XXII. STUDIES ON CARBONIC ACID COMPOUNDS AND HYDROGEN ION ACTIVITIES IN BLOOD AND SALT SOLUTIONS.

A CONTRIBUTION TO THE THEORY OF THE EQUATION
OF LAWRENCE J. HENDERSON AND K. A. HASSELBALCH.

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INTRODUCTION

K. A. HASSELBALCH in 1916 introduced a formula with the help of which it is possible to determine the hydrogen ion concentration of the blood from the amount of its combined and dissolved carbonic acid, basing his equation upon the work of L. J. Henderson carried out from 1908–1910. Henderson employed the then generally known equation for the first dissociation of carbonic acid, namely,

$$\gamma \frac{C_H C_{HCO'_3}}{C_{H_2CO_3}} = K_1.$$

Applied to the determination of the C_{H^+} of the blood he got

$$C_{H^+} = \frac{C_{H_2CO_3}}{C_{HCO_3^-}} \times \frac{K_1}{\gamma}.$$

By substituting the best known values at the time for combined and dissolved CO_2 , for the first dissociation constant of carbonic acid and for the dissociation of bicarbonate, he found a value for C_{H^+} which corresponded fairly well to the reaction of the blood as it was thought to be at that time. Henderson [1909–1910] concluded from his calculations that the major portion of combined carbonic acid in the blood was in the form of bicarbonate.

Hasselbalch [1916] determined in the same sample of blood (and serum) C_{H^+} , $C_{HCO_3^-}$ and $C_{H_2CO_3}$, and found that C_{H^+} was the same as calculated by substituting in the equation the value of $\frac{K_1}{\gamma}$ for a solution of pure sodium bicarbonate. He thought he could infer from this that all the combined carbonic acid of the blood was in the form of bicarbonate and that the C_{H^+} of the blood could be estimated by means of the equation when $C_{H_2CO_3}$ and $C_{HCO_3^-}$ were known.

As investigations on kindred subjects progressed it became clear the theory could only be recognised as a first approximation—a view which a knowledge of S. P. L. Sørensen's *Studies on Proteins* [1915–1917] strongly supported—and the question immediately arose, how is it possible the calculated and experimental values of C_{H^+} can coincide when the suppositions of the calculation are inadequate?

It further became evident from experience gradually accumulated regarding the C_{H^+} measurements by the Hasselbalch-Michaelis principle (shaking method combined with minimal immersion), that experimental difficulties were present which had not been entirely overcome, since measurements with various electrodes gave constant differences. And as the Henderson-Hasselbalch equation seemed to be destined to play an important rôle in physiology and pathology it was necessary to subject both the measurements and the theories which formed the basis of the equation to a further test.

The present work therefore has a double object, viz.:

(1) to investigate whether the Henderson-Hasselbalch equation gives correct results when the measurements are carried out by another method than that of Hasselbalch;

(2) to develop a theory connecting the amount of carbonic acid in the blood with its reaction.

In connection with this a number of points have naturally arisen concerning the distribution of ions between blood cells and serum, and a series of experiments on the reactions in simple watery bicarbonate solutions in equilibrium with different tensions of CO_2 have been made.