendency of acidity, then the  $pH$  of the resulting solution should read 4.109. Alas, the actual reading was 2.758, which happens to be the  $pH$  of the mean hydrogen ion concentration in the resulting solution. I, therefore concluded that best expression of the central tendency of acidity in a series of solutions can be proven by