

ESSENTIAL FATTY ACIDS IN INFANT NUTRITION

III. CLINICAL MANIFESTATIONS OF LINOLEIC ACID DEFICIENCY ¹

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An extensive clinical study is being made to evaluate the role of the essential fatty acids in infant feeding. After careful explanation of the nature of the study, the mothers of several hundred infants have chosen to participate. The chief criteria of selection are that the parents seem anxious to cooperate and that the infants are normal neonates. The individual subjects include children of physicians, medical students as well as those seen in the Well Baby Clinics. As an integral part of the study the healthy young infants are given one of 5 different milk mixtures which vary in their content of fat and linoleic acid. One group received a milk mixture practically devoid of fat and because of the unsatisfactory progress of a number of the infants, this phase of the study has been terminated. The findings seem worthy of presentation at this time.

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MATERIAL AND METHODS

Twenty-seven infants received a skim milk mixture which supplied 1.4% of the Calories as fat (0.1 gm%) with <0.1% of the Calories as linoleic acid (<0.04 gm%). Protein constituted 15% of the Calories with carbohydrate supplying the remainder of the Caloric intake. The milk contained added vitamins and iron and was prepared so that when diluted with equal parts of water there were 63 Cal./100 ml (19 Cal./oz.). Solid foods were added to the diet, beginning with cereals at three months of age, and at monthly intervals thereafter, fruits, vegetables and meats were given. The infants were maintained on the low-fat regimen for periods varying from two weeks to 12 months. Linoleic acid as trilinolein was added to the diet of three infants and as natural fat by changing to one of the other milk mixtures in 9 instances. Ethyl arachidonate was used in the diet of one infant. Tripalmitin was added to the diet of another. Three infants were shifted to a milk mixture containing only saturated fat. The subjects were examined regularly by the same pediatricians, particular attention being given to growth, development, illnesses, the number and character of the stools, and to the condition of the skin. Periodic determinations of the blood serum unsaturated fatty acids were made by the method of alkaline isomerization (Wiese and Hansen, '53).

RESULTS

Clinical features of the group as a whole

The infants readily accepted the milk low in fat content. Vomiting and regurgitation did not occur and weight gain was adequate in most instances. In general, progress was satisfactory except for the following 4 outstanding features:

Character of stools. The occurrence of frequent, large, dark-brown, sirupy bowel movements was a distinguishing symptom in 25 of the 27 infants. In three instances it was necessary to change the type of feeding because of loose stools.

Perianal irritation. Raw red exuding areas often developed in the diaper region. The usual therapeutic measures had no effect on the severe lesions in 14 of the infants.

Abnormalities of the skin. Of the 24 infants who were fed on the milk preparation low in fat for at least one month, changes in the skin were observed in 15. Characteristically, there developed dryness and leathery thickening of the skin which could be detected readily by inspection and palpation. Soon desquamation was noted. This was particularly apparent in the colored infants where the fine, flaky, white scales stood in contrast to the dark background (fig. 1). Annoying exudation often occurred in the body folds and the raw exuding surface in the intertriginous areas became a disconcerting feature to both the mothers and the attending physicians.

Serum lipid findings. At three months of age the serum lipids were determined in 16 infants receiving the low-fat diet. The levels of dienoic and tetraenoic fatty acids were uniformly low and those for the trienoic acid relatively high compared with three-month-old infants who received fat and linoleic acid in the diet. The mean values for the di-, tri- and tetraenoic acids were 3.3, 4.9 and 2.8% of the total fatty acids, respectively.

When symptoms of fat deficiency were marked, it was at the discretion of the pediatrician-in-charge to add specific fatty acids to the diet, or to change the milk preparation to one containing fat. In each instance wherein the milk mixture was changed to one containing linoleic acid or the low-fat diet was supplemented with linoleic acid, the diarrhea stopped, the rash in the diaper region disappeared, the raw exuding areas in the intertriginous folds cleared and the skin gradually returned to a normal soft velvety texture. The serum lipids reflected the dietary change. By the diligent use of local therapy and the addition of solid foods to the diet, 4 of the infants were maintained satisfactorily on the low-fat milk for 6 months and three for 12 months. After the addition of solid foods, the serum di- and tetraenoic acids were found to increase gradually and the trienoic acid to decrease.

