plasma, transform it into lecithin and that thus the red blood corpuscles play a part in the transportation and metabolism of fat. Our interest in the problem has been in relation to the alterations in permeability of the red blood corpuscle accompanying changes in the composition of its lipid constituents. The frequently cited data of Knudson obtained in his study of fat absorption of dogs are of unquestioned accuracy, but their physiological significance may be made more apparent if represented in terms of molecular equivalents. At any time during absorption, the millimolar increase of cholesterol, present as esters, plus 2 x the millimolar increase of lecithin, obviously represent the increase, in millimols, of the fatty acid present in combination with cholesterol and as phosphatide. The remainder may be supposed to exist almost entirely as neutral fat and soap.

Figure 1 represents the data, based on these calculations, obtained in an experiment on a dog, weighing 7.5 kg., following the administration of 50 g. of olive oil. Knudson's data have been recalculated on the same basis and show close agreement to our own results. It therefore does not seem necessary to present all of our data in detail.

Conclusions.—During the absorption of fat the maximum increase in total fatty acid in the red blood corpuscle is usually observed at the end of 2 to 4 hours. The increase of the combined fatty acids is somewhat delayed, the maximum being noted usually at the end of 6 hours.

Though occasionally the increase in cholesterol esters and lecithin in the corpuscle is more marked, as a rule it represents less than 20% of the total increase in fatty acids.

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Distribution of Unsaturated Fatty Acids in the Blood During Fat Absorption.

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This paper considers the effect of the ingestion of olive oil on the distribution of unsaturated fatty acids in the plasma and corpuscles. Dogs were used as the experimental animals. After a 12 hour period of fasting, a specimen of blood was taken for analysis. A

definite amount of olive oil was then given by stomach tube and additional specimens of blood were collected at the end of 2, 4 and 6 hours. Analyses were made of the plasma, as well as of the whole blood. These were treated with the alcohol-ether mixture, according to the well-known method of Bloor. To insure complete extraction of the lipids from the corpuscles, the extractions were repeated several times. The iodine number of the extracted lipids was determined by a micro-modification of Hanus' method, essentially as described by Gibson and Howard.[1] This procedure has been found to give reliable results both in previous work[2] and in the present experiments.

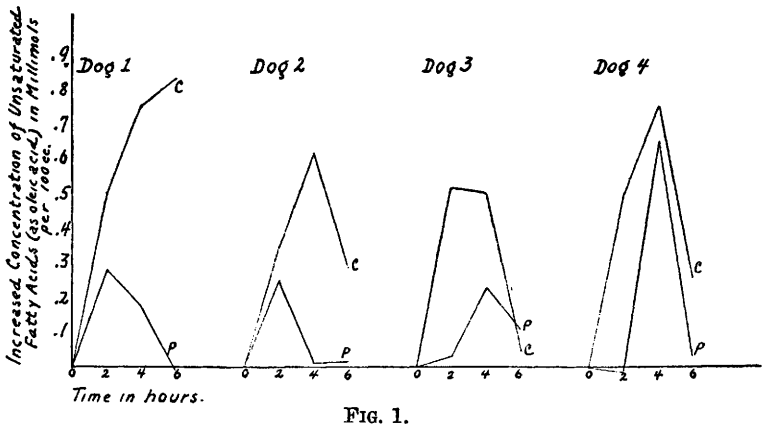

FIG. 1.

The results are represented by the curves in the accompanying figure. Dog 1, weighing 7.3 kg., received 50 cc. of olive oil; Dog 2, weighing 15.6 kg., received 65 cc.; Dog 3, weighing 11.1 kg., received 60 cc.; Dog 4, weighing 7.5 kg., received 50 cc. As shown by the curves, the increase in concentration of unsaturated fatty acids was always greater in the corpuscles (*C*) than in the plasma (*P*). The increase, however, was very small considering the amounts of fat administered. Taking Dog 4 as an example, the volume of blood, assuming it to be approximately 8.5% of the body weight, was about 635 cc. The maximum increase in the concentration of the unsaturated fatty acids was observed in this case at the end of 4 hours after administration and amounted to 0.7 millimols of oleic acid per 100 cc. of whole blood. Accordingly, at this time, there was in circulation 4.45 millimols, or 1.25 g. of oleic acid more than at the beginning of the experiment. This was only about

[1] Gibson, R. B., and Howard, C. P., *Arch. Int. Med.*, 1923, **32**, 1.

[2] Bodansky, M., *J. Biol. Chem.*, 1925, **63**, 239.

one-half of the increase in total fatty acids, which at the end of 4 hours amounted to 1.27 millimols per 100 cc. of whole blood, or 2.3 g. of fatty acid (in terms of oleic acid). Considering the red blood corpuscles alone, the average maximum increase of the unsaturated fatty acids was .68 millimols, which is only about one-third of the total fatty acid increase (average of 1.92 millimols).

It is difficult to explain why after the administration of olive oil the increase in total and saturated fatty acids, particularly in the corpuscles, should be greater than the increase in oleic acid. This observation, first made by the author in 1924, is in agreement with a similar finding of McClure and Huntsinger[3] that the increased concentration of lipids in the blood which follows the absorption of oleic acid is not solely the result of accumulation of this substance. Either the oleic acid undergoes saturation, or what is more likely, saturated fat is mobilized from the fat depots during fat absorption.

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Relation of Hemolysis to the Primary Penetration of Fatty Acids Through the Red Cell Membrane.

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The hemolytic action of fatty acids may be attributed to the combined effects of injury of the erythrocyte at its surface and secondary penetration. It is obvious, however, that in high concentrations of the hemolytic agent, the damage to the membrane may in itself be sufficient to cause the dissolution of the cell, in which case the factor of permeability is of negligible importance. On the other hand, if the concentration is sufficiently low, the change in the red blood cell membrane may be so slight that a condition is approached in which primary penetration of the fatty acid may be regarded as the sole factor involved in the process.

That under certain conditions measurement of the rate of hemolysis also determines the rate of permeability of the hemolytic agent has been considered elsewhere[1] and is supported by the observation that the hemolytic action of fatty acids parallels their behavior in a

[3] McClure, C. W., and Huntsinger, M. E., *J. Biol. Chem.*, 1928, **76**, 1.

[1] Bodansky, M., *J. Biol. Chem.*, 1928, **79**, 241.