Communications

Fatty Acid Absorption and Chylomicrons

Singer, Sporn, and Necheles [*Science* **118**, 723 (1953)] state: "The absorption pathway of long-chain fatty acids is still controversial." The evidence they cite, however, indicates that some misunderstanding may still persist with regard to the exact nature of the issues involved.

The objective of my original experiments (*1*) quoted by Singer *et al.* was to see whether differences could be detected between the absorption of olive oil on the one hand, and the absorption of its contained fatty acids on the other, since at that time it was generally maintained (*2*) that glycerides could be absorbed only after complete hydrolysis to fatty acids and glycerol. Several differences were found, and as a result of this and many other experimental studies, we concluded that the basic concept of the lipolytic hypothesis—that is, the necessity for complete hydrolysis—was incorrect. Our view that lipolysis need only be partial during absorption has since been amply confirmed (*3, 4*) by the use of isotope-labeled fats.

As early as 1946 (*5*), I pointed out that the partition of lipid molecules between the water and the oil phase might determine the mode and pathway of absorption. Thus, long-chain fatty acids were difficult to remove from the oil into the water phase under the conditions prevailing in the upper intestine. They thus passed into the body in the particulate fat in the chyle and caused an increase in the number of chylomicrons in the systemic blood; in the absence of carrier glyceride, saturated long-chain fatty acids were poorly absorbed. Shorter chain fatty acids, on the other hand, were more easily removed into the water phase and were not found in the chyle. It was thought that they might pass with other water-soluble substances in the portal blood. Thus it was concluded that saturated fatty acids were partitioned between the oil and water phases according to chain length and water solubility, and that this differential distribution affected their absorption.

This "partition hypothesis" has been completely confirmed by the studies of Chaikoff and his colleagues, using isotope-labeled fatty acids (*6–8*). It was unfortunate that these workers stated in their first paper (*6*) that their observations on the absorption of stearic acid in corn oil were contrary to the partition hypothesis and that this factual misstatement has been repeated by other authors (*9–11*). So far as I am concerned, there is not, and has never been, any controversy with regard to the pathway of absorption of saturated fatty acids; they behave precisely as predicted on the basis of the partition hypothesis (*12*).

The absorption of unsaturated fatty acids is more complicated. Consideration of my original data (*1*) shows that oleic acid could behave in two different ways. If it was fed as a glyceride ester fine intraluminar emulsification occurred and the oleic acid passed mainly in particulate form in the chyle glycerides. When free oleic acid was fed alone however, no intraluminar emulsification was observed, and there was no evidence of particulate absorption during the course of the experiment, although significant amounts of oleic acid were absorbed. Under different circumstances, however, oleic acid may be finely emulsified in the intestinal lumen, and if this should occur, particulate absorption of oleic acid alone might result.

Reiser (*13*), Tidwell (*14*), and Singer *et al.* claimed that their experiments on unsaturated fatty acid absorption do not agree with mine; they are different from mine, both in design and objective. Particulate absorption appears to be occurring in their experiments, but it was not observed in mine. A more precise definition of the intraluminar conditions in the experiments of Reiser, Tidwell, and Singer *et al.* might be interesting.

Unsaturated fatty acids, especially oleic acid, are normally eaten as constituent fatty acids of most dietary glycerides, and they pass largely with the oil phase. We still do not know what happens under abnormal conditions of defective particulate absorption. These are the aspects of the problem with which my studies have been concerned, and they do not necessarily conflict with the observations quoted by Singer, Sporn, and Necheles, the objective of which has been to study fatty acid absorption itself, with which the partition hypothesis—a concept of the mechanism of absorption of dietary glycerides—is only secondarily concerned.

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We do not doubt the general truth of the partition hypothesis of fat absorption, but the results of some of our experiments may modify it.

When oleic acid was introduced into a Thiry loop of intestine, fine, intraluminar emulsification *did* occur, although bile and pancreatic juice were *not* present. Furthermore the oleic acid disappeared from the loop, and an abundant chylomicronemia gave evidence of its particulate absorption (*1, 2*).

