

the amplitude of these spikes increased, and a fast convulsive activity began to appear ($C_{2,3,4}$), increasing in amplitude within the following 5 sec ($D_{3,4}$). This epileptiform activity disappeared 3 min later (E). Within 6 min of SCh application, the spikes reappeared in doublet form ($F_{2,4}$), which, however, developed gradually to massive epileptiform discharges in the following time period (G, H, I: 3,4). After cessation of the seizure activity (K) doublets reappeared ($L_{2,4}$) following an inactivation period lasting for about 1 min. Occasionally, the intermittent high amplitude sharp waves appeared and developed into the high frequency epileptiform activity ($M_{2,4}$). During seizure activities pupillary dilatation was observed in all experiments.

Figure 2 illustrates the effect of topical SCh on the cortical single cell activity and the correlation between ECoG and single cell discharge pattern in a typical experiment. Single shock stimulation of the left pyramid above decussation elicited two spikes recorded extracellularly from the left postcruciate gyrus in depth of 1.8 mm from the cortical surface (A_1). Spontaneous activity did not occur in the control (B). Within 2 min after topical application of a 20% SCh-solution to the postcruciate gyrus near the recording microelectrode, the antidromic response remained unchanged, but a small neuron began to discharge spontaneously (A_2), which lasted only for about 1 min (not illustrated). This cortical cell being not activated by antidromic stimulation (nonpyramidal

tract neuron) was reactivated within 3 min and delivered bursts composed of 3–6 spikes at constant 2-msec-intervals (C). Within 7 min these bursts occurred less frequently, but a tonic discharge appeared (D), and the large pyramidal tract neuron also delivered high frequency bursts (E, F). ECoG showed no waves in the control because of low amplification. However, after topical SCh, small or large sharp waves appeared (G, H, I, K, M: 1). The large sharp waves coincided with strong bursts of a large neuron and the small waves with burst of a small neuron (G and H; respectively). Sharp waves without corresponding burst were also common ($I_{1,2}$). Synchronization of the unit discharge, i.e., tonic activity, usually associated with flattening of the ECoG (K and L: 1,2). In M, low voltage rhythmic waves (1) appearing in ECoG during bursting activity of a nonpyramidal tract neuron (2) was recorded in fast sweep.

The results of this work clearly showed that topical SCh is a potent convulsant, bringing the single cortical neurons to bursting activity and tonic discharge. The close correlation between ECoG and unit activity suggests, on the other hand, that a) the small waves in the ECoG may be produced by the bursting activity of the small cortical cells; b) the large sharp waves may occur either without participation of any spike activity, or during very strong bursting activity of many cortical cells in concert; c) the flattening periods in the ECoG may appear during tonic activity of the cortical cells without bursting.

Morphological appearance of fat in the epithelial cells of different portions of the intestines in mice

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Summary. Absorption of administered fat in the small intestine of mice as judged morphologically in semi-thin sections demonstrates a proximal to distal gradient, being greatest in the mid-jejunal area, but less in the duodenum and ileum. The criterion of the amount and size of fat droplets in intestinal epithelial cells, however, does not necessarily give a reliable indication of the efficiency of fat absorption in the different segments of the intestine.

Numerous investigations on the course of fat absorption have been performed in the past decade with the aim of elucidating the mechanism of fat uptake by the epithelial cells in the small intestine¹. While much attention has been given to the ultrastructure and molecular levels, the course of fat absorption in the different portions of the intestine as a whole has been somewhat neglected. Most of the fat in a normal diet is sequestered in the duodenum and this process is so efficient that the more distal segments are not normally exposed to a substantial amount of fat. That the distal portions are capable of absorption is not doubted; even the cecum and colon of some species have been shown to have a fat-absorbing capacity². This ability may be of medical importance, especially in extensive resection of the small intestine or in pathological conditions of the proximal small intestine. Recently, Sabesin et al.³ demonstrated that distal portions of the intestines of rats perfused with fat were less efficient in absorbing lipids than proximal portions of the small intestine.

