Post Scripta.

While this book was printed *H. A. Krebs* and *W. A. Johnson* (*Enzymologia*, 4, 148, 1937) published a paper bearing closely on the C_4 theory of respiration. According to these authors the C_4 are but members of a more complicated cycle in which oxaloacetate combines with „triose" to form citrate. Citrate on its turn is oxidised, step by step, into succinate, succinate into oxaloacetate which again combines with triose. The carbohydrate is thus oxidised *via* citrate.

Undoubtedly, much can be said in favour of this theory, which, if found correct, would necessitate a thorough revision of this book.

Citric acid has occupied also my laboratory *(F. L. Breusch)* for some time, for its close chemical relation to C_4, and the analogous behaviour of the citrico- and malico-dehydrogenase, both suggest a catalytic function. We can corroborate most of the observations of *Krebs* and *Johnson*. We think, however, that the observations of these authors are capable of a different interpretation. Our experiments rather suggest, that the cycle, even if it exists, has but a minor part in the total oxygen uptake of muscle.

This is not the place to enter discussion and I am quoting our observations merely as an apology for publishing this book unchanged.

In another paper *H. A. Krebs* showed (Perspectives in Biochemistry, Cambridge University Press, 1937) that in the oxidative processes of *Bacterium coli* fumaric acid can replace oxygen. He arrives at the conclusion that the system of succinic-fumaric acid, together with its dehydrogenase plays, as catalytic H transmitter, an important rôle also in bacterial metabolism.

I want to mention here a few further observations, made since the foregoing pages were written.

Parnas and *Szankowski* (Enzymologia *3*, 220, 1937) have found oxaloacetate equivalent to pyruvate as H acceptor of triose and have given herewith strong support to the theory of the *Pasteur* Reaction, presented in this book.

H. v. Euler and *M. Malmberg* (Z. f. physiol. Chem. *242*, 85, 1937) have found vitamin P active in promoting the formation of reticulocytes in scurvy, giving thus a new evidence for the biological activity of this substance. The authors find a certain synergism between C and P.

I have been informed that a laboratory, with which I had the pleasure of collaborating a few years ago, has also tried the effect of hesperidine combined with minute doses of vitamin C in scorbutic guinea pigs. These experiments, performed simultaneously and independently, have led to results identical with those of *Bentsáth*. Unfortunately, however, *Bentsáth* himself was unable to corrobrate his previous findings in a later series of experiments. The results of a third laboratory were equally negative. It is evident, that there is a further unknown factor still, responsible for this variation. May be, a new and labile accessory food factor is hiding behind these discrepancies and I am afraid, much work will be needed, till their final cause will be revealed.

During the last weeks, at the discussions of the *Solvay* conference at Bruxelles, it became clear to me that the „ascorbic acid oxidase" is not merely an oxidase. As mentioned on p. 77, *Hopkins* and *Morgan* showed that „ascorbic acid oxidase" activated ascorbic acid also in its reaction with glutathion, speeding up the reduction of dehydro-ascorbic acid by SH. The function of the enzyme is thus primarily not to oxidise, but to *activate* ascorbic acid. In presence of O_2 the activation will reveal itself in an increased oxidation of ascorbic acid and the activator will act as an oxidase. The „ascorbic acid oxidase" is thus a new example of a protein, activating a smaller molecule and ascorbic acid is an example of a vitamin activated within the cell. *v. Euler* expressed similar views.

It has been reported by *Lawrence, McCance* and *Archer* (Brit. med. J. No. 3995, 1937) that succinic acid, applied in two

diabetic patients, had no effect on acidosis. This suggests, that the cases, observed by *Korányi* responded more favourably, than many diabetic patients will do. Undoubtedly, acidosis represents a very complicated problem and more experience will be needed to arrive at definite conclusions and to find out whether succinic acid is useful at all fighting acidosis. There can be little doubt about the effect of succinate on acetone formation is certain experimental conditions and in tissue slices, which effect can readily be demonstrated. The system, composed of a human patient and a clinician is too involved and many things might happen in such a complex system.

I want to mention a paper at last, published by *L. F. Leloir* and *M. Dixon*, wich reached me but lately (Enzymologia, 2, 81, 1937). This paper deals in part with the action of pyrophosphate, which substance strongly inhibits respiration. According to these authors, to the one of whom we owe much of our knowledge of respiration, pyrophosphate has an action analogous to malonate, poisoning the succino-dehydrogenase in a specific way. Its inhibitory effect on resipration is explained by its action on the C_4 system. The action of pyrophosphate is thus a further evidence for the correctness of views presented in this book.

Oct. 18, 1937.