The Thiry loop often contained traces of excreted fat. However, with the large amounts of fatty acid that we used, we consider that, essentially, there was only a water phase, and that carrier fats and glycerides were not available for the degree of absorption that we have observed. The degree of chylomicronemia in the experiments with oleic acid introduced into the Thiry loop sometimes was equal to that observed following the oral feeding of 0.5 g/kg of body weight of olive oil. Therefore, in our experiments, the pathway of absorption of long-chain fatty acid was not determined by either oil phase or glyceride carriers; that is, the fatty acid did *not* behave precisely as predicted on the basis of the partition hypothesis.

In analyzing physiological phenomena, we believe that, in the first place, a simple experiment must be performed, narrowing down the latitude of the experimental conditions to as few factors as possible. Therefore, we have not considered whether fatty acids are normally eaten by the rat as "constituent fatty acid of most dietary glycerides."

"A more precise definition of the intraluminar conditions" in our Thiry fistulas would not help in our opinion, to explain or to shake the doubtless absorption of long-chain fatty acid as chylomicrons from a loop devoid of bile, pancreatic juice, glyceride carriers, or oil phase.

Our experiments on absorption of fatty acid *per se* are a minor point in the investigation of fat absorption in general but our scope was the investigation of basic physiological phenomena.

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Effect of Elemental Sulfur in the Diet on Load-Extension Hysteresis in Single Wool Fibers

As has already been demonstrated by means of radioactive sulfur as a tracer, sulfur in the diet of sheep is metabolized and appears in wool after a period of 2 wk or less. It has been of great interest, therefore, to discover whether variations in the amounts of sulfur could be correlated with measurable differences in the structure or physical properties of wool. The x-ray diffraction patterns of wool are characteristic of α-keratin but are so diffuse that very slight structural changes are difficult to detect even with the most precise techniques and measurements. There is some slight indication of sharpening of the fiber interferences with increasing amounts of silver in the diet.

Wool samples were secured from sheep of the same age and breed, at the same time. Their basal ration, fed *ad libitum,* contained 0.05 percent sulfur. The only variable was the addition to this standard diet of 0 to 0.7 percent of powdered sulfur, the actual amounts added being 0, 0.20, 0.25, 0.40, 0.55, 0.60, and 0.70 percent. By all odds, the most sensitive method of evaluation of any effects has been the careful determination of elongation of single fibers as a function of applied load. A special, very sensitive piece of apparatus was constructed from an analytic balance such that analytic weights could be added in steps. As the load was applied to the single fibers, an elongation was quantitatively measured by a long pointer and a magnified scale. Enough individual measurements were made of single fibers of each type to assure statistical soundess at constant temperatures and humidity. Remarkable reproducibility has been found in the stress-strain curve, both with loading and with removal of the weights.

For wool with no additional sulfur in the diet, there is very nearly perfect recovery, so that the loop of tension and relaxation is extremely narrow. However, the area measured by a planimeter for wool corresponding to 0.7 percent sulfur in the diet is more than 3 times that of the loop for 0.2 percent sulfur. The intermediate percentages of sulfur also give intermediate values for the hysteresis loop areas.

It is clear, therefore, that sulfur has been metabolized and added to the disulfide linkages between the keratin molecules in the wool fibers. As the number of these bridges statistically placed between molecules increases, there is a greater tendency to retention of the extended configuration of the fiber and resistance to relaxation upon removal of the load. These highly quantitative experiments by a well-known and traditional technique have demonstrated, therefore, the correlation between sulfur in the diet and sulfur in the wool fibers, and the results point clearly to the fact that there should actually be quantitative differences in mechanical behavior of the wool fibers in textiles as a function of the number of disulfide linkages and in terms of metabolism of sulfur in the diet of sheep.

Detailed descriptions of the apparatus and the hysteresis loops will be published elsewhere.

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