The Essential Fatty Acids

A. T. JAMES, PH.D.

IN SOME studies of the fatty acid composition of lipids from human blood,[1] it was found that the composition of the human erythrocyte was remarkable for its constancy. This fact prompted an investigation of lipid synthesis by the erythrocyte by incubating sterile whole blood with CH_3-labeled acetate.[2] After a 5-hour incubation not only the red cell lipids but also the plasma lipids were found to be labeled.

Separation of the long chain fatty acids on the gas-liquid chromatogram followed by collection of the fractions and determination of their specific activity, demonstrated that labeling existed not only in all the common saturated and unsaturated acids but also in linoleic and arachidonic acids.

TABLE I

Specific Activities of Long Chain Fatty Acids Isolated from Red Cell and Plasma Lipids after Incubation with Labeled Acetate (counts/min/mg)

Acid	Red cell neutral fat	Plasma neutral fat	Red cell phospholipid	Plasma phospholipid
Lauric	325	1030	255	760
Myristic	660	520	506	612
Palmitic	132	180	41.0	570
Stearic	203	312	87.0	122
Linoleic + linolenic	—	61.0	34.0	31.0
Oleic	60	377	37.0	40.0
Arachidonic	Not determined	Not determined	18.1	207

In Table I are shown the specific activities of a variety of fatty acids isolated from the lipids of whole blood in a typical experiment.

The fatty acids synthesized by the red cell are incorporated into neutral fat and phospholipid which are exchanged with the plasma lipoproteins.

The linoleic and linolenic acids in the plasma neutral fat have a specific activity of one-fifth of that of oleic acid and may therefore represent a turnover of the same order. It is of some interest to note that in the original experiments of Stetten and Schoenheimer on the use of tracers in the biosynthesis of fatty acids the isolated linoleic acid possessed 0.02 atom per cent excess of deuterium compared with 0.06 for oleic acid.

The presence of radioactive label in the linoleic plus linolenic acids isolated from whole blood does not furnish proof of their biosynthesis since two possibilities exist:

(1) An exchange process such as:

$$\text{linoleic acid} \rightleftharpoons \text{degradation product} + \text{acetate} \quad \text{acetate} \rightleftharpoons \text{acetate pool}$$

(2) Synthesis from acetate or from some unessential fatty acid and acetate.

The small amounts of material so far available have prevented a stepwise degradation that would accurately define the position of the label. Those experiments carried out so far have shown part of the activity to exist in the azelaic acid obtained by oxidative degradation.

Nevertheless, this synthetic activity of the red cell, when taken together with the exchange of lipids with plasma lipoproteins, does raise the question of the importance of dietary linoleic and arachidonic acids for the human. The precise requirements, if any, of these acids for the adult human has yet to be defined. In recent years many suggestions have been made, particularly by Sinclair,[4,5] that some human diseases were caused by dietary insufficiency of the essential fatty acids. Such insufficiency would be expected to be detectable in the blood

From National Institute for Medical Research, The Ridgeway, Mill Hill, London N. W. 7.

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levels of humans suffering from these diseases since Mukherjee *et al.*[6] demonstrated a marked fall in di- and tetraenoic acids in the plasma of rats when fed a fat-deficient diet.

Such studies as have been made on (a) adults suffering from coronary artery disease[7] and (b) children suffering from idiopathic hypercalcemia[8] have failed to demonstrate significantly lower blood levels of linoleic plus linolenic and arachidonic acids than those found in control subjects.

Since neither the detailed function nor the required level of intake of these unsaturated fatty acids is understood, at this stage it would be useful to devote less time to sermonizing and more time to experimentation on the subject of essential fatty acids.

REFERENCES

1. James, A. T. and Lovelock, J. E.: A preliminary investigation of the fatty acid composition of blood lipids from rabbit, ox, rat and normal and atherosclerotic humans; in *The Blood Lipids and the Clearing Factor*. Palais des Acadamien, Brussels, 1957, p. 94.
2. James, A. T., Lovelock, J. E., and Webb, J.: The biosynthesis of fatty acids by human red blood cells. *Biochem. J.* 66: 60P, 1957.
3. Stetten, D., Jr. and Schoenheimer, R.: The conversion of palmitic acid into stearic and palmitoleic acids in rats. *J. Biol. Chem.* 133: 529, 1940.
4 Sinclair, H. M.: Letters to the Editor: Deficiency of essential fatty acids and atherosclerosis, etcetera. *Lancet* 1: 381, 1956.
5. Sinclair, H. M.: Fats and disease. *Lancet* 2: 101, 1956.
6. Mukherjee, S., Achoya, K. T., Deuel, H. J., and Alfin-Slater, R. B.: The nature of the lipides in rat blood. *J. Biol. Chem.* 226: 845, 1956.
7. James, A. T., Lovelock, J. E., Webb, J., and Trotter, W. R.: The fatty acids of the blood in coronary-artery disease. *Lancet* 1: 705, 1957.
8. James, A. T., Webb, J., Stapleton, T., and Macdonald, W. B.: Essential fatty acids and idiopathic hypercalcemia of infancy. *Lancet* 1: 502, 1958.