To date, a morphological definition of the role of each segment of the small and large intestine in fat absorption is lacking. It is the aim of this communication to offer a morphological picture of the process of fat absorption in the different segments of the intestine at the light microscopical level, using semi-thin sections of resin-embedded material stained specifically for fat.

In order to involve the different segments of the intestine in the process of fat absorption, a fasting period of 2–3

days is necessary to empty the gut of food content. Fasted mice were force-fed massive doses of commercial triglycerides (Mazola oil; 0.10–0.15 ml/g b.wt) over 2–3 days by gastric intubation. The various segments of the intestine were sampled measuring from the pyloric-duodenal junction (PDJ) distally. When the cecum and colon contained fat, these segments were also sampled. Small pieces were cut from each sample and fixed according to routine methods for electron microscopy. 1–3 μ m thick sections were cut and stained with p-phenylene diamine⁴. Morphologically, fat appears as small droplets concentrated in the supranuclear region, presumably in the Golgi region, in the epithelial cells of the proximal-most portion of the small intestine (duodenum; first 4 cm from the PDJ). In addition, scattered, fine droplets occur in the apical cell area. Distal to the duodenum (4–20 cm from the PDJ) an abrupt increase in the content and size of fat droplets can be noted. The apical portions of some cells are completely filled with droplets of varying sizes. In the more distal portions of the small intestine (ileum; approximately 20 cm from the PDJ to the cecum), the amount of detectable fat decreases gradually. In the cecum and proximal colon a limited number of fat

1 R. R. Cardell, S. Badenhansen and K. R. Porter, *J. Cell Biol.* 34, 123 (1967).

2 R. L. Snipes, *Acta anat.* 99, 435 (1977).

3 S. M. Sabesin, P. R. Holt and S. B. Clark, *Lipids* 10, 840 (1975).

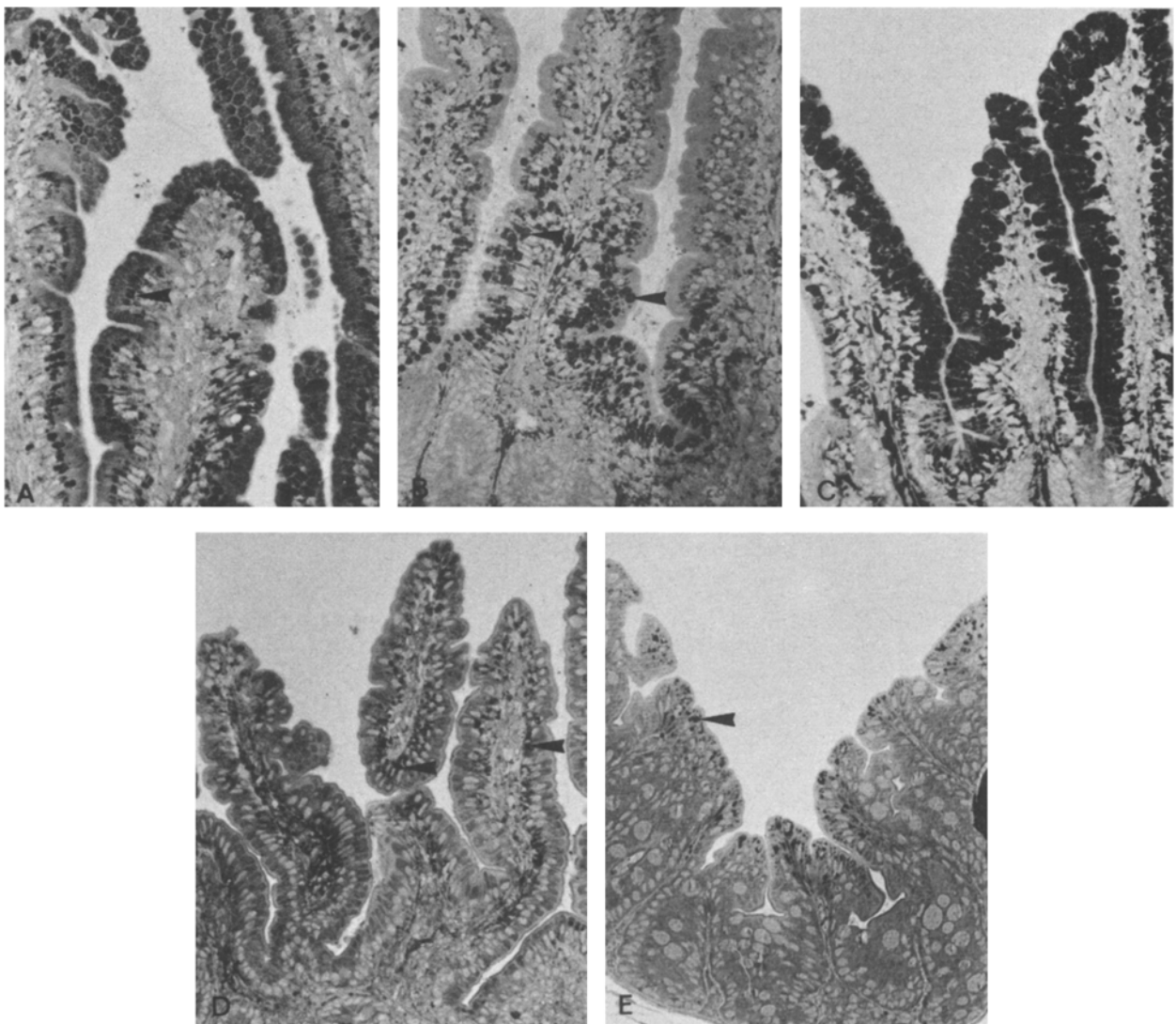
4 R. L. Snipes, *Microsc. Acta* 79, 127 (1977).

