McKim,[1] H. Lowenburg,[2] Geo. T. Grinnan,[3] H. B. Weiss,[4] J. Mitchell Clarke,[5] Herbert Brown,[6] W. deB. MacNider,[7] A. W. Sellards,[8] V. Pleth[9] and many more.

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## ON THE SWELLING OF PROTEIN COLLOIDS. A REPLY.

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Professor Fischer's rejoinder seems to me to call for no modification of my original statement. But, in that he has at length undertaken to consider the question of the quantitative relation between change of volume of a colloid and change of hydrogen-ion concentration, I wish to make the following additional remarks:

First, Fischer is mistaken in supposing that I have admitted or that there is in fact any evidence that the hydrogen-ion concentration in any part of the body can ever vary as widely as in those solutions of his to which attention has been called. The present state of knowledge upon variations of the hydrogen-ion concentration in the body may be illustrated by Michaelis's extensive studies of venous blood.[10] The data fall into three groups: (I) 64 measurements on 28 normal specimens; (II) 34 measurements on 17 pathological specimens from cases of diabetes, nephritis, and edema, which therefore involve conditions contemplated by Fischer's theories; (III) 38 measurements on 19 pathological specimens representing various other diseases. The data are summarized in the following table:

TABLE I.—VALUES OF $p_H$ FOR VENOUS BLOOD (MICHAELIS).

| | I. | II. | III. |
|---|---|---|---|
| High | 7.67 | 7.67 | 7.74 |
| Low | 7.49 | 7.50 | 7.42 |
| Mean | 7.58 | 7.58 | 7.62 |
| Range | 0.18 | 0.17 | 0.32 |

Evidently the values of $p_H$ for venous blood, both in normal and in pathological conditions, are liable to very small variations. In a single case of diabetic coma just before death Michaelis observed a value of $p_H$ of 7.12.

[1] Gordon F. McKim, personal communication (1914).

[2] H. Lowenburg, *J. Am. Med. Assoc.*, **63**, 1906 (1914).

[3] Geo. T. Grinnan, *Virg. Med. Semi-Month.*, **20**, 523 (1916).

[4] H. B. Weiss, *J. Am. Med. Assoc.*, **68**, 1618 (1917); *Ohio State Med. J.*, **13**, 595 (1917).

[5] J. Mitchell Clarke, *Brit. Med. J.*, **2**, 239 (1917).

[6] Herbert Brown, personal communication from Flanders received Sept. 1, 1917.

[7] W. deB. MacNider, *J. Exp. Med.*, **23**, 171 (1916); *Ibid.*, **26**, 19 (1917); *Proc. Soc. Exp. Biol. Med.*, **14**, 140 (1917).

[8] A. W. Sellards, "Acidosis and Clinical Methods," Cambridge, 1917.

[9] V. Pleth, personal communication, 1917.

[10] L. Michaelis, "Die Wasserstoffionenkonzentration," Berlin, **1914**, pp. 101–105.

Such observations are the sole evidence that the normal reactions of the blood can suffer substantial change, even for a few hours.

Secondly, according to Fischer's measurements, these variations of $p_H$ which Michaelis has observed in the venous blood of nephritics, diabetics, etc., involve a change of swelling of gelatin plates of less than 2%. Fischer's estimate of a 50% change of volume is therefore illusory and his further remarks are irrelevant.

Professor Fischer must demonstrate very much wider variations of hydrogen-ion concentration than are now known to occur within the organism or very much greater changes in swelling within physiological ranges than are now known, before there can be any ground for accepting his theories.

This is not the place to enter upon a discussion of the physiology of respiration or the changes in volume of the blood corpuscles. But in order to avoid misunderstandings I venture to say that Fischer's interpretations of both phenomena seem to me contrary to the evidence.[1]

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## NOTES.

**Rapid Organic Combustions of Substances Containing Nitrogen.**—In a note "On Rapid Organic Combustions"[2] the use of cerium dioxide as a catalyst deposited on asbestos was supplemented by cupric oxide, and it was shown that by the addition of the lead peroxide-minium mixture the method could be used for determining carbon and hydrogen in substances containing nitrogen also. The lead peroxide which was obtained by us was found to be very unsatisfactory, and this same trouble was mentioned recently by Wise in connection with the micro method.[3] At first we abandoned the use of the lead peroxide altogether, and by keeping the latter part of the cupric oxide at a comparatively low temperature some fair results were obtained. When, however, a very active catalyst was used a large amount of nitric acid was formed and in one series of experiments the tube, after 8 runs, was finally completely clogged on account of the formation of a basic copper nitrate. The lead peroxide mixture is usually placed about 5 cm. beyond the cupric oxide and must be kept at about 300–320°[4] in order to avoid the decomposition of any lead nitrate formed.[5] The

[1] Cf. Haldane, J. S., "Organism and Environment as Illustrated by the Physiology of Breathing," New Haven, 1917; Barcroft, J., "The Respiratory Function of the Blood," Cambridge (England), 1914; Höber, R., "Physikalische Chemie der Zelle und der Gewebe," Leipzig, 1914.

[2] Reimer, THIS JOURNAL, **37**, 1636 (1915).

[3] Wise, *Ibid.*, **39**, 2055 (1917).

[4] Dennstedt, "Anleitung zur vereinfachten Elementaranalyse," III Aufl., p. 66, Hamburg, 1910.

[5] Lead nitrate decomposes rapidly at 357°. Baekeland, THIS JOURNAL, **26**, 391 (1904); Morgan, *J. Phys. Chem.*, **8**, 416 (1904). We could not find any specific data on the temperature of decomposition of the basic copper nitrates.