A considerable amount of data has accumulated in regard to disturbance of the acid-base balance in both experimental and pathological conditions. The normal variations in the alkali reserve of blood and plasma have been well established (Peters, Barr, and Rule; and Van Slyke), but comparatively little attention has been paid to the extent of the normal variation in hydrogen ion concentration of the plasma.

This report presents data on the variation of the plasma pH in normal persons, together with parallel observations on the alkali reserve and on oxygen contents and capacities. The data are also utilized to show the relationship between $pK_1$ (of Hasselbalch's equation) values of plasma and of whole blood.

Through the courtesy of Dr. S. Goldschmidt and Dr. A. Light and their students, and in cooperation with their regular laboratory work on the physiology of the blood in the Department of Physiology in this University, we obtained venous blood from twenty-seven normal medical students. Every sample was taken without stasis from an elbow vein by the same person, Dr. Light, through a sterile dry needle into Pyrex tubes containing mineral oil and neutral powdered potassium oxalate to make 0.3 per cent. The samples were all taken at the beginning of the laboratory period between 10 and 11 a.m. after an hour's lecture and therefore under uniform conditions. They were all taken in April, 1922.

A portion of the blood was centrifuged at once for about three-quarters of an hour in a full, stoppered tube and the plasma removed with the usual precautions. The pH determinations were made by Cullen's colorimetric method. The readings were
### Normal Plasma pH

#### TABLE I.

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* Average values of Peters, Bulger, and Eisenman, and of Gram and Norgaard.

† Calculated from Hasselbalch's equation using Bohr's coefficient 0.511 for whole blood at 35° (relative solubility coefficient 0.920).

‡ Calculated from cell volume using Bohr's relative solubility coefficient of 0.81 for red cells and 0.975 for plasma.
all made between 20 and 25°C. and corrected to the pH values at 38°C. by the equation

$$\text{pH}_{38} = \text{pH}_r + 0.01(t^\circ - 20^\circ) - 0.22,$$

where $t^\circ$ = temperature of the reading.

The [CO₂] content determinations were made with Van Slyke's constant volume apparatus. The oxygen content and capacity measurements were made with Van Slyke and Stadie's technique.

![Graph](attachment:image.jpg)

**Fig. 1.**

using the short form of Van Slyke's apparatus. We are indebted to Dr. J. H. Austin for these oxygen determinations. The whole blood [CO₂] contents were determined on twenty-three of the samples, and on fourteen of these parallel plasma [CO₂] content determinations were made.

The results are given in Table I and in Figs. 1, 2, 3, and 4.
Normal Plasma pH

Fig. 2.

Fig. 3.
Fig. 4. • = Δ pK₁ values calculated from Hasselbalch’s equation using Bohr’s coefficient 0.511 for whole blood at 38° (relative solubility coefficient 0.920). + = Δ pK₁ values calculated from cell volume using Bohr’s relative solubility coefficient of 0.81 for red cells and 0.975 for plasma.

Hydrogen Ion Concentration.

The pH of the plasma varied from 7.28 to 7.41. Twenty-one of the twenty-seven determinations lay between 7.35 and 7.40. The maximum variation in pH was 0.13 pH. Even if one assumed that the two extreme values of 7.28 and 7.41 were in error by 0.02 pH (and in the opposite direction) it is evident that any pH values of plasma, measured at 38°, between 7.3 and 7.4 must be accepted as normal.

It is probable that in a similar number of normals taken at random there would be greater variations than in this group where the conditions of age, time of day, activity, occupation, etc., were so uniform.

It is felt that these data lend support to the view that the ordinary normal individual and day by day variations in the reaction of the blood are greater than has been supposed.
Normal Plasma pH

Total [CO₂] Content of Blood and Plasma.

In Fig. 1 the total [CO₂] contents of blood and plasma are plotted against pH. Within these normal limits of pH and [CO₂] content there is apparently no systematic relation between the variables, pH and [CO₂] content. In Fig. 2 the whole blood [CO₂] contents are plotted against hemoglobin contents. Again, for this normal range, there is no apparent relation between the level of blood [CO₂] and hemoglobin content.

In order to determine what influence the hemoglobin content of the blood exercised on the position of the blood in the acid-base diagram the blood [CO₂]-pH points of Fig. 1 have been replotted on a larger scale in Fig. 3 and have been divided into four groups according to oxygen capacities—17.7 to 18, 18 to 20, 20 to 22 and 22 to 25 volumes per cent.

It is evident that within this normal range of hemoglobin content any changes in the position of the [CO₂]-pH points on the diagram due to varying hemoglobin are negligible in comparison with the other variations that occur normally.

Difference between Whole Blood and Plasma pK₁.