droplets is observed (figure). After these time periods of fat administration, neither diarrhea nor steatorrhea occurred in any of the animals.

This proximal-distal gradient is particularly emphasized by the prefasting and massive doses of fat administered. In normal chow-fed animals, distal portions of the intestine are scarcely exposed to fat^{5,6}. Also after administering small doses of fat, the proximal portions absorb so efficiently that distal segments are exposed to small amounts of fat only. The fed or fasting state of the animal at the time of fat administration also plays an important role in the appearance of fat in the various intestinal segments. In fasted animals, the intestines are largely empty and thus the availability of fat to all segments of the intestine is favored. Although the duodenum is the portion which is most probably exposed to the most constant flow of fat, morphologically it appears to contain less fat than lower in the jejunum. As recently suggested by Sabesin et al.³, however, after perfusion of lipids in different parts of the small intestine, the greater amount

of fat morphologically is not necessarily a true indication of the amount of fat actually absorbed in the sense of being built into chylomicra and transported into lacteals. Indeed, the increased amount in the form of huge fat droplets may indicate a defect in packaging and transport in the segments distal to the duodenum. If this be the case, then one must speculate that the duodenum is more efficient in this process, and thus large quantities do not accumulate in this region. This could indicate a cellular mechanism in the duodenum which is lacking, or more probably, less well developed in more distal segments. The observation of smaller amounts of fat in the ileal-cecal regions may indicate a different uptake mechanism perhaps due to a differing membrane which could influence the speed of diffusion of fat into these portions of the intestine.

- 5 H. Davenport, *Physiology of the Digestive Tract*. Year Book Medical Publ. Inc., Chicago 1971.
- 6 R. L. Snipes, *Lab. Invest.* 78, 179 (1968).



Different regions of the intestine of lipid-fed mice. Semi-thin sections of Epon-embedded material stained with p-phenylene diamine. $\times 240$. *A* Duodenum (within the first 4 cm distal from PDJ). Absorbed fat is concentrated in the Golgi zone (arrow). The cell apices are filled with very fine fat droplets. *B* Duodenal-jejunal junction (approximately 6 cm distal from PDJ). Some epithelial cells contain large fat droplets (arrows). *C* Jejunum (16 cm distal from PDJ). Most of the epithelial cells lining the villi are filled with huge, osmophilic fat droplets. *D* Ileum (at cecal junction). Very little fat (arrows) is found in the epithelial cells as compared to regions shown in *A-C*. *E* Cecum. Small fat droplets (arrow) are located in the surface epithelial cells.