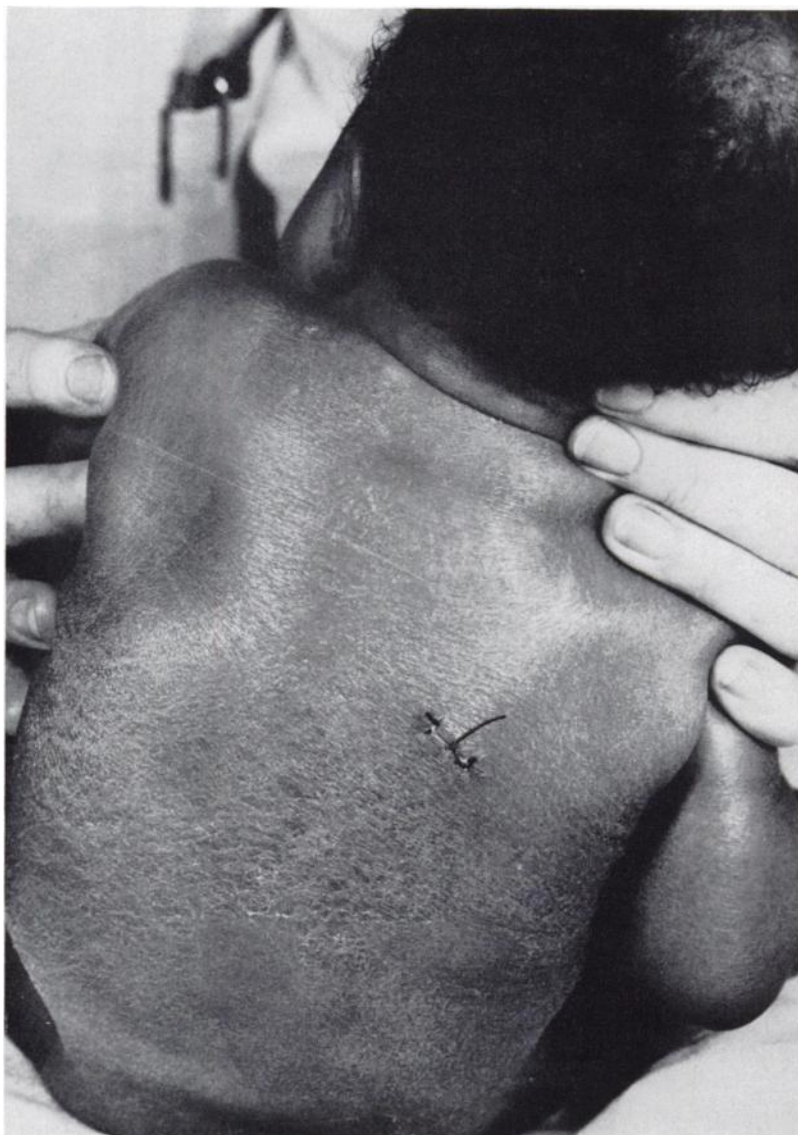


Fig. 1 Typical appearance of skin of 10-week-old infant given a skim milk mixture lacking linoleic acid.

Observations concerning individual infants

The relationship which exists between dietary linoleic acid and the condition of the skin in young infants, as well as the correlation between these two features and the blood serum levels of unsaturated fatty acids are illustrated by reference to the case histories of several infants.

Case 19: A female negro infant with a birth weight of 2850 gm was fed the milk mixture low in fat beginning on the third day of life. Her stools were semi-formed and numbered 5 to 6 daily. By 10 weeks of age her entire skin became dry and scaly as illustrated in figure 1. Later there developed a parchment-like texture with fissuring in the post-auricular areas. At three months cereal was added to the diet without any demonstrable change in the condition of the skin. Six weeks later linoleic acid, as trilinolein, was given by dropper directly into the mouth before each feeding in an amount to equal 2% of the daily Caloric intake. After one week of supplementation, the skin became soft and smooth except for some excoriation in the diaper area. After three weeks the linoleic acid was discontinued, and 10 days later pureed fruits and vegetables were added to the diet. The skin remained of normal texture although the low-fat milk was continued until one year of age. While fed the low-fat milk mixture alone the blood serum levels for the 2- and 4-double-bond fatty acids were characteristically low with a high level for the 3-double-bond fatty acid. With the addition of linoleic acid to the diet the dienoic acid rose as indicated in table 1.

