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# THE PARTICULATE ABSORPTION OF FAT: ITS DIRECT DEMONSTRATION IN A NORMAL HUMAN

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Two theories dominate the modern concept of lipid absorption from the small intestine: a) the *hydrolysis* theory first propounded by Pfluger (1900)[1] and later elaborated by Verzar and McDougall (1936)[2] and b) the *partition* theory of which the main advocates have been Professor A. C. Frazer and his associates (1938 *et seq.*)[3,4,5,6] in England.

In brief, the hydrolysis theory states that fat, prior to absorption, must be completely hydrolyzed to fatty acids and glycerol. Glycerol, being water soluble, is absorbed as such while the fatty acids combine with bile salts to form a water soluble complex. Following absorption, the fatty acids and gylcerol are recombined within the intestinal epithelial cells through an intermediate process of phosphorylation.

The partition theory contends that, in addition to the hydrolized components, neutral fat may be physically absorbed in a chemically unaltered form providing that it is first emulsified to exceedingly fine droplets. Conditions favorable to the formation of such an emulsifying system are present in the intestine, and much indirect, circumstantial evidence has been put forward to substantiate the validity of the theory. This evidence has been derived chiefly from such methods as analysis of contents in isolated intestinal loops and tracing the absorption of stained oil after its ingestion by animals. Wotton and Zwemer[7] administered various fats prestained with Sudan IV to cats. By sacrificing the animals at intervals of 1 to 4 hours, they observed the stained fats in various stages of absorption through the intestinal mucosa. These authors produced excellent and convincing photographs of the process although they did not attempt to prove that the fat administered and that absorbed were chemically identical. Heretofore, such work could not be corroborated in humans for obvious reasons. With the advent of a suitable instrument for small bowel mucosal biopsy[8], it occurred to us that the direct demonstration of fat absorption in a normal human might be possible.

The purpose of this paper is to confirm and extend, by *direct visual observation,* the previous experimental evidence that particulate absorption of unhydrolyzed fat can occur in man. No attempt is made to debate the relative merits of either of the previously described theories of fat absorption or the quantitative contribution of either mechanism to the absorption of fat.

## MATERIALS AND METHOD

Three factors were essential to the success of the experiment: 1) a normal human subject, 2) a means of obtaining an adequate specimen of intestinal mucosa

