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Acid-Base Balance and the Distribution of Fat in the Blood.

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The mechanism of fat transport from and to the tissues is obscure. The fat content of the blood has been determined both experimentally and clinically in a variety of conditions, by a number of investigators.[1] It has been generally assumed that an increased amount of fat in the blood signified the transfer of fat from one site to another for the purposes of storage or metabolism. A review of this subject suggested to us that most of the conditions in which lipemia had been reported were characterized by the tendency for the acid-base balance to be shifted towards the acid side. This parallelism has been previously noted in the case of diabetes.[2, 3, 4] However, the same relationship is evident if one considers such clinical states as starvation, hemorrhage and nephritis and such experimental conditions as severe exercise, pancreatic diabetes and phlorhizination.[1] It, therefore, seemed worthwhile to investigate the effects of experimentally induced changes in acid-base balance upon fat transport as indicated by lipemia.

"Acid" and "alkaline" salts were administered intravenously or by mouth to normal dogs. Various salts were used (ammonium chloride, ammonium lactate, sodium bicarbonate and sodium lactate) to obviate the influence of specific ions. Blood samples were taken at hourly intervals for 4-6 hours after the salt administration and analyzed for total blood fat[5] of the whole blood and serum respectively, and for carbon dioxide-combining power. Hematocrit readings were made to determine the partition of the fat between the red blood cells and the blood plasma.

During the course of these experiments it became of interest to determine whether particular organs were important to the results which we obtained on normal animals. Accordingly the above pro-

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1 Peters, J. P., and Van Slyke, D. D., *Quantitative Clinical Chemistry (Interpretations)*, Springfield, 1932.

2 Gunnar Blix, *Studies on Diabetic Lipemia*, Lund, 1925.

3 Allen, F. M., *J. Metab. Research*, 1922, **2**, 238.

4 Curtis, A. C., Sheldon, J. M., and Eckstein, H. C., *Am. J. Med. Sciences*, 1933, **186**, 548.

5 Bloor, W. R., *J. Biol. Chem.*, 1928, **77**, 53.

cedures were performed on depancreatized, hypophysectomized, and eviscerated animals respectively. In the last mentioned group of animals an anesthetic was necessary. However, control experiments on anesthetized normal animals showed that the anesthetic (nembutal) employed did not influence the results.

The results of changes in the acid-base balance, by whatever means, were uniformly consistent in all our experiments. It will, therefore, suffice to present 2 typical experiments (Fig. 1) and a composite graph summarizing our results as a whole (Fig. 2). Since the control values for blood fat varied between wide limits in different animals, our results in Fig. 2 are expressed as percentage rise or fall from the control values.

The data show that changes in the acid-base balance have no significant influence on the fat content of the whole blood. It is evident, however, that a fall in the carbon dioxide-combining power is associated with a rise in the serum fat, while a rise in the carbon dioxide-combining power is accompanied by a fall in the serum fat. These results must be interpreted as indicating a shift of fat from the red blood cells to the plasma and vice versa, under the influence of disturbances in the acid-base equilibrium. The presence or absence of the pancreas, the hypophysis or the liver and abdominal viscera had no influence on the nature of the results obtained.

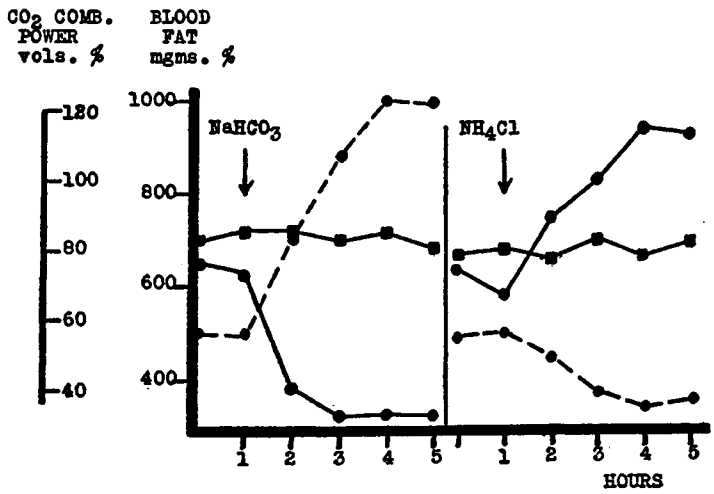

FIG. 1.

Two experiments on the same normal dog, showing the influence of experimentally induced increase and decrease of the carbon dioxide combining power upon the whole blood fat and serum fat respectively. The broken lines indicate carbon dioxide combining power. The continuous lines with the solid squares represent the whole blood fat. The continuous lines with the round dots represent the serum fat.