Case 54: This female negro infant weighed 1680 gm at birth and was placed on the low-fat milk mixture on the third day of life. At one week of age (during an epidemic of staphylococcus aureus, phage type 81) she developed a breast abscess which responded to incision, drainage and antimicrobial therapy. After receiving the low-fat milk for 7 days, she began having large, loose brown stools (8 to 10 per day). Within 4 weeks the skin was noted to be taut, shiny, and marked excoriation was present in the diaper area. The skin

TABLE 1
Blood serum levels of di- tri- and tetraenoic acids for individual infants in relation to intake of linoleic acid

| CASE NO. | DIET | DURATION | DIENOIC ACID ¹ | TRIENOIC ACID ¹ | TETRAENOIC ACID ¹ |
|----------|--|----------|---------------------------|----------------------------|------------------------------|
| 19 | Skim milk | 3 months | 2.9 | 6.9 | 4.0 |
| | Skim milk + 2% Cal. as linoleic acid (trilinolein) | 2 weeks | 10.1 | 4.0 | 2.8 |
| | Skim milk + cereals, fruit, vegetables and meats | 9 months | 15.8 | 2.8 | 8.6 |
| 54 | Skim milk | 3 months | 2.2 | 5.5 | 1.5 |
| | Skim milk + 2% Cal. as palmitic acid (tripalmitin) | 6 weeks | 3.1 | 5.8 | 0.3 |
| | Milk containing 7.3% Cal. as linoleic acid | 6 weeks | 37.9 | 2.8 | 10.2 |
| 39 | Skim milk | 6 weeks | 1.1 | 5.7 | 1.2 |
| | Skim milk + 2% Cal. as arachidonic acid (ethyl arachidonate) | 1 month | 1.4 | 6.3 | 3.4 |
| | Skim milk | 3 months | 2.8 | 7.1 | 2.0 |
| 22 | Skim milk, topical olive oil | 3 weeks | 3.0 | 6.3 | 1.9 |
| | Milk containing 1.3% Cal. as linoleic acid | 2 months | 16.7 | 2.5 | 7.1 |

¹As percentage of total fatty acids in serum.

changes became more severe with flaking and denudation of the intertriginous folds. At two months of age the infant was given a fat supplement of tripalmitin to equal 2% of the daily Caloric intake. Although supplementation was continued for 6 weeks, no improvement was noted nor did any significant change occur in the serum levels of unsaturated fatty acids. When 4 months of age, the infant was admitted to the hospital because of staphylococcal pyopneumothorax which gradually responded to appropriate therapy. After the first two weeks of hospitalization the low-fat milk mixture was changed to one containing 42% of the Calories as saturated fat. Again no improvement of the skin was noted. Next the diet was changed to a milk mixture containing liberal amounts of linoleic acid and within two weeks, the skin had become soft and moist with no desquamation. There was also a prompt increase in the di- and tetraenoic acid levels of the serum with a decrease in trienoic acid. The values for the serum fatty acids are shown in table 1.

Case 39: A male negro infant, one of twins, weighing 1550 gm at birth was fed the low-fat milk mixture beginning on the second day of life. After one week he developed voluminous stools (3 to 8 per 24 hours) and by 4 weeks of age, the diaper region was severely excoriated despite local therapeutic measures. At 6 weeks of age definite generalized skin changes were noted which consisted of desquamation, denudation and palpable thickening. Due to intermittent edema the other twin (case 40) was given a low-salt milk which contained liberal quantities of linoleic acid. No abnormalities of the skin occurred in this twin (fig. 2). Ethyl arachidonate³ in an amount equal to 2% of the daily Calories was fed by dropper before each feeding to the affected infant with slow improvement over the next 5 weeks; however, the changes were by no means as striking as those seen in the infants who were given trilinolein. The relatively poor response to arachidonic acid may have been due to impurity of the product as

³ Kindly supplied by Dr. Ralph T. Holman, Hormel Institute.

indicated in a personal communication from Dr. Ralph Holman. Serum levels for the unsaturated fatty acids initially reflected the low intake of linoleic acid, but there was only a slight rise in tetraenoic acid and no change in di- and trienoic acid levels during supplementation as indicated in table 1.



Fig. 2 Appearance of skin of 6-week-old twins. A, Given a skim milk mixture lacking linoleic acid. B, Given a milk mixture containing linoleic acid.

