The Transport of Fatty Acids Across the Cell Wall

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INTENSIVE research efforts of the past few years have led to some understanding of the transport of lipids in the blood and lymph. Their transport across cell walls, an equally complex and interesting subject, has, however, remained completely obscure. Although a complete study of this problem necessarily involves several different lipids in a number of different lipoprotein combinations, the recent information that the most probable form in which fatty acids reach the cell is as the albumin complex prompted us to study this simple lipoprotein first.

For this study we used the Ehrlich mouse ascites tumor because of the ease of making *in vitro* preparations of these cells which could be used in metabolic studies with some confidence that essentially normal reactions were being carried out. Later studies could be performed with other cells such as those from liver or adipose tissue. Experiments were carried out in the conventional Warburg apparatus with washed cells. Substrates used were carboxy-labeled palmitic acid in buffer or as its albumin complex and biosynthetic albumin from ascitic fluid of mice fed phenylalanine-3-C^{14}.

When palmitic acid alone was added to the incubated cells, it was metabolized, since $C^{14}O_2$ appeared in the center wells. However, this oxidation was somewhat irregular and incomplete, ceasing when about 30 per cent of the palmitic acid had been oxidized. After separation of the cells, the supernatant solution retained about 9 per cent of the total C^{14} activity.

When palmitic acid was added as its albumin complex, oxidation, as attested by the appearance of $C^{14}O_2$ in the center well, was regular, and continued for at least 90 minutes. In this case, an average of about 29 per cent of the counts remained in the supernatant solution. When the two substrates were oxidized by the same cells, the differences were even more striking. When the complex containing radioactive albumin was used, no $C^{14}O_2$ appeared in the center well and all the activity remained in the supernatant solution.

From these data, it appears probable that the function of albumin in the fatty acid-albumin complex is one of solubilization and transport to the cell wall and not of aiding in the passage through the wall.

To investigate this aspect further, palmitate or its albumin complex was incubated with normal and KCN-inhibited cells. In the presence of KCN, no oxidation of palmitate occurred, but the proportion of activity in the cell wall was greater than for the normal cells. Evidently active cell metabolism is not necessary for adsorption of fatty acid onto the cell wall.

From the results of these experiments a picture of absorption of fatty acids by cells is becoming clearer. The albumin complex aids in solubilizing and dispersing the fatty acid and in presenting it to the cell wall. At this point, a distribution between the lipid-containing cell surface and the albumin takes place. The fatty acid adsorbed onto the cell wall is then activated and drawn within the cell to be oxidized. The transport of the fatty acid within the cell is still unknown but could possibly be investigated by the same methods.

The transport of other lipids into or out of cells has received some preliminary attention.

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Shapiro, Chowers and Rose[1] have carried out studies in which fat-depleted adipose tissue (from fasted rats) was incubated with various types of lipids, the changes in concentration of which were followed. It was found that fatty acids, simple esters and glycerides were readily taken up by the tissue whereas lecithin and cholesterol esters were not. Stearic acid-1-C^{14} was also absorbed and oxidized by the tissue. James, Lovelock, and Webb,[2] studying the synthesis of fatty acids by red cells, found that fatty acids synthesized *in vitro* are not released into the medium unless serum α-lipoproteins are present in it. This appears to be a distribution in the reverse direction to that of the fatty acid-albumin complex.

From these very preliminary studies, it is evident that this complex and obscure subject is of great importance to the metabolism of lipids by the cell. Many further experiments will be necessary before a clear understanding of these phenomena will be obtained.

REFERENCES

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2. James, A. T., Lovelock, J. E., and Webb, J.: The biosynthesis of fatty acids by human red blood cells. *Biochem. J.* 66: 60, 1957.