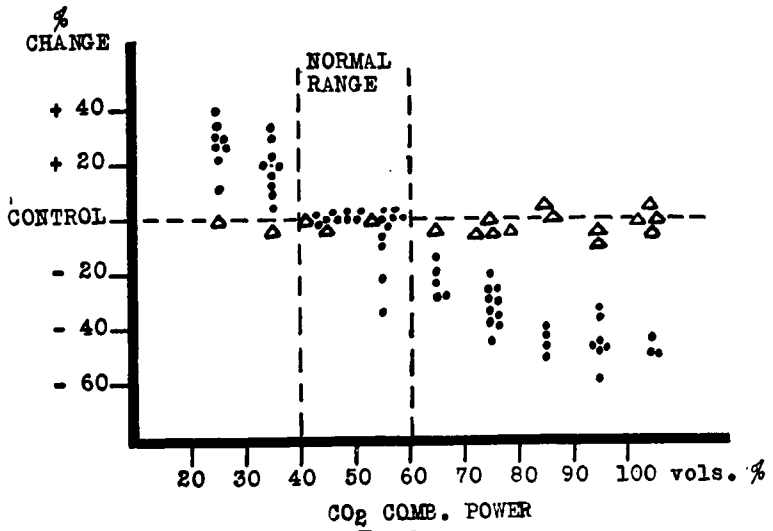

FIG. 2.

Summary of all our results in percentage change from the control values, to obviate the large normal variation in the latter. The round dots represent serum fat. The hollow triangles represent whole blood fat. Note that the serum fat is influenced by the carbon dioxide combining power, while the whole blood fat is not.

The term "lipemia" has been used indiscriminately to denote increases in the fat content of the whole blood, the plasma or the serum according to which medium the observers happened to direct their attention. It is evident from our results that increases in fat content of the whole blood and serum are not necessarily parallel, nor do they have the same significance as regards fat transport. A lipemia of the whole blood must indicate a transfer of fat from the tissues to the blood, and if the increased blood fat is carried to a distant organ or tissue, this would constitute the transport of fat. It is equally clear, however, that when fat is determined in the serum only, any lipemia so observed may indicate only a shift of fat across the membrane of the red blood cell into the plasma, without any increase in the total fat of the blood, and without any participation of the fixed tissues.

A review of the literature on lipemia, in the light of our present results, does not allow an unequivocal answer to the question of the relationship between the acid-base balance and fat transport. This is due to the fact that there has been no uniformity in the methods of fat analysis or in the use of whole blood or serum for the determinations.[6] Our results indicate that those determinations which

[6] Nissen, N. I., *Alimentary Lipæmia in Man*, Copenhagen, 1933. (Contains extensive bibliography on lipemias.)

were made on serum cannot be used to establish the relationship and, for the short experimental periods which we used, no transport of fat was observed. It is apparent that further work, using analysis of whole blood, is necessary. It may be noted, however, that even the shift of fat from red blood cells to plasma may have some significance as regards fat transport, since it represents a higher concentration of fat in that portion of the blood which is immediately concerned with the transfer of food stuffs to the tissue cells.

Conclusions. 1. A reciprocal relationship has been shown to exist between the carbon dioxide combining power of the blood and the concentration of total fat in the blood serum. 2. Changes in serum fat content produced by altering the acid-base balance are not accompanied by changes in the fat content of the whole blood, within the duration of our acute experiments. 3. The changes in serum fat are therefore the result of a shift of fat between the red blood cells and the blood plasma. 4. The significance of serum and whole blood lipemias as regards fat transport, is discussed.

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Effect of Certain Yohimbine Derivatives upon Arterial Strips.

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Previous work by F. Meyer,[1] Hamet,[2, 3] Weger[4] and others indicates that the yohimbine radicle exhibits a rather marked antisympathicomimetic action in various organs. Some investigators have studied various isomers of yohimbine with similar results but our present work deals with several newly formed HCl salts of the yohimbine radicle in the form of ethyl, allylamine, butyl, diethylaminoethyl, phenyl and allyl derivatives.* Essentially, these derivatives behave similarly to yohimbine HCl but ethyl yohimbine

[1] Meyer, F., *Arch. f. d. ges. Physiol.*, 1912, 223.

[2] Hamet, M., *Comp. rend. Acad. d. sc.*, 1925, **180**, 2074.

[3] Hamet, M., *Comp. rend. Soc. de Biol.*, 1931, **108**, 963.

[4] Weger, P., *Comp. rend. Soc. de Biol.*, 1927, **96**, 801.

* The yohimbine derivatives used in this research were made by Professor David Worral of Tufts College, Medford, Mass.