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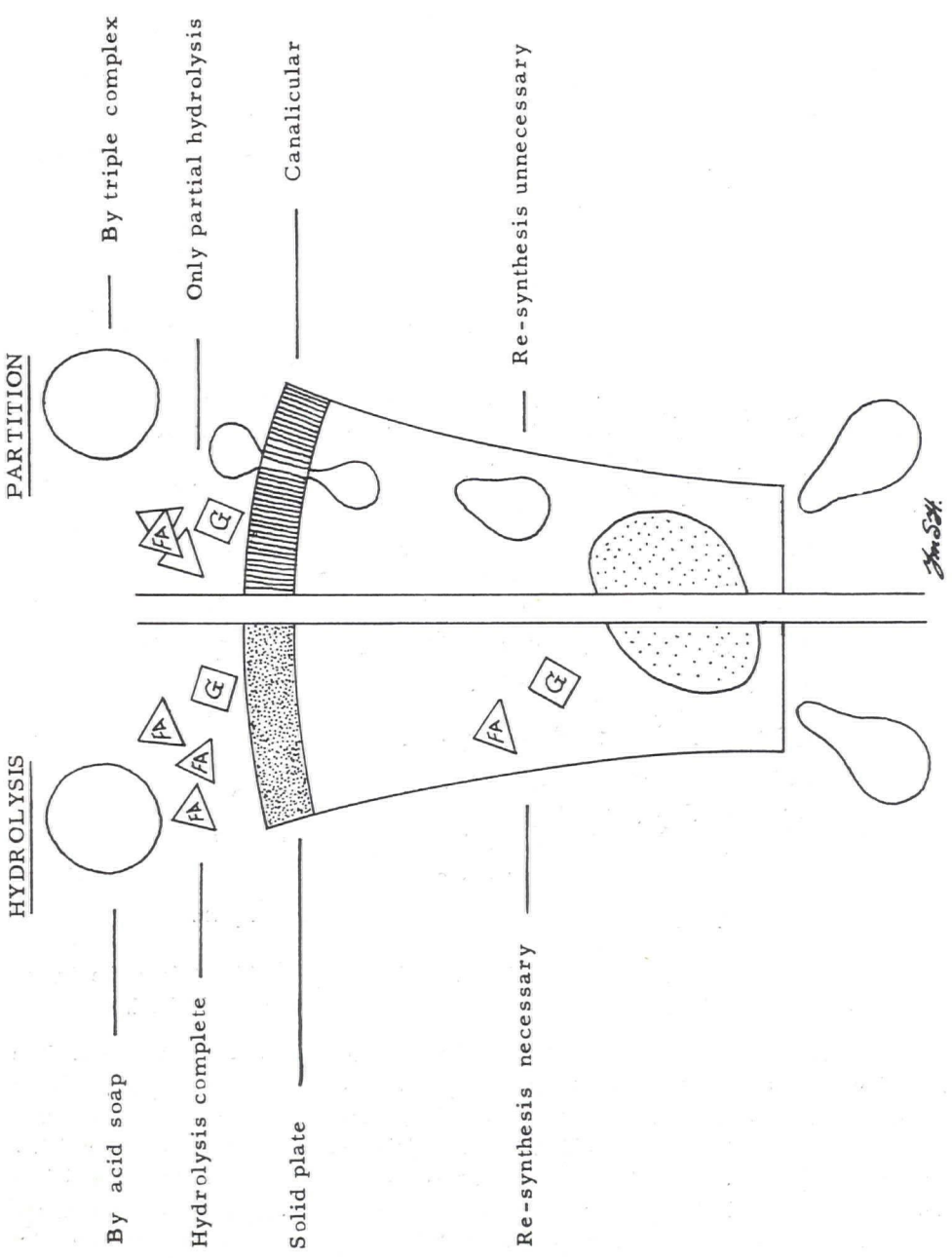


Figure 1

Schematic illustration contrasting the hydrolytic and partition theories of intestinal fat absorption. The chief points of variance are: a) the means by which ingested fat is emulsified within the intestinal lumen, b) the extent of hydrolysis or chemical breakdown of the fat, c) the mode of passage through the free border of the epithelial cell, and d) the need for chemical resynthesis within the cell.

at a suitable interval after the administration of fat, and 3) a neutral fat which could readily be identified in the intestinal epithelial cells.

The subject of this experiment is a normal male exhibiting no evidence of organic alimentary disease by history, physical examination, or labortory test.

The biopsy specimen was obtained by a Crosby capsule illustrated in figure 2 and succinctly described by its inventor[8]:

> "It consists of a capsule containing a rotating knife which is spring activated and triggered by suction. The suction first draws a bit of mucosa into the capsule before the knife is sprung. The capsule is held captive by a polyethylene tube 2 mm. in diameter which also serves to transmit suction and to retrieve the capsule."

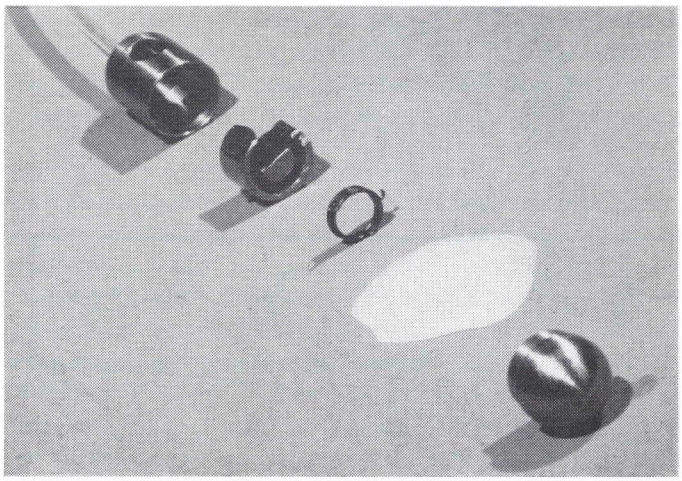

Figure 2

Crosby capsule disassembled to illustrate the component parts.