Case 22: This female negro infant weighed 3000 gm at birth. On the 7th day of life she was started on the milk mixture very low in fat content and at three weeks of age developed the typical skin features of fat deficiency. Changes in the character of the stools were only moderately severe. The opportunity arose to ascertain whether liberal amounts of topically applied olive oil would effect a therapeutic response or a change in the serum 2-, 3- and 4-double-bond fatty acids. The mother used the oil for three weeks with no alteration either clinically or chemically. Since no improvement had occurred, the infant's diet was changed to a milk mixture

which provided moderate amounts of linoleic acid (1.3% of the Calories) and within one week improvement in the skin was noted. Three weeks after the diet was changed the skin appeared normal. The values for the serum lipids are presented in table 1.

DISCUSSION

From the data presented it has been demonstrated quite definitely that young healthy infants within a relatively short time may develop symptoms when given diets extremely low in fat. Previous studies by von Gröer ('19) and von Chwalibogowski ('37) with infants on low-fat diets disclosed no changes in the skin. On the other hand, in short term studies using diets low in fat, Holt and coworkers ('35) found that one of three infants developed skin changes. Of special interest have been the observations of Hansen and Wiese ('44) on an infant with chylous ascites. This subject remained on a low-fat diet for almost two years and developed eczematous patches intermittently, a chronic dermatitis following prickly heat and a refractory impetiginous eruption. Infants with steatorrhea when maintained on relatively low fat intakes for long periods of time also have developed skin eruptions (Luzzatti and Hansen, '44). Indirect evidence that dietary fat may be of importance in the maintenance of a healthy skin has been supplied by observations on patients with eczema (Hansen and coworkers, '47).

It is not surprising that skin changes may develop in young infants inasmuch as one of the first outstanding evidences of fat deficiency in experimental animals was an abnormality of the skin (Burr and Burr, '29). It should be pointed out that only in young animals deprived of fat for relatively long periods of time are distinct skin changes demonstrable. In more mature animals evidences of fat deficiency are slower to develop and are not clear-cut. The likelihood of maintaining infants on a diet low in linoleic acid becomes less as the child grows older because cereal grains which are fed at an early age contain appreciable quantities of linoleic acid.

That there are individual variations in the susceptibility of the skin to changes in the kind and amount of fat in the diet is a distinct possibility. This is illustrated in our study by the larger proportion of negro infants who developed demonstrable skin changes compared with those of Latin-American and Anglo-Saxon extraction. Nevertheless, an abnormality of the skin as evidence of the lack of a specific fatty acid is indicated from the results of feeding various fats of known composition. For example, tripalmitin fed as 2% of the Caloric intake as well as saturated fats to equal 42% of the Calories did not improve the condition of the skin. In contrast, supplementation with trilinolein at a 2% Caloric intake of linoleic acid brought about striking improvement in the skin. On the basis of studies of the unsaturated fatty acids in blood serum, Wiese and coworkers ('58) found minimal normal levels were associated with diets which provided 1 to 2% of the Calories as linoleic acid. Also, optimum levels of intake of linoleic acid seemed to be in the range of those found in breast milk, namely 4 to 5% of the Caloric intake. This level of intake of linoleic acid resulted in optimum Caloric efficiency (Adam and coworkers, '58).

SUMMARY AND CONCLUSIONS

In an infant feeding study it was found that young infants fed on a skim milk diet extremely low in fat and linoleic acid, though otherwise nutritionally adequate, showed certain signs and symptoms. Within a short time, most of the 27 infants developed frequent large stools. Perianal irritation was a disconcerting feature in most instances. Within a matter of weeks alterations in the skin were discernible in the majority of infants. The first sign observed was dryness, then thickening and later desquamation with oozing in the intertriginous folds. These changes were particularly marked in the negro infants. Addition of saturated fatty acids to the diet did not improve the skin. On the other hand, the addition of linoleic acid as trilinolein to constitute 2% of the daily Caloric intake

restored the skin to a normal soft moist texture and appearance within one to two weeks. If the milk mixture was changed to 2 to 5% of the Calories with total fat constituting 42% of the Calories, restitution of the skin was equally as prompt. When a milk mixture containing 1.3% of the Calories as linoleic acid was given, the skin returned to normal in two to 4 weeks. In one instance, arachidonic acid given as the ethyl ester at a 2% Caloric level required about 5 weeks for the skin to return to normal. The serum of all the infants on the low-fat diet had extremely low values for the di- and tetraenoic acids and high values for trienoic acid which values changed with the addition of linoleic acid to the diet. The dienoic acid values reflected the dietary intake most markedly. Arachidonic acid administration did not change the dienoic acid level. It is concluded that young infants require linoleic acid in their diet.

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