When both whole blood and true plasma [CO₂] contents are available as well as the plasma pH the data may be utilized to determine the difference between whole blood and plasma pK₁ values, in a manner similar to that used by Peters, Bulger, and Eisenman.

For the purpose of calculation, a plasma pK₁ of 6.10 was assumed¹ and from the pH and [CO₂] content of the plasma, the [H₂CO₃] of the plasma was calculated from Hasselbalch’s equation

\[
\text{pH} = \text{pK}_1 + \log \frac{[\text{BHCO}_3]}{[\text{H}_2\text{CO}_3]}
\]

For details of this calculation see the paper on technique (Austin and coworkers). From the plasma [H₂CO₃] using Bohr’s solubility coefficient of 0.541 the CO₂ tension at 38° was calculated.

Using this same tension the blood pK₁ values were calculated in two ways. In the first, Bohr’s blood solubility coefficient at 38°

¹ The arbitrarily selected value of 6.10 is probably nearly correct. We have recently, on three human plasmas, determined pK₁ electrometrically and obtained 6.081, 6.090, and 6.106.
of 0.511 was used to calculate the blood $[H_2CO_3]$ and from this, and the measured value of blood $[CO_2]$ content, the pK$_1$ of the blood was obtained. The difference between this and the plasma pK$_1$, is given in Column 10 of Table I ($\Delta$pK$_1$, a).

Warburg, and later, Peters and coworkers have criticized the use of the average value of 0.511 for blood solubility on the ground that the variation in cell volume should be included in the estimation of the CO$_2$ that is dissolved in whole blood. This contention seems correct and the problem is presented of what value to use for cell CO$_2$ coefficient. Peters accepts Bohr's values for plasma and cells and uses the equation $(0.7118-0.1205C) pCO_2 = [H_2CO_3]$ where $C$ = the cell volume.

Using this equation the values for $\Delta$pK$_1$ were calculated and are given in Column 11 of Table I ($\Delta$pK$_1$, b). The cell volumes were calculated from Peters' value of 0.465 for the oxygen capacity: cell volume ratio which agrees with the values of Gram and Norgaard.

Both the $\Delta$pK$_1$ values calculated from Bohr's blood solubility coefficient and those calculated from Peters' equation are plotted against cell volume in Fig. 4. Since our pH values are all between 7.30 and 7.40 the influence of pH variations is negligible. It is evident that there exists, over this normal range, a rather large variation in $\Delta$pK$_1$ values.

It is also evident that the average value of $\Delta$pK$_1$ of 0.05 calculated by the Bohr solubility factor is about 0.01 higher than the average of the values calculated from Peters' equation. Our results are not of a nature to throw light on the question as to which values are the more accurate. It is worth while, however, to call attention to the difference in the assumptions involved in the two methods. In the first method, the assumption is that Bohr's value of 0.511, established on defibrinated ox blood, is identical with that for normal human blood. The assumption in the equation of Peters, Bulger, and Eisenman—which is derived from the equation $\left(\frac{555}{760} \times [\text{volume of plasma} \times 0.975 + \text{volume of cells} \times 0.81] = H_2CO_3\right)$—is the validity of Bohr's calculation that the relative solubility of CO$_2$ in red cells, as compared with water, is 0.81. Bohr calculated this from his plasma and whole blood coefficients by assuming a cell volume for his defibrinated ox blood of one-third. The desirability of correcting the whole
blood pK₁ values on the basis of cell volume is unquestioned in
the pathological conditions involving changes in cell volume.
It seems important also, as Peters and coworkers have done, to
establish the normal variation upon the same assumption used in
calculating the abnormal. Until the solubility coefficients for
normal human blood and cells have been more accurately estab-
lished, one may arbitrarily choose one or the other of these alter-
native assumptions. For determining the correction for any given
cell volume we may, since Δ pK₁ = 0 when cell volume = 0,
draw that line from the origin which passes as a median through
the Δ pK₁ value at normal cell volume. In Fig. 4 two such lines
are drawn, the upper is the median through the Δ pK₁ values cal-
culated from Bohr's whole blood solubility coefficient, the lower
the median through the values calculated from Bohr's plasma and
red cell solubility coefficients.

SUMMARY.
Venous blood was obtained under uniform conditions from
twenty-seven normal individuals.
On twenty-three of these specimens whole blood [CO₂] content,
and oxygen content and capacity were determined, and on sixteen
of these true plasma [CO₂] content was also determined.
From these data the difference between the pK₁ of whole blood
and plasma has been calculated. The assumptions involved in
this calculation are discussed.

pH determinations were made by the colorimetric method on
the plasma of these bloods. The pH of the plasma at 38° varied
between 7.28 and 7.41. The significance of this normal variation
is discussed.

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THE NORMAL VARIATIONS IN PLASMA HYDROGEN ION CONCENTRATION
Glenn E. Cullen and Howard W. Robinson


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