A Statistical Approach to the Problem of Acid Secretion by the Gastric Glands*

Gladys R. Bucher

Mundelein College for Women and Northwestern Medical School, Chicago, Illinois

It was the purpose of this research to secure a large number of observations and deduce by statistical methods the answers to the following questions: (1) How do the chemical constituents containing chloride vary with the rate of secretion? (2) How do these constituents vary with respect to one another? (3) Which relationships contribute the most useful information toward answering the paramount question, at what concentration does the cell of the gastric gland secrete the hydrochloric acid?

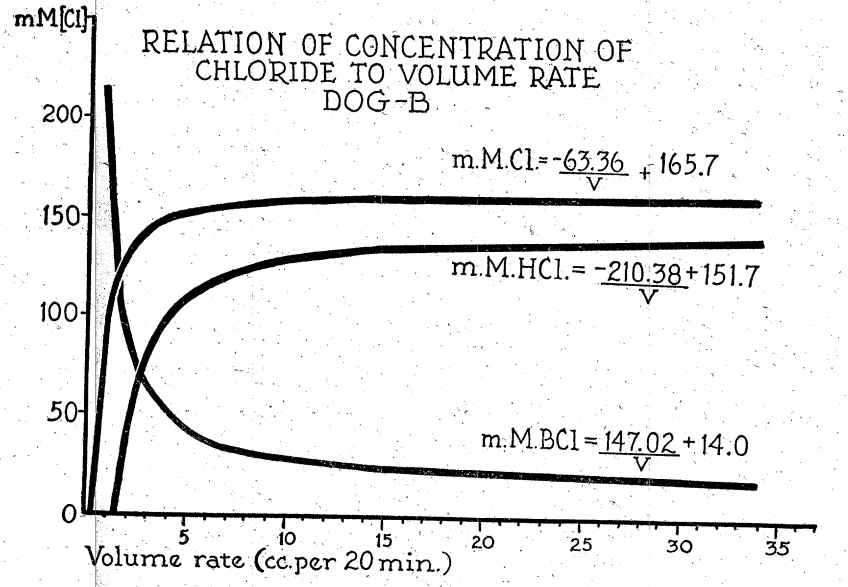

Fig. 1.

We have used dogs provided with pouches of the total stomach. The secretory stimulant was a constant amount of histamine administered subcutaneously every 10 minutes. This dose was varied during part of the work to secure all ranges of volume-rates. Collections were made every 20 minutes. Total and free acid was determined by titration. Total chlorides were determined by the Volhard titration method. The neutral chloride was taken as the difference between the total and acid chloride values.

One hundred separate samples were collected and analyzed on each of two dogs. In addition, 183 samples were collected from 6 dogs and these pooled into 9 large samples on the basis of volume-rate in 20 minutes. The data on each sample consisted of the following: neutral chloride output, neutral chloride concentration, acid chloride output, acid chloride

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concentration, total chloride output, total chloride concentration, and the volume. All relationships were studied by a method of "least squares", which determined a linear equation that mathematically and graphically would express the trends of the data. The general form of the equations obtained is $y = a + bx$. The validity of these curves was measured in a degree by the probable errors of the constants a and b or by the standard error of estimate. The mathematical results of all our experiments display amazing uniformity. When the observed values were plotted about the theoretical lines, the degree of fit was most gratifying.

The outputs of both total and acid chlorides were found to increase with the volume-rate, the total chloride output increasing more rapidly. The mathematical difference between these equations expresses the relationship of neutral chloride output to the volume-rate. The neutral chloride output also increased but at a very slow rate. When all lines are extended to the volume-rate axis, meaningless values are indicated for it would appear that a neutral chloride output can exist in the absence of a total chloride output. We feel certain that at minute volume-rates, the relationships cease to be linear and deviate to describe curves that pass through the origin.

After the manner employed by Lim (1), these linear expressions were converted into hyperbolic functions expressing the relationship of concentration to the volume-rate. These curves are seen in Fig. 1 for the dog B. The asymptotic nature of these curves is self evident. If the volume-rate is extrapolated to infinity, the maximum concentration of total chloride approaches 165.7 mM and that of the acid chloride, 151.6 mM as maximum value, while the concentration of the neutral chloride approaches a minimum at 14 mM. Since all the curves level off at experimentally possible volume-rates, this extrapolation is justifiable. The significance of these curves near the origin is meaningless again, until after the point at which they intersect.

When the relationships of the concentrations to each other were studied, the results could also be expressed by straight lines. As the acidity increased, the total chloride concentration increased and the neutral chloride concentration decreased. Applying the "least squares" method to the data was found to be no more accurate than to derive the relationship from the output equations. This relationship is subject to large errors regardless of the way the equation is obtained: i.e. fitted or derived. Our experiments have yielded statistically significant results showing that:

(1) As the volume-rate increases, the outputs of total chloride, acid chloride and neutral chloride all increase in the order given, beginning with total chloride increasing most rapidly.

(2) The concentrations of the various chlorides bear a hyperbolic relationship to the volume-rate; those for total chloride and acid chloride increasing with the volume while that for neutral chloride decreases.

(3) The concentrations when studied as functions of the volume, all display asymptotic maximum or minimum values when the volume is extrapolated to infinity. This extrapolation is justified for the limits are reached at volume-rates experimentally attainable. Average values for these limits from our 3 experiments are:

Maximum total chloride	165.7 mM
Maximum acid chloride	152.6 mM
Minimum neutral chloride	13.1 mM

(4) The concentration of total chloride increases in a direct linear manner with the acidity, while the neutral chloride concentration decreases. These linear functions must be limited to the maximum and minimum values as determined by the hyperbolae obtained from the output equations. Extrapolations beyond these limits are meaningless.

Because the output studies can be manipulated to express concentration relationships as well as show the limits under which the relationships are valid and significant, we feel that the output to volume-rate studies contribute the most useful information relevant to the question; at what concentration is each of chloride constituents secreted by the cells.

BIBLIOGRAPHY

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