This technic permitted the convenient injection of a liquid fat into the lumen of the intestine through the same port from which the biopsy was obtained.

The subject swallowed the capsule on the evening prior to the experiment. The following morning the capsule was found by fluoroscopy to lie in the right lower quadrant of the abdomen and 173 cm. (68 inches) from the incisor teeth as measured by markings on the tube. Ten milliliters of Lipiodol®* (28 per cent iodine by weight) were then injected through the tubing. Because of the viscosity of this material, 5 minutes elapsed during the injection. Fifteen minutes later the biopsy was taken, the capsule withdrawn, and the specimen was immediately immersed in formolcalcium fixative.

## RESULT

After suitable fixation, sections were cut on the freezing microtome. Some sections were stained with Flaming Red and hematoxylin for demonstration of neutral fat and general tissue architecture.

In other sections the lipid was stained metachromatically. Particulate lipid was seen along the lumenal border, within the epithelial cells, and within the subepi-

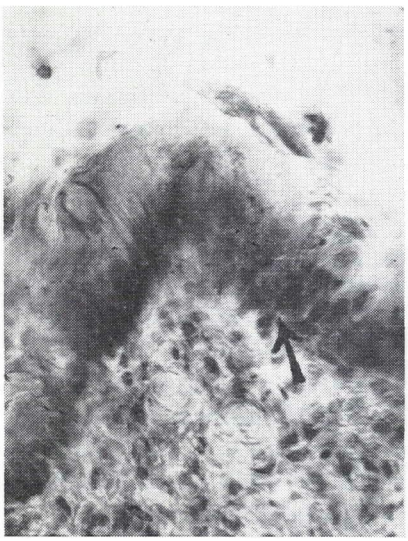

Figure 3

Small intestinal mucosa. Fine droplets of fat lie along the lumenal border of epithelium. Arrow points to tear drop shaped lipid droplets near the basal portion of the epitheial cell. Flaming Red and hematoxylin stain, 480x.

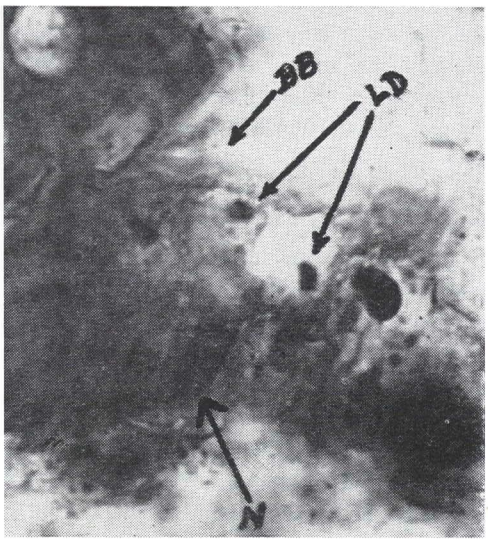


Figure 4

Higher power view of figure 1. Arrow labeled *N* points to cell nucleus; arrow labeled *BB* points to brush (striated) border; arrows labeled *LD* point to lipid droplets within 2 adjoining cells. The droplets appear as black masses in this photograph.

