

The Problem of the Essential Fatty Acids in Relation to Human Nutrition

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IN CONTRADISTINCTION to most clinicians who presently are concerned with the problem of the dietary significance of essential fatty acids our interest has been of long duration. As pediatricians, quite naturally, our chief objective has been to attempt to define the role of linoleic acid in infant feeding and it may be said that our approach has been conservative. To pursue our endeavors it has been necessary to carry on considerable work with chemical methods as well as with experimental animals, which studies have been carried on in collaboration with Hilda F. Wiese. A number of persons have assisted in these investigations (acknowledgments of which may be found in *Pediatrics* 21: 494, 1958).

Shortly after the turn of the century it was the accepted clinical practice to remove fat from the diet of the child with eczema. Seldom, if ever, in the author's experience was this procedure of benefit to the infant. Because of this apparent therapeutic failure, the idea was entertained that dietary fat actually may be advantageous to the child. After the observations of Burr and Burr on the essentiality of certain fatty acids, there was distinct support of this idea. It was observed that a number of infants with intractable eczema responded favorably when fat rich in the unsaturated fatty acids was added to their diet; hence, it seemed logical to pursue studies in the field of lipid metabolism. A number of years were spent in

developing chemical methods which would allow one to measure specific unsaturated fatty acids in the blood serum of small infants. In working with William R. Wilson at Yale it was our good fortune to develop a semimicrogravimetric technic wherein it was possible to separate the saponifiable from the nonsaponifiable lipid fractions. For example, in so doing, it was no longer necessary to make assumptions regarding the composition of the material which was separated with cholesterol in the unsaponifiable portions of the blood serum. Extension of the basic principles of this procedure to the study of the phospholipid fraction revealed that the average molecular weight of the phospholipid fatty acids was higher than that which had been assumed. It was also demonstrated that the average iodine number of the cholesterol ester fatty acids was higher than the fatty acids present as glycerides and phospholipids.

It was our good fortune to find that young dogs were especially suitable animals for study of the dietary significance of the essential fatty acids. For example, when young puppies were placed on a diet very low in fat it was observed that within a few weeks there developed a thickening of the skin, desquamation, later loss of hair, with oozing of the feet and running of the ears. Even after the animals had been in despicably bad shape for several years, it was possible to restore the animals to complete normalcy when the diet contained linoleic acid in adequate amounts. Spectacular changes also were demonstrated in the histologic structure of the skin. Both the gross and the microscopic findings could be correlated with the level of linoleic acid in the diet. More significant, however, was that the above features could be correlated with the level of the 2-, 3-, and 4-double bond fatty acids of the blood

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serum. With the development of the alkaline isomerization method of chemical analysis, the results of which correlated so well with the gross and microscopic appearance of the skin, it was felt that one was in the position of attempting to learn something definitive about the role of linoleic acid in the diet of infants.

The use of low-fat diets in the feeding of infants seemed fully justified, first, because a number of pediatricians considered this to be the method of choice for feeding premature and small infants and second, the experience of some observers indicated satisfactory progress with this type of dietary regimen. Thanks to grants from the United States Department of Agriculture, Institute of Home Economics, Human Nutrition Research Division, Washington, D. C.; Baker Laboratories, Inc., Cleveland, Ohio; and Gerber Products Company, Fremont, Michigan, it has been possible to carry on rather extensive clinical studies in infant feeding wherein the only variable has been the substitution of carbohydrate for fat. Only preliminary reports have been made inasmuch as the studies are still under way; however, we may mention a few features which have been demonstrated.

Serum Lipid Findings: Good correlations have been found between the linoleic acid in the diet of infants and the blood serum levels of the di-, tri-, and tetraenoic acids. Because of the variations which occur in the level of the total fat in the blood from individual to individual as well as in the same individual from time to time it has been found more meaningful to express the values for the di-, tri-, and tetraenoic acid in terms of "per cent of the total fatty acids" rather than in milligrams per cent. This also holds for the fatty acids present as phospholipids, cholesterol esters, as well as glycerides. With a low fat diet the most marked changes are decreases in both the di- and tetraenoic acid levels of the blood serum. On the other hand, the trienoic acid level increases. When the diet contains liberal quantities of linoleic acid there is a distinctly higher level of the dienoic acid in the blood serum and to a lesser extent also of the tetraenoic acid, whereas the trienoic acid values drop. Dienoic acid seems to be the chief fatty acid present as

cholesterol ester. The greatest change in the trienoic acid value occurs in the phospholipid fraction although the levels of di- and tetraenoic acids in this acetone-insoluble fraction also vary directly with the linoleic acid in the diet.

Clinical Evidence of Fat Deficiency in Infants: Rather remarkable has been the observation that young infants fed on diets low in fat frequently develop definite changes in the skin consisting of dryness and desquamation, denudation, and exuding in the body folds. It has been demonstrated that this skin abnormality disappears completely within a week to ten days after adding 2 per cent of the calories as linoleic acid to the diet or changing to a milk mixture containing liberal amounts of linoleic acid. It may be conjectured that this observation is of some clinical significance because some 20 years ago in a rather comprehensive clinical study it was observed that eczematous skin eruptions occurred seven times more frequently in artificially fed infants than in infants who were entirely breast fed. The speculation has been made that contributing to this phenomenon is the fact that mother's milk contains 4 to 5 per cent of the calories as linoleic acid compared to about 1 per cent of the calories in the usual cow's milk formulas used in the artificial feeding of infants. In other words, in the consideration of factors which are concerned with maintenance of the integrity of the skin, dietary linoleic acid is of distinct significance.

Caloric Consumption in Relation to Linoleic Acid in the Diet: In view of the many studies which have been carried out to quantitate the caloric requirements of infants it seems rather remarkable that observations have been made which indicate that infants given diets extremely low in fat tend to consume a greater number of calories than when their diet contains fat. It has been found that in babies given diets extremely low in fat the addition of 1 per cent of the calories as linoleic acid decreases caloric consumption. Perhaps it should not be so surprising that dietary linoleic acid affects caloric consumption when one realizes that one of the earliest observations made on rats maintained on fat deficient diets was growth failure. Also, it has been found that young puppies de-

velop severe inanition when maintained on fat-deficient diets in spite of iso-caloric consumption of food compared with healthy control animals. The late Dr. William R. Brown maintained himself on a diet extremely low in fat for a period of six months. Metabolic studies indicated that his responses were the same as those found in fat deficient rats. Unfortunately, the enzymatic mechanisms concerned with caloric efficiency, as yet, are not known.

Finally, one may say that a feature which is rather disconcerting to the speaker is the likelihood of continued confusion in this field by failure to name specific fatty acids when speaking of dietary "essential fatty acids." Too often a rather loose term is used to connote

more than one unsaturated linkage in the fatty acid chain. It is believed that the development of simpler methods of determination will lead to a better understanding of the exact role played by linoleic acid in infant nutrition. However, alkaline conjugation methods with spectrographic readings for specific fatty acids have been found to give satisfactory results in relation to gross and histologic features which are indicative of the dietary need for the essential fatty acids. It is further conjectured that when the dietary as well as metabolic significance of linoleic acid is better understood in infant feeding the groundwork will be laid for a real understanding of the role played by specific fatty acids in the nutrition of adult human subjects.