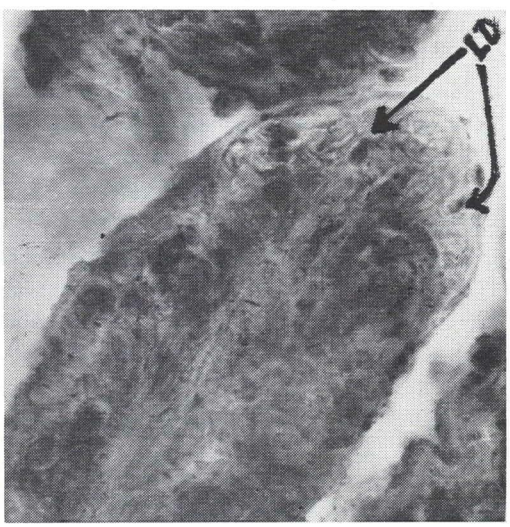


Figure 5

Small intestinal mucosa after metachromatic staining and silver nitrate treatment, 480x. *LD* arrows indicate lipid droplets which were pink after metachromatic staining and were brown after treatment with silver nitrate.

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Kindly supplied by Mr. Lee Riegler representing E. Fougera & Co., Inc.

thelial structures of the villus itself. In the epithelial cells the droplets often assumed a tear drop shape with the pointed end directed away from the intestinal lumen. Larger aggregates of the pink-red staining lipid were found in the lacteals. When the metachromatically stained lipid particles had been localized and mapped, they were treated with silver nitrate solution. Silver nitrate reacts with iodine to form silver iodine which then appears brown-black in section. The brown-black bodies thus demonstrated (figure 5) conformed to the droplets previously described, indicating that the lipid was similar to that which had been injected.

## DISCUSSION

Lipiodol® was chosen for this experiment because of its inherent iodine label. Lipiodol® represents poppyseed oil and iodine chemically compounded. Poppyseed oil consists of the glycerol esters of various fatty acids, *viz.*, oleic, linoleic, linolenic, palmitic, and stearic acids. The percentage of palmitic and stearic acids is very low because a high concentration of these saturated glyceryl esters would render the oil incapable of combining with large amounts of iodine. Of the unsaturated fatty acids, linoleic constitutes 65 per cent, oleic 30 per cent, and linolenic 5 per cent. The poppyseed oil is iodinated by hydriodic acid which adds the iodine across the double bonds of the unsaturated fatty acids as illustrated by the following equation[9]:

$$
\begin{array}{l}
CH_3 - (CH_2)_7 - CH = CH - (CH_2)_7 - COOCH_2 \\
CH_3 - (CH_2)_7 - CH = CH - (CH_2)_7 - COOCH + 3\ HI \\
CH_3 - (CH_2)_7 - CH = CH - (CH_2)_7 - COOCH_2 \\
\qquad\qquad\qquad\quad \mathrm{I} \\
CH_3 - (CH_2)_7 - CH - CH_2 - (CH_2)_7 - COOCH_2 \\
\qquad\qquad\qquad\quad \mathrm{I} \\
CH_3 - (CH_2)_7 - CH - CH_2 - (CH_2)_7 - COOCH \\
\qquad\qquad\qquad\quad \mathrm{I} \\
CH_3 - (CH_2)_7 - CH - CH_2 - (CH_2)_7 - COOCH_2
\end{array}
$$

It is apparent that Lipiodol® is not an easily dispersed mixture but rather a true chemical compound in which the iodine is strongly bound. Iodinated fat is not normally present in the intestinal tract. Therefore, it is our contention that the iodine staining material demonstrated in the sections represents, in fact, the Lipiodol® injected at the precise mucosal area from which the biopsy was taken.

Because this same lipid was distributed along the free border of the epithelial cell, demonstrated in continuily passing through the free border, found within the epithelial cells, and also seen within the substance of the villus, it is our further contention that this lipid was absorbed physically and without hydrolysis or other chemical alteration.

The technics described in this report are being extended and elaborated to further study fat absorption in pertinent disease states.

## SUMMARY

The partition theory of intestinal fat absorption has been supported by considerable indirect evidence accumulated over the past 20 years. The particulate absorption of fat has been demonstrated in laboratory animals. To this evidence we add the direct, visual observation of physical passage through the intestinal mucosa of a labeled fat in